Clinical outcomes after mix-and-match implantation of diffractive multifocal intraocular lenses with +2.75 and +4.00 diopter add powers

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SUBJECT AREAS
Ophthalmology
Abstract

Background
To evaluate the clinical outcomes of bilateral mix-and-match implantation of diffractive multifocal intraocular lenses (IOLs) with different add powers.

Methods
We retrospectively reviewed the medical records of 18 patients who underwent bilateral mix-and-match implantation of diffractive multifocal IOLs with different add powers. Multifocal IOLs with add powers of +2.75 diopters (D) and +4.00 D were implanted into the patients’ dominant and nondominant eyes, respectively. At 1 and 3-month postoperatively, monocular and binocular visual acuity was measured using logMAR charts and manifest refraction was performed. Specifically, logMAR charts were used to measure uncorrected distance visual acuity (UDVA), uncorrected intermediate visual acuity (UIVA), uncorrected near visual acuity (UNVA), and corrected distance visual acuity (CDVA). Defocus curves, contrast sensitivity, and patient satisfaction were assessed at 3-month postoperatively.

Results
Binocular logMAR measurements (mean ± standard deviation) at 3-month postoperatively were 0.01±0.04 (UDVA), 0.16±0.05 (UIVA), and 0.11±0.07 (UNVA). Postoperative spherical equivalent was -0.43±0.35 D and -0.39±0.21 D in the dominant and nondominant eyes, respectively. Defocus curves showed significant differences between -1.50 and -4.00 D among binocular, dominant, and nondominant eye measurements, except between -2.50 and -3.00 D. Eyes implanted with +2.75 and +4.00 D IOLs showed good contrast sensitivity under photopic and mesopic conditions. Over 80% of patients reported high satisfaction with their near vision.

Conclusions
Bilateral mix-and-match implantation of diffractive multifocal IOLs with add powers of +2.75 D and +4.00 D showed good near, intermediate, and far vision.

Background
Technological developments, including the development of multifocal intraocular lenses (IOLs), have
resulted in maximization of vision quality via cataract surgery. Bifocal IOLs show improvements in near and far distance visual acuity and emphasize near visual acuity. In general, bifocal IOLs of the same type and with the same add power for each eye are bilaterally implanted. However, several studies reported insufficient intermediate visual acuity with bilateral bifocal IOLs. The need for better intermediate distance visual acuity has led to efforts to improve the uncorrected intermediate visual acuity (UIVA) of these IOLs. For example, multifocal IOLs with extended depth of focus (EDOF) and trifocal IOLs have been developed and widely commercialized. However, trifocal IOLs showed more prominent background shadows than did bifocal IOLs, and EDOF IOLs have are limited in their ability to improve uncorrected near visual acuity (UNVA). Thus, there are still no IOLs available that improve vision across all ranges.

To overcome the limitations of available IOLs, efforts have been made to expand the range of vision by implanting different types of multifocal IOLs in each eye of a subject. Several studies have reported a good range of vision after bilateral mix-and-match implantation of multifocal IOLs. However, studies that evaluate clinical outcomes after implantation of diffractive multifocal IOLs with different add powers are scarce. Therefore, we aimed to evaluate clinical outcomes after implantation of TECNIS® IOLs with near addition powers of +2.75 diopters (D) in the dominant eye and +4.00 D in the nondominant eye.

Methods
We conducted this retrospective observational case series with the approval of the Institutional Review Board of the Asan Medical Center and the University of Ulsan College of Medicine (Seoul, South Korea). The study adhered to the tenets of the Declaration of Helsinki and followed good clinical practice guidelines. All patients provided written informed consent to allow their medical information to be included for analysis and publication.

