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Review

The effects of premium intraocular lenses on presbyopia treatments

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ABSTRACT

Background: Presbyopia has become a global disease affecting the world's aging population. Among various treatments, cataract extraction and intraocular lens (IOL) implantation have become the most popular and common methods of presbyopia correction. During the twentieth century, IOLs have underwent significant innovation and advancements to meet the patients' high demands for functional vision at all distances.

Main Text: To meet the increasing needs for excellent near and intermediate vision for daily activities, some premium IOLs with more than one focus have been developed, for example, the refractive MfIOLs, diffractive MfIOLs, extended depth of field (EDOF) IOLs, and accommodating IOLs (AIOLs) were introduced to meet this need. In addition, the add-on MfIOLs have been explored as promising supplementary IOLs for pseudophakic presbyopia. When selecting the MfIOLs, the IOLs' features, patients' characteristics, preoperative eye conditions, and treatment expectations should be considered.

Conclusions: In this review, we focus on the multifocal IOLs (MfIOLs) commonly used for presbyopia correction and systematically summarized their optical designs and clinical outcomes. More evidence-based studies are required to provide guidelines for MfIOL selection, provide maximum visual benefits, and develop personalized visual solutions in the future.

1. Background

Presbyopia is affecting an increasing number of aging population, and its treatment has become a major research focus in ophthalmology.[1] Currently, presbyopia is described as “a condition of age rather than aging and, as such, is devolved from the lamentable situation where the normal age-related reduction in amplitude of accommodation reaches a point when the clarity of vision at near cannot be sustained for long enough to satisfy an individual's requirements”.[1] Although the specific mechanism responsible for such decreased accommodation is still being debated, Helmholtz's theory is the one that is most broadly accepted.[2] According to this theory, the contraction of the ciliary muscle increases the thickness and decreases the diameter of the crystalline lens, leading to increased lens curvature and lenticular power and changes in the focal length.[1] Due to decreasing lens elasticity as people age, lenses also become opaque, resulting in cataract, which is why many methods used to correct presbyopia do not achieve optimal results.[2,3]

“Ideal” presbyopia correction should restore accurate focusing and maintain the emmetropic level for decades.[1] Theoretically, refilling the capsular bag with a clear but elastic substance may be the best way to replay lenses, however, efforts in this direction have, to date, been unsuccessful.[4] Currently, the most common methods of correcting presbyopia include spectacles or contact lenses,[1,5,6] drugs,[7,8] refractive surgery,[5,9,10] scleral surgery,[11,12] and intraocular lens (IOL) implantation.[13–15] Among these methods, cataract phacoemulsification and IOL implantation are the most widely accepted and popular methods for correcting presbyopia in elderly people.

2. Intraocular lens (IOL) for presbyopia correction

After lens extraction, an eye will lose 20–30% of its total refractive power, but IOL implantation can correct the refractive error.[2] The past few decades have witnessed a revolutionary development of IOLs. Some studies have introduced or compared the advanced materials, focal points, and optical designs of different IOLs. This review summarizes the IOLs used for presbyopia correction, which can be divided into the following categories: monofocal IOLs (MIOLs), multifocal IOLs (MfIOLs), extended depth of field (EDOF) IOLs, and accommodating IOLs (AIOLs).

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EDOF IOLs are a special category of MfIOLs, and are reviewed in a separate section.

2.1. Monofocal IOLs (MIOLs)

Theoretically, MIOLs only provide patients with one focus for distance vision, however, some patients are able to achieve satisfactory distance and near vision without spectacles, which is called *pseudo adjustment*.[5] Researchers have generally agreed that this adjustment is caused by residual high-order aberrations or astigmatisms of the post-operative eye, or by patients happening to have small pupils, enabling a pinhole effect to expand the depth of focus.[5] Another way of correcting presbyopia is to use bilateral MIOL implantation to achieve "monovision" for patients. Generally, the dominant eye is corrected for hyperopia and the non-dominant eye for myopia, causing superimposition of a focused image on a defocused one.[16,17] Through brain processing and adaptation, sharp vision can thus be obtained. Nevertheless, "monovision" may lead to poor stereoacuity, and some patients cannot adapt to such anisometropia.[14,16,17] Due to the inevitable drawbacks of MIOLs, other IOLs have been developed to correct presbyopia.

2.2. Multifocal IOLs

Presbyopia is generally regarded as a monofocal condition because patients experience clear distance vision but blurred intermediate and near vision. Effective strategies mainly aim to produce multifocality or extend the depth of focus.[14] MfIOLs generally provide functional vision at two or more focal distances. Compared with the MIOLs, MfIOLs provide patients with better intermediate and near visual acuity (VA), which are particularly important because most daily activities such as driving, reading, and operating devices, are performed at intermediate and near distances.[4] However, MfIOLs inevitably disperse light energy, leading to decreased contrast sensitivity and increased optical disturbances (glare, halos, dysphotopsia, etc.).[18] Fortunately, the advances in IOL technology in recent decades have promoted the development and improved function of MfIOLs.

This review classifies MfIOLs into refractive, diffractive, and hybrid refractive-diffractive optical types and systematically summarizes their designs and features.

