CURRENT OPINION

Small-aperture strategies for the correction of presbyopia

H. Burkhard Dick

Purpose of review

The recent scientific literature provides evidence of long-term results with small-aperture corneal inlays, as well as new evidence from a multicenter postmarket study of small-aperture intraocular lenses (IOLs) and early reports of the use of topical agents for presbyopia correction through pupil constriction. The field of small-aperture optics is growing and changing rapidly.

Recent findings

This article reviews what is known to date about various small-aperture optics platforms, including a posterior chamber IOL, add on device, corneal inlay, contact lenses, and pupil-constricting drops. Additionally, the impact of small-aperture technologies on light perception and visual performance, as well as the relative merits of monocular versus binocular small apertures are discussed.

Summary

Small-aperture optics are a dynamic, physiologic solution to the problem of presbyopia. They are effective throughout the range of accommodation loss and in pseudophakia. Small-aperture optics offer an opportunity to improve vision in presbyopes with and without cataracts. In some forms, they may also be able to reduce the impact of aberrations or improve vision in eyes with corneal irregularities, scars, or iris damage.

Keywords

corneal inlay, enhanced depth of focus, pinhole, presbyopia, small aperture

INTRODUCTION

Humans have applied the concept of small-aperture optics for centuries, beginning with the early camera obscura and pinhole cameras, and continuing today with advanced surgical devices to improve vision in presbyopes with and without cataracts.

Channeling light through a small aperture – whether artificial, induced, or natural – blocks incident stray light and unfocused light from the periphery. This sharpens vision and extends the depth of field, or the distance from a visual target that remains in focus when looking at the target. A small aperture also minimizes the impact of corneal aberrations on vision. The relationship between higher order aberration (HOA) and pupil size is well known. With a smaller pupil, it is primarily paraxial light rays – which are less susceptible to optical imperfections – that reach the retina, while light rays from the more aberrated peripheral cornea are blocked. However, smaller pupils also transmit less total luminance to the retina, which might be expected to influence visual performance.

There are now corneal inlays, contact lenses, intraocular lenses (IOLs) and topical miotic drops that rely on the principles of small-aperture optics for presbyopia correction, either commercially available or in development. This article reviews each of these small-aperture platforms, including recently published outcomes. We will also address the latest information on the impact of small-aperture technologies on light perception and visual performance, as well as the relative merits of monocular versus binocular small apertures.

PART I: SMALL-APERTURE PLATFORMS

Posterior chamber intraocular lens

The IC-8 small-aperture IOL (AcuFocus, Irvine, California, USA) is a single-piece hydrophobic

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KEY POINTS

- Channeling light through a small aperture – whether artificial, induced, or natural – blocks incident stray light and unfocused peripheral light, extending the depth of field and minimizing the impact of corneal aberrations on vision.
- Six months after implantation with a small-aperture posterior chamber IOL in one eye, 99, 95, and 79% of patients achieved 20/32 or better binocular UDVA, UIVA, and UNVA, respectively.
- Safety and efficacy of a small-aperture corneal inlay for presbyopia correction has been well documented, including both objective and subjective, patient-reported outcomes.
- Newer formulations of topical drops aimed at presbyopia treatment use a combination of agents to achieve a small pupil while reducing unwanted side effects.
- Perceived brightness is greater than what would be expected from theoretical calculations based on aperture size, and this effect is likely due to neuroadaptation.

acrylic IOL intended for implantation in the capsular bag, with modified C haptics, and an overall diameter of 12.5 mm. The biconvex aspheric optic is 6.0 mm in diameter with a 360-degree square posterior edge. The embedded annular mask has an outer diameter of 3.23 mm and a central aperture measuring 1.36 mm in diameter (Fig. 1).

The IC-8 IOL is CE marked and is commercially available in select markets in Europe, Australia and New Zealand. The lens is currently in clinical trials in the United States. Results from a multicenter postmarket European trial were recently published [1▪▪]. Patients ($n = 105$) with bilateral cataract were implanted with the IC-8 IOL in one eye, with a refractive target of –0.75 D, and an aspheric, colorless, monofocal IOL in the fellow eye with a plano target. Six months after implantation, monocular uncorrected distance visual acuity (UDVA) was 0.87 logMAR (20/23), uncorrected intermediate acuity (UIVA) was 0.83 logMAR (20/24), and uncorrected near acuity (UNVA) was 0.66 logMAR (20/30).

