

Clinical evaluation of the Crystalens AT-45 accommodating intraocular lens

Results of the U.S. Food and Drug Administration clinical trial

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PURPOSE: To evaluate the 12-month U.S. phase II clinical trial results of the Crystalens AT-45 (eyeonics, Inc.) intraocular lens (IOL) used to provide uncorrected distance, intermediate, and near visual acuities in patients having cataract extraction and to compare in a substudy the contrast sensitivity and near visual acuity in patients with the Crystalens AT-45 IOL and those receiving a standard IOL.

SETTING: Fourteen clinical sites throughout the U.S. for efficacy and 3 non-U.S. sites for safety and efficacy.

METHODS: Patients 50 years or older had small-incision cataract extraction with implantation of the Crystalens AT-45 IOL. Unilateral implantation was followed by fellow-eye implantation. Postoperatively, uncorrected distance, near, and intermediate visual acuities were determined. Near and intermediate visual acuities were tested through a distance correction to eliminate potential pseudoaccommodative effects of residual myopia and corneal cylinder. A substudy tested contrast sensitivity under mesopic conditions with and without glare, as well as visual acuity in a subset of Crystalens AT-45 patients and a control group receiving a standard IOL.

RESULTS: A total of 263 patients participated in the U.S. clinical trial and had 1 year of follow-up. Near visual acuities through the distance correction of 20/40 (J3) or better, monocularly and bilaterally, respectively, were seen in 90.1% and 100%; intermediate near visual acuities were seen in 99.6% and 100%. More than half the bilaterally implanted Crystalens AT-45 patients achieved uncorrected near acuity of 20/25 (J1) or better through the distance correction, and 84% achieved 20/32 (J2) or better. In the substudy, monocular near vision through the distance correction of 20/25 (J1) or better was seen in 50.4% with the Crystalens AT-45 IOL and in 4.7% with the standard IOLs. Mesopic contrast sensitivity results with and without glare for the Crystalens AT-45 were similar to those with standard monofocal IOLs. Nearly all patients (74 patients; 97.3%) who bilaterally were within 0.50 diopter of plano postoperatively achieved 20/32 (J2) or better uncorrected near, intermediate, and distance visual acuities.

CONCLUSIONS: The Crystalens AT-45 accommodating IOL provided good uncorrected near, intermediate, and distance vision in pseudophakic patients. Contrast sensitivity with the Crystalens AT-45 was not diminished relative to standard monofocal IOLs, and near and intermediate visual performance was significantly better than with standard IOLs.

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The Crystalens AT-45 (eyeonics, Inc.) multipiece silicone posterior chamber accommodating intraocular lens (IOL) received U.S. Food and Drug Administration (FDA) approval in November 2003 to correct aphakia and in August 2004 to correct presbyopia following cataract extraction

and to provide near, intermediate, and distance vision without spectacles.¹ It is the first IOL approved by the FDA that provides accommodation postoperatively, so that many patients are able to see near and intermediate targets as well as the usual distance target. This spectacle-free near vision is

not common with single focal point IOLs in patients of an age group likely to have had significant decline in the ability to accommodate.

Loss of accommodation occurs as the human crystalline lens experiences profound optical and physical changes with increasing age.^{2,3} These lens changes include increased mass, thickness, and hardness; increased posterior and anterior surface curvature; and possible changes in the distribution of the refractive index.³ Ciliary muscle, on the other hand, appears to retain its function through 80 years of age.⁴

The Crystalens AT-45 is a biconvex lens with a 4.5 mm optic and flexible hinged-plate haptics that allow forward movement of the optic during accommodative effort to provide near and intermediate vision in pseudophakic patients. The lens design incorporates grooves, or hinges, across the plates adjacent to the lens optic that allow for forward and backward movement of plate-haptic lenses against the vitreous face. The proposed mechanism of the Crystalens AT-45 IOL is that with accommodative effort, there is a redistribution of the ciliary muscle mass that causes increased vitreous pressure and forward movement of the IOL.

The feasibility study of this IOL was published earlier.⁵ In this report, we present the 12-month follow-up results of the U.S. FDA phase III clinical trial of the Crystalens AT-45 IOL used to correct aphakia and designed to provide uncorrected distance, intermediate, and near vision after implantation into an intact capsular bag following cataract surgery. In addition, we present results of a contrast sensitivity sub-study, conducted to determine whether the small Crystalens AT-45 optic is associated with any decrease in contrast sensitivity or increase in glare symptoms when

compared with a standard monofocal IOL. Results of the substudy comparing patients' uncorrected near acuity with the Crystalens AT-45 with that of patients with a standard monofocal IOL are also presented.

PATIENTS AND METHODS

Study Design

Fourteen clinical investigators in the U.S. participated in this prospective multicenter clinical trial and enrolled 415 eyes of 263 consecutive qualified cases for evaluation of effectiveness and safety. Three non-U.S. investigators provided safety data only. Effectiveness of the lens was assessed by evaluating near, intermediate, and distance visual acuities. Safety of the lens was assessed by recording the incidence of adverse events and complications and included data from the unilateral (primary eyes) as well as from the fellow eye. A patient questionnaire was administered to determine patient satisfaction, subjective vision quality, and occurrence of visual disturbances. Study follow-up was planned to be for 3 years. The bilateral survey was slightly different in format from the unilateral survey. However, questions related to patient satisfaction and night driving (including halos and glare) were asked in an identical manner.

The contrast sensitivity substudy was conducted in the second phase in which bilateral implantations were performed. It was designed to compare unilateral contrast sensitivity, with and without glare, in eyes implanted with the Crystalens AT-45 to the contrast sensitivity of a matched population of eyes implanted with a standard IOL. Tests were done under extremely low-light conditions to simulate vision in the presence of poor illumination and a larger pupil in the presence and absence of glare. Testing was performed through the distance correction. Contrast sensitivity testing was to be performed 3 to 6 months postoperatively. However, if posterior capsule opacification (PCO) was detected at the 3-month to 6-month examination, testing was delayed until after a posterior capsulotomy had been performed. All contrast sensitivity results are monocular.

Patients

Prior to enrollment in the study, potential study participants were evaluated to determine eligibility, and the investigator explained the study purpose and procedures. Eligible patients were those who were required to have cataract extraction and IOL implantation surgery, were 50 years or older, had no ocular pathology, no more than 1.00 diopter (D) of corneal astigmatism, and had the potential for best corrected visual acuity (BCVA) of 20/32 or better in both eyes. Written informed consent was obtained, and a baseline preoperative examination that included measurement of uncorrected and best corrected distance and near visual acuities, intraocular pressure (IOP) by applanation tonometry, and slitlamp examination was performed. Enrolled patients who did not have cataract extraction by phacoemulsification, did not have an intact capsule with an intact capsulorhexis, or had zonular rupture were excluded from the study at the time of surgery. The standard monofocal IOL patients recruited to participate as controls in the contrast sensitivity substudy had to meet the same eligibility criteria as the Crystalens AT-45 patients and had to provide written informed consent.

For the substudy, the Crystalens AT-45 group was composed of the first 126 eyes that met the inclusion criteria. The standard

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Drs. Colvard, Dell, Doane, Fine, Hoffman, Packer, and Slade were investigators in the U.S. Food and Drug Administration (FDA)-approved clinical study sponsored by eyeonics, Inc. Dr. Slade was the medical monitor for this study.

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Dr. Cumming is an employee of and stockholder in Eyeonics; Dr. Colvard is a stockholder in Eyeonics; and Drs. Dell, and Doane are consultants to Eyeonics. No other author has a financial or proprietary interest in any product mentioned.

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IOL group was composed of 64 consecutive eyes of qualified patients who had cataract extraction by phacoemulsification, were implanted with a standard monofocal IOL, and were scheduled to reach the 3-month to 6-month postoperative period during the bilateral phase of the clinical trial. The inclusion criteria for patients implanted with a standard IOL were identical to those of patients participating in the Crystalens AT-45 study.