2.2.1. Refractive Multifocal IOL (MfIOLs)

2.2.1.1. Rotationally symmetric refractive MfIOLs. As summarized in Table S1, a classic refractive MfIOL is rotationally symmetric, which is characterized by five concentric aspheric refractive zones on the anterior surface of the IOL that facilitate distance and near vision.[19] This MfIOL category includes the Array SA40N, ReZoom NXG1, M-flex 630 series, and FIL611PV IOLs. The Array SA40N was approved by the United Sates Food and Drug Administration (FDA) in 1997. It distributes incident light in proportions of 50% for far distance, 37% for near distance, and 13% for middle distance.[19] Previous studies have reported superior distance and near vision for Array SA40N IOLs over MIOLs, with tolerable optical disturbances.[20] Compared with other MfIOLs, Array SA40Ns provide distance VA like that of AIOLs (e.g., Crystalens) or diffractive MfIOLs (e.g., TwinSet), but with higher patient satisfaction.[21]

To reduce photic disturbances, another refractive MfIOL—the ReZoom NXG1 IOL (Advanced Medical Optics, United States)—was produced, with a modified square edge that can decrease the incidence of posterior capsular opacity (PCO).[19] ReZoom NXG1s performed better than MIOLs for distance vision under photopic conditions, but worse under mesopic conditions.[22] Gierek-Ciaciura et al. found better uncorrected distance visual acuity (UDVA) with ReZoom NXG1s compared with Array SA40Ns, and worse uncorrected near visual acuity (UNVA) compared with diffractive and hybrid refractive-diffractive MfIOLs.[23]

Thereafter, Rayner Intraocular Lenses Ltd., United Kingdom, introduced the M-flex 630 series MfIOLs and reported satisfactory distance and intermediate VA. The series provides different near additions ranging from 30 to 50 cm. Researchers found no significant differences in UNVA between near additions of +3.0 D and +4.0 D, whereas uncorrected intermediate visual acuity (UIVA) was better with the +3.0 D model.[24] Another refractive MfIOL model (FIL611PV) resulted in worse UDVA and UNVA but better UIVA compared with a diffractive MfIOL.[25]

Taken together, compared with MIOLs, rotationally symmetric MfIOLs provide better distance VA and restore near VA to some extent. However, the additional focus inevitably causes decreased contrast sensitivity, more photic disturbances, and decreased spectacle independence at near distances. Although some refractive MfIOLs are designed with aspheric surfaces to improve the visual quality, problems such as pupil dependence, tilt, and decentration can still affect visual outcomes.[26]

2.2.1.2. Rotationally asymmetric refractive MfIOLs. Rotationally asymmetric refractive MfIOLs are designed with two segments with different refractive indexes—one for distance vision and the other for near vision.[27] The aspheric transition between the two segments reflects the incident light from the optical axis, preventing blurred vision caused by the interference and diffraction.[28,29] Following more advanced optical design, asymmetric refractive MfIOLs provide improved visual outcomes compared with symmetric refractive MfIOLs (Table S2).

Table 1 presents the clinical outcomes for rotationally asymmetric refractive MfIOLs. The Lentis (Netherlands) Mplus series was the first asymmetric refractive MfIOL on the market. Previous studies have reported improved distance vision, higher contrast sensitivity, less halo and glare, and better image quality with Mplus series IOLs.[13,30,31] The series includes an LS-312 model with a C-loop haptics and an LS-313 model with a plate haptics, with different near addition powers from +1.5 D to +3.0 D. A previous study showed satisfactory VA of Mplus LS-312 MF30,

Table 1
Main clinical outcomes of eyes implanted with rotationally asymmetric refractive MfIOLs.

Study	Model[a]	UDVA (log MAR)[b]	UIVA (log MAR)[b]	UNVA (log MAR)[b]	SE (D)[b]
Muñoz, 2011[16]	LS312 MF30	0.05 ± 0.10	0.13 ± 0.12	0.11 ± 0.13	0.30 ± 0.33
Alio, 2011[33]	LS312 MF15	0.20 ± 0.14	0.19 ± 0.11	0.45 ± 0.19	−0.13 ± 0.61
	LS312 MF30	0.14 ± 0.11	0.20 ± 0.13	0.21 ± 0.10	−0.09 ± 0.48
McNeely, 2016[30]	bilateral LS-312 MF30	−0.08 ± 0.08	0.36 ± 0.07	0.11 ± 0.11	−0.05 ± 0.41
	blended LS-312 MF20 & LS-312 MF30	−0.07 ± 0.07	0.38 ± 0.12	0.12 ± 0.11	0.02 ± 0.43
	bilateral SBL-3	***−0.05 ± 0.10***	***0.38 ± 0.10***	***0.10 ± 0.14***	***−0.03 ± 0.47***
McNeely, 2017[35]	LS312 MF30	−0.07 ± 0.07	0.36 ± 0.09	0.1 ± 0.07	0.02 ± 0.38
	SBL-3	***−0.06 ± 0.09***	***0.36 ± 0.09***	***0.05 ± 0.01***	***0.00 ± 0.45***
Shodai, 2017[34]	LS-313 MF30	−0.05 ± 0.12	0.10 ± 0.12 (BUIVA)	0.25 ± 0.22	0.26 ± 0.42
	LU-313 MF30T	−0.03 ± 0.13	0.13 ± 0.14 (BUIVA)	0.18 ± 0.17	0.12 ± 0.43
Nakajima, 2020[32]	Comfort LS-313 MF15	0.05 ± 0.13	0.23 ± 0.17	0.52 ± 0.20	0.00 ± 0.42

Abbreviations: MfIOL, multifocal intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; SE, spherical equivalent; BUIVA, best uncorrected intermediate visual acuity.

[a] MfIOL model SBL-3 was displayed in bold italics.

[b] Data presented as mean ± standard deviation (SD).

with peaks at distance and near foci.[18] Alió et al. compared the LS-MF15 and LS-MF30 IOLs and found better UDVA and UNVA for the LS-MF30 and better UIVA for the LS-MF15.[32] Also, the design of another Lentis IOL (LU-313 MF30T) managed to correct astigmatism and provide excellent VA.[33]

In 2016, another representative segmented refractive MfIOL, SBL-3, was produced by Lenstec Optical Group Ltd., United Kingdom. Its anterior surface comprises a sector-shaped distance-vision zone in the upper part and a sector-shaped near-vision zone in the lower part, providing a continuous and variable diopter.[34] What makes the SBL-3 different from the Lentis Mplus series is the inferonasal placement of the near segment.[29] As shown in Table 1, SBL-3s provided satisfactory bilateral distance and near VA, and no significant differences were found compared with the Lentis Mplus series. In addition, blended implantation of LS-312 and SBL-3 IOLs produced higher quality of vision (QoV) scores and fewer visual disturbances than bilateral Lentis Mplus LS-312 and bilateral SBL-3 IOLs.[29]