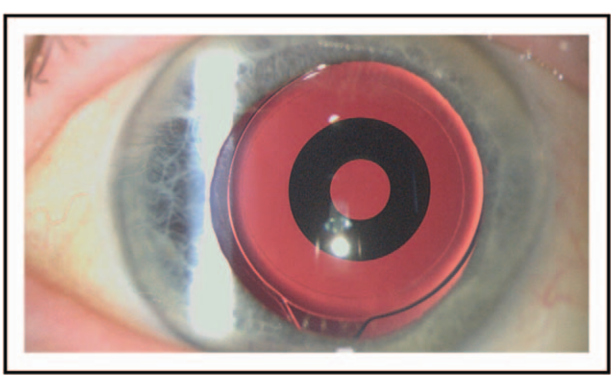

FIGURE 1. IC-8 intraocular lens 1 week after femtosecond laser-assisted cataract surgery using the Catalys Precision Laser System (Johnson & Johnson, Santa Ana, California, USA).

Binocularly, 99, 95, and 79% of patients achieved 20/32 or better UDVA, UIVA, and UNVA, respectively. The vast majority of patients (95.9%) reported they would have the procedure again, while four patients (4.1%) said they would not. Most (84.8%) reported using spectacles occasionally to never, 9 patients (8.6%) reported using them 50% of the time, and 7 patients (6.7%) reported using them often to most of the time [1▪▪].

The eyes with the monofocal IOLs had significantly better monocular contrast sensitivity than the eyes with the small-aperture IOLs at 1.5, 3.0, 6.0, and 12.0 cpd ($P < 0.003$). Eyes with the monofocal IOL had significantly better monocular mesopic contrast sensitivity with glare than eyes with the small-aperture IOL eyes at 1.5, 3.0, and 6.0 cpd ($P < 0.0001$). However, binocular contrast sensitivity matched the monocular contrast sensitivity achieved in the monofocal IOL eye [1▪▪].

Patients in this study and others have demonstrated very good tolerance to residual refractive error, making a small-aperture IOL more forgiving and diminishing the need for intraoperative orientation or aberrometry systems. In the European multicenter trial, mean UIVA and UNVA remained at 20/25 and 20/32, respectively, for up to 1.5 D of residual astigmatism in eyes with the small-aperture IOL. In fact, there were no clinical or statistical differences between eyes with at least 0.75 D of cylinder and those with 0.76–1.50 D [1▪▪].

Ang also reported that astigmatic patients in a single-site prospective clinical trial who were implanted with an IC-8 IOL without any additional astigmatic management were able to tolerate up to 1.50 D (and in some cases, even 2.00 or 2.50 D) of refractive astigmatism [2▪]. Mean UDVA in this study was 0.08 ± 0.08 logMAR (20/24) at 1.50 D of cylinder defocus, 0.18 logMAR $\pm$ 0.08 (20/30) at 2.00 D of defocus, and 0.24 logMAR $\pm$ 0.07 (20/35) at 2.50 D of defocus. Eight of 10 patients achieved 20/25 or better vision with 1.50 D of cylinder defocus, and all patients were 20/30 or better. The author notes that this small-aperture IOL may be able to bridge the gap between monofocal and monofocal toric IOLs for correction of low levels of astigmatism [2▪].

