Static and Dynamic Factors Associated With Extended Depth of Focus in Monofocal Intraocular Lenses

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• PURPOSE: To analyze factors affecting depth of focus (DOF) and near vision functionality in eyes implanted with aspheric monofocal intraocular lenses (IOLs).
• METHODS: This prospective study included 111 eyes of 74 patients that underwent phacoemulsification with monofocal IOL implantation. Ninety-one normal eyes were randomized to receive aberration-free (n = 30) or negative-spherical aberration (SA) IOLs (n = 61). Twenty post–hyperopic femto-LASIK eyes received aberration-free IOLs. Corneal higher-order aberrations (SA, coma, trefoil, and corneal asphericity) for a 6 mm pupil were measured by Scheimpflug tomography. Ray-tracing metrics (visual Strehl optical transfer function [VSOTF], effective range of focus [EROF], sphere shift [SS], EROF−SS), pupil size measurements at far and near, and ocular and corneal SA were obtained using ray-tracing aberrometry. Distance-corrected near visual acuity (DCNVA) and subjective defocus curves up to ±4.0 diopters were evaluated.
• RESULTS: Multivariable logistic regression found corneal profile and IOL type to be determinants of extended DOF with monofocal IOLs. The aberration-free IOL group showed significantly better DCNVA and higher total SA than the negative-SA group. Post–hyperopic LASIK eyes showed significantly better DCNVA; higher negative SA, coma, and Q value ($P < .05$), and smaller pupil size ($P = .05$) than normal eyes implanted with aberration-free IOLs.
• CONCLUSION: Corneal profile and type of IOL implanted were the most important factors influencing near vision functionality with aspheric monofocal IOLs. Higher positive SA in the aberration-free group potentially led to better DCNVA than the negative-SA group in normal eyes. Hyperprolate corneas had better DOF curves and DCNVA than normal corneas. NOTE: Publication of this article is sponsored by the American Ophthalmological Society. (Am J Ophthalmol 2020;216:271–282. © 2020 Elsevier Inc. All rights reserved.)

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One of the major challenges with the aging eye is the gradual loss of accommodation, known as presbyopia. Although the technology to successfully restore true accommodation does not yet exist, implantation of modern presbyopia-correcting intraocular lenses (IOLs) at the time of cataract surgery can correct refractive error at distance and provide patients with improved intermediate and near vision, for near-complete spectacle independence. However, not all patients are candidates for or able to afford presbyopia-correcting IOLs; as such, monofocal IOLs remain a mainstay of cataract surgery.

It has long been observed that some patients have unaided functional near visual acuity after cataract surgery with monofocal IOLs targeted for emmetropia. Small pupil diameters resulting in a pinhole effect were initially thought to be a determining factor in this phenomenon of unexpectedly good near vision,[1] but Nakazawa and associates subsequently attributed the apparent accommodation to greater depth of field.[2] Pseudoaccommodative effect, or unexpected extended depth of focus from nonaccommodative mechanisms, was also observed in patients who underwent conventional photorefractive keratectomy (PRK) for myopia. Pseudoaccommodation, independent from ciliary muscle contraction and zonular apparatus, has been related to the increase in corneal spherical aberration (SA) following PRK surgery.[3]

Over time, it gradually became accepted that specific amounts of SA[4–7] and coma[8–11] may increase overall depth of focus (DOF). We have previously demonstrated that simulation of both positive and negative SA using adaptive-optics technology can enhance depth of focus up to 2 diopters (D).[6] Multifocality of the cornea[9,11–13] and against-the-rule astigmatism (ATR)[11,14] have also been shown to influence DOF.

After Bellucci and associates[15] and Piers and associates[16] demonstrated that IOLs designed to neutralize aberrations, and specifically SA, could improve quality of vision, IOL manufacturers began to develop aspheric IOLs. Aspheric IOLs with negative SA are now typically implanted with the goal of neutralizing some or all of the average cornea's +0.27 μm of SA for a 6 mm pupil size.[17] Aspheric aberration-free IOLs that preserve the pre-existing corneal aberrations are also available.

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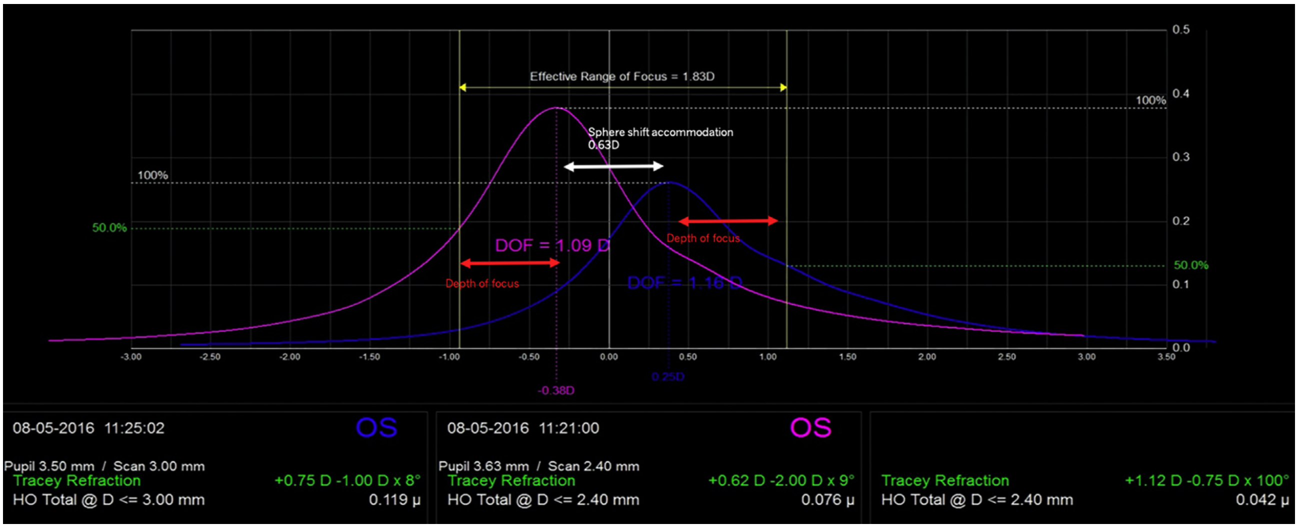

FIGURE 1. Ray-tracing aberrometry objectively compares refraction and higher-order aberrations at distance and near to provide the following measurements: visual Strehl optical transfer function (VSOTF): an optical wavefront error–derived metric that predicts visual acuity; effective range of focus (EROF): range of focus with acceptable blur; sphere shift (SS) accommodation: difference between distance and near refraction (distance from peak to peak of VSOTF curves); depth of focus (EROF − SS): difference between effective range of focus and sphere shift accommodation.