According to previous studies, the VAs, refraction, contrast sensitivity, and patients' satisfaction for rotationally asymmetric refractive MfIOLs were better than for symmetric refractive MfIOLs.[28] However, considering the asymmetric design, surgeons' decisions about the placement of the near segments are crucial.[28] Interestingly, McNeely et al. claimed that combining low near additions in the dominant eyes and the high near additions in the fellow eyes can improve patients' visual postoperatively outcomes.[29]

2.2.2. Diffractive MfIOLs

Another way to redirect light is diffraction. Based on Whitman's diffraction principle, diffractive MfIOLs combine monofocal and toric designs, with a diffractive element splitting the incoming light into various foci.[35] Briefly, four diffraction orders are produced: 0 for the distant focus, first order for the near focus, and the other orders that fail to converge on the focus, mainly producing higher-order aberrations (HOAs).[35,36] Generally, diffractive MfIOLs can be divided into bifocal and trifocal models based on the focus number.

2.2.2.1. Bifocal diffractive MfIOLs. Of all the bifocal diffractive MfIOL series and models, AMO's TECNIS series is the most representative, with the ZM900, ZMA00, and ZMB00 models having high near addition power (+4.0 D), and the ZLB00 and ZKB00 models having lower near addition of +3.25 D and +2.75 D, respectively (Table S3). Kim et al. compared three (ZLB00, ZKB00, and ZMB00) models with different near additions.[36] As summarized in Table 2, no significant differences were found for the UDVA, contrast sensitivity, or aberrations among the three TECNIS models, but the ZMB00's UNVA was better, at 33 cm, than that of the other two models.[36,37] Nevertheless, the comfortable working distance for most people is around 40–60 cm, and IOLs applying low near additions help to improve the intermediate vision to some extent.[36] ZKB00s with low near additions can provide patients with satisfactory UIVA and UNVA, and 98.4% of the patients' spherical equivalents (SEs) at the intermediate and near distances are within ±1 D (Table 2).[38] Compared with other MfIOLs, ZM900s provided better UDVA, UNVA, and refraction stability than a refractive MfIOLs (e.g., ReZoom) and a refractive-diffractive MfIOLs (e.g., ReSTOR).[23] Compared with refractive AIOLs, ZMA00s with high near additions were slightly inferior to AIOLs in improving intermediate vision and reducing optical disturbances, but the UNVA was better than that provided by AIOLs.[39]

2.2.2.2. Trifocal diffractive MfIOLs. Although the high near addition of bifocal MfIOLs ensures satisfactory distance and near vision, demands are increasing for intermediate vision based on changes in people's lifestyles. Reducing the near additions of bifocal MfIOLs helps to improve intermediate VA to some extent, and another promising method is to produce an additional focus at the intermediate distance.[40] Here, we introduce two representative trifocal diffractive MfIOLs.

The FineVision (PhysIOL, Belgium) series incorporates a special diffractive profiles with different diffractive steps by combining two kinoforms, producing three main foci on the anterior surfaces of the IOLs (Table S4).[35,41] In theory, the first-order diffraction of the first kinoform provides an addition of +3.5 D for near focus, the first-order diffraction of the second kinoform provides an addition of +1.75 D for intermediate focus, and the second-order diffraction of the second kinoform enhances near focus. In combination, three foci are produced, with light energy reduced by about 15%.[35,42,43] The FineVision series comprises three models (Micro F, POD F, and POD FT) with similar optical designs and refractive powers. Comparisons of the three models suggested that Micro Fs with larger optics provide the best vision for large-pupil patients, whereas POD FTs can improve the stability of IOLs, making them less prone to decentration or tilting (Table 3).[44] Several studies have compared the FineVision series with EDOF IOLs and found that trifocal MfIOLs provided better UNVA than the EDOF MfIOLs, but generated more optical disturbances, such as halo and glare.[45]

RayOne (Rayner, United Kingdom) is another pure diffractive trifocal MfIOL with a diffractive grating design. It has 16 diffractive rings in the central 4.5 mm zone on the optic anterior surface, and the percentages for light energy splitting are 52% for far distance, 22% for intermediate

Table 2
Main clinical outcomes of eyes implanted with bifocal diffractive MfIOLs.

Study	Model[a]	UDVA (log MAR)[b]	UIVA (log MAR)[b]	UNVA (log MAR)[b]	SE (D)[b]
Gierek-Ciacuira, 2010[24]	ZM900 (+4.0 D)	0.14 ± 0.02	NA	0.12 ± 0.03	0.22 ± 0.09
	ReZoom (refractive)	***0.11 ± 0.01***	***NA***	***0.20 ± 0.04***	***0.37 ± 0.16***
	ReSTOR IOL (diffractive and refractive)	***0.17 ± 0.02***	***NA***	***0.11 ± 0.03***	***0.29 ± 0.09***
Pepose, 2014[40]	ZMA00 (+4.0 D)	−0.05 ± 0.10 (high-contrast)	0.18 ± 0.15 (high-contrast)	0.04 ± 0.13 (high-contrast)	−0.09 ± 0.34
Chang, 2014[38]	ZMB00 (+4.0 D)	0.01 ± 0.12	0.27 ± 0.18 (67 cm)	0.15 ± 0.11 (33 cm)	−0.16 ± 0.50
Kim, 2015[37]	ZMB00 (+4.0 D)	0.07 ± 0.07	NA	0.11 ± 0.09 (33 cm) 0.15 ± 0.08 (40 cm) 0.18 ± 0.08 (50 cm)	0.04 ± 0.23
	ZLB00 (+3.25 D)	0.05 ± 0.04	NA	0.13 ± 0.08 (33 cm) 0.14 ± 0.08 (40 cm) 0.14 ± 0.07 (50 cm)	−0.10 ± 0.22
	ZKB00 (+2.75 D)	0.07 ± 0.06	NA	0.17 ± 0.07 (33 cm) 0.15 ± 0.07 (40 cm) 0.10 ± 0.05 (50 cm)	−0.04 ± 0.28
Kretz, 2015[39]	ZKB00 (+2.75 D)	0.13 ± 0.18	0.16 ± 0.16 (0.09 ± 0.15 binocular)	0.11 ± 0.19 (0.04 ± 0.15 binocular)	−0.04–0.00[c]

Abbreviations: MfIOL, multifocal intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; SE, spherical equivalent; NA, not available.
[a] MfIOL models of refractive design was displayed in bold italics.
[b] Data presented as mean ± standard deviation (SD).