Examination Methods

Effectiveness of the IOL was assessed by measuring near acuity at 16 inches/40 cm with the distance corrected near visual acuity but no reading add, uncorrected near visual acuity at 16 inches, and best corrected near visual acuity at 16 inches through the distance correction with the minimal reading add to obtain the best corrected near acuity; intermediate visual acuity at 32 inches through the distance correction to obtain the best corrected intermediate visual acuity through the distance correction, for which a standard reading lamp with a 60-watt bulb was provided to each site by the sponsor and shone directly onto the card; intermediate visual acuity, uncorrected intermediate acuity at 32 inches bilaterally, uncorrected distance acuity, and best corrected distance visual acuity. Measurements of near and intermediate vision were made through the distance correction to eliminate potential pseudoaccommodative effects of residual myopia and corneal cylinder.

Safety of the lens was assessed through the incidence of adverse events and complications and included data from primary eyes and all eyes (primary and fellow eyes) from the 14 U.S. investigators as well as the data from the 3 non-U.S. investigators. Safety was determined by the incidence of cumulative and persistent adverse events as compared to the FDA Grid of Historical Controls. Cumulative adverse events consist of the total number of adverse events reported at any time during the 12 months of postoperative follow-up, including the 1-year visit. Each report of a single adverse event was included in the cumulative total. Persistent adverse events are those events present at the 1-year postoperative visit only. A questionnaire (U.S. patients) was mailed to patients to determine patient satisfaction, subjective vision quality, and occurrence of visual disturbances. Patients completed these surveys in their homes, reducing the effects of surgeon presence.

Axial length measurements were performed using the Axis-II biometer with immersion (Quantel Medical) or partial coherence interferometry with the IOLMaster Interferometer (Zeiss-Humphrey), along with manual K-readings. Applanation biometry was used in some eyes in the phase II portion of the study. Short axial length was defined as ≤ 22.79 mm, median axial length as > 22.79 mm to < 24.36 mm, and long axial lengths as > 24.36 mm.

Add power was measured monocularly at 16 inches. The add was determined by adding plus lenses over the patient's distance correction in $+0.25$ D increments, with visual acuity evaluated at each increment. This process was continued until $+0.50$ D of additional plus did not improve the patient's near visual acuity. The add recorded was the additional plus power added to the distance correction up to the point where the patient's near visual acuity ceased to improve.

Distance visual acuity and contrast sensitivity were measured with the StereoOptical Optech X1600 vision tester, a stand-alone unit that contains ETDRS targets and allows control of luminance. Distance visual acuity testing was performed at a standardized luminance level of 85 cd/m^2 (ie, photopic lighting). Contrast sensitivity was tested at a standardized luminance level of 3 cd/m^2 (mesopic lighting conditions).

Intermediate and near visual acuities were evaluated with the MN Read acuity chart (Lighthouse Company), which is a text reading card using sentences of 13 words and 47 letters in length. Luminance and testing distance at each clinical site was standardized. The reading card was consistently held at 32 inches for measurement of intermediate vision or 16 inches for measurement of near vision. Recently, there has been much discussion regarding measurement of speed reading. This was not done because no such standard existed in 2000.

The contrast sensitivity test consisted of Functional Acuity Contrast Test sine wave-grating patches arranged in 5 series, labeled A through E. Each of the 5 series contained 8 sine wave-grating patches numbered 1 through 8. The spatial frequency of the sine wave gratings progressively increased by a factor of 2 as the patient progressed from series A to series D. The change in spatial frequency between series D and series E increased by a factor of 1.5. Spatial frequency was measured in cycles per degree (cpd) and progressed in the following manner: series A, 1.5 cpd; series B, 3 cpd; series C, 6 cpd; series D, 12 cpd; series E, 18 cpd. Eighteen cycles per degree approximates the visual angle subtended by the 20/20 Snellen line. Patients in both the Crystalens AT-45 and standard IOL control groups were tested in an identical manner.

Contrast sensitivity testing measures the spatial and contrast discrimination of the visual system when measured through the distance correction. Typically, this testing measures the minimum contrast threshold at which a target of a certain spatial frequency (cpd) can be resolved by an observer. Contrast sensitivity is then represented as the reciprocal of the minimum resolvable contrast, and this value is typically transformed to a logarithmic scale. For example, if the minimum target contrast resolved (also known as the contrast threshold) is 1%, the contrast sensitivity is $1/0.01$ or 100, which is equivalent to 2 log units. Resolving a 0.1% contrast target equates to a contrast sensitivity of 3 log units. Alternatively, a decrease in contrast sensitivity of 0.1 log units means that to resolve a target at the baseline contrast, its spatial frequency must be decreased by approximately 0.1 log units, that is, the target size must be increased approximately 1 Snellen line.

To determine the effect of glare on contrast sensitivity, a 3 lux glare source was added to the 3 cd/m^2 luminance testing level. To eliminate any effect of refractive error on the measurement of contrast sensitivity, testing was performed with the patient wearing the appropriate distance correction. Patients were dark adapted for 10 minutes before having mesopic contrast sensitivity testing. Pupil size was measured with either a Colvard or a Proceon pupillometer, with luminance set at the same mesopic level (3 cd/m^2).

The conversion table provided for the Optech Model X1600 was used to convert contrast sensitivity patch scores to contrast sensitivity values. These contrast sensitivity values were converted to logarithms. The maximum target contrasts supplied were 14.29%, 10.0%, 8.33%, 12.5%, and 25% for the 1.5, 3, 6, 12, and 18 cpd targets.

Study Device

The Crystalens AT-45 is a modified plate-haptic high-refractive index silicone IOL containing an ultraviolet filter and is designed for implantation in the capsular bag (Figure 1). The lens is hinged adjacent to the optic and has small T-shaped polyimide loops on the ends of the plate haptics. At the 2 tips of each of the polyimide loops are 2 small disks, round on the right and oval on the left. When the round disk is on the right, the lens is oriented with the hinge on its anterior surface. The overall length (loop-tip to loop tip) is 11.5 mm, while the overall length, measured from

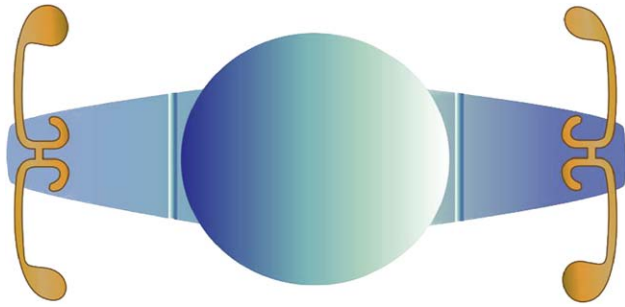


Figure 1. The Crystalens AT-45 accommodating IOL. A posterior chamber modified plate-haptic IOL containing a high-refractive-index silicone material with an ultraviolet filter. The lens is hinged adjacent to the optic and has small T-shaped polyimide loops on the ends of the plate haptics. The overall length (loop tip to loop tip) is 11.5 mm, while the overall length, as measured from the ends of the plate haptics, is 10.5 mm. The optic diameter is 4.5 mm and the recommended A-constant in the FDA study was 119.0. Correct anterior–posterior placement of the Crystalens AT-45 can be confirmed by the asymmetric haptic tip construction.

the ends of the plate haptics, is 10.5 mm. The optic diameter is 4.5 mm.

