

Synchrony dual-optic accommodating intraocular lens

Part 2: Pilot clinical evaluation

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PURPOSE: To evaluate the clinical outcomes of an accommodating dual-optic intraocular lens (IOL).

SETTING: Private practice and university centers.

METHODS: A prospective noncomparative case series with retrospective control comprised 21 patients (26 eyes) scheduled for small-incision extracapsular cataract extraction by phacoemulsification with implantation of the Synchrony dual-optic accommodating IOL (Visiogen) (accommodating IOL group) and 10 patients who had small-incision extracapsular phacoemulsification with implantation of a monofocal, single-optic IOL at least 6 months previously (control group). Patients were examined 1, 3, 6, and 12 months after surgery. Defocus curves in the accommodating IOL group were compared with those in the control group. The main outcome measures were postoperative distance uncorrected and best corrected visual acuity; near uncorrected, distance corrected, and near corrected visual acuity; and accommodative range based on defocus curves.

RESULTS: Twenty-four eyes were available at the 6-month follow-up visit. All eyes had best corrected distance visual acuity of 20/40 or better, and 19 eyes (79%) had an uncorrected distance visual acuity of 20/40 or better. Uncorrected near visual acuity was 20/40 or better in all eyes. With distance correction, 23 eyes (96%) had an acuity of 20/40 or better at near. Defocus curve analysis suggested a mean accommodative range of 3.22 diopters (D) \pm 0.88 (SD) (range 1.00 to 5.00 D) in the accommodating IOL group and 1.65 \pm 0.58 D in the control group (range 1.00 to 2.50 D) ($P < .05$).

CONCLUSION: The Synchrony dual-optic IOL shows promise as an option to provide accommodative function in pseudophakic patients.

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The efficiency of a single-optic accommodating intraocular lens (IOL) based on optic shift principles is dependent on the optical power of the displaced lens. To circumvent this constraint, a single-piece, dual-optic, foldable silicone IOL (Synchrony, Visiogen) was designed with an exaggerated high-plus-power moving optic coupled to a low-power static minus lens joined by spring haptic.⁷ When implanted in the capsular bag, bag tension compresses the optics, reducing their separation. The compression of the lens system stores strain energy in the connecting haptics. Once accommodative effort ensues, the zonules relax, releasing tension on the capsular bag and thus allowing release of the stored energy in the spring system with anterior displacement of the anterior optic.

Initial prototypes of this design were constructed, and studies of biocompatibility in a rabbit model have been

reported.⁸ After these investigations, a pilot study to study the safety and function in human subjects was initiated. We report the results of this pilot clinical trial.

PATIENTS AND METHODS

All tenets of the Helsinki Declaration for the Protection of Human Subjects in Medical Research were strictly observed (World Medical Association. Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects. 41st World Medical Assembly, Hong Kong, 1989 [online]. Available at <http://www.fda.gov/oc/health/helsinki89.html>. Accessed August 29, 2006), and independent Institutional Review Board approval was secured. Prospective patients were offered the opportunity to participate in a clinical trial to have cataract surgery with implantation of an experimental single-piece, dual-optic accommodating IOL. All patients participating in the study were fully informed of their involvement in

a research study. To acknowledge this, patients were required to sign a written informed consent. The original signed document was kept in the patient's file, and a copy was provided to the patient.

The prospective study was conducted from October 2003 through February 2005. Patients considered for inclusion were 40 years or older with visual loss and cataract that required removal, had the ability to fully comprehend the informed consent, and were considered likely to adhere to the postoperative examination schedule and demands. Exclusion criteria included visual impairment in the fellow eye, corneal astigmatism greater than 2.00 diopters (D), significant anterior segment pathology including glaucoma or potentially occludable angles, capsule exfoliation, ocular inflammation or poor pupil dilation, and systemic disease such as autoimmune disease and diabetes.

Before surgery, all patients had a complete ophthalmic examination that included measurement of best corrected distance and near acuities in each eye, distance corrected near visual acuity, and the minimum amount of addition (add) required to achieve best corrected near visual acuity. Biometric measurements included corneal curvature, anterior chamber depth (ACD), lens thickness, and axial length. Lens thickness was measured by immersion A-scan. Axial length and ACD were measured with the IOLMaster (Carl Zeiss Meditec) if the signal-to-noise ratio was higher than 2.5. When the signal-to-noise ratio was below 2.5, immersion A-scan was used to measure axial length and ACD. These measurements were entered into a theoretical model eye that was modified to describe the appropriate power distribution of the plus and minus components of the dual-optic IOL for each individual patient.