This retrospective study included 18 patients who underwent cataract surgery with bilateral mix-and-match implantation of a TECNIS® +2.75 D multifocal IOL (ZKB00, Johnson & Johnson Vision, Santa Ana, CA, USA) into the dominant eye and a TECNIS® +4.00 D multifocal IOL (ZMB00, Johnson &
Johnson Vision) into the nondominant eye by one surgeon (HT) at the Cataract and Refractive Surgery Clinic of Asan Medical Center from March 2015 to February 2016. Patients who met the following inclusion criteria were included: (1) older than 18 years, (2) preexisting corneal astigmatism less than +1.00 D, and (3) visual acuity greater than 0.1 logMAR as measured with a potential acuity meter. Patients were excluded from the analyses if they had (1) optical opacities or pathology on slit-lamp examination, (2) previous corneal surgeries, (3) ocular trauma, (4) intraocular surgery, (5) severe dry eyes, (6) corneal disease, (7) ocular infection, or (8) collagen vascular disease or other autoimmune diseases.

**Measurements**

All subjects underwent comprehensive ophthalmological examinations preoperatively, including logMAR visual acuity measurements of monocular and binocular uncorrected distance visual acuity (UDVA), UIVA, UNVA, corrected distance visual acuity (CDVA), corrected intermediate visual acuity (CIVA), and corrected near visual acuity (CNVA). Preoperative assessments also included autorefraction and keratometry (Canon R-50, Canon USA Inc., Huntington, NY, USA), slit-lamp examinations (Haag-Streit, Gartenstadtstrasse, Köniz, Switzerland), biometry (IOL Master 500, Carl Zeiss Meditec, Jena, Germany), and corneal topography (Orbscan, Bausch & Lomb, Rochester, NY, USA). Each patient’s dominant eye was determined prior to surgery using the hole-in-the-card test wherein the patient looks at a target through a 1 inch hole in the center of a card held at one arm’s length, with only one eye open at a time, to determine which eye saw the target.

The ophthalmic examinations conducted at 1 and 3-month after surgery included logMAR measurements of monocular and binocular UDVA, UIVA, UNVA, and CDVA. Autorefraction and keratometry were also performed. Intermediate visual acuity was measured at 60 cm. Near visual acuity was measured at 33, 40, and 50 cm, with near visual acuity expressed as the average of visual acuity at these distances. In addition, monocular and binocular defocus curves were obtained at 3-month postoperatively by measuring monocular or binocular visual acuity at 4 m starting from distance correction and then defocusing with added lenses in half-diopter steps from -4.50 D to 0.00 D.
Contrast sensitivity was measured at 3-month postoperatively, using the Functional Acuity Contrast Test of the Ophtec 6500 view-in test system (Stereo Optical Co, Inc., Chicago, IL, USA) with stimulus spatial frequencies between 1.5 and 18 cycles per degree under photopic (target luminance = 85 candelas per square meter [cd/m²]) and mesopic (target luminance = 3 cd/m²) conditions.

Finally, patients were asked to complete a questionnaire regarding their overall satisfaction, the occurrence of visual symptoms, and their dependence on spectacles for near and far vision. Overall satisfaction was assessed using a 5-point Likert scale: 1 = very dissatisfied, 2 = dissatisfied, 3 = neither satisfied nor dissatisfied, 4 = satisfied, and 5 = very satisfied. Visual symptoms (glare, halo, and visual disturbances at night or in the dark) were scored on a 5-point scale from 1 (absent symptoms) to 5 (severe symptoms). Patients were also asked if they would recommend bilateral mix-and-match implantation of multifocal IOLs to their friends or relatives, with allowed responses being yes or no.