It would be desirable to be able to identify preoperatively which eyes are most likely to achieve greater DOF and near vision functionality with a monofocal IOL. However, the interplay of all the various factors affecting DOF remains unclear. We hypothesized that with new diagnostic technologies, it may be possible to further elucidate the factors contributing to DOF. Moreover, we also anticipated that eyes having undergone previous hyperopic LASIK surgery resulting in hyperprolate corneas would naturally have greater DOF and respond differently than eyes with normal corneas.

In this study, we analyzed various anatomic, surgical, and subjective and objective parameters that may influence near visual outcomes.[18,19] Most of these factors were subjected to multivariable logistic regression to identify those factors that are most strongly associated with functional near visual acuity (distance-corrected near visual acuity [DCNVA] of J3 or better) following the implantation of contemporary aspheric IOLs with 2 different aberration profiles in eyes with normal or hyperprolate corneas.

METHODS

THIS PROSPECTIVE, SINGLE-CENTER STUDY RECRUITED 111 eyes (91 normal and 20 post–hyperopic femto-LASIK eyes) of 74 cataract patients scheduled to undergo phacoemulsification with an aspheric monofocal IOL targeting emmetropia. To address our hypothesis, we deliberately included eyes that had previously undergone hyperopic femtosecond laser–assisted in situ keratomileusis (FS-LASIK) surgery, leaving the corneas hyperprolate in shape. Twenty hyperprolate eyes were implanted with an aberration-free IOL (enVista MX60E; Bausch & Lomb, Bridgewater, NJ). Ninety-one eyes with virgin (normal) corneas were randomized to receive either an aberration-free IOL (30 eyes) or a negative-SA IOL (ZCB00; Johnson & Johnson Vision, Santa Ana, CA) (61 eyes) from February 2018 to June 2019. Randomization was open ended and was based on the weekday when the surgery was performed (ie, all eyes that underwent cataract surgery on a specific day of the week received only 1 type of IOL. IOL calculation was performed using optical biometry with swept-source OCT (IOLMaster 700; Carl Zeiss Meditec AG, Jena, Germany) and Barret Universal II formula. Written informed consent was obtained from all patients prior to the start of the study. The study was approved by the Medical University of South Carolina institutional review board and followed the tenets of the Declaration of Helsinki. All surgeries were performed by a single experienced surgeon (K.M.R.) at the Storm Eye Institute at the Medical University of South Carolina.

• **INCLUSION AND EXCLUSION CRITERIA:** Cataract patients aged 40 years or older who were scheduled to undergo cataract surgery with implantation of an aberration-free (MX60E) or negative-SA (ZCB00) monofocal IOL were included in the study. The enVista MX60E IOL is an aspheric aberration-free lens (zero SA) designed not to induce or modify the SA of the cornea. The Tecnis ZCB00 IOL has SA of −0.27 μm for a 6 mm pupil and is designed to correct the average positive SA (+0.27 μm) of the cornea. Owing to already increased negative SA in post–hyperopic LASIK corneas, the manufacturer of the ZCB00 IOL does not recommend its implantation in such eyes. Thus, in the current study, eyes with hyperprolate corneas received only the aberration-free MX60E IOL.

Exclusion criteria were previous ophthalmic surgery (other than hyperopic refractive surgery); potentially challenging cases (eg, small nondilating pupils, corneal pathologies such as corneal scars, ocular herpes, corneal dysplasia, or corneal/conjunctival lesions that may interfere with topographic measurements); history of other eye conditions such as glaucoma, uveitis, diabetic retinopathy, and retinal detachment; complications during the perioperative period; zonular dehiscence; or other neural or retinal conditions that could impair visual performance. Patients with active eye allergies or other inflammatory signs were also excluded.

• **STUDY PARAMETERS:** Patients were examined between 1 and 3 months post cataract surgery. Uncorrected distance visual acuity and corrected distance visual acuity (CDVA) at 20 feet were measured using the ETDRS chart. Distance-corrected near visual acuity (DCNVA) at 33 cm was assessed using a standard Jaeger chart. Defocus curves were generated for both aberration-free MX60E IOL (normal and hyperprolate eyes separately) and negative-SA ZCB00 IOL groups. For the generation of defocus curves, each eye was first corrected for best distance visual acuity using a distance eye chart; a series of positive and negative lenses were then placed in front of the patients' eye to produce defocus; visual acuity with each level of defocus was measured. The defocus was introduced from ±0.50 D to ±4.00 D, with increments of 0.50 D.

Scheimpflug imaging (Pentacam HR; Oculus, Wetzlar, Germany) was used to measure corneal asphericity (Q value), corneal higher-order aberrations (HOAs) including corneal SA, coma, and trefoil at a pupil size of 6 mm. Ray-tracing aberrometry (iTrace; Tracey Technologies, Houston, Texas, USA) was carried out to assess HOAs (ocular and corneal), visual Strehl optical transfer function (VSOTF) for far and near, effective range of focus (EROF), sphere shift (SS), and pupil size measurements at far and near. The VSOTF is an optical wavefront error-derived metric used to measure the objective visual performance of patients. It is calculated as follows:

$$\text{VSOTF} = \frac{\text{the area under the contrast sensitivity} - \text{weighted optical transfer function}}{\text{the area under the contrast sensitivity} - \text{weighted optical transfer function for a diffraction limited eye}}$$

Ray-tracing aberrometry can estimate objective DOF directly from wavefront measurements using various retinal image quality metrics. DOF measured with such methods is defined as the range of defocus error that degrades the retinal image quality to a certain level of the maximum value.[20] Thus, ray-tracing aberrometry that objectively compares refraction and HOAs at a distance and near target can be used to determine EROF, SS, and EROF−SS.[21] EROF is the range of focus with acceptable blur and is calculated as the difference in diopters between the near and distance DOF curves at the threshold value of 50% VSOTF.[22] It is an objective measure of both the true accommodation and pseudoaccommodation. SS is the true accommodative ability of the eye and is measured as the difference in the spherical equivalent of ray-tracing refraction for the distance and near DOF curves (measured from peak to peak).[21] In general, for a young eye, there exists a significant amount of true accommodation, whereas in a presbyopic or pseudophakic eye there exists little or no true accommodation.[22] EROF−SS is a measure of apparent accommodation in a pseudophakic eye, beyond that predicted by the optical properties of the IOL. It is calculated as the difference between EROF and true accommodation (EROF−SS) (Figure 1).