All surgeries were performed by the same surgeon (I.L.O.) using standard phacoemulsification via a clear corneal or scleral incision. A capsulorhexis ranging in diameter from 4.5 to 5.5 mm was created, and the nucleus and cortical material were removed using an endocapsular technique followed by careful polishing of the inner surface of the anterior lens capsule. Intraoperative requirements for implantation of the dual-optic accommodating IOL were an intact and centered continuous curvilinear capsulorhexis smaller than the anterior optic of the IOL (5.5 mm), an intact posterior capsule, and no evidence of zonular rupture. If these criteria were met, the dual-optic IOL was implanted in the capsular bag. The wound was enlarged to 4.5 mm and, in a single-step procedure, the 2 optics were placed through the

capsulorhexis into the capsular bag with a folding forceps. The ophthalmic viscosurgical device was thoroughly aspirated, with careful attention to the space behind the posterior optic and the gap between the 2 optics. The wound was then secured with a single 10-0 nylon suture (Figure 1, A to D).

After surgery, all patients were treated with atropine 1%, 1 drop at the end of the procedure and 1 drop on the first postoperative day; topical prednisolone acetate 1% for 6 weeks; and ofloxacin 0.3% for 1 week.

In accordance with the study protocol, examinations were performed at fixed intervals that included 1 day, 1 week, and 1, 3, 6, and 12 months after surgery. Postoperative examinations included slitlamp evaluation, applanation tonometry, visual acuity measurements, keratometry, retinoscopy, subjective refraction, and elevation corneal topography (Orbscan II, Bausch & Lomb). Particular attention was paid to the assessment of corneal clarity, anterior segment inflammation, prelenticular or interlenticular opacification, angle occlusion, IOL centration and orientation, iris anatomy, and posterior segment status.

Uncorrected and best corrected distance visual acuities were measured on a logMAR Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 4 m with luminance standardized to 85 cd/m² using the Vector Vision CVS 1000 light box. Near visual acuity testing was performed at 16 inches using a standard Rosenbaum chart (Precision Vision). Distance corrected near vision was tested through the phoropter, and a determination of the minimum amount of add needed to reach 20/20 (J1⁺) on the near chart was made. Visual acuities were recorded in logMAR units for ease of statistical analysis.

Defocus curves were generated to characterize near function. The untested eye was occluded, and the best distance correction was placed in the phoropter or trial lens set. Plus lenses were added in 0.50 D steps, and the visual acuity was recorded at each step. Defocus was continued until the baseline best corrected visual acuity (BCVA) had fallen by at least 3 lines. Returning to the best distance correction, the procedure was repeated with the addition of minus lenses in 0.50 D steps. Defocus was continued until acuity had fallen by at least 3 lines. Accommodative range was defined by the range of lens powers beyond which distance visual acuity was reduced by 2 lines on the ETDRS chart.

A cohort of 10 patients who had uneventful cataract extraction at the University of California San Francisco (UCSF) at least 6 months earlier served as a retrospective control. Institutional Review Board approval was obtained from the UCSF Committee for Human Research, and informed consent was obtained from all control group participants. Patients who had cataract surgery with implantation of a single-optic standard acrylic IOL (AcrySof MA60AC, Alcon Corp.) or silicone IOL (SI40NB, Allergan Inc) and a BCVA of 20/20 or better were included. In the control group, defocus curves were generated using the protocol described above and compared with curves generated by patients who received the dual-optic IOL.

Statistical analysis was performed with Stata 7.0 for Windows (Stata Corp.)

RESULTS

In this feasibility study, 26 eyes of 21 patients were enrolled at the single participating site for implantation of the dual-optic accommodating IOL. All patients were Hispanic, and 14 (67%) were women. The mean age in this group was 64 years (range 40 to 79 years). Cataract surgery and