Surgical Technique

The FDA required use of only 1 formula, and the Sanders, Retzlaffi, Kraff/Theoretical (SRK/T) was chosen. An A-constant of 119.0 was used in the clinical trial to determine the IOL power in all study eyes. The refractive target for the first eye implanted (primary eye) was -0.5 D to avoid the possibility of a postoperative hyperopic refraction. Lens power in fellow eyes was based on the same formula, but consideration was given to the refractive outcome in the primary eye. Surgery to implant the Crystalens AT-45 was performed using standard microsurgical techniques and local or topical ophthalmic anesthesia. A curvilinear capsulorhexis of between 4.0 mm and 6.0 mm was recommended and was made with the surgeon using his or her standard technique, and the cataract was extracted by phacoemulsification. The IOL was implanted with a forceps without folding into the intact capsular bag through a clear corneal or scleral tunnel incision no larger than 4.0 mm, with the surgeon using his or her standard instrumentation and technique. The Crystalens AT-45 IOL was not implanted if the capsular bag was not intact or if there were zonular rupture. The incision was closed according to the surgeon's discretion. Capsulotomy by neodymium:YAG (Nd:YAG) (if necessary) was not to be performed until at least 3 months after implantation of the Crystalens AT-45 IOL.

Statistical Analyses

Because the FDA requires 92.5% of IOL implanted eyes to have a best corrected distance acuity of 20/40 or better, the hypothesis tested in the main study was that at least 92.5% of Crystalens AT-45-implanted eyes will achieve postoperative 20/40 or better at a significance level of $P \leq 0.05$. That is, best corrected distance visual acuity following implantation of the Crystalens AT-45 is equivalent to (no worse than) best corrected distance visual acuity following implantation of standard IOLs. The hypothesis was tested by means of the chi-square test. The Fischer exact test was used to compare differences in percentage of eyes with

visual acuity of 20/40 among different age groups after stratification to decades: <60 , 60 to <70 , 70 to <80 , and ≥ 80 .

The hypothesis tested in the substudy was that contrast sensitivity results, with and without glare, for the Crystalens AT-45-implanted patients was equivalent to (no worse than) that of patients implanted with a standard IOL. Functional Acuity Contrast Test scores were converted to log (base 10) units of contrast sensitivity. When no patch could be recognized, the log contrast sensitivity was assumed to be the log contrast sensitivity for the highest contrast patch (patch 1) minus 0.15 log units, which is the log unit difference in contrast sensitivity between 2 patches. The clinically relevant difference in mean patch score of 0.8 represented 80% of a 1 unit change in patch score. The equivalent value in log units was 80% of 0.15 log units, or 0.12 log unit of contrast sensitivity. Thus, the clinically relevant difference in the mean log contrast sensitivity between the 2 IOL groups was less than $+0.12$ log units.

Mean and standard deviation of the log contrast sensitivity were calculated for the 2 lens groups separately. The F-test was used to compare the standard deviations of the log contrast sensitivity between the 2 lens groups. If the upper 95% confidence limits were larger than 0.12 log units, the alternative hypothesis of "the Crystalens AT-45 is no worse than a standard IOL" was rejected. Patients who were unable to resolve even the highest contrast patch at a given spatial frequency were assigned a contrast sensitivity score equal to that associated with patch 1 $- 0.15$ log units. This assumes that the next highest contrast patch would have been recognized if such a patch had been available in the testing.

Due to the statistically significant difference in the mean age between the 2 IOL groups, a regression model was used to adjust the log contrast sensitivity difference between the 2 lens groups. The log contrast sensitivity of the Crystalens AT-45 IOL was also stratified by the pupil size (<5.5 mm and ≥ 5.5 mm) to determine whether this had any effect on contrast sensitivity.

RESULTS

Demographics and Surgical Information

This prospective multicenter U.S. clinical trial of the Crystalens AT-45 IOL was conducted between March 22, 2000, and February 27, 2002. Fourteen clinical investigators in the U.S. and 3 investigators outside the U.S. participated and enrolled consecutive qualified cases. Enrollment was performed in 2 phases. In phase I, 100 eyes received the Crystalens AT-45 IOL unilaterally and were followed for 3 to 6 months. Data from these phase I eyes were included in analyses of effectiveness variables. In phase II, patients received the Crystalens AT-45 bilaterally and will be followed for 3 years. The first eye implanted in phase II was termed the primary eye, and the second eye was termed the fellow eye. The U.S. investigators enrolled 263 patients (263 primary eyes), and those primary eyes, were included in the efficacy and safety analyses. The non-U.S. investigators enrolled 61 patients (eyes), and data from the first implanted eye were included in the safety analyses only. Thus, the safety cohort consisted of all implanted eyes for a total of 324 eyes. A minimum of 2 weeks was required between the primary and the fellow

implantations. All cataracts extracted in the study were senile cataracts.

At the 12-month follow-up reported here, data on 246 of 263 primary eyes were available for analysis. Enrolled patients had a mean age of 70.0 years \pm 8.0 (SD) (range 49.5 to 87.8 years). Most (95.1%) were white, and 56% were women. Mean preoperative refractive error, expressed as manifest refractive spherical equivalent (MRSE), was -0.197 ± 0.615 D (range -2.88 to $+2.25$ D). Cataract extraction was performed through a clear corneal incision in 77.9% (205 of 263) of primary eyes. The range of axial lengths of eyes in the clinical trial was 21.0 to 26.6 mm and the dioptric power range of the IOLs was 16.5 to 27.5 D. A total of 19.8% of primary eyes and 19.7% of fellow eyes had a scleral tunnel incision. Mean incision size was 3.55 ± 0.30 mm (range 2.50 to 4.50 mm) in the primary eyes, and mean capsulorhexis size was 5.05 ± 0.61 mm (range 4.0 to 7.0 mm). The IOL was implanted in 10 eyes in which the capsulorhexis was 7.0 mm or greater, larger than the 4.0 to 6.0 mm recommended. In 2 of these eyes, the patient's postoperative refraction was greater than -1.0 D. Nearly all implantations (98.8%) were reported to have been "easy" or "very easy" to perform. One IOL could not be placed in the capsular bag; 1 haptic was placed in the bag and the other in the sulcus. This eye was included in safety data analysis only.

Combined Distance and Near Visual Acuity

Combined uncorrected distance and uncorrected near visual acuity of 20/40 or better was achieved by 78.8% (189 of 240) of the primary eyes with unilateral Crystalens AT-45 IOLs at 1 year; bilaterally, the same combined acuities were achieved by 96.7% (119 of 123) of patients. Two of the 240 primary eyes in the study cohort had both uncorrected distance and uncorrected near visual acuity worse than 20/40, but both these eyes were correctable to 20/40 or better for both distance and near acuity. An evaluation of a subset of the primary eyes—those that refracted within 0.5 D of plano—showed 87.7% of primary eyes unilaterally had both uncorrected distance and uncorrected near visual acuity of 20/40 (J3) or better. It is of interest that those patients within ± 0.5 D bilaterally achieved excellent uncorrected acuities; 97.3% achieved J2 or better uncorrected near acuity, 100% achieved J1 or better uncorrected intermediate acuity, and 98.6% achieved 20/25 or better uncorrected distance acuity 1 year postoperatively. One primary eye had both uncorrected distance and uncorrected near acuities worse than 20/40. Seventy-four eyes refracted within 0.5 D of plano in both eyes. Their combined uncorrected distance, intermediate, and near binocular visual acuities are shown in Figure 2.

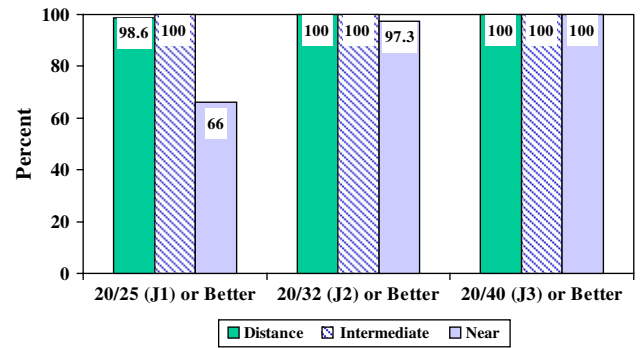


Figure 2. Uncorrected bilateral visual acuity in patients within 0.50 D of plano in each eye 12 months postoperatively (N = 74).