• **STATISTICAL ANALYSIS:** Data analysis was performed using SPSS software, version 17.0 (SPSS Inc, Chicago, Illinois, USA). Simple binary logistic regression was performed to evaluate the effect of various parameters on the likelihood of obtaining DCNVA of J3 or better (functional near vision, an indirect measure of DOF) vs DCNVA worse than J3. Factors analyzed in the study included patient's age, pupil size, IOL type (aberration-free MX60E vs negative-SA ZCB00 monofocal IOL), corneal profile (normal vs hyperprolate), corneal asphericity (Q value), corneal HOAs (including SA, coma, trefoil), total HOAs measured with Scheimpflug tomography (Pentacam HR), ocular and corneal HOAs, VSOTF, EROF, SS, and EROF−SS measured with ray-tracing aberrometry (iTrace). Odds ratio (OR) with 95% confidence interval was calculated to study the association of these factors with DCNVA. Any variable having a P value $< .2$ in binary logistic regression was selected as a candidate for multivariable logistic regression, as the traditional significance level ($P < .05$) may fail to identify variables known to be important. Multiple logistic regression examines the interplay of different independent variables on the dependent variable and retains only those independent variables that show strong association with the dependent variable. Variables that had P value $< .05$ in the multiple logistic regression were retained in the model and adjusted ORs were calculated for them.

Study variables were compared between the 2 IOL groups (aberration-free MX60E vs negative-SA ZCB00

TABLE 1. Association of Various Independent Variables With the Likelihood of Achieving Good Distance-Corrected Near Visual Acuity (J3 or Better) as Analyzed With Simple and Multiple Logistic Regression

	Simple Binary Logistic Regression (N = 111 Eyes)			Multiple Logistic Regression (N = 111 Eyes)		
			95% CI for EXP(B)			95% CI for EXP(B)
Independent Variables	Sig. ($P < .2$)	Odds Ratio	Lower-Upper	Sig. ($P < .05$)	Adjusted Odds Ratio	Lower-Upper
Sex (categorical)						
Female (reference category)		1				
Male	.876	1.070	0.459-2.496			
Age	.023[a]	0.937	0.885-0.991	NR	NR	
Intraocular lens type (categorical)						
Negative-spherical aberration (reference category)		1			1	
Aberration-free	<.001[a]	5.778	2.352-14.195	.045[b]	2.889	1.023-8.155
Corneal profile (categorical)						
Normal (reference category)		1			1	
Hyperprolate cornea	<.001[a]	11.368	3.667-35.24	.006[b]	6.000	1.693-21.262
Pupil size	.022[a]	0.561	0.342-0.920	NR	NR	
Sphere shift	.863	1.026	0.767-1.372			
EROF−SS	.843	0.989	0.886-1.104			
Corneal spherical aberration (Scheimpflug – 6 mm pupil)	.009[a]	0.817	0.703-0.950	NR	NR	
Corneal coma (Scheimpflug – 6 mm pupil)	.098[a]	0.925	0.844-1.014	NR	NR	
Corneal trefoil (Scheimpflug – 6 mm pupil)	.323	0.940	0.830-1.063			
Corneal total HOA (Scheimpflug – 6 mm pupil)	.081[a]	1.089	0.990-1.199	NR	NR	
Q value (Scheimpflug imaging)	.011[a]	0.817	0.698-0.955	NR	NR	
Ocular spherical aberration (ray tracing – natural pupil size)	.418	0.742	0.360-1.527			
Corneal spherical aberration (ray tracing – natural pupil size)	.420	0.591	0.164-2.124			
Spherical aberration difference between far and near (ray tracing – natural pupil size)	.721	0.873	0.413-1.843			
Near VSOTF	.886	1.009	0.888-1.147			
Far VSOTF	.410	0.936	0.801-1.095			

EROF = extended range of focus; Exp (B) = Odds ratio; HOA = higher-order aberration; NR = not retained; Sig. = significance; SS = sphere shift; VSOTF = visual Strehl optical transfer function.

[a]Variables with P value < .2 in simple binary logistic regression were analyzed in multiple logistic regression.

[b]Variables that were retained in multiple logistic regression model are shown here.

group, normal eyes only) and 2 corneal profiles (normal vs hyperprolate, MX60E only). Normality of the scale data was tested using the Shapiro-Wilk test. For normally distributed scale data, the means of the 2 groups were compared using the independent *t* test; for ordinal data or non-normally distributed scale data, nonparametric Mann-Whitney *U* test was used. *P* values less than .05 were considered statistically significant.

Defocus curves for the subjectively measured DOF at varying levels of defocus were also compared between the 2 IOL groups (aberration-free MX60E vs negative-SA ZCB00 in normal eyes) and the 2 corneal profiles (normal vs hyperprolate in MX60E-implanted eyes).

To evaluate the role of objectively measured DOF metrics (EROF, SS, EROF−SS) on DCNVA, these were compared between the good near vision group (J3 or better) and poor near vision group (worse than J3) and their correlation with DCNVA was studied.

RESULTS

SIXTY-ONE EYES WITH NORMAL CORNEAS RECEIVED negative-SA ZCB00 IOLs and 30 eyes with normal corneas received aberration-free MX60E IOLs. Twenty eyes with hyperprolate corneas were also included in the study; all of these eyes received MX60E IOLs.