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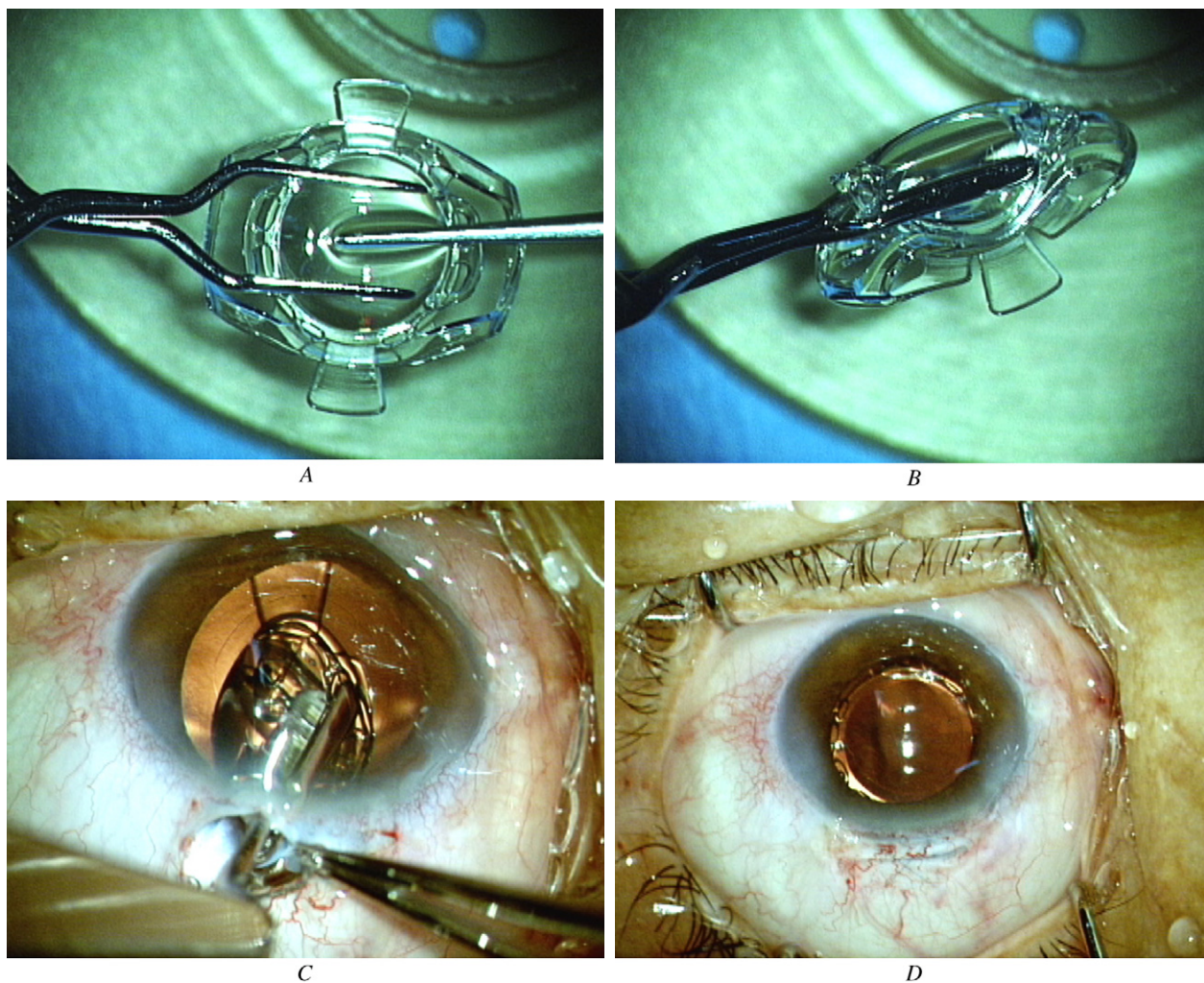


Figure 1. A and B: The 2 optics of the Synchrony dual-optic accommodating IOL are compressed together using a forceps, stabilizing the IOL, which can then be folded using a standard folding forceps. C: The folded complex can then be inserted through a 4.5 mm scleral wound and guided through a 4.5 to 5.5 mm diameter capsulorhexis. D: The dual-optic accommodating IOL is seen in the capsular bag. Note the overlap of the capsulorhexis edge over the anterior optic.

implantation of the dual-optic IOL was uneventful in all 26 eyes (Figure 2). However, 1 patient died of pneumonia after the first month of follow-up. Another patient had a large-diameter capsulorhexis and IOL decentration. The dual-optic IOL was subsequently exchanged for a single-piece monofocal hydrophobic acrylic IOL. This procedure was uneventful. The 2 eyes of these 2 patients were excluded from analysis.

Follow-up data were available for all 24 eyes through the first 6 months of follow-up. Eleven of the 24 eyes (46%) completed 1 year of follow-up.

The mean preoperative astigmatism was 0.67 ± 0.48 D (SD) (range 0.25 to 2.00 D). At the 1-month examination, the mean residual astigmatism was 1.07 ± 0.62 D (range 0 to 2.25 D); it decreased to 0.36 ± 0.35 D (range 0 to

1.00 D) at the 12-month examination ($P = .017$, 2-sided paired Student *t* test). Visual acuity measurements at baseline and the follow-up examinations are shown in Table 1.