The IC-8 IOL has also provided good visual outcomes in post-LASIK [3] and post-RK [4] eyes. These patients are typically highly motivated to maintain

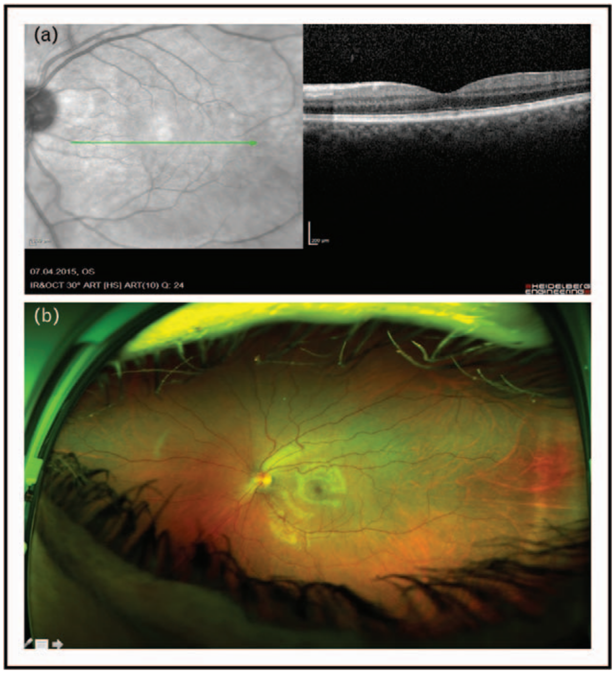

FIGURE 2. (a) Macular SD OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) after implantation of an IC-8 IOL. (b) Widefield retinal imaging showing 200° fundus photography using Daytona (Optos Inc. Marlborough, Massachusetts, USA) in an eye after implantation of an IC-8 IOL.

spectacle independence after cataract surgery, but many physicians consider them unsuitable candidates for implantation of other presbyopia-correcting IOLs. The greater degree of forgiveness of a small-aperture IOL could be beneficial in postrefractive eyes in which a greater deviation from target refraction can be expected, due to the unpredictability of IOL power calculations in such eyes.

Small-aperture IOLs also offer an opportunity to improve vision in eyes with scars, iris damage, or corneal irregularities that could be masked by the opaque annulus. Most diagnostic examinations can be performed after IC-8 lens implantation (Fig. 2a and b).

Add on, sulcus-implanted IOL

The XtraFocus device (Morcher, Stuttgart, Germany) is a foldable hydrophobic acrylic aperture, designed to be implanted in the ciliary sulcus of pseudophakic patients in an add on configuration. It has a black, opaque 6.0 mm diaphragm with a 1.3-mm central opening and 14.0 mm overall diameter (Fig. 3). The occlusive part of the device has a concave–convex design to prevent contact with the primary IOL, which can be any monofocal IOL, including a toric lens (Fig. 4). The black acrylic material of the XtraFocus device has the unique feature of being transparent to infrared light. The XtraFocus pinhole implant has been CE marked in Europe since 2016.

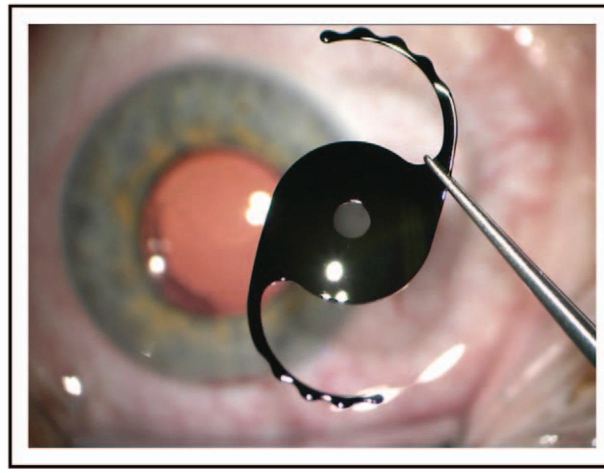

FIGURE 3. Overview of the XtraFocus pinhole device (Morcher, Stuttgart, Germany) before intraocular implantation into the ciliary sulcus (view through the OR microscope).

Several recent case reports have found the device to be effective in improving near visual acuity and managing irregular astigmatism in complex eyes [5▪,6▪,7]. However, routine use for the correction of presbyopia in normal eyes has not been studied.

Small-aperture add on designs similar to that of the Morcher lens have been tested in cadaver eyes to evaluate centration, tilt, and safety of supplementary sulcus-fixated lenses [8].