**Surgical technique**

After instillation of topical anesthesia (0.5% proparacaine hydrochloride), the phacoemulsification surgery was performed. A continuous curvilinear capsulorrhexis marker with a 6.0-mm diameter was used to reference the corneal plane. The main clear corneal incision was made using a 2.2-mm keratome, followed by capsulorrhexis using a capsulorrhexis needle. Phacoemulsification was performed using either the Infiniti® or Centurion® phacoemulsifier (Alcon Laboratories, Inc., Fort Worth, TX, USA). Using an injector, a +2.75 D multifocal IOL was implanted into the capsular bag of the dominant eye, and a +4.00 D multifocal IOL was implanted into the capsular bag of the nondominant eye. The target postoperative refraction was emmetropia in both eyes. All patients were administered 0.5% gatifloxacine ophthalmic solution (Gatiflo®, HANDOK, Seoul, South Korea) and prednisolone eye drops (Pred-Forte®, Allergan, Dublin, Ireland) for 1-month postoperatively.
Results are expressed as the mean ± standard deviation. Differences between preoperative and postoperative data were assessed using the Wilcoxon signed-rank test. Values for the defocus curves for both eyes, the dominant eye, and the nondominant eye were analyzed by the Kruskal-Wallis test with the Bonferroni correction. All statistical analyses were performed using SPSS® version 21 software (IBM, SPSS Inc., Chicago, IL, USA). Differences were considered statistically significant for \( P \) values of less than 0.05.

Results
The study included 18 patients (10 female and 8 male), of mean age 65.8 ± 5.7 years (range, 55–76 years). Preoperative subject and ocular characteristics are summarized in Table 1. Table 2 shows preoperative and postoperative spherical equivalent (SE) and monocular visual acuity. At 3-month postoperatively, monocular logMAR UDVA, logMAR UIVA and logMAR UNVA of the dominant eye were 0.04±0.05, 0.16±0.05 and 0.17±0.10, respectively. And monocular logMAR UDVA, logMAR UIVA and logMAR UNVA of the nondominant eye were 0.04±0.05, 0.30±0.12 and 0.11±0.07, respectively. Postoperative monocular SE, logMAR UDVA, logMAR UIVA, logMAR UNVA and logMAR CDVA were all significantly better than preoperative values. Also significant differences were found between preoperative and postoperative binocular visual acuity for logMAR UDVA, logMAR UIVA, and logMAR UNVA (Table 3). At 3-month postoperatively, binocular logMAR UDVA, logMAR UIVA and logMAR UNVA were 0.01±0.04, 0.16±0.05 and 0.11±0.07, respectively.

The binocular and monocular defocus curves are shown in Figure 1. Binocular defocus curves showed a better range of postoperative vision when compared with each monocular defocus curve across all distances. Visual acuity between -1.50 D and -4.00 D differed significantly among the 3 defocus curves (+2.75 D multifocal IOL, +4.00 D multifocal IOL, and binocular), with the exception of between -2.50 D and -3.00 D (\( P = 0.001 \) for -1.50 D, 0.003 for -2.00 D, 0.003 for -3.50 D, and 0.002 for -4.00 D). Defocus curves between -3.50 D and -4.00 D differed significantly for comparisons of binocular and +2.75 D multifocal IOL monocular vision (\( P = 0.003 \) for -3.50 D and 0.001 for -4.00 D) and between -1.50 D and -2.00 D for comparisons of binocular and +4.00 D multifocal IOL monocular vision (\( P = 0.001 \) for -1.50 D and 0.002 for -2.00 D). Defocus curves between -1.50 D and -4.00 D also
differed significantly for comparisons of +2.75 D multifocal IOL and +4.00 D multifocal IOL monocular vision, with the exception of between -2.50 D and -3.00 D (P = 0.001 for -1.50 D, 0.007 for -2.00 D, 0.006 for -3.50 D, and 0.007 for -4.00 D).

As shown in Figure 2, good contrast sensitivity was demonstrated under both photopic and mesopic conditions in eyes implanted with +2.75 D and +4.00 D multifocal IOLs, with no significant differences at any spatial frequency.

Sixteen subjects completed satisfaction questionnaires at 3-month postoperatively. Thirteen subjects (81.3%) reported that they were satisfied or very satisfied with their near vision, with an average satisfaction score of 4.4 ± 0.9. Only one subject (6.3%) reported occasionally needing glasses for near vision after surgery. Regarding the rate of visual symptoms, 4 (25.0%) subjects reported glare and halo symptom scores >3 (average score: 2.4 ± 0.9) and 3 (18.8%) patients scored symptoms of visual disturbances at night or in the dark at ≥3 (average score: 2.3 ± 0.9) (Table 4).