Table 3
Main clinical outcomes of eyes implanted with trifocal diffractive MfIOLs.

Study	Model	UDVA (log MAR)[a]	UIVA (log MAR)[a] (80 cm)	UNVA (log MAR)[a] (40 cm)	UNVA (log MAR)[a] (25 cm)	SE (D)[a]
Vryghem, 2013[42]	FineVision	0.06 ± 0.09	0.05 ± 0.19	0.11 ± 0.12	NA	0.10 ± 0.37
Poyales, 2019[45]	FineVision Micro F	0.02 ± 0.01	0.21 ± 0.02	0.13 ± 0.02	0.29 ± 0.02	−0.03 ± 0.08
	FineVision POD F	0.00 ± 0.01	0.16 ± 0.04	0.11 ± 0.12	0.31 ± 0.10	−0.09 ± 0.07
	FineVision POD FT	0.04 ± 0.02	0.17 ± 0.02	0.10 ± 0.07	0.32 ± 0.08	−0.17 ± 0.10
Ferreira, 2019[47]	RayOne	−0.02 ± 0.08	0.00 ± 0.10	0.01 ± 0.12	NA	−0.07 ± 0.29
	FineVision POD F	−0.01 ± 0.06	0.04 ± 0.07	0.02 ± 0.11	NA	−0.25 ± 0.35

Abbreviations: MfIOL, multifocal intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; SE, spherical equivalent; NA, not available.
[a] Data presented as mean ± standard deviation (SD).

distance, and 26% for near distance.[46] Compared with the FineVision series, both FineVision and RayOne models provided satisfactory distance, intermediate, and near VA (Table 3). The defocus curves were similar for the two groups, and both provided the best UNVA at −3.0 D (33 cm). At an intermediate distance, the VA decreased less than 0.2 log MAR within the range of −2.5 to −1.0 D (40–100 cm).[46] RayOne therefore provides patients with excellent VA at all distances, together with improved refractive accuracy.

2.2.3. *Hybrid refractive-diffractive MfIOLs*

Although MfIOLs provide satisfactory VA at all distances, they inevitably cause photic disturbances, such as halo and glare, and decrease contrast sensitivity, mainly due to increased aberrations and decreased energy from the light dispersion. To solve this problem, *apodization* is used to gradually reduce the diffraction step from the center to the periphery of some diffractive MfIOLs. Alternatively, combined diffraction and refraction can redistribute incoming light across different foci.[47]

2.2.3.1. Bifocal refractive-diffractive MfIOLs. The AcrySof IQ ReSTOR is a new bifocal refractive-diffractive MfIOL produced by the Alcon Company, USA. The IOL's optic center smoothly decreases in step heights from the center to the periphery, and the peripheral zone is pure refractive for distance vision.[19,35] The refractive-diffractive design improves light transmission and reduces light dispersion, providing a smooth transition between different foci without compromising contrast sensitivity (Table S5). Pedrotti et al. compared the AcrySof IQ ReSTOR SV25T0 and SN60D1 models and found better VA for the SV25T0 at 50–70 cm and better VA for the SN60D1 at 30–40 cm.[48] The AcrySof IQ ReSTOR SN60AD3 was also compared with a refractive ReZoom MfIOL and a diffractive Tecnis MF ZM900 MfIOL (Table 4). The refractive ReZoom had worse UNVA than the other models. The level of spectacle independence was 80% in patients implanted with ZM900s and SN60AD3s, but 70% for those implanted with ReZooms. MfIOLs with a diffractive design have therefore been recommended for patients with high demands for near VA.

The AT LISA series produced by Carl Zeiss Meditec Company, Germany, is another typical refractive-diffractive MfIOL, consisting of bifocal 809M and trifocal 839M models, and 909M and 939MP models with an astigmatism-correcting function.[49] Compared with the ReSTOR SN6AD1, both IOLs exhibited excellent VA at all distances, but the intermediate VA was not as good as the near VA, and the level of spectacle independence was 69% for the 809M and 65% for the SN6AD1.[50]

Another MfIOL in this category is the Eyecryl (Biotech Vision Care, India) Actv, the optic of which consists of a refraction region-diffraction region-refraction region progression from the center to the periphery. Haldipurkar et al. compared the Actv IOL with the ReSTOR SN6AD1 and found no significant differences in VA, visual quality, or defocus curve between the two groups. However, the Actv provided better contrast sensitivity and fewer optical disturbances than the SN6AD1 under mesopic conditions.[47]

The Acri series from Acritec Industries, Germany, is another type of refractive-diffractive MfIOL (Table S5); for instance, the Acri LISA 366D is an aspheric MfIOL consisting of a main zone and a phase zone. The main zone handles distance and near foci, with light distributions of 65% and 35%, respectively.[51] The phase zone reduces the light loss that causes HOAs, decreases optical disturbances and improves the visual quality.[51] Also, the Acri LISA 366D has an aspheric surface to reduce corneal aberrations, and its sharp optic edge is designed to prevent PCO. Previous studies reported that the Acri LISA 366D provided excellent distance and near VA and contrast sensitivity, and was suitable for patients with high demands for contrast sensitivity.[51,52] Thereafter, the Acri Twin system of 737D and 733D models were designed to minimize the visual

Table 4
Main clinical outcomes of eyes implanted with bifocal refractive-diffractive MfIOLs.