Corneal inlay

The IC-8 IOL design was based on that of the Kamra intracorneal inlay (CorneaGen, Seattle, Washington, USA) that preceded the IOL and is commercially available in the U.S., Europe, and around the world. The small-aperture corneal inlay is suitable for

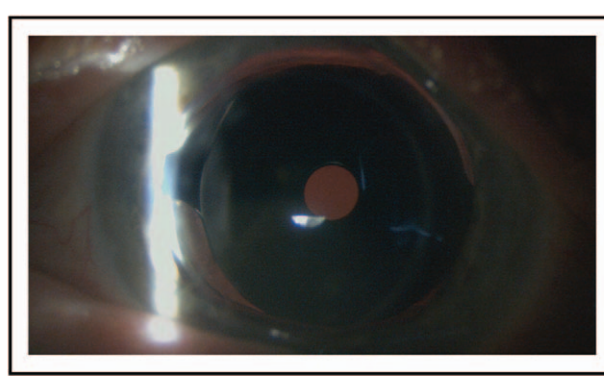

FIGURE 4. XtraFocus pinhole device implanted in front of a monofocal IOL (slit lamp photograph).

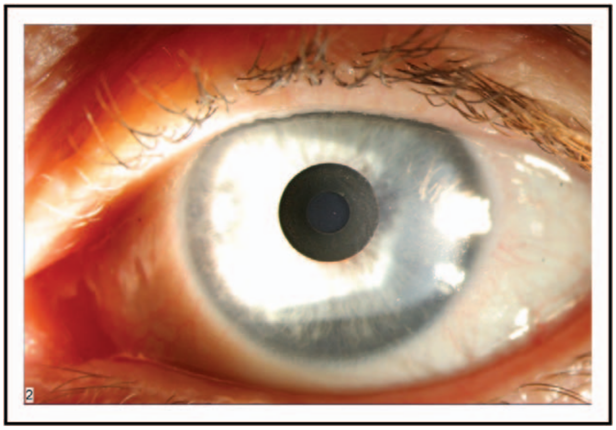

FIGURE 5. Well centered KAMRA corneal inlay implanted in a 5.0 mm corneal pocket created by the iFS femtosecond laser (Johnson & Johnson).

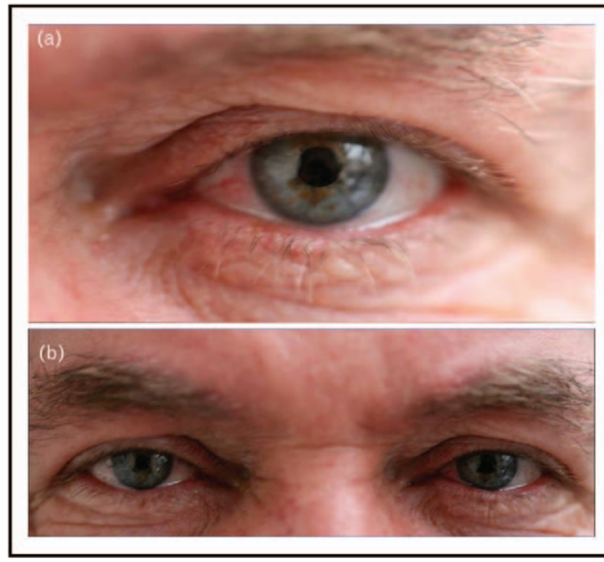

FIGURE 6. (a) KAMRA corneal inlay after implantation into the left eye. (b) Both eyes of the same patient (overview photo demonstrating the cosmetic effect): right eye without KAMRA inlay, left eye with intracorneal KAMRA inlay.

presbyopes with healthy crystalline lenses. They are removable and less invasive than intraocular options.

The Kamra inlay is a thin (6.0 μm), microperforated, opaque inlay with a 1.6-mm central aperture and a total diameter of 3.8 mm that is implanted in a femtosecond laser-created deep stromal pocket (Fig. 5). Safety and efficacy, including both objective and patient-reported outcomes, have been well documented in the published literature.