Discussion
In the current study, we demonstrated that bilateral mix-and-match implantation of multifocal IOLs with add powers of +2.75 D and +4.00 D showed good near, intermediate, and far vision. We implanted multifocal IOL with add power of +4.00 D into the nondominant eye for near visual acuity, which was relatively high add diopter compared to previous studies, based on the fact that Asians have lower amplitudes of accommodation and thus need higher add powers compared to Caucasians.11 Previously, patients who underwent implantation of bilateral +4.00 D multifocal IOLs have reported problems with intermediate vision, although their near visual acuity was good.12 Bilateral implantation of +2.50 D and +3.00 D multifocal IOLs resulted in good near vision and noninferior intermediate and distance vision compared with bilateral implantation of +2.50 D multifocal IOLs.8 Unilateral implantation of TECNIS® +2.75 D, +3.25 D and +4.00 D multifocal IOLs resulted in similar monocular UDVA, and UNVA was best in patients who underwent diffractive multifocal IOL implantation with add power of +2.75 D at 50 cm.13 Bilateral implantation of the TECNIS® +2.75 D and +3.25 D multifocal IOLs resulted in good binocular UIVA (0.07 ± 0.11 logMAR)
but relatively inferior binocular UNVA (0.25 ± 0.11 logMAR). On the basis that mix-and-match implantation of multifocal IOLs with different add powers may be more beneficial than bilateral implantation of multifocal IOLs with the same add power for subjects who desire spectacle independence, we evaluated clinical outcomes after bilateral mix-and-match implantation of diffractive multifocal IOLs with different add powers. A +2.75 D multifocal IOL was implanted into the dominant eye, and a +4.00 D multifocal IOL was implanted into the nondominant eye. The spectacle plane add power of multifocal IOLs differs from the IOL plane add power. For example, the spectacle plane add powers of the TECNIS® +2.75 D, +3.25 D, and +4.00 D multifocal IOLs are +2.01 D, +2.37 D, and +3.00 D, respectively. In the present study, depending on the spectacle plane add powers of the IOLs, visual acuity in the 0.00 D to -3.00 D range of binocular defocus curves was 0.1 logMAR or better. Binocular visual acuity at -3.50 D was better than 0.2 logMAR. On the other hand, a previous study found that the second peak of the binocular defocus curve was at -2.00 D, and the visual acuity at -2.50 D was about 0.0 logMAR. Then, visual acuity dropped sharply at values below -2.50 D, being 0.2 logMAR and 0.3 logMAR at -3.00 D and -3.50 D. Recently introduced TECNIS® EDOF IOLs provide an elongated focal area but not multiple foci. Therefore, these IOLs could provide better intermediate vision than other currently available multifocal IOLs. However, UIVA from our study was better than that of subjects who underwent bilateral implantation of TECNIS® EDOF and TECNIS® +4.00 D multifocal IOLs. Although binocular defocus curves showed that the visual acuity in the 0.00 D to -1.50 D range in a previous study were similar to those in the present study, the earlier study found that visual acuity decreased at values below -2.00 D. Several studies have evaluated methods to overcome the inferior UNVA following implantation of EDOF IOLs. For example, according to the CONCERTO prospective case series study in which EDOF IOLs were implanted into both eyes of 411 subjects, 299 had emmetropia target (non-monovision) and 112 had micro-monovision. The mean UNVA of the micro-monovision and non-monovision groups were 0.17 logMAR and 0.21 logMAR, respectively, with the former being inferior to UNVA in our study. To sum up, bilateral mix-and-match implantation of diffractive multifocal IOLs
with add powers of +2.75 D and +4.00 D can be the good alternatives of implantation of EDOF IOL for intermediate visual acuity, with better near visual acuity, too.