Near Visual Acuity through Distance Correction

At 1 year, near acuity measured through the distance correction to eliminate the pseudoaccommodative factors of myopia and astigmatism was 20/25 (J1) or better in 24.8% (60 of 242), 20/32 (J2) or better in 54% (130 of 142), and 20/40 (J3) or better in 90.1% (337 of 369) of primary eyes unilaterally (Figure 3). Twenty-four primary eyes (9.9%) and 8 fellow eyes (6.3%) had unilateral near acuity through distance correction worse than 20/40 (J3). Eight of these 32 eyes had ocular pathology: 3 eyes with macular degeneration, 2 eyes with cystoid macular edema (CME), 2 with guttata, and 1 with a corneal scar. Six eyes had PCO, and no cause could be identified for the remaining 16 eyes. Distance corrected near visual acuity in these eyes ranged from 20/50 to 20/80. Bilateral implantation was associated with a substantially larger proportion of eyes in each visual acuity category. Bilaterally, near acuity measured through distance correction was 20/25 (J1) or better in 64 of 124 (51.6%), 20/32 (J2) or better in 83.9% (104 of 124), and 20/40 (J3) or better in 100% (124 of 124). Data stratified by age showed that all age decade

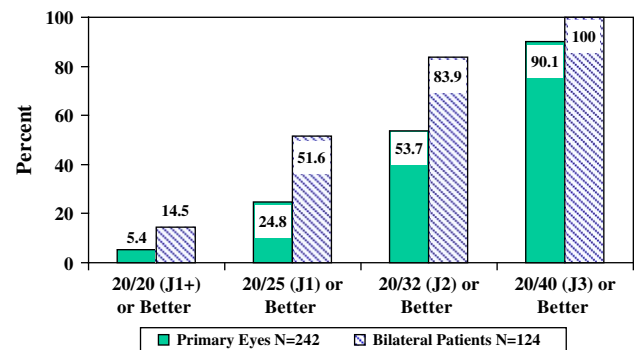


Figure 3. Near visual acuity through distance correction 12 months postoperatively.

groups achieved good near acuity measured through distance correction.

There was no statistically or clinically significant difference in near acuity measured through distance correction between the eyes implanted with the low-power, intermediate-power, or high-power lenses, suggesting that IOL power had no effect on the accommodative function of the Crystallens AT-45 IOL. There were no statistically significant differences in near acuity between short, medium, or long axial lengths in primary eyes. Overall, axial length and the power of the implanted lens appeared to have no effect on the accommodative properties of the Crystallens AT-45 IOL.

Uncorrected Near Visual Acuity

At 1 year, 43% (104 of 241) of the primary eyes had uncorrected near visual acuity of 20/25 (J1) or better, 69.7% (168 of 241) had 20/32 (J2) or better, and 88.4% (213 of 241) had 20/40 (J3) or better. Bilaterally, 72.6% (90 of 124) had uncorrected near visual acuity of 20/25 (J1) or better, 93.5% had 20/32 (J2) or better, and 98.4% (122 of 124) had 20/40 (J3) or better (Figure 4). Near vision was tested with the MN reading card at a distance of 16 inches (40 cm), the measurement being standardized by having a 40 cm cord attached to the reading card with the end aligned with the eye. For purposes of this article, near acuity was converted into Jaeger because more ophthalmologists are familiar with Jaeger values. While there is no direct conversion from LogMAR to Jaeger, the conversion was done by comparing the type size on Lighthouse International reading cards.

Of the 28 (11%) primary eyes with uncorrected near visual acuity worse than 20/40 (J3), 13 had a hyperopic postoperative spherical equivalent greater than +0.5 D. Nine of these eyes had sight-limiting ocular pathology including macular degeneration, corneal guttata, and CME. In the remaining 6 eyes, no specific cause could be identified. The 2 bilaterally implanted patients who failed to achieve uncorrected near visual acuity of 20/40 or better were hyperopic.

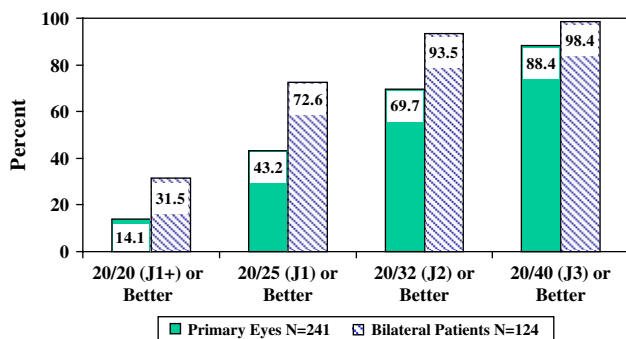


Figure 4. Uncorrected near visual acuity 12 months postoperatively.

Table 1 shows uncorrected near visual acuity stratified by postoperative refractive error. A total of 66.9% of primary eyes within ± 0.5 D of plano achieved uncorrected near visual acuity of 20/32 (J2) or better compared with 25% of eyes that were hyperopic more than 0.5 D. The difference between the groups was statistically significant ($P < .0001$). Both near acuity through distance correction and uncorrected near visual acuity were unaffected by age ($P > .05$) for primary eyes and for all patients bilaterally. Uncorrected near acuity was 20/40 (J3) or better in up to 94% of eyes, irrespective of age decade.

Near Acuity with Add

At 1 year, 100% (242 of 242) of primary eyes and 100% of bilaterally implanted eyes were correctable to 20/40 (J3) or better near acuity through distance correction with add and approximately 99% were correctable to 20/32 (J2) or better. For 20/25 (J1) or better and 20/20 (J1+) or better, the percentages were 96% and 70%, respectively. All bilaterally implanted patients had near acuity through distance correction with add of 20/25 (J1) or better, and 87% were 20/20 (J1+) or better. Patient age had no effect on visual outcome. The mean add power required to achieve the patient's best corrected near acuity was reduced from $+2.37 \text{ D} \pm 0.35$ at the baseline preoperative evaluation to $+1.20 \text{ D} \pm 0.44$ at 12 months for primary eyes. This reduction in required add power of approximately 50% was statistically significant ($P < .0001$).

The distribution of required add power was significantly different when baseline values were compared with 12-month values. Preoperatively, no primary eyes could achieve a best corrected near acuity with less than +1.00 D of add power, and only 2.7% of eyes (7 of 262) could achieve best corrected near acuity with less than +1.50 D of add power. In contrast, at 12 months, 22.1% (53 of 240) of eyes implanted with the Crystallens AT-45 lens required an add power of less than +1.00 D and an additional 45% (108 of 240) of eyes required +1.00 D to +1.25 D of add. Only 6% (14 of 240) of Crystallens AT-45 implanted eyes required an add of +2.00 D or more at 12 months, compared with 88.2% (231 of 262) preoperatively.

Intermediate Visual Acuity

Intermediate visual acuity through the distance correction is shown in Figure 5. Over 95% of primary eyes were 20/25 (J1) or better, and 99% were 20/32 (J2) or better at 1 year. Only 1 primary eye had intermediate acuity worse than 20/40, which was attributable to macular degeneration and PCO at the 1-year examination. All bilaterally implanted patients had intermediate acuity through distance correction of 20/25 (J1) or better, and 98% of these patients were 20/20 (J1+) or better at 1 year. Intermediate vision

Table 1. Uncorrected near VA by MRSE at 12 Months: primary eyes.