Postoperatively, no patient lost lines of BCVA. At the 6-month follow-up examination, the mean postoperative spherical equivalent was -0.52 ± 0.77 D. Twelve of the 24 eyes (50%) were within ± 0.50 D of plano, and 17 (70.8%) were within ± 1.00 D. Nineteen eyes (79.2%) had an uncorrected distance acuity of 20/40 or better and 5 eyes, of 20/50, 20/60, and 20/80 as a result of residual wound-related astigmatism and myopia related to IOL calculation. The best spectacle-corrected distance acuity was 20/40 or better in all study eyes at all follow-up examinations. A substantial improvement in uncorrected near acuity was observed at every follow-up visit; at the 6-month

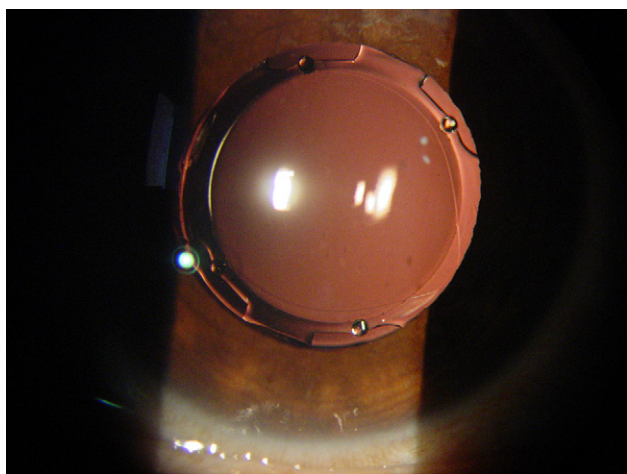


Figure 2. High-power slitlamp photograph of the dual-optic accommodating IOL seen through a dilated pupil 11 months after implantation. Note the absence of interlenticular, anterior, or posterior capsule opacification.

visit, all eyes achieved 20/40 (J3) or better and 17 eyes (70.8%) had an acuity of 20/25 (J1) or better ($P < .001$, Fisher exact test). At 6 months, 23 eyes (95.8%) had distance corrected near visual acuity of 20/40 (J3) or better. All 11 eyes achieved distance corrected near visual acuity of 20/40 or better at the 12-month visit, with 7 eyes (63.6%) having an acuity of 20/25 (J1) or better.

The mean distance corrected near visual acuity was stable throughout the duration of the study (Table 1). It was 0.17 ± 0.15 at 1 month, 0.14 ± 0.15 at 3 months, 0.14 ± 0.16 at 6 months, and 0.14 ± 0.09 at 12 months ($P = .946$, Kruskal-Wallis test). The mean minimum add required to

reach J1⁺ (20/20) at the 6-month study visit was 0.73 ± 0.66 D (range 0 to 1.75 D). This value remained stable at the 1-year follow-up visit (0.70 ± 0.51 D; range 0 to 1.50 D). At the 6-month follow-up, 17 eyes (70.8%) required 1.00 D or less of add to reach J1⁺.

Defocus curves generated for the dual-optic IOLs ($n = 24$) at 6 months and for monofocal single-optic IOLs ($n = 10$) are shown in Figure 3. The curves show that eyes with the dual-optic IOL had a reduced rate of visual acuity loss (mean accommodative range 3.22 ± 0.88 D; range 1.00 to 5.00 D) with defocus than eyes with a standard monofocal IOL (mean accommodative range 1.65 ± 0.58 D; range 1.00 to 2.50 D) ($P < .05$).

Slitlamp examination showed mild to moderate anterior capsule opacification (ACO) in 4 eyes (16.6%) at 6 months. All 24 eyes had 360-degree overlap of the capsulorhexis over the anterior optic of the IOL. There were no cases of capsule contraction, severe ACO, or phimosis of the capsulorhexis (Figure 2). Visually significant posterior capsule opacification was evident in 1 eye (4.2%) at the 6-month visit. A neodymium:YAG posterior capsulotomy had not been performed in this eye at the time of this report. No additional complications or adverse events were observed during the 12-month follow-up.

DISCUSSION

In this pilot study, we sought to investigate the feasibility of correcting aphakia with a dual-optic IOL and initiate a study of the accommodative function of this lens. The results suggest that a dual-optic IOL can be successfully and safely implanted using contemporary small-incision phacoemulsification techniques, the lens appears to be

Table 1. Visual acuity data.