Study	Model[a]	UDVA (log MAR)[b]	UIVA (log MAR)[b]	UNVA (log MAR)[b]	SE (D)[b]
Gierek-Ciaciura, 2010[24]	SA60D3	0.17 ± 0.02	0.36 ± 0.07	0.11 ± 0.11	−0.05 ± 0.41
	ReZoom	***0.11 ± 0.01***	***NA***	***0.20 ± 0.04***	***0.37 ± 0.16***
	ZM900	***0.14 ± 0.02***	***NA***	***0.12 ± 0.03***	***0.22 ± 0.09***
Pedrotti, 2018[49]	SN6AD1	0.02 ± 0.08	0.29 ± 0.12 (60 cm)	0.05 ± 0.08 (40 cm)	−0.06 ± 0.22
	SN6AD2	0.00 ± 0.09	0.00 ± 0.08 (60 cm)	0.28 ± 0.11 (40 cm)	−0.06 ± 0.27
Alfonso, 2007a[54]	Acri Tec737D	0.04 ± 0.06 (BCDVA)	NA	0.06 ± 0.09 (BCNVA)	0.07 ± 0 .56
	Acri Tec 733D	0.14 ± 0.13 (BCDVA)	NA	0.02 ± 0.12 (BCNVA)	0.06 ± 0.63
Alfonso, 2007b[52]	Acri LISA 366D	0.13 ± 0.20	NA	0.01 ± 0.05	NA
Fernández-Vega, 2007[91]	Acri Tec 447D	0.02 ± 0.04 (BCDVA)	0.04 ± 0.03 at 33 cm (BCIVA); 0.21 ± 0.08 at 70 cm (BCIVA)	0.04 ± 0.03 (BCNVA)	−0.09 ± 0.48
Alio, 2011[33]	Acri LISA 366D	0.11 ± 0.11	NA	0.12 ± 0.11	0.13 ± 0.48
Wang, 2015[56]	BB MFM 611	−0.05 ± 0.13	NA	0.15 ± 0.14	0.69 ± 0.49
	BB MF 613	0.02 ± 0.14	NA	0.20 ± 0.17	0.75 ± 0.49

Abbreviations: MfIOL, multifocal intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; SE, spherical equivalent; BCDVA, best corrected distance visual acuity; BCIVA, best corrected intermediate visual acuity; BCNVA, best corrected near visual acuity; NA, not available.
[a] MfIOL models with refractive design were displayed in bold italics.
[b] Data presented as mean ± standard deviation (SD).

disturbances common with MfIOLs. Alfonso et al. found that combining these two models significantly improved VA and contrast sensitivity, but some patients could not adapt to the unequal light distribution between their eyes (Table 4).[53]

The Acriva Reviol (VSY Biotechnology, Netherlands) series has three models: MFM 611, 613, and 625. Previous studies compared the MFM 611/625 with the Acri LISA and ReSTOR SN6AD3, but observed no significant differences in VA at all distances, contrast sensitivity, or photic disturbances (Table 4)[54,55]; hence, the choice of MfIOL mainly depends on the patients' preferences.

2.2.3.2. Trifocal refractive-diffractive MfIOLs. OptiVis (Aaren Scientific, United States) is a far-dominant refractive-diffractive MfIOL that handles three foci by alternating the refractive and diffractive zones. The multifocal posterior surface consists of three zones: the first refractive zone for distance and intermediate vision, the second apodized diffractive zone for distance and near vision, and the third refractive zone to improve contrast sensitivity (Table S5).[56] Dyrda et al. found that OptiVis provided good VA at all distances, although the level of spectacle independence was 16% for distance vision and 50% for near vision (Table 5).[56]

Another trifocal refractive-diffractive MfIOL is the widely used AT LISA tri 839MP from Carl Zeiss Meditec Company, Germany, which consists of a central trifocal zone and a peripheral bifocal zone. The light dispersion is 50% for far distance, 20% for intermediate distance, and 30% for near distance (Table S5). Compared to the EDOF ZXR00 MfIOL, the 839MP had better UNVA but produced more photic disturbances. The level of spectacle independence was 54% for the 839MP and 64% for the ZXR00.[57] For patients with high expectation for spectacle independence, the 839MP model is a better option.

The AcrySof IQ PanOptix is a single-piece aspheric trifocal refractive-diffractive MfIOL developed by Alcon Laboratories, USA, in 2015, which is widely used for presbyopia correction.[58] Unlike the usual design of intermediate focus at a distance of 80 cm, the intermediate focus of PanOptix is at 60 cm, providing a more comfortable working distance for most people. The innovative features of the PanOptix IOL are summarized in Table S5. Unlike the common trifocal MfIOLs, the PanOptix applies a patented ENLIGHTEN optical technology to redistribute the light energy and minimize the energy loss.[59,60] A previous study involving patients with bilateral PanOptix implantations reported excellent VA at all distances, particularly for intermediate VA (Table 5).[59] Three months postoperatively, the researchers also reported high levels of spectacle independence.[59] Although 89% of patients reported halo disturbance, the photic effect was mild and the overall satisfaction was high. Compared with the TECNIS Symfony ZXR00, the PanOpitx produced significantly better UNVA, although halo and glare optical disturbances were more frequently reported.[61]

Table 5
Main clinical outcomes of eyes implanted with trifocal refractive-diffractive MfIOLs.

Study	Model[a]	UDVA (log MAR)[a]	UIVA (log MAR)[a]	UNVA (log MAR)[a]
Dyrda, 2018[57]	OptiVis	0.13 ± 0.12	0.54 ± 0.31	0.20 ± 0.14
Webers, 2020[58]	AT LISA tri 839MP	−0.05 ± 0.07	0.01 ± 0.03	0.04 ± 0.07
Sudhir, 2019[59]	AcrySof IQ PanOptix	0.00 ± 0.09	0.00 ± 0.11 (60 cm) 0.09 ± 0.11 (80 cm)	0.01 ± 0.09
Farvardin, 2021[62]	AcrySof IQ PanOptix	0.03 ± 0.11	0.20 ± 0.11	0.23 ± 0.11

Abbreviations: MfIOL, multifocal intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity.
[a] Data presented as mean ± standard deviation (SD).