Table 1 presents the findings of logistic regression. Patients' age, IOL type, corneal profile, pupil size,

TABLE 2. Comparison of Study Variables Between the 2 Intraocular Lens Types (Normal Corneas Only)

Variable	IOL Type: Normal (ZCB00) (N = 61), Mean ± SD	IOL Type: Normal (MX60E) (N = 30), Mean ± SD	*P* Value[b]
Age	71.2 ± 5.7	72.0 ± 8.2	.572
Corneal spherical aberration (Scheimpflug – 6 mm pupil)	0.34 ± 0.12	0.34 ± 0.13	.873
Corneal coma (Scheimpflug – 6 mm pupil)	0.08 ± 0.31	0.06 ± 0.33	.762
Corneal trefoil (Scheimpflug – 6 mm pupil)	−0.06 ± 0.40	−0.14 ± 0.26	.463
Total corneal HOA (Scheimpflug – 6 mm pupil)	0.59 ± 0.35	0.54 ± 0.32	.549
Q value (Scheimpflug imaging)	−0.30 ± 0.19	−0.35 ± 0.18	.450
Ocular spherical aberration (ray tracing – natural pupil size)	0.01 ± 0.03	0.02 ± 0.07	.001[a]
Corneal spherical aberration (ray tracing – natural pupil size)	0.02 ± 0.02	0.03 ± 0.03	.024[a]
Difference spherical aberration (ray tracing – natural pupil size)	0.00 ± 0.03	0.03 ± 0.08	.489
Near VSOTF	0.50 ±0.22	0.44 ± 0.24	.245
Far VSOTF	0.44 ± 0.22	0.34 ± 0.15	.096
SS	0.31 ± 0.27	0.46 ± 0.41	.062
EROF	1.68 ± 0.81	2.02 ± 1.15	.117
EROF−SS	1.37 ± 0.65	1.56 ± 0.85	.391
Pupil size at far (mm)	2.9 ± 0.6	3.3 ± 0.6	.008[a]
Pupil size at near (mm)	2.6 ± 0.4	2.6 ± 0.5	.685
UDVA	0.07 ± 0.10	0.13 ± 0.15	.161
CDVA	0.01 ± 0.06	0.03 ± 0.05	.090
DCNVA	0.42 ± 0.24	0.29 ± 0.16	.008[a]

CDVA = corrected distance visual acuity; DCNVA = distance-corrected near visual acuity; EROF = effective range of focus; HOA = higher-order aberrations; IOL = intraocular lens; SS = sphere shift; UDVA = uncorrected distance visual acuity; VSOTF = visual Strehl optical transfer function.

[a]Variables with *P* value < .05.

[b]*P* value for comparison between normal (negative spherical aberration IOL) and normal (aberration-free IOL).

corneal HOAs measured with Scheimpflug tomography (Pentacam HR), and corneal asphericity (Q value) were found to be predictors of achieving DCNVA of J3 or better by simple logistic regression ($P < .2$). These factors were further analyzed in multiple regression to exclude confounding effects and generate adjusted ORs for the retained parameters. Multiple regression retained only the IOL type (aberration-free MX60E vs negative-SA ZCB00) and corneal profile (hyperprolate vs normal) in the model. The probability of obtaining DCNVA of J3 or better was higher with the aberration-free MX60E IOL than with the negative-SA ZCB00 IOL (adjusted OR = 2.889, $P = .045$). The probability of obtaining DCNVA of J3 or better was greater in eyes with hyperprolate corneas compared to normal corneas, when implanted with the same aberration-free MX60E IOL (adjusted OR = 6.000, $P = .006$). Other factors analyzed were not retained in the multiple logistic regression model.

To further investigate which factors were associated with DCNVA of J3 or better in normal eyes, we excluded 20 eyes with hyperprolate corneas and again performed simple binary logistic regression with 91 normal eyes. In this subanalysis, only the IOL type was associated with better near vision outcomes ($P < .2$); eyes implanted with the aberration-free MX60E IOL had statistically significant higher probability (OR = 2.889, $P = .045$) of obtaining DCNVA of J3 or better. No other factors (pupil size, corneal HOAs [SA, coma, trefoil, total HOA] measured with Scheimpflug tomography, ocular and corneal SA measured with ray tracing, EROF−SS, sphere shift, Q value) demonstrated statistical significance in simple logistic regression (ie, all other factors had $P > .2$).

Tables 2 and 3 present the comparison of study variables between the 2 IOL types and between the 2 corneal profiles. Intergroup comparison between the aberration-free MX60E (normal eyes) and negative-SA ZCB00 (normal eyes) revealed statistically significantly

TABLE 3. Comparison of Study Variables Between Normal and Hyperprolate Corneas (MX60E Only)

Variable	Normal (MX60E) (N = 30), Mean ± SD	Hyperprolate (MX60E) (N = 20), Mean ± SD	*P* Value[b]
Age	72.0 ± 8.2	66.2 ± 9.3	.047[a]
Corneal spherical aberration (Scheimpflug – 6 mm pupil)	0.34 ± 0.13	−0.22 ± 0.36	<.001[a]
Corneal coma (Scheimpflug – 6 mm pupil)	0.06 ± 0.33	−0.42 ± 0.68	.014[a]
Corneal trefoil (Scheimpflug – 6 mm pupil)	−0.14 ± 0.26	−0.28 ± 0.44	.322
Total corneal HOA (Scheimpflug – 6 mm pupil)	0.54 ± 0.32	1.11 ± 0.56	<.001[a]
Q value (Scheimpflug imaging)	−0.35 ± 0.18	−0.74 ± 0.36	<.001[a]
Ocular spherical aberration (ray tracing – natural pupil size)	0.02 ± 0.07	−0.01 ± 0.08	.003[a]
Corneal spherical aberration (ray tracing – natural pupil size)	0.03 ± 0.03	−0.01 ± 0.05	<.001[a]
Difference spherical aberration (ray tracing – natural pupil size)	0.03 ± 0.08	0.02 ± 0.06	.890
Near VSOTF	0.44 ± 0.24	0.52 ± 0.57	.835
Far VSOTF	0.34 ± 0.15	0.51 ± 0.75	.968
SS	0.46 ± 0.41	0.42 ± 0.42	.565
EROF	2.02 ± 1.15	2.32 ± 1.84	.572
EROF−SS	1.56 ± 0.85	2.02 ± 1.53	.127
Pupil size at far (mm)	3.3 ± 0.6	2.6 ± 0.7	.001[a]
Pupil size at near (mm)	2.6 ± 0.5	2.3 ± 0.4	.050
UDVA	0.13 ± 0.15	0.15 ± 0.17	.680
CDVA	0.03 ± 0.05	0.04 ± 0.09	.714
DCNVA	0.29 ± 0.16	0.18 ± 0.18	.012[a]

CDVA = corrected distance visual acuity; DCNVA = distance-corrected near visual acuity; EROF = effective range of focus; HOA = higher-order aberrations; SS = sphere shift; UDVA = uncorrected distance visual acuity; VSOTF = visual Strehl optical transfer function.