Near VA	MRSE (D)		
	Myopia > -0.50 D (n = 59)	Within 0.50 D of Plano (n = 167)	Hyperopia > +0.50 D (n = 20)
	n (%)	n (%)	n (%)
20/20 (J1+) or better	18 (31.0)	16 (9.8)	0 (0.0)
20/25 (J1) or better	43 (74.1)	60 (36.8)	1 (5.0)
20/32 (J2) or better	54 (93.1)	109 (66.9)	5 (25.0)
20/40 (J3) or better	59 (100)	146* (89.6)	9* (45.0)
Worse than (J3) 20/40	0 (0.0)	17 (10.4)	11 (55.0)

MRSE = manifest refractive spherical equivalent; VA=visual acuity

*P<.001 for significant difference between groups

was tested at a distance of 32 inches (80 cm), the measurement being standardized by having an 80 cm cord attached to the MN reading card with the end aligned with the eye.

Distance Visual Acuity

Uncorrected distance visual acuities at 1 year are shown in Figure 6. Acuity of 20/25 or better was achieved by 68.0% (166 of 244) of the primary implantations and 20/32 or better by 80.7%. Of the 27 of 244 eyes that did not achieve uncorrected distance visual acuity of 20/40 or better, 20 had significant postoperative refractive error, ranging from -0.87 to -2.875 D, 4 had ocular pathologies (macular degeneration, CME), 2 had PCO, and no specific cause could be identified in the remaining 2 eyes. Bilaterally, uncorrected distance acuity of 20/25 or better was achieved in 91.9%, 20/32 or better by 97.6%, and 20/40 or better by 98.4%.

When uncorrected distance acuity was stratified by postoperative MRSE (Table 2), 60% (99 of 165) of eyes with postoperative refraction within ±0.50 D of plano

read the 20/20 or better line. This compares with 6.8% (4 of 59) eyes with myopia greater than -0.50 D and 35.0% (7 of 20) of eyes with hyperopia of more than +0.50 D, and this difference was statistically significant (P<0001).

Best corrected distance visual acuity of 20/25 or better was achieved by 97% (235/243) of primary eyes and by all bilaterally implanted patients. A total of 99.2% of the primary eyes had best corrected distance acuity of 20/40 or better. All patients with bilateral Crystalens AT-45 implantations achieved 20/25 or better. Only 2 implanted eyes did not achieve a best corrected distance acuity of 20/40 or better at 1 year: 1 eye had macular degeneration and the other eye had PCO.

Safety

The safety data comprise both U.S. and non-U.S. clinical sites. Three non-U.S. sites provided safety data only.

The incidence of cumulative and persistent adverse events for the cohort of all 324 primary implantations was less than the incidence reported in the FDA Grid of Historical Controls, with the exception of the cumulative

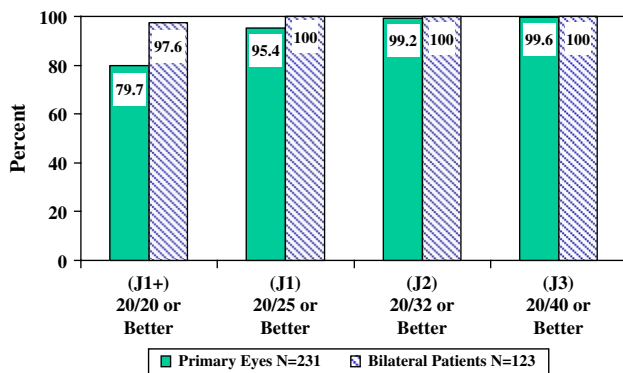


Figure 5. Intermediate visual acuity through distance correction 12 months postoperatively.

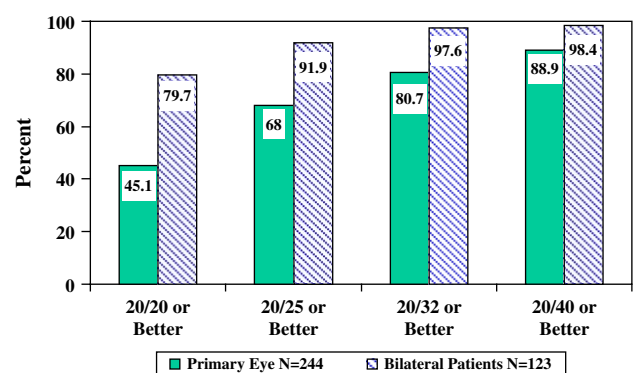


Figure 6. Uncorrected distance visual acuity with the Crystalens AT-45 IOL 12 months postoperatively.

Table 2. Uncorrected distance VA by MRSE at 12 Months: primary eyes.

Distance VA	MRSE (D)		
	Myopia > -0.50 D (n = 59)	Within 0.50 D of Plano (n = 165)	Hyperopia > +0.50 D (n = 20)
	n (%)	n (%)	n (%)
20/20 or better	4 (6.8)*	99 (60.0)	7 (35.0)*
20/25 or better	15 (25.4)	143 (86.7)	8 (40.0)
20/32 or better	28 (47.5)	155 (93.9)	14 (70.0)
20/40 or better	38 (64.4)	160 (97.0)	19 (95.0)
Worse than 20/40	21 (35.6)	5 (3.0)	1 (5.0)

MRSE = manifest refractive spherical equivalent;

VA = visual acuity

* $P < .0001$ for significant difference between groups

report of endophthalmitis and the cumulative report of CME, diagnosed by fluorescein angiography (Table 3). In no case was there a statistically significant difference between the incidence of adverse events reported in the clinical study and the FDA Grid of Historical Controls.

Persistent (present at the 12-month visit) CME was reported in 3 eyes. In 1 case, significant residual cortex was observed. A decision was made to leave the residual cortex

Table 3. Cumulative and persistent adverse events: primary eyes.

Adverse Event	n/N (%)	FDA Grid
12-month cumulative adverse events	1/324 (0.3)	0.3%
Endophthalmitis	1/324 (0.3)	2.2%
Hyphema	0/324 (0.0)	0.3%
Hypopyon	0/324 (0.0)	0.1%
IOL dislocation	12/324 (3.7)	3.0%
Cystoid macular edema	0/324 (0.0)	0.1%
Pupillary block	0/324 (0.0)	0.3%
Retinal detachment	2/324 (0.6)	0.8%
Secondary surgical	0/324 (0.0)	NA
Intervention	1/324 (0.3)	NA
Iridectomy	1/324 (0.3)	NA
Vitreotomy	0/324 (0.0)	NA
Repositioning of lens	0/324 (0.0)	NA
Lens removal	0/324 (0.0)	NA
Lens replacement		
Other		
12-month persistent adverse events	0/298 (0.0)	0.3%
Corneal edema	2/298 (0.7)	0.3%
Iritis	3/304 (0.9)	0.5%
Cystoid macular edema	0/304 (0.0)	0.4%
Raised IOP requiring treatment		

IOP = intraocular pressure

*CME 7 of 13 (54%) of the reported cases were diagnosed by fluorescein angiography and had a best corrected distance acuity of 20/32 or better at the time of diagnosis. At 1 year, only 1 eye had a best corrected distance acuity of 20/40, but CME was not the etiology.

in the eye, and the patient remained on topical ophthalmic medications to control inflammation and IOP. Best corrected near visual acuity of 20/25 and best corrected distance visual acuity of 20/32 were reported for this eye. In the second case, fluorescein angiography performed at the 1-year visit revealed no peripheral leakage and suggested resolution of the CME. Best corrected distance and near acuity were 20/32 in this eye. In the third case, slitlamp examination revealed presence of 1 of the Crystallens AT-45 lens haptics in the sulcus and the other haptic in the capsular bag. At the 12-month examination, best corrected distance acuity was 20/40.

Endophthalmitis was reported in 1 non-U.S. eye. The patient presented with severe endophthalmitis 1 week postoperatively. With treatment, the endophthalmitis had resolved by the 1-month visit; however, an epiretinal membrane was diagnosed and uncorrected distance acuity remained at 20/400. At the last recorded visit, the uncorrected distance acuity had improved to 20/200. The investigator concluded that the initial diagnosis of endophthalmitis was not lens related but a result of the patient's poor personal hygiene.