According to the results for contrast sensitivity test of the current study, both multifocal IOLs demonstrated good contrast sensitivity under photopic and mesopic conditions. Furthermore, eyes implanted with diffractive multifocal IOLs with +4.00 D add powers showed better contrast sensitivity than eyes implanted with diffractive multifocal IOLs with +2.75 D add powers, albeit the differences were not significant. Contrast sensitivity under photopic and mesopic conditions without glare was similar to the results of previous studies of bilateral implantation of the TECNIS® bifocal IOLs and of bilateral implantation of an EDOF IOL and a TECNIS® +4.00 D multifocal IOL.\textsuperscript{9,14}

In terms of subject satisfaction, we found that 25.0% had moderate glare and halo symptoms, while 18.8% reported night vision problems. These findings were inferior to those of the CONCERTO study.\textsuperscript{16} On the other hand, these results are superior to those of previous studies with implantation of bilateral multifocal IOLs.\textsuperscript{18,19} In addition, the rate of spectacle independence was higher in our study than in the CONCERTO study. Our findings that 93.8% of subjects reported that they would recommend mix-and-match implantation of diffractive multifocal IOLs with +2.75 D and +4.00 D add powers to their friends and relatives indicated that despite some visual problems, these symptoms did not have a significant impact on overall satisfaction.

Our study had several limitations, including the small number of eyes and the lack of a control group. Nonetheless, we demonstrated that UIVA and UNVA following mix-and-match implantation of diffractive multifocal IOLs with +2.75 D and +4.00 D add powers was not inferior to those following bilateral implantation of EDOF IOLs or bilateral implantation of an EDOF IOL and a diffractive trifocal IOL.\textsuperscript{20,21} Further research is needed on the bilateral implantation of other types of multifocal IOLs, especially trifocal and EDOF IOLs, to determine which combination of IOLs could provide superior UIVA, extended visual acuity range on defocus curves, and high spectacle independence at all distances.

Conclusions
In summary, we evaluated clinical outcomes after mix-and-match implantation of diffractive multifocal IOLs with +2.75 D and +4.00 D add powers and demonstrated good near, intermediate, and far vision with a high degree of patient satisfaction. Therefore, mix-and-match implantation of +2.75 D and +4.00 D multifocal IOLs can be a good option for subjects who do not want to depend on glasses after cataract surgery.

**Abbreviations**

CDVA: Corrected distance visual acuity; CPD: Cycles per degree; D: Diopters; EDOF: Extended depth of focus; IOL: Intraocular lenses; logMAR: Logarithm of the minimal angle of resolution; MR: Manifest refraction; SE: Spherical equivalent; UDVA: Uncorrected distance visual acuity; UIVA: Uncorrected intermediate visual acuity; UNVA: Uncorrected near visual acuity

**Declarations**

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**Availability of data and materials**

The datasets of the current study are available from the corresponding author on reasonable request.

**Authors’ contributions**

Involved in conception and design (JHL, HL, HT) and conduct of the study (JHL, JAL, AY); collection, management and interpretation of data (JHL, HL, JAL, AY); data analysis (JHL, HL, JYK, HT); writing the article (JHL, HL); and preparation, review, and approval of the manuscript (JHL, HT). JHL contributed to the manuscript as the first authors. HT contributed to the manuscript as the corresponding authors.

**Ethics approval and consent to participate**

This study was performed in accordance with the tenets of the Declaration of Helsinki. Approval to conduct this study was obtained from the Institutional Review Board of the Asan Medical Center.
(Seoul, Republic of Korea). Informed written consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

No conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

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Tables
Table 1. Demographic and clinical characteristics of study subjects
|                                      | MRSE           | LogMAR UDVA | LogMAR UIVA | LogMAR UNVA | Logζ |
|--------------------------------------|----------------|-------------|-------------|-------------|------|
| Preoperative                         |                |             |             |             |      |
| Dominant eye                         | 0.55 ± 1.99    | 0.36 ± 0.31 | 0.64 ± 0.25 | 0.58 ± 0.30 | 0.0  |
| Non-dominant eye                     | 0.21 ± 2.05    | 0.38 ± 0.35 | 0.62 ± 0.27 | 0.58 ± 0.30 | 0.0  |
| 1-month postoperative                 |                |             |             |             |      |
| Dominant eye                         | -0.43 ± 0.44   | 0.06 ± 0.07 | 0.16 ± 0.10 | 0.19 ± 0.09 | 0.0  |
| Non-dominant eye                     | -0.35 ± 0.37   | 0.07 ± 0.12 | 0.29 ± 0.08 | 0.13 ± 0.09 | 0.0  |
| P value*                             | <0.001         | 0.002       | <0.001      | 0.003       |      |
| 3-month postoperative                 |                |             |             |             |      |
| Dominant eye                         | -0.43 ± 0.35   | 0.04 ± 0.05 | 0.16 ± 0.05 | 0.17 ± 0.10 | 0.0  |
| Non-dominant eye                     | -0.39 ± 0.21   | 0.04 ± 0.05 | 0.30 ± 0.12 | 0.11 ± 0.07 | 0.0  |
| P value*                             | <0.001         | 0.002       | 0.001       | 0.005       |      |

Results reported as means ± standard deviations.

MRSE = manifest refraction spherical equivalent; UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity; CDVA = corrected distance visual acuity.

*Compared with preoperative values.
Table 3. Binocular visual acuity in patients with mix-and-match implantation of diffractive multifocal intraocular lenses with different add power

|                      | Preoperative | 1-month postoperative | P value* | 3-month postoperative | P | 
|----------------------|--------------|-----------------------|----------|-----------------------|---|
| logMAR UDVA          | 0.31 ± 0.31  | 0.02 ± 0.04           | 0.007    | 0.01 ± 0.04           |   |
| logMAR UIVA          | 0.56 ± 0.23  | 0.14 ± 0.07           | 0.007    | 0.16 ± 0.05           |   |
| logMAR UNVA          | 0.48 ± 0.25  | 0.10 ± 0.10           | 0.017    | 0.11 ± 0.07           |   |
| logMAR CDVA          | 0.09 ± 0.13  | 0.01 ± 0.03           | 0.084    | 0.01 ± 0.03           |   |

Results reported as means ± standard deviations.

UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity; CDVA = corrected distance visual acuity.

*Compared with preoperative values.

Table 4. Results for questionnaire about overall satisfaction, visual symptoms and dependence on spectacles

| Questionnaire                                      | Response (average score/rate) |
|----------------------------------------------------|-------------------------------|
| Overall satisfaction                                | 4.4 ± 0.9, very satisfied or satisfied: 81.3 % |
| Needing for near glasses after surgery             | 4.8 ± 0.6, occasionally need near glasses |
| Glare and halo symptoms                             | 2.4 ± 0.9, over score 3: 25.0% |
| Visual disturbance at night or dark place           | 2.3 ± 0.9, over score 3: 18.8 % |
| Recommendation for mix-and-match implantation      | Yes : 93.8 %                  |

Results reported as means ± standard deviations.

IOL = intraocular lenses.

Satisfaction scale; 5 = very satisfied; 1 = very dissatisfied; Need for near glasses; 5 = not at all; 1 = always needed. Scale of discomfort due to visual symptom; 5 = severe symptoms; 1 = absent symptoms.

Figures
Figure 1

Binocular and monocular defocus curves for patients after bilateral mix-and-match implantation of diffractive multifocal intraocular lenses with +2.75 and +4.00 diopter add powers. * P < 0.05. IOL, intraocular lens.

Figure 2

Contrast sensitivity test under photopic and mesopic conditions in patients with mix-and-match implantation of diffractive multifocal intraocular lenses with +2.75 and +4.00 diopter add powers. CPD, cycles per degree.