2.2.4. Extended depth of field (EDOF) MfIOLs

The additional foci of MfIOLs can provide better VA at certain distances, but the depth of focus is usually limited, leading to poor image quality. The recent introduction of EDOF technology has led to consistent visual performance in response to light. EDOF IOLs are generally based on two principles: the first is decreasing the spherical aberration and extending the depth of focus, such as the Isopure (PhysIOL, Belgium), Acrisof Vivity (Alcon, USA), and Tecnis Eyhance (Johnson & Johnson, USA) MIOLs.[14,35,62] However, the EDOF IOLs based on asphericity have larger spherical aberration, which may lead to binocular photic phenomena.[63] The second is using the pinhole principle to elongate the focus, such as the IC-8 (Acufocus, USA) and XtraFocus piggyback (Morcher GmbH, Germany) MIOLs.[35,64] The blurred vision resulting from defocus is proportional to pupil diameter. Although a small pupil can expand the eye's depth of field, it would also influence diffraction and optical aberrations and reduce the field of view.[14] Unlike bifocal or trifocal MfIOLs, which have biphasic defocus curve profiles, the defocus curves of EDOF MfIOLs are smooth and steady, without decay or energy loss at intermediate to far distances.[65] Through special diffraction grating, the EDOF MfIOLs extend a focus into a *focal line*, which can enhance depth of focus or range of vision and eliminate the overlapping of near and distant images caused by traditional MfIOLs.[64] We next summarize some commonly used EDOF MfIOLs on the market.

The TECNIS Symfony ZXR00 is a multifocal-EDOF IOL produced by Johnson & Johnson (USA), which was approved by the FDA in 2016.[66] It combines a wavefront-design aspheric anterior surface with an achromatic diffractive posterior surface and uses proprietary echelette technology (Table S6).[64,66] Cochener et al. examined 411 patients' VA at 4–6 months after bilateral implantation of ZXR00, and the mean UDVA, UIVA, and UNVA were 0.95, 0.81, and 0.69, respectively.[67] Comparing with MIOLs, ZXR00 showed some inherent defects, including optical disturbances and low contrast sensitivity, but were considered tolerable by patients, who rated them highly.[68] Another study by Gil et al. compared the ZXR00 with some bifocal MfIOLs (the SVT250, ZKB00, ZLB00, and AT LISA 809M) and a trifocal MfIOL (the AT LISA Tri 839MP) and found that the ZXR00 produced a single peak in the defocus curve from intermediate to far distance.[65] For patients who expect good intermediate VA, the ZXR00 is more effective.

The Artis Symbiose (Cristalens Industrie, France) is designed with a patented through-focus phase profile with extended sharp vision at near to intermediate distances and high contrast sensitivity at far distances.[69] To date, studies regarding the Artis Symbiose have been mainly theoretical, and clinical trials are needed to provide more evidence for clinical application.

Another EDOF MfIOLs is the Mini WELL Ready IOL (SIFI, Italy), featured with positive and negative spherical aberrations in three different optic zones (Table S6). Previous studies have confirmed the stability and effectiveness of the Mini WELL in providing excellent VA at all distances with few night visual disturbances.[66,70] Postoperative questionnaires also indicated high levels of spectacle independence and patient satisfaction, and the incidences of postoperative dysphotopsia and optical disturbances for the Mini WELL were lower than those for the ZXR00.[66]

In addition to the clinically available EDOF MfIOLs, some experimental EDOF techniques also showed promising results. For example, the peacock eye optical element was designed to focus an incident plane wave into a segment of the optical axis.[71] The double peacock eye element produces two successive focal segment which covers the required depth of focus, and demonstrates better image quality at the focal points and smaller aberration than MfIOLs.[71] Another EDOF technique, light sword lenses, is an asymmetric refractive element with angular variation of optical power.[72] Experimental results showed that light sword lenses produced consistently good quality images at a wide range of distances from 25 to 33 cm to infinity, and a recent clinical study showed their acceptable VA and high-quality contrast sensitivity at near and distant vision.[73] Overall, all these new EDOF designs represent promising alternatives for presbyopia correction in clinical applications.

2.2.5. Accommodating intraocular lens (AIOLs)

AIOLs are designed to maintain the natural accommodation ability of the eyes' refractive system, which can change the IOL's refractive power with the help of ciliary muscular contractions.[74] AIOL optics are usually composed of the same material with the same refractive index and without any optical microstructures, such as diffraction grating or refractive zones, which reduces optical disturbances.[25] According to their optic designs, AIOLs mainly include single-optic, dual-optic, and deformable surfaces, etc. (Table S7).

2.2.5.1. Single-optic AIOLs. Single-optic AIOLs are usually connected with flexible haptics, allowing the optics to convert the contraction of the ciliary muscle into power for the accommodation ability of eyes (Table 6)[74]; for example, the 1CU produced by HumanOptics Company, Germany, can adjust its axial position according to ciliary muscle contraction and relaxation, within a range of +16–26 D.[75] The Crystalens IOL series produced by Bausch and Lomb Company, Canada, is a hinged plate-haptic AIOL made from a third-generation silicone elastome. The ciliary muscle contraction redistributes Crystalens AT-45 across the vitreous base and eventually leads to axial displacement and refractive power change of the optic.[76] Another typical single-optic AIOL is the Tetraflex KH3500 (Lenstec, United States), which has a 5°angle between the optic and haptics and an edge designed to reduce PCO. Previous evidence confirmed that single-optic AIOLs provided comparable VA with MfIOLs, but generated significantly less halo or glare.[77] However, since single-optic AIOLs can only move less than 1 mm in the eyes, which results in limited refractive change and accommodation.[78] Another risk associated with single-optic AIOLs is capsular contraction syndromes, which can alter the intended position of the IOL optic. Asymmetric capsular contractions force one of the plate haptics to vault anteriorly and the other posteriorly, resulting in astigmatism.[19]