Patient Survey

Of the unilaterally implanted patients who completed a survey, most (84 of 88, or 95.4%) reported improvement in their quality of vision at 1 year. Only 4 of 88, or 4.6%, reported no improvement. Of the 130 patients implanted bilaterally, 91.2% (115 of 126) reported that they were very satisfied, somewhat satisfied, or satisfied with their visual outcome, 2.4% were undecided, and 6.3% were somewhat dissatisfied with their outcome.

Spectacle Independence

One hundred twenty-eight patients implanted bilaterally with the Crystallens IOL were asked to complete

a patient survey. The survey was administered in 1 of 3 ways: (1) an ophthalmic technician read out the questions and checked the answers, (2) the patient was placed into a room alone and asked to complete the survey, and (3) the patient took the survey home and returned it at a later date. The survey revealed that 25.8% did not wear glasses. In addition, 47.7% reported that they wore glasses 10 to 25% of the time.

Posterior Capsule Opacification

The incidence of posterior capsule opacification in this study was higher than the incidence reported for some lenses with a 360-degree square edge. The square edge on the Crystalens AT-45 IOL extends for only 240 degrees; there is no square edge where the optic abuts the plates. An Nd:YAG capsulotomy was performed in 37 of 263, or 14.1%, of primary eyes. Most were performed at the 3-month to 6-month or the 11-month to 15-month visits. The visual acuity in 29 of 37 (78%) of these eyes was 20/32 or better prior to the Nd:YAG capsulotomy. Post-Nd:YAG, uncorrected distance acuity was 20/32 or better in 64.7%; uncorrected near acuity was 20/32 or better in 89.1% and 20/25 or better in 81.0%, respectively. Best corrected distance visual acuity was 20/32 or better in 100%. The procedure was reported to have no significant deleterious effect on any measure of visual acuity, and there were no reports of post-Nd:YAG capsulotomy cases of CME or retinal detachment.

Stability

Stability data showed 84% of eyes had a mean change of MRSE from the target refraction (-0.25 D in first eye, plano in second eye) within ± 0.50 D between 1 to 3 and 3 to 6 months, and 85% between 3 to 6 and 11 to 12 months postoperatively. The mean change in MRSE between 1 to 3 and 3 to 6 months was -0.03 D and between 3 to 6 and 11 to 15 months was $+0.13$ D.

Predictability of Visual Outcomes

The predictability of visual outcomes was excellent. Of 126 patients implanted bilaterally, 1 year postoperatively, 74 (59.1%) had refractions in both eyes within the target refractions of -0.50 to plano in the first eye and plano in the second eye.

Contrast Sensitivity Substudy

A total of 126 Crystalens AT-45 IOL patients and 64 standard IOL (control=9 different lens models including silicone, acrylic, and Collamer) patients were enrolled at 8 investigational sites. The Crystalens AT-45 IOL and

standard IOL groups were similar in sex (Crystalens AT-45: 57% female, standard IOL: 58%); race (Crystalens AT-45: 94% white, standard IOL: 91%); and mean pupil size (Crystalens AT-45: 4.4 ± 0.9 mm; standard IOL: 4.6 ± 0.7 mm). However, there was a statistically significant difference in age ($P = .004$) between the Crystalens AT-45 patients (mean 70.1 ± 8.0 years; range 49.5 to 87.8 years) and the standard IOL patients (mean 73.8 ± 9.1 ; range 52.1 to 89.1 years). The age difference was significant only at the 1.5 and 3 cpd targets with glare. Age-adjusted results were very similar to the unadjusted data.

Results of mesopic contrast sensitivity testing with and without glare source are shown in Figures 7 and 8. At each spatial frequency, the upper 95% confidence limits for the difference in the mean log contrast sensitivity between the 2 IOL groups was less than $+0.12$ log units (the clinically relevant delta value). Thus, the study hypothesis that contrast sensitivity in the Crystalens AT-45 IOL group was no worse than that in the control group even in the presence of glare was demonstrated.

The glare source had minimal effect on contrast sensitivity in both groups, decreasing mean scores by 0.01 to 0.08 log units. The upper 95% confidence limits for the differences in the mean log contrast sensitivity with glare between the 2 lens groups were all less than $+0.12$ log units. There were no clinically or statistically significant differences between the 2 lens groups in the absence of glare.

Twenty Crystalens AT-45 IOL and 7 standard IOL patients had pupil diameters equal to or greater than 5.5 mm. A comparison of contrast sensitivity results between the 2 groups showed no clinically or statistically significant differences in the presence of glare except at the 6 cpd spatial frequency (Figure 9). At 6 cpd, the mean contrast sensitivity was 1.24 log units with glare for the Crystalens AT-45 eyes versus 1.55 log units for the 7 standard IOL patients.

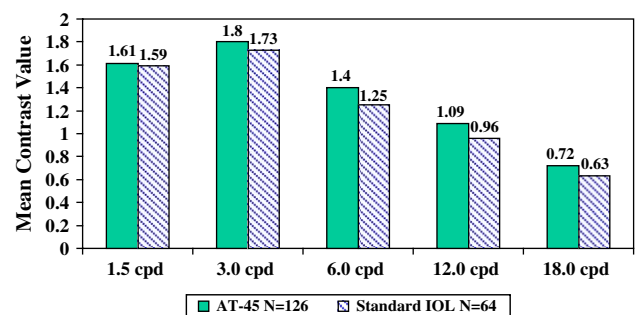


Figure 7. Log contrast sensitivity without glare 3 to 6 months postoperatively. Crystalens AT-45 IOL versus standard IOLs. No statistically significant differences between the lens groups were seen at 1.5 cpd through 18 cpd.

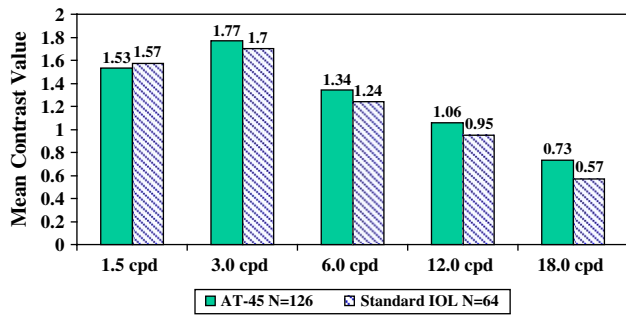


Figure 8. Log contrast sensitivity with glare 3 to 6 months postoperatively; Crystalens AT-45 IOL versus standard IOLs. No statistically significant differences between the lens groups were seen at 1.5 cpd through 18 cpd.

Visual Acuity Results

The differences between the groups in uncorrected monocular near visual acuity through the distance correction were substantial, with 89.3% of Crystalens AT-45 IOL patients and only 35.9% of standard IOL patients achieving 20/40 (J3) or better ($P < .0001$). For 20/32 (J2) or better near, the percentages were 50.4% for the Crystalens AT-45 and 4.7% for the standard IOL (Table 4). For intermediate visual acuity through the distance correction (Table 5), significantly more eyes implanted with a Crystalens AT-45 IOL achieved 20/20 (J1+) or better visual acuity than those implanted with a standard IOL (75.2% vs 20.3%, $P = .049$).

Range of Accommodation

Combined monocular best distance corrected near acuity and intermediate and near visual acuity through the distance correction for the Crystalens AT-45 IOL and the standard IOL groups are shown in Figure 10. A total of 88.4% of Crystalens AT-45 patients achieved 20/40 (J3) or better at distance, intermediate, and near versus only 36% of control patients. For 20/32 (J2), the

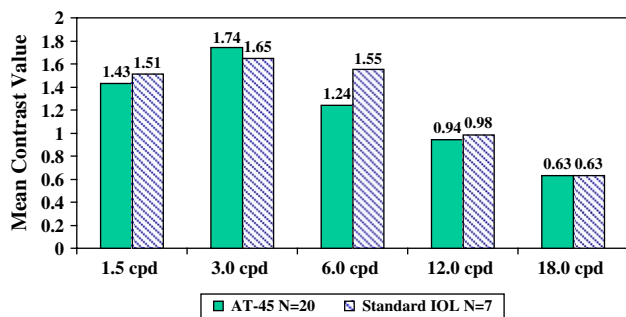


Figure 9. Mesopic contrast sensitivity with glare: pupil ≥ 5.5 mm.