Three-year data from the U.S. clinical trials has recently been published [9■■]. In this study, mean monocular UNVA at three years was J2, mean UIVA was 20/25, and mean UDVA was 20/20. Binocular UDVA was 20/16. The mean range of depth of focus at 0.2 logMAR (20/32) or better improved from approximately 1.7 D preoperatively to approximately 3.0 D at 12 months and to more than 3.5 D at 0.3 logMAR (20/40) [9■■]. Late hyperopic refractive shifts and topographic changes have been reported with the inlay. However, these seem to be linked to shallower implantation [10,11■]. In a large, 4-year study in nearly 3000 patients, less than 1% of inlays were removed due to haze or refractive shift [12■■].

In addition to deep implantation, achieving optimal results also requires attention to ocular surface health and a slightly myopic target in the inlay eye. This is most often achieved through a dual procedure, in which the patient undergoes both inlay surgery and laser vision correction, either simultaneously, as described recently by Moshirfar *et al.* [13■], or as planned sequential procedures. It has been reported that binocular mean UNVA improved from 20/32 to 20/20 at 12 months and remained stable through 48 months in a large study of patients treated with the sequential approach [12■■].

Small-aperture inlays may also be combined with a monofocal IOL in pseudophakic patients to increase intermediate and near visual acuity and improve spectacle independence (Fig. 6a and b). Patients implanted with an inlay in the nondominant eye in combination with monofocal IOLs achieved UNVA that was, on average, two lines better than bilateral cataract patients without inlays [14■].

Contact lenses

Small-aperture contact lenses were proposed as early as the 1950s and some models, such as the EyeLike Noan Pinhole contact lenses (Koryo EyeTech, Seoul, Korea) have been tested and sold internationally. Earlier studies reported relatively poor resolution at near and a greater loss of distance vision compared to other small aperture modalities. Given that a contact lens is designed to move freely on the tear film, it is not an ideal platform for small aperture optics, as movement of the contact lens on the eye may not keep the aperture centered.

Pupil-constricting drops

Finally, several companies are currently exploring various agents for pharmacological pupil constriction. Frequent use of miotic agents has been associated in the past with unwanted side effects, such as headache, nausea, and ciliary spasm, and serious adverse events, including chronic inflammation, pigment dispersion, posterior synechiae, and induction of retinal detachment [15].

Newer formulations aimed at presbyopia treatment use a combination of agents to achieve a small pupil while reducing the side effects. Among these are LiquidVision PRX-100 (Presbyopia Therapies, Coronado, California, USA), a combination of aceclidine and tropicamide; PresbiDrops/CSF-1 (Orasis Pharmaceuticals, Herzliya, Israel), with unknown components; and FOV Tears, a combination of pilocarpine 0.247%, phenylephrine 0.78%, polyetheleneglycol 0.09%, nepafenac 0.023%, pheniramine 0.034% and naphazoline 0.003%.

There are few published articles on pharmacological pupil constriction for presbyopia. Most of what is known is from anecdotal reports or early pilot studies several years ago that do not appear to have been repeated or extended. Two recent reviews of topical approaches provide more detail about these reports and about the pharmacology involved [15,16].

The noninvasiveness of a topical approach would be a significant advantage. However, a topical drop requires daily use and would be entirely reliant on patient motivation and compliance with the drop regimen. To be successful, a pupil-constricting drop must be comfortable and well tolerated, as well as free from serious adverse events when used chronically. Rapid onset of action and/or long duration of effect would also be desirable characteristics.

PART II: SMALL APERTURE OPTICS TOPICS OF INTEREST

Effects of reduced light transmission

It has been proposed that reducing the amount of light reaching the retina through a small aperture could reduce retinal image quality or cause an unwanted reduction in contrast sensitivity.

Trindade *et al.* for example, theorized that patients implanted with the Morcher add on small-aperture device would struggle in low-light conditions. However, only one of the 21 patients in their prospective case series complained of reduced acuity under low-light conditions [7]. The authors surmised that the Stiles-Crawford effect, in which pupil luminance is not proportional to the pupillary area because of differing degrees of brightness from central and peripheral rays, was responsible for the unexpected tolerance.