[a]Variables with *P* value < .05.

[b]*P* value for comparison between normal (negative spherical aberration intraocular lens) and hyperprolate corneas (aberration-free intraocular lens).

better mean DCNVA in the aberration-free MX60E group (*P* =.008). The comparison of defocus curves for the 2 IOL groups also showed better DOF in the aberration-free MX60E group beyond the defocus level of ±0.5 D, although statistical significance was reached at defocus levels of −3.5 D (*P* = .028), −2.5 D (*P* = .028), −1.5 D (*P* = .047), and +2.0 D (*P* = .043) (Figure 2). Mean CDVA was slightly better in the negative-SA ZCB00 group; however, the difference did not reach statistical significance (*P* = .090). VSOTF at far was also higher in the negative-SA ZCB00 group than in the aberration-free MX60E group, although the difference between the 2 groups did not reach statistical significance (*P* = .096). The aberration-free MX60E group also showed statistically significant higher mean ocular and corneal SA (ray-tracing aberrometry) than the negative-SA ZCB00 group.

Figure 3 provides a representative chart of the objective depth-of-focus metrics (EROF, SS, EROF−SS) measured using ray-tracing aberrometry; EROF in a MX60E-implanted normal cornea was better than in the ZCB00-implanted normal cornea. Correspondingly, the mean EROF and EROF−SS were higher in the aberration-free MX60E group; however, the difference was not statistically significant (Tables 2 and 3).

Intergroup comparison between normal and hyperprolate corneas, both implanted with MX60E IOL, revealed significantly better mean DCNVA in eyes with hyperprolate corneas (*P* = .012) (Tables 2 and 3). Correspondingly, the defocus curves for hyperprolate corneas showed better DOF than normal corneas when both were implanted with MX60E IOLs, with statistically significant differences for defocus levels −4 D to −1.5 D and +1 D to +4 D (Figure 4). Mean CDVA was comparable between the 2 groups (normal eyes vs hyperprolate eyes) (Tables 2 and 3). There were statistically significant differences in mean age, corneal HOAs (SA, coma, trefoil, total HOA) measured with Scheimpflug tomography, corneal asphericity (Q value), ocular and corneal SA measured with ray tracing, and pupil size (at far and near) between the eyes with normal corneas and those with hyperprolate corneas ($P \leq .05$).

It is important to note that EROF in an eye with hyperprolate cornea is usually higher than in those with normal cornea (Figure 3). Correspondingly, the mean EROF and EROF−SS were higher in the hyperprolate corneas;

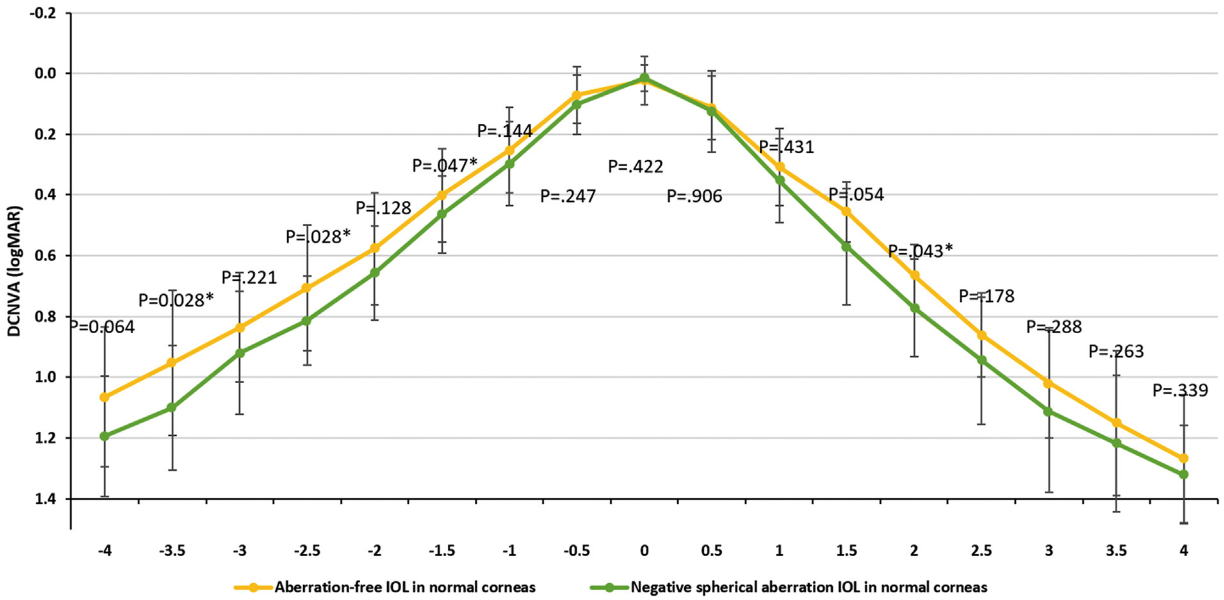

FIGURE 2. Comparison of defocus curves of the 2 intraocular lens (IOL) types (aspheric neutral, aberration-free IOL vs aspheric negative-spherical aberration IOL) implanted in eyes with normal corneas.

however, the difference was not statistically significant (Tables 2 and 3).

There were no correlations between DCNVA and EROF, SS, or EROF−SS (Figure 5A-C). Mean EROF, SS, and EROF−SS were also found to be comparable between eyes with DCNVA J3 or better (n = 34) and those worse than J3 (n = 77) (Table 4).

DISCUSSION

CONTRARY TO CONVENTIONAL WISDOM, PSEUDOPHAKIC eyes implanted with monofocal IOLs may exhibit extended DOF or pseudoaccommodative characteristics. Several ocular factors (visual acuity, pupil size, retinal eccentricity, ocular aberrations, and age) have been related to ocular DOF[23,24]; however, the relative effect of these factors on DOF remains unclear. Denoyer and associates[25] found that aberration-free IOLs had statistically significantly better best-corrected near vision subscale score (using the Activities of Daily Vision Scale) and better quality of near vision than negative-SA IOLs.[26] Rocha and associates[5] showed good DCNVA with spherical (nonaspheric) IOLs compared to negatively aspheric IOLs. In some other studies, higher-order aberrations, particularly SA and coma-like aberrations, have been found to increase DOF and improve near vision functionality.[5,6,9,25,27] Additional factors including corneal astigmatism (ATR),[11,14] corneal multifocality,[9,11–13] pupil size,[1,7,11,13,28] and axial length[28] have also been found to influence DOF following implantation of monofocal IOLs.