Table 4. Contrast sensitivity substudy: uncorrected monocular near VA through distance correction 3 to 6 months postoperatively.

Visual Acuity	Lens Group			
	AT-45 (n = 121)		Standard IOL (n = 64)	
	N	(%)	N	(%)
20/20 (J1+) or better	2	(1.7)	0	
20/25 (J1) or better	31	(25.6)	0	
20/32 (J2) or better	61	(50.4)	3	(4.7)
20/40 (J3) or better	108	(89.3)*	23	(35.9)*
20/41 to 20/100	13	(10.7)	40	(62.5)
Worse than 20/100	0		1	(1.6)

*Difference between the lens groups for 20/40 or better is significant ($P \leq .0001$)

percentages were 50% for the Crystalens AT-45 group and 4.7% for the standard lens group.

Add Power

The add power required to achieve monocular best correct near acuity in the 2 groups in the contrast sensitivity substudy is shown in Table 6. The mean add for the Crystalens AT-45 IOL group was +1.24 D (range 0.00 to +2.50 D), while the mean add for the standard IOL group was +2.32 D (range +1.00 to +3.00 D). This difference was statistically significant ($P < .0001$). In the Crystalens AT-45 IOL group, 62.6% required an add of 1.5 D or less to achieve their monocular best corrected near acuity, whereas only 3.1% of the standard IOL group achieved their best corrected near acuity with an add of 1.5 D or less.

DISCUSSION

Several surgical options for providing near vision in pseudophakic patients have been evaluated with varying

Table 5. Contrast sensitivity substudy: intermediate visual acuity through distance correction 3 to 6 months postoperatively.

Visual Acuity	Lens Group			
	AT-45 (n = 121)		Standard IOL (n = 64)	
	n	(%)	n	(%)
20/20 or better	91	(75.2)	13	(20.3)
20/25 or better	115	(95.0)	44	(68.8)
20/32 or better	118	(97.5)	53	(82.8)
20/40 or better	120	(99.2)*	60	(93.8)*
20/41 to 20/100	1	(0.8)	4	(6.3)

*Difference between the lens groups for percentages of 20/40 or better is significant ($P = .049$)

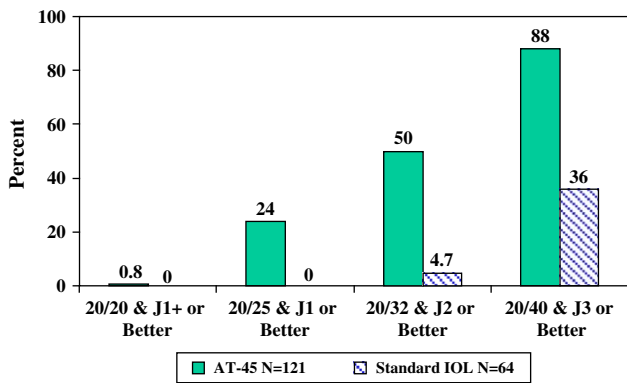


Figure 10. Combined distance and near and intermediate visual acuities through the distance correction with the Crystalens AT-45 IOL versus standard IOLs monocularly 3 to 6 months postoperatively.

degrees of success, including monovision,^{6,7} implantation of corneal inlays,⁸ and implantation of multifocal⁹⁻¹¹ and posterior chamber IOLs. Magnetic resonance imaging studies have established the continued functionality of the ciliary body with aging and demonstrated that the ciliary muscle retains much of its contractility in older patients.⁴ However, none of the current modalities of IOL designs use the natural physiology of the ciliary muscle following cataract removal to enable the patient to see at near. The Crystalens AT-45 multipiece silicone posterior chamber IOL was specifically designed to allow the lens to move forward to provide accommodation upon increased vitreous cavity pressure resulting from ciliary muscle constriction.

Cumming and Kammann¹² introduced the concept of posterior chamber accommodating IOLs with the aim of allowing pseudophakic accommodation by a change in

Table 6. Contrast sensitivity substudy: add power 3 to 6 months postoperatively.

Add Power Over Distance Correction	AT-45 (n = 126)		Standard (n = 64)	
	n	(%)	n	(%)
< 1.0 D	19	(15.1)	0	0.0
1.0 to < 1.5 D	60	(47.6)	2	(3.1)
1.5 to < 2.0 D	41	(32.5)	5	(7.8)
2.0 to < 2.5 D	5	(4.0)	18	(28.1)
2.5 to < 3.0 D	1	(0.8)	38	(59.4)
3.0 to < 3.5 D	0		1	(1.6)
3.5 to < 4.0 D	0		0	
Total	126	100.0	64	(100.0)
Mean ± SD (D)	1.24 ± 0.39		2.32 ± 0.36	
Range (D)	0.00 to 2.50		1.00 to 3.00	

*Difference between the Crystalens IOL and the standard IOL was statistically significant ($P < .0001$).

power affected by forward movement of the lens. This movement of an accommodating IOL optic along the axis of the eye is attributed to the ability of the ciliary muscle to move a silicone plate-haptic IOL optic forward, resulting from an increase in vitreous cavity pressure.¹³ The increase in vitreous cavity pressure created on ciliary muscle contraction results in the anterior movement of the IOL optic and was demonstrated by the increased length of the vitreous cavity in eyes following administration of pilocarpine.¹⁴ Maximum posterior positioning or vaulting of a plate lens in the capsular bag space,¹⁵⁻¹⁸ placing the optic up against the vitreous face, allows the optic to move forward most efficiently on an increase in vitreous cavity pressure.

The prospective multicenter clinical trial described here establishes the ability of an accommodating IOL, the Crystalens AT-45, to provide patients with good uncorrected and distance corrected near, intermediate, and distance visual acuities. Near visual acuities of 20/40 (J3), 20/32 (J2), or 20/25 (J1) or better through the distance correction were achieved by 90.1%, 53.7%, and 24.8%, respectively, of all patients implanted in 1 eye with a Crystalens AT-45 IOL. Distance corrected near acuities were even better in the bilaterally implanted patients, with 83.9% achieving 20/32 (J2) or better and 51.6% achieving 20/25 (J1) or better. For intermediate acuity through the distance correction, 99.2% had 20/32 (J2) or better monocularly, 97.6% had 20/20 (J1+) or better, and 100% had 20/32 or better bilaterally. These results demonstrate the accommodating function of the Crystalens AT-45 IOL when the pseudoaccommodative factors of myopia and cylinder are not contributing to near and intermediate acuities.

Uncorrected near acuity values for the Crystalens AT-45 IOL were better than those measured through the distance correction, presumably because of the pseudoaccommodative factors mentioned earlier. While 73% of eyes in this study had uncorrected near acuity of 20/25 (J1) or better, the percentage dropped to 52% when near acuity was measured through the distance correction. However, near acuities for the Crystalens AT-45 IOL, measured through the distance correction were still better than the near acuity values in published reports for standard monofocal IOLs.^{11,19}

Furthermore, a comparison of near visual results for the Crystalens AT-45 accommodating IOL in this main study with the results from the monofocal control arm of the substudy reveals substantial differences. Approximately half the eyes with the Crystalens AT-45 IOL had near acuity through the distance correction of 20/25 (J1) or better, compared with only 4.7% having this near acuity with the standard monofocal lens. Differences between the 2 lens types were also evident for intermediate vision, with 20/20 (J1+) or better through the distance correction

achieved by 75.2% of the Crystalens AT-45 eyes compared with only 20.3% of standard monofocal IOL eyes. These results provide further evidence of the accommodative abilities of the Crystalens AT-45 IOL.