Using an adaptive optics simulator, Artal and Manzanera evaluated perceived brightness when small apertures (3.0 mm and 1.6 mm in diameter) were presented monocularly to the participant [17▪▪]. They found perceived brightness to be 1.24 to 1.51 times greater than what one would expect from theoretical calculations based on the aperture size. About 1/3 to 1/5 of the greater-than-expected perceived brightness effect could be explained by the Stiles-Crawford effect, but most of the effect was unexplained. Additionally, the authors theorized, neuroadaptation and binocular effects could further increase perceived brightness in real visual settings [17▪▪].

In a later publication, these authors evaluated perceived brightness in the two eyes of patients implanted monocularly with Kamra small aperture inlays [18▪▪]. Patients implanted with the inlay exhibited an enhanced brightness perception compared to their untreated fellow eye – again, larger than what could be expected due the Stiles-Crawford effect. Neural adaptation could be responsible.

A related issue is whether the discrepancy in light transmission between pupils of two different sizes matters when a small aperture is implanted or induced monocularly. The Pulfrich effect is an optical phenomenon characterized by a distorted perception of object motion induced by an interocular marked difference in retinal luminance. When this optical phenomenon is present, the path of a pendulum appears as an elliptical rather than a lateral movement. Reports suggest that any Pulfrich effect with a small aperture inlay is very small; patients seem to neuro-adapt to reduced illuminance in the treated eye. This would be expected to be the case with a small-aperture IOL, as well, although it has not been studied.

Ultimately, of course, researchers and clinicians want to know whether small-aperture optics affect contrast sensitivity, contrast acuity, or visual performance. Numerous studies have now shown some reduction in monocular contrast sensitivity under some lighting conditions or at some spatial frequencies, but minimal change to binocular contrast sensitivity. Elling *et al.* for example, reported discrete reduced contrast sensitivity under binocular mesopic conditions with glare in eyes with a small-aperture inlay, compared to the control group, but the difference was not statistically significant [14▪]. Small aperture inlays have previously been shown to provide better contrast sensitivity than multifocal IOLs. And, in the European multicenter trial of the IC-8 IOL, contrast acuity was equivalent between the IC-8 and monofocal IOL eyes [1▪▪].

Monocular versus binocular

Contemporary applications of small-aperture optics principles have most often taken a monocular approach, with a device implanted in one eye to improve binocular near vision while maintaining binocular distance vision. However, given that small-aperture technologies have a minimal effect on monocular distance, does it make sense to use them bilaterally for ideal summation and clear focus at all distances?

Stereoacuity is a concern with any monocular solution. One author, testing young patients in dim light, found a deterioration in stereopsis at near and intermediate distances, as well as a loss of binocular summation at some distances in patients wearing a small-aperture contact lens, especially when combined with monovision [19]. These findings may or may not apply to real-world conditions in presbyopes with an implanted monocular small-aperture in better lighting conditions.

We know that monocular small-aperture surgery with a myopic target produces results that are quite different from monovision. Even small amounts of monovision (0.75 D) with a contact lens can reduce stereopsis, with the effect increasing with a greater degree of difference between the eyes. But, in a prospective study in 60 patients, there was no significant change in stereoacuity six months after monocular Kamra inlay implantation [20].

My colleagues and I compared six cases in which patients undergoing cataract surgery were implanted bilaterally with the IC-8 IOL to 11 cases in which patients received the IC-8 in one eye and an aspheric monofocal in the fellow eye: Bilateral implantation of the IC-8 IOL resulted in an extended range of focus, with better intermediate and near vision than monocular implantation. However, satisfaction was higher in the monocular group [21■■]. Larger studies are needed to confirm which approach is superior.

CONCLUSION

Small-aperture optics are a dynamic, physiologic solution to the problem of presbyopia. They are effective throughout the range of accommodation loss and in pseudophakia. The small-aperture corneal inlay has proven to be a safe and effective solution for presbyopes with healthy lenses. The new category of small-aperture IOLs is likely to continue to expand as we learn more about how these IOLs can not only extend the depth of focus and reduce HOAs from peripheral light rays, but (in the case of the IC-8) also correct refractive error and provide tolerance to residual error. Additionally, small-aperture lenses provide new opportunities for the therapeutic treatment of eyes with irregular astigmatism or other abnormalities.

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Conflicts of interest

The author is Consultant to AcuFocus.

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