2.2.5.2. Dual-optic AIOLs. A dual-optic AIOL consists of two independent optical elements, and the distance between them alters as the capsule bag contracts and changes the refractive power accordingly. At present, the Synchrony (Visiogen, United States) and Sarfarazi (Bausch and Lomb, United States) are the only dual-optic AIOLs available on the market (Table S7). The Synchrony IOL uses two optical elements—one positive-power anterior optic and one negative-power posterior optic—to provide emmetropia. This dual-optic AIOL can produce 2.2 D power per 1 mm of movement compared with the 1 D of a single-optic AIOL.[74] The Sarfarazi is another dual-optic AIOL produced by Bausch and Lomb, with accommodation up to 4.0 D.[74] Previous studies have proved that dual-optic AIOLs can provide better VA, higher contrast sensitivity, and lower incidence of PCO than single-optic AIOLs.[79,80] However, dual-optic AIOLs also have limited accommodation amplitude, which depends on the elasticity of the capsule bag. The forward movement of the anterior optic increases the distance between the image space nodal point and the retina, resulting in magnification of the image[74]; therefore, the effect of dual-optic AIOLs in practice largely depends on patients' personal characteristics.

Table 6
Main clinical outcomes of eyes implanted with AIOLs.

Study	Model[a]	UDVA (log MAR)[b]	UIVA (log MAR)[b]	UNVA (log MAR)[b]	SE (D)[b]
Saiki, 2010[74]	1CU	0.00 ± 0.10	NA	0.51 ± 0.36	−0.26 ± 0.41
Marchini, 2007[77]	Crystalens AT-45	0.02 ± 0.01	NA	NA	−0.1 ± 0.5
	1CU	0.04 ± 0.07	NA	NA	−0.2 ± 0.9
	MIOL	***0.04 ± 0.02***	***NA***	***NA***	***−0.3 ± 0.2***

Abbreviations: AIOL, accommodating intraocular lens; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; SE, spherical equivalent; MIOL, monofocal intraocular lens; NA, not available.

[a] MIOL models were displayed in bold italics.

[b] Data presented as mean ± standard deviation (SD).

2.2.5.3. Other AIOLs. Besides the aforementioned AIOLs, another category of deformable surface AIOLs exists, which is represented by NuLens (Ben-Nun, Israel) and designed with a silicone oil filling. This type of AIOL generally has an anterior reference plane with a central round hole and a posterior piston. When the ciliary muscle contracts or relaxes, the capsule diaphragm causes the flexible gel to thin or bulge, resulting in an increase or decrease in IOL optical power until the best image is obtained on the retina.[81,82] Alió et al. reported the 1-year follow-up results for 10 patients with NuLens AIOL and showed that UNVA reached a peak at 3 months and stabilized at 9 months postoperatively. However, clinical evidence of this AIOL's effectiveness is still limited.

Other underdeveloped AIOLs include switchable electro-optic diffractive lenses based on electrical control, and MAG-driven active shift AIOLs and smart AIOLs based on temperature control.[74,83] The AkkoLens Lumina AIOL (Akkolens International B.V., Netherlands) slides on the plane perpendicular to the optical axis to provide a continuous variable-focus lens (Table S7).[84] A previous study showed that Luminas produced significantly better UIVA and UNVA than MIOLs at a 1-year follow-up, without compromising contrast sensitivity.[84] Fluidvision (Powervision, United States), another clinically available AIOL, changes the refractive index through fluid displacement. When the haptics are subject to accommodative forces, silicone oil is pushed into the optic through fluid channels that connect the haptics to the optic, changing the AIOL's refractive index, which provides much better biocompatibility with the uvea and lens capsule than a single-optic AIOL.[85] Taken together, the recently developed AIOLs can achieve comparable UDVA and significantly better UIVA and UNVA than MIOLs, with fewer side effects. Nevertheless, their accommodation effects are limited, and large sample size clinical trials are needed prior to clinical application.

2.2.6. Add-on MfIOLs

Since MIOLs can only provide a focus at far distances, patients with MIOL implantations often experience pseudophakic presbyopia. Nowadays, supplementary MfIOL implantation is considered as an effective treatment for pseudophakic presbyopia by combining an add-on MfIOL in the ciliary sulcus with a MIOL in the capsule.[86,87] The most common add-on MfIOLs include the trifocal 1stQ Add-On series (Medicontur Medical Engineering Ltd., Germany), bifocal DIFFRACTIVA Diff-sPB (HumanOptics, Germany), and the bifocal M-Flex Sulcoflex (Rayner Surgical GmbH, United Kingdom) (Table S8). The 1stQ AddOn MfIOL can provide excellent UDVA and UNVA without complications or optical disturbances, and it performs better at near distances than trifocal MfIOLs in capsular bags.[87,88] For the bifocal Diff-sPB, the best UNVA was reported at 30 cm, with 100% patient satisfaction.[86] No severe postoperative complications were observed, and halo and glare were mild, confirming the safety of the Diff-sPB.[86] Schrecker et al. reported the results for two other bifocal add-on MfIOLs—the refractive Sulcoflex 653F and the diffractive MS 714 PB Diff—combined with MIOLs in pseudophakic patients.[89] Both add-on MfIOLs provided excellent VA at all distances, while the diffractive MS 714 PB Diff performed better at a distance of 40 cm and caused significantly fewer optical disturbances than the refractive Sulcoflex 653F.[89] Add-on MfIOLs are therefore promising IOLs for pseudophakic presbyopia correction.

3. Selection of MfIOLs

The development of various advanced MfIOLs has met people's demands for high-quality vision and spectacle independence at all distances. However, inevitable optical disturbances, including halo and glare, are the inherent shortcomings of MfIOLs. In clinical practice, strict selection criteria based on the MfIOLs' characteristics, patients' expectations, and preoperative conditions should be used.[18,23,90]

3.1. Implantation strategies

Nowadays, *mix and match* strategy is common for presbyopia correction. Bilateral implantation of MfIOLs with different near-distance additions is known to improve VA and spectacle independence without affecting stereovision and contrast sensitivity. Some studies have compared the *mix and match* implantation of EDOF MfIOLs with the bilateral implantation of trifocal MfIOLs; the EDOF group exhibited better UDVA but inferior UIVA and UNVA than the trifocal group.[64] Also, binocular intolerance to different light distributions between eyes may occur with *mix and match* implantations.[91]

3.2. Precautions for selecting presbyopia patients

For patients who opt for implanted MfIOLs to achieve better functional vision, accurate preoperative assessment is essential.[13] This includes reviewing the patients' medical histories for relevant medical conditions, medications currently used, and other risk factors, such as diabetes and immunosuppressive conditions, that may affect surgical outcomes.[92] Also, patients' psychological states and endurance should be assessed. Since there may be a long neuroadaptation process of several months following MfIOL implantation, patients who are psychologically unstable or intolerable of visual disturbances may not be suitable for MfIOL implantations.