The present study was designed to investigate the effects of multiple factors that may enhance DOF and improve near vision in pseudophakic patients implanted with contemporary aspheric monofocal IOLs. Simple binary logistic regression revealed that patient's age, IOL type, corneal profile, pupil size, HOAs (SA, coma, total HOAs) measured with Scheimpflug tomography (Pentacam HR), and corneal asphericity (Q-value) have at least some association with improved DOF, measured indirectly as DCNVA of J3 or better ($P < .2$); however, multiple regression found that only IOL type (aberration-free MX60E better than negative-SA ZCB00) and corneal profile (hyperprolate better than normal) significantly affect the probability of obtaining DCNVA (J3 or better).

Compared with the negative-SA group, the aberration-free group exhibited both statistically significant superior visual acuity beyond the defocus level of ±0.5 D and better mean DCNVA. Increasing SA (both positive and negative, up to a threshold value) is known to expand DOF and improve near visual acuity.[6] In the present study, better mean DCNVA obtained with the aberration-free IOL is likely owing to the statistically significantly higher ocular and corneal SA (ray-tracing aberrometry) in the aberration-free group compared with the negative-SA group. Implantation of the IOL with zero SA in normal eyes retains the positive corneal aberrations associated with DOF, improving near vision outcomes. By contrast, implantation of negative-SA IOL neutralizes the positive SA of the cornea, thus reducing the amount of ocular SA and decreasing DOF and DCNVA.

Mean CDVA was slightly better in the negative-SA ZCB00 group (20/23.6 vs 20/26.6 in the MX60E group,

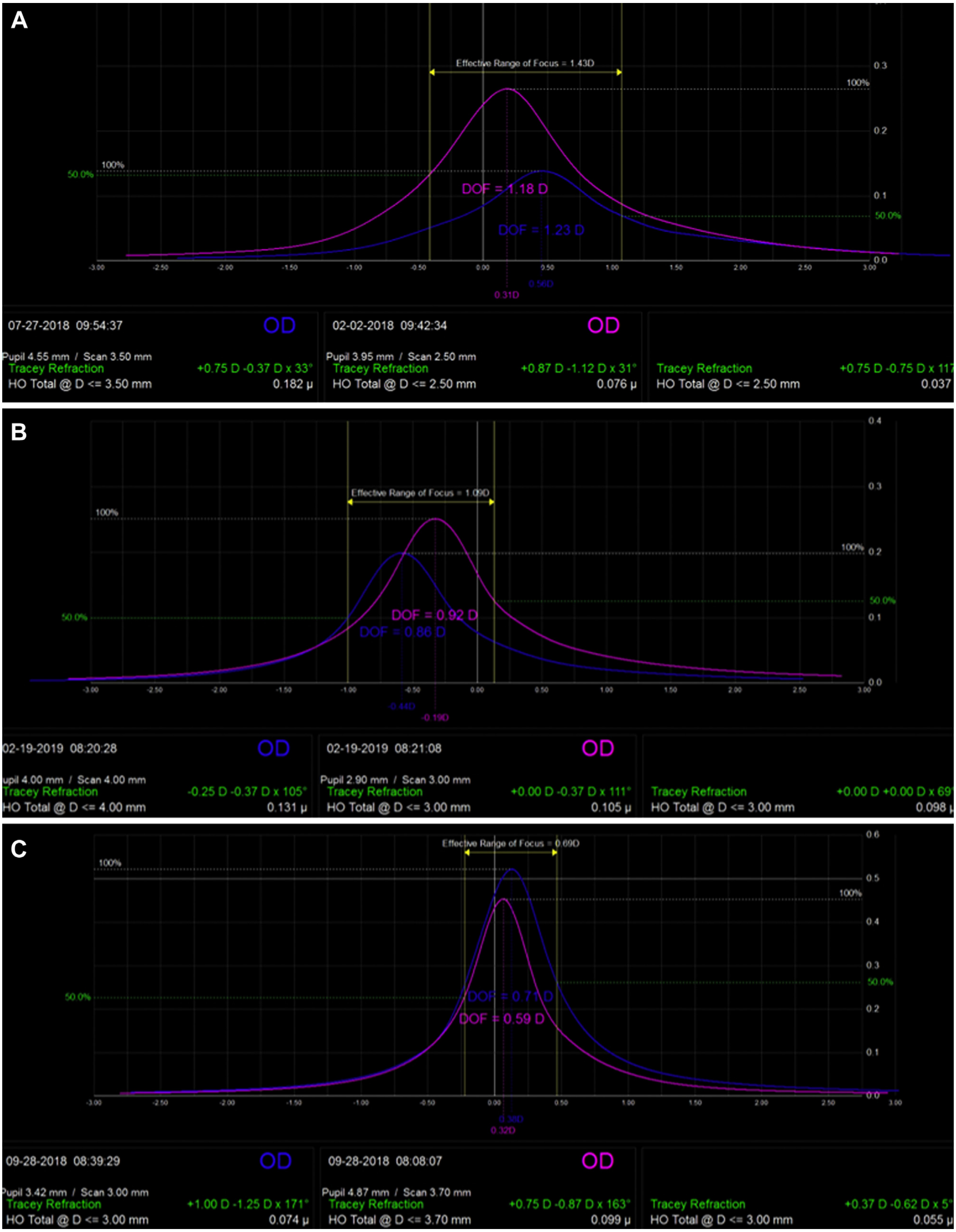

FIGURE 3. Representative figures of the objective depth-of-focus metrics (effective range of focus [EROF], sphere shift [SS], EROF−SS), measured using ray-tracing aberrometry for the 3 subgroups: eyes with (A) hyperprolate cornea implanted with an aberration-free intraocular lens (IOL); (B) normal cornea implanted with an aberration-free IOL; and (C) normal cornea implanted with a negative spherical aberration IOL. DOF = depth of focus.