Parameter	Preop (n = 24)	Number (%)		
		3 months (n = 24)	6 months (n = 24)	12 months (n = 11)
Uncorrected distance visual acuity 20/40 or better	—	15 (63)	19 (79)	9 (82)
Best spectacle corrected distance visual acuity 20/40 or better	—	24 (100)	24 (100)	11 (100)
Uncorrected near acuity				
J1 or better	3 (13)	16 (67)	17 (71)	7 (64)
J3 or better	7 (29)	23 (96)	24 (100)	10 (100)
Best corrected near acuity				
J1 or better	5 (21)	24 (100)	24 (100)	11 (100)
J3 or better	8 (33)	—	—	—
Distance corrected near acuity				
J1 or better	—	11 (46)	12 (50)	7 (64)
J3 or better	—	23 (96)	23 (96)	11 (100)

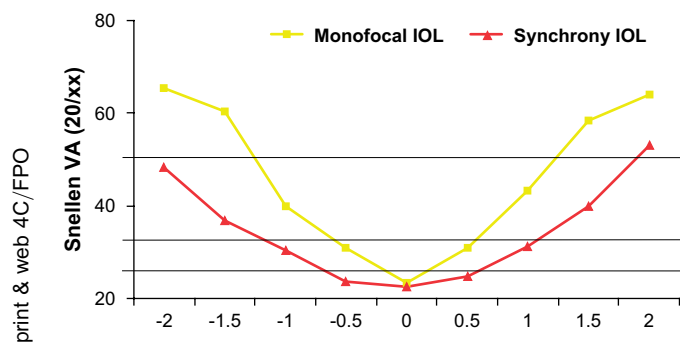


Figure 3. Defocus curves generated in 10 eyes with a monofocal IOL compared to 24 eyes with the dual-optic IOL. The x-axis indicates the power in diopters of the defocusing lens placed in front of the tested eye through which the visual acuity (y-axis) was measured. The accommodative amplitude was defined by the range of defocus lens power through which visual acuity was maintained to within 2 lines on the ETDRS chart.

reasonably well tolerated, and the dual-optic design appears to produce improved range of focus compared to a monofocal IOL.

Although subjective methods that typically measure visual acuity in the setting of a presumed accommodative stress might reasonably be expected to be indicative of an individual's near-vision function, none reliably distinguishes between pseudoaccommodation (eg, as a result of multifocality) and a true change in the conjugation power of the eye. It is possible that the dual-optic design introduces a multifocal effect or enhanced depth of focus that might account for these findings. Retinoscopic methods that include skiascopy, infrared optometry, and wavefront analysis can, in theory, provide an objective method of measuring accommodative change; however, all have proven far more challenging in the research setting than is immediately obvious.⁹ The measuring device or experimental setup frequently interferes with or requires alteration of typical accommodative cues, leading to significantly reduced measured accommodative amplitudes, even in cooperative subjects. Moreover, the convergence that accompanies accommodation can present alignment difficulties during measurement as the target is moved. Although this effect can be circumvented by pharmacologic stimulation of accommodation, recent evidence suggests this technique does not accurately represent physiologic accommodation.¹⁰

Nevertheless, best distance corrected near vision better than 0.3 logMAR (20/40 or J3) in 96% of patients is consistent with a degree of accommodative function, as is the comparison of defocus curves generated from eyes with the dual-optic IOL as opposed to those with the monofocal IOL, and suggests proof of principle for the function of a dual-optic accommodating IOL as well as rudimentary

indicators of clinical efficacy. It should be acknowledged that this preliminary study primarily directed toward feasibility and safety used a control group that was neither concurrent nor strictly matched by demographics or examiners. A nonstandardized Rosenbaum card was used, and this might also limit the direct comparison of the case and control cohorts. Moreover, the definition of accommodative range applied to the defocus curve interpretation (visual acuity maintained within 2 lines on the ETDRS chart) is necessarily arbitrary, but direct qualitative comparison of the defocus curves, as seen in Figure 3, indicates that better visual acuity is maintained through defocus with the dual-optic IOL than with the monofocal IOL.

Because the principle of action of this IOL design is based on axial displacement of the anterior plus-power optic, demonstrated changes in ACD and optic separation under subjective accommodative stimulus or pharmacologic stimulus might confirm the mechanism of action and the accommodative function suggested by subjective measures of near vision. These studies, which used ultrasound biomicroscopy of the anterior segment, will be reported separately; initial results show optic displacement consistent with the intended biomechanical function.

Although we recognize the current limitations of accommodation measurement techniques, we are encouraged by the initial results. The data we report appear to support the proposition that a dual-optic system can be designed that will produce an accommodative change in the conjugation power of the eye through anterior and posterior displacement of the anterior optic. This pilot study represents a small cohort of patients with limited follow-up. Larger long-term studies are required to reveal the long-term stability, evolution, and characteristics of the accommodative function suggested. Future studies will seek to incorporate objective measurement techniques under development as well as functional visual tests and quality-of-life assessment.

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