More importantly, regarding patients' ophthalmic conditions, those with high degrees of astigmatism, irregular astigmatism, or other forms of corneal dystrophy or degeneration are not suitable for MfIOL implantations.[93] Patients with macular diseases or abnormal structures and children with varying physiological features are also unsuitable. Therefore, eye examinations and assessments before MfIOL implantations should be careful and individualized. Most MfIOLs require large pupil sizes to facilitate the efficient use of incident light. The larger the pupil is, the more zones of an MfIOL's optic can be used.[92,94] By contrast, small pupils require higher capsulorhexis technology because MfIOLs are more sensitive to decentered capsulorhexis. Other conditions, such as eccentric pupils or iris coloboma, can lead to MfIOL dysfunction, which is an absolute contraindication for MfIOL implantation.[95]

When choosing a suitable MfIOL, the patient's lifestyle and vision requirements should also be considered; for example, for patients who frequently read books, use mobile devices, or work on computers, the EDOF MfIOL, which provides excellent UIVA, should be suitable.[13] For patients who requires good visual quality at night, the MfIOLs with excellent contrast sensitivity under mesopic conditions may be a better choice.

Postoperative astigmatism correction is vital for vision recovery. One study reported that the VA provided by MfIOLs is directly proportional to the degrees of residual astigmatism in eyes implanted with MfIOLs.[96] Toric MfIOLs have an anterior or posterior surfaces that provide multifocality, and toric surfaces that provide astigmatism correction; therefore, patients with high astigmatism may choose toric MfIOLs, such as the AcrySof IQ ReSTOR SN6AD1 or the Tecnis Symfony Toric, to provide the best visual quality.

3.3. The choice of MfIOLs

3.3.1. MfIOLs diopter

An appropriate MfIOL diopter is the basis for successful postoperative vision.[92] First, the axial length should be measured using A-scan ultrasound or IOL Master (Carl Zeiss Meditec Company, Germany), and the central corneal diopter should be determined by automatic or manual corneal curvature measurement or corneal topography. Finally, the total diopter of the MfIOL should be calculated using the calculation formulae, such as the Hoffer Q, Holladay, and SRK/T, etc.[92]

3.3.2. MfIOL implantation site

As mentioned in the previous sections, an MfIOL can be implanted in the capsule bag or in the ciliary sulcus as an add-on IOLs. Add-on MfIOLs have been reported to provide similar postoperative visual outcomes to the conventional intracapsular method.[97] Nevertheless, intraocular pigment deposits and dysphotopsia have been reported more frequently for add-on MfIOLs.[98]

3.3.3. MfIOLs' optical design

Over decades of development, MfIOLs have been produced with various edges, haptics, materials, and focus additions. Unlike MfIOLs with round and blunt edges, MfIOLs with sharp and square optic edges can prevent the migration of epithelial cells at the posterior capsule interface and therefore prevent PCO.[99] Also, haptic deformation and bending caused by anterior capsule contraction play a key role in IOL decentration and tilting, which significantly affect visual quality. Bozukova et al. carried out *in vitro* and *in vivo* experiments and proved that double C-loop haptics are suitable for manufacturing high-quality IOLs.[99] Considering MfIOLs' focus addition, some manufacturers use low near addition to provide excellent intermediate vision and accommodate patients' increasing needs to work at intermediate distances.[100] Low near addition MfIOLs can also provide lower incidence of optical disturbances and higher levels of spectacle independence and patient satisfaction.[36] However, more studies should be carried out to assess the effects of optical designs on postoperative visual outcomes.

4. Conclusions

In recent decades, IOLs have developed rapidly alongside various advanced models and continuous technological innovation. Although MfIOLs have inherent disadvantages, the development of MfIOLs over the past few decades has significantly improved presbyopia patients' quality of life. Our review has listed some representative MfIOLs and summarized the clinical outcomes of the most common models. In general, choices of MfIOLs should be based on the patients' eye conditions, daily requirements for vision at different distances, functional statuses, and the characteristics of different MfIOLs. More large-scale clinical trials of MfIOLs for presbyopia correction are needed to provide patients with maximum benefits from MfIOLs implantation. Also, the inherent defects of MfIOLs such as light energy loss, and the potential risks of EDOF technology, such as HOAs are still issues that still need to be solved, and global awareness is lacking regarding the distinct types of MfIOLs. According to recent studies, the topics about "improving intermediate vision", "providing full range vision", and "continuous focus" may still be the priorities for the MfIOLs market in the future.

Study Approval

Not applicable.

Author Contributions

The authors confirm contribution to the paper as follows: Conception and study design: Yanan Zhu; Writing the original draft: Yanan Zhu and Yueyang Zhong; Review and editing: Yueyang Zhong and Yanyan Fu; Supervision and funding acquisition: Yanan Zhu. All authors have read and approved the final version of the manuscript.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Abbreviations

AIOL	Accommodating intraocular lens
EDOF	Extended depth of field
FDA	United Sates Food and Drug Administration
HOA	Higher-order aberration
IOL	Intraocular lens
MIOL	Monofocal IOL
MfIOL	Multifocal IOL
PCO	Posterior capsular opacity
SE	Spherical equivalent
UDVA	Uncorrected distance visual acuity
UIVA	Uncorrected intermediate visual acuity
UNVA	Uncorrected near visual acuity
VA	Visual acuity

Appendix A. Supplementary data

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