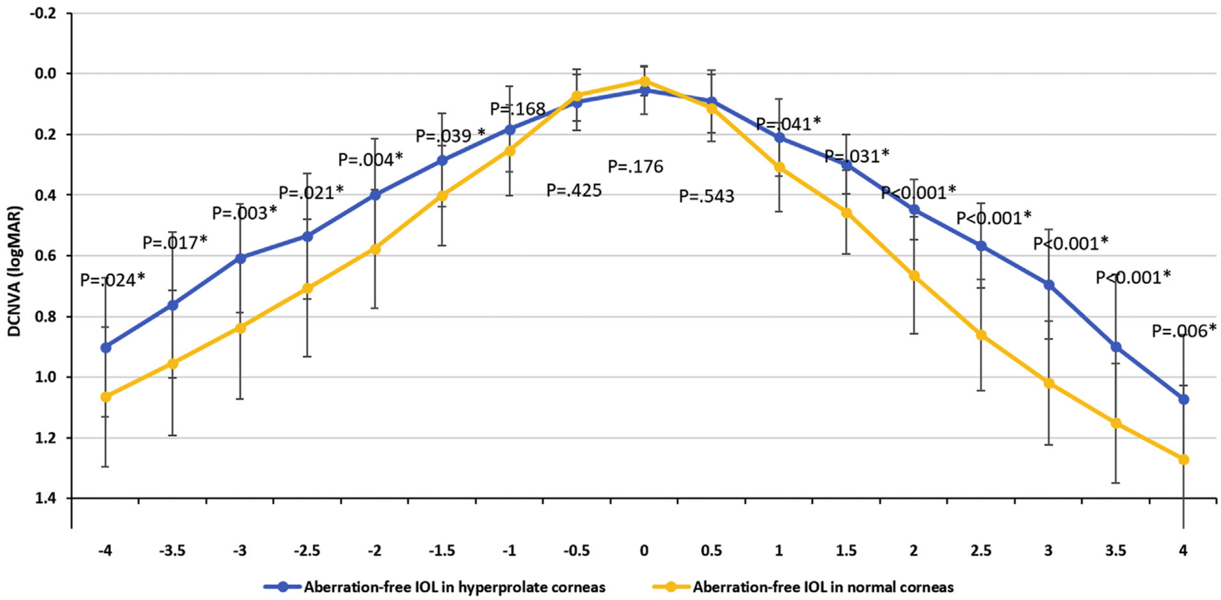

FIGURE 4. Comparison of defocus curves of the 2 corneal profiles (hyperprolate vs normal), both implanted with aberration-free intraocular lens (IOL). DCNVA = distance-corrected near visual acuity.

although statistically not significant). Our results corroborate the previous study by Denoyer and associates,[25] who demonstrated statistically significantly better mean DCNVA and comparable CDVA between the aberration-free and negative-SA groups. In contrast, Nanavaty and associates[26] showed no difference in the mean DCNVA as well as mean CDVA between the negative-SA and spherically neutral IOL. This might be simply owing to different populations or owing to the implantation of a negatively aspheric IOL with lower negative SA (−0.20 μm) that might not have neutralized all the SA and retained some depth of focus and DCNVA. HOA and SA are known to be pupil dependent; as such, the differences in the pupil size of the study eyes may also be responsible for the differences in visual outcomes discussed above.

With significantly better DCNVA in the aberration-free MX60E group and better CDVA in the ZCB00 group (although statistically not significant), it may be reasonable to conclude that patients undergoing monofocal IOL implantation may benefit from the implantation of a negative-SA IOL in the dominant eye (possibly allowing better CDVA or visual quality) and an aberration-free IOL in the nondominant eye (potentially allowing better DCNVA). A modified monovision approach that involves inducing SA in the nondominant eye has previously been shown experimentally to improve DOF and achieve better binocular summation than with traditional monovision.[29] Although such a strategy may benefit patients undergoing monofocal IOL implantation, patients desiring a high level of spectacle independence at far, intermediate, and near distances may be better off choosing a presbyopia-correcting IOL.

Bakaraju and associates[4] and Rocha and associates[6] have reported that both positive and negative SA can enhance DOF; our study findings seem to corroborate this. Retaining natural corneal HOAs, specifically positive SA in normal eyes, by using an aberration-free IOL or inducing negative aberrations in the eye (following hyperopic ablation in the present study or by an appropriately designed IOL in the future) may enhance near vision without significantly compromising the distance visual outcomes. Rocha and associates[6] also showed that introduction of both positive and negative SA (up to ∼±0.6 μm) significantly expanded DOF (by ∼2.0 D) at a pupil size of 6 mm and this benefit began to plateau and decline at higher levels. Bakaraju and associates[4] found that SA more negative than −0.15 μm showed a slightly higher DOF than their respective positive counterparts.

Modifications in corneal asphericity (Q value) following refractive surgery are known to influence DOF. Hyperprolate corneas generated following hyperopic LASIK tend to show a significant change in the corneal asphericity toward values more negative than −0.6 owing to the increased prolateness of the cornea. We included eyes with hyperprolate corneas in the current study to evaluate the effect of corneal asphericity and negative SA on DOF. With significantly higher values of negative corneal asphericity (−0.74 hyperprolate vs −0.35 in normal) and significantly higher amount of negative SA (−0.22 μm) than the normal corneas (+0.34 μm) ($P < .001$), hyperprolate corneas were found to have greater subjective DOF (defocus curve) and significantly better DCNVA (20/30.4) than achieved in eyes with the normal corneas (20/39) when implanted with aberration-free IOLs.

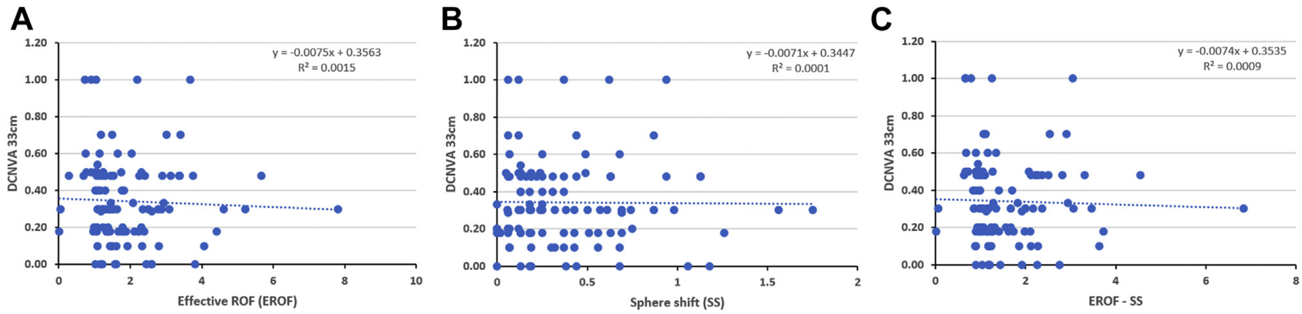

FIGURE 5. Correlation between distance-corrected near visual acuity (DCNVA) and objective measurements of accommodation: (A) effective range of focus (EROF), (B) sphere shift (SS), and (C) difference between effective range of focus and sphere shift accommodation (EROF−SS).

TABLE 4. Comparison of Mean Extended Range of Focus, Sphere Shift, and EROF−SS Between Eyes With Distance-Corrected Near Visual Acuity J3 or Better and Those Worse Than J3

Variable	DCNVA Worse (N = 77) Mean ± SD	DCNVA Better (N = 34) Mean ± SD	*P* Value
Sphere shift (SS)	0.36 ± 0.36	0.38 ± 0.32	.575
Extended range of focus (EROF)	1.89 ± 1.27	1.89 ± 0.91	.243
EROF−SS	1.55 ± 1.01	1.51 ± 0.77	.409

DCNVA = distance-corrected near visual acuity; EROF = extended range of focus; SS = sphere shift.

A few studies[8–11] also reported coma-like aberrations, particularly vertical coma, to be significantly associated with DOF. Consistent with the findings of these studies, our current study also found coma-like aberrations to have at least some association with the likelihood of achieving good near vision. Further, the aberration-free implanted eyes with hyperprolate corneas demonstrated significantly greater coma-like aberrations that may potentially contribute to enhanced DOF. In contrast, Rocha and associates[6] and Lim and associates[28] found that coma-like aberrations may not contribute to DOF.

Depth of focus of the human eye serves as a mechanism of blur tolerance. Although DOF can be expanded with increasing SA or coma, modifying HOA beyond a threshold value to enhance DOF may cause reduction in contrast sensitivity and degradation of image quality. Identifying the threshold to which aberrations can be increased to enhance DOF without compromising image contrast is still a matter of investigation, although there is some evidence to suggest that the best compromise of subjective DOF and objective contrast sensitivity may be reached with ocular SA between 0.07 μm and 0.10 μm for 6 mm pupil.[30]

In the present study, corneal SA measured with ray-tracing aberrometry (iTrace) did not seem to affect the probability of achieving good near vision ($P = .420$); however, Scheimpflug tomography (Pentacam HR) SA was significantly associated with good near vision outcomes (DCNVA of J3 or better). These differences in the association of corneal SA measured with the 2 devices on the likelihood of achieving good near vision might be owing to the differences in pupil size at which the measurements were taken (fixed 6 mm pupil with the Pentacam vs natural pupil ∼2.6 mm with iTrace).

Depth of focus also varies widely with object luminance and pupil diameter.[31] Smaller pupils are known to enhance DOF[1,7,11,13,28,32]; for instance, Elder and associates[33] and Lim and associates[28] found that pupil size less than ∼2.5-2.6 mm resulted in better near visual acuity with monofocal IOLs. Similar to the literature, the present study also found an inverse relationship between pupil size and likelihood of obtaining good near vision (J3 or better). The concept of pinhole optics has been successfully used in corneal inlays[34] (1.6 mm) and IOLs[35] (1.36 mm) and various presbyopia-correcting drops that aim to enhance DOF by inducing pupillary miosis. Similarly, in our study, pupil size (near) was smaller in the hyperprolate group compared with the normal group (both implanted with aberration-free IOLs), though the difference was only borderline significant ($P = .05$). Of note, in the present study, pupil size was not found to be a factor strong enough to be retained in the multiple logistic regression model. Consistent with the results of present study, Nanavaty and associates[14] and Fukuyama and associates[12] also did not find pupil size to be a significant factor affecting pseudoaccommodation.

In addition to DOF, pupil size is known to affect retinal illuminance, which in turn influences contrast sensitivity.[36] At low light conditions, reduced retinal illuminance associated with small pupil area causes reduction in neural contrast sensitivity. Therefore, at low stimulus luminance (eg, the 2 cd/m^2 modeled), reducing pupil diameter from 6.0 mm to 3.0 mm will halve neural contrast sensitivity, resulting in a 50% drop in the VSOTF in addition to any changes in VSOTF caused by optics.[7,37] At high light levels, where neural contrast sensitivity becomes independent of retinal illuminance, smaller pupils (1.0-3.0 mm) have been found to be more effective in expanding DOF.[37] As the pupil size increases, the effects of aberrations become more pronounced. Hickenbotham and associates[7] suggested that the benefits of a smaller pupil can possibly be combined with added negative SA to improve depth of focus beyond that possible by individual technologies. Such an approach may also help improve DOF under lower illumination.

Simple myopic ATR astigmatism of up to 1.5 D has been documented to improve DOF of pseudophakic eyes, possibly explained by conoid of Sturm[14,38]; however, since this is also known to compromise distance visual acuity, we did not include ATR astigmatism in the present study. This inclusion, however, would not affect our study findings, as our study parameter, DCNVA, would effectively eliminate any pseudoaccommodation related to ATR astigmatism and residual defocus in study eyes.

Although our subjectively measured DOF (defocus curve) corroborates the mean DCNVA findings in the aberration-free MX60E and negative-SA ZCB00 groups, objectively measured DOF metrics (EROF, SS, and EROF−SS) were comparable between the 2 IOL groups and the 2 corneal profiles (normal vs hyperprolate). Correspondingly, these variables showed no statistically significant difference between the eyes with DCNVA of J3 or better and those worse than J3. We also found no correlation between these objectively measured accommodation variables (EROF, SS, EROF−SS) and DCNVA. Although the absence of a correlation between SS (objective measure of true accommodation) and DCNVA in pseudophakic eyes implanted with monofocal IOL was expected, the absence of a correlation between EROF−SS or EROF (a measure of true accommodation + pseudoaccommodation) was unexpected. Overall, the findings of the present study seem to suggest that ray-tracing objective metrics of accommodation may not necessarily predict DCNVA outcomes.

In conclusion, the present study revealed that corneal aberration profile and IOL type are the most important parameters affecting the probability of achieving extended depth of focus (near vision outcomes of J3 or better) with an aspheric monofocal IOL targeted for distance correction. In normal eyes, aberration-free IOLs are likely to produce higher positive SA and better DCNVA than a negative-SA IOL. This is certainly the case in eyes with hyperprolate corneas.

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