Of the 2 study groups tested identically, a best corrected near acuity of 20/30 or better was achieved by 100% of the standard monofocal group and 99.2% of the Crystalens AT-45 group. From this it was concluded that the age difference between the 2 groups was of no significance.

The postoperative near add powers (mean +1.24 D) required in the eyes to achieve the best potential near acuity were significantly lower than those measured for the standard IOL (mean +2.32 D) measured in the substudy. These data further suggest evidence of accommodation. In the Crystalens AT-45 group, 62.6% required an add of 1.5 D or less to achieve the monocular best corrected near acuity, whereas only 3.1% of the standard IOL group achieved their best corrected near acuity with an add of 1.5 D or less.

Patients also achieved good distance vision without correction. Uncorrected distance acuities of 20/40 or better were achieved in 88.9% of unilaterally implanted patients and in nearly all patients (98.4%) with the Crystalens AT-45 IOL in both eyes. These outcomes for uncorrected distance acuity support the A-constant of 119.0 and use of the SRK/T formula for the Crystalens AT-45 IOL and the consistency of the location of the plate-haptic lens along the axis of the eye, with the broad range of axial lengths in the eyes with the IOL (ie, 21.0 to 26.6 mm), and of IOL powers implanted (16.5 to 27.5 D).

Best corrected distance acuity of 20/25 (J1) or better was achieved in 96.7% of eyes with monocular Crystalens AT-45 IOLs and in 100% of patients with an IOL in both eyes. Patients with minimum postoperative refractive error (within 0.50 D of plano) had better uncorrected near acuities and uncorrected distance acuities, underscoring the importance of accurate preoperative biometry and keratometry. Furthermore, as would be expected, patients who were more hyperopic postoperatively ($>+0.50$ D) had reduced uncorrected near vision (45% 20/40 [J3] or better) than patients who were more myopic (>-0.50 D), all of whom achieved uncorrected near acuities of 20/40 (J3) or better.

Combined visual acuities of 20/40 or better distance and J3 or better near were achieved in 78.8% of the Crystalens AT-45 patients implanted monocularly and in 96.7% implanted bilaterally at 1 year in the main clinical trial. The increase with bilateral implantation may be due to the refractive target being -0.50 D in the primary implanted eyes and plano in the fellow eyes. Combined uncorrected distance, intermediate, and near binocular acuities were even better in the 74 patients (148 eyes) who were within ± 0.50 D of plano in both eyes. A total of 100%, 100%,

and 97.3% had 20/32 (J2) or better visual acuity for distance, intermediate and near, respectively. In the substudy at 3 to 6 months postoperatively, 88% of the Crystalens AT-45 IOL eyes achieved 20/40 or better distance combined with J3 or better near compared with 36% of eyes that achieved these combined acuities with the standard IOLs. For 20/32 or better distance combined with J2 or better, the percentages were 50% for the Crystalens AT-45 IOL eyes compared with 4.7% for the standard IOL eyes. These combined acuities attest to the restoration of functional distance as well as near vision following cataract surgery and implantation of this accommodating IOL.

The safety study results were consistent with the values reported in the FDA Grid of Historical Controls for other monofocal IOLs. The cases of persistent iritis and cumulative macular edema were slightly above the FDA Grid values. Persistent iritis occurred in 1 eye in which a significant amount of cortex was left in the capsule postoperatively and in another eye with persistent CME. However, the best corrected distance acuity at 12 months was 20/25 for this latter eye and the uncorrected near acuity 20/25 (J1) and distance corrected near acuity 20/32 (J2). No lens dislocations were reported in this clinical trial, and the rate of Nd:YAG capsulotomy (13.3%) was within the range previously reported for other silicone IOLs.^{20,21} Post-Nd:YAG capsulotomy, best corrected distance acuity was 20/25 or better in 94% (32/34) and 20/32 or better in 100% of the eyes. Post-Nd:YAG acuities of uncorrected near vision were 100% (20/40 [J3] or better), 89.1% (20/32 [J2] or better) and 81.0% (20/25 [J1] or better), respectively. The near acuity with distance correction following Nd:YAG capsulotomy was unchanged. Further evidence of the safety of the Crystalens AT-45 IOL was the lower rate of visual disturbances, specifically glare, halos, and night driving vision, reported in this clinical trial than reported for a standard IOL by Steinert et al.¹¹ No IOL had to be explanted for complaints of halos or glare, decenetration, or unusual alignment.

The Crystalens AT-45 IOL substudy was conducted to address concerns regarding glare and loss of contrast sensitivity possibly related to the small optic of the Crystalens AT-45 lens. We compared near visual acuity through the distance correction of the Crystalens AT-45-IOL patients with that of patients implanted with a standard monofocal IOL. We tested under extremely low-light conditions to simulate vision in the presence of poor illumination and a larger pupil in the presence and absence of glare.

The results demonstrated that the small optic of the Crystalens AT-45 IOL was not associated with greater loss of contrast or increased glare symptoms than observed with a standard monofocal IOL. In contrast to these findings, studies of zonal-progressive and diffractive multifocal IOLs have shown a significant reduction in contrast

sensitivity compared to monofocal control lenses.^{11,22} Importantly, the contrast sensitivity results for the monofocal control arm were consistent with results of contrast sensitivity testing in patients with standard monofocal IOLs reported by Featherstone et al.²³

The Crystalens AT-45 lens test populations were not age matched to the Featherstone et al. study cohort, nor were these groups of patients “best case.” Additionally, the contrast sensitivity testing performed in Crystalens AT-45 patients was unilateral because the Crystalens AT-45 patients were tested in their primary surgical eye only, while Featherstone et al.’s population consisted of bilaterally implanted patients who were tested binocularly. Studies have shown that binocular contrast sensitivity is increased over unilateral contrast sensitivity by a factor of 1.414 (square root of 2).²⁴ A comparison of the binocular contrast sensitivity data reported by Featherstone et al. and the contrast sensitivity data for the Crystalens AT-45 and the standard IOL control group transformed to binocular contrast sensitivity by multiplying by a factor of 1.414 confirm that the results of contrast sensitivity testing performed with the Crystalens AT-45 IOL are consistent with the published data.

When adjusting for the baseline age difference that existed between the treatment groups, mesopic contrast sensitivity results with and without glare in the Crystalens AT-45 group were consistent with those achieved in the control group. This finding was also consistent with data reported by Sloane et al.²⁵ on contrast sensitivity in different age groups. In Sloane et al.’s study, under mesopic conditions (1.07 cd/m²) at a target spatial frequency of 4 cpd, mean contrast sensitivity decreased from approximately 1.6 log units in younger patients with a mean age of 23 years to 1.2 log units in older patients with a mean age of 74 years. This equates to a very minimal decrease of approximately 0.0078 log units per year. This supports and is consistent with the minimal age effects observed in this substudy in which the difference in mean age for the 2 treatment groups was only 3.7 years.

The glare source had minimal effect on contrast sensitivity in either substudy group, decreasing mean scores by 0.01 to 0.08 log units in each group. These results confirm that contrast sensitivity in the Crystalens AT-45 group was no worse than that in the control group even in the presence of the glare source, indicating that patients implanted with the Crystalens AT-45 IOL perform as well as patients implanted with a standard IOL in contrast sensitivity testing under low-light situations in the presence of glare.

Contrast sensitivity results in the 7 standard lens patients with larger pupils are anomalous and inconsistent with published results. Contrast acuity has been shown to decrease in pseudophakic patients with increasing pupil diameter. For example, Knorz et al.²⁶ demonstrated that

mean Reagan acuity at low contrast decreased by more than 1 line with increasing pupil diameter from 3.5 mm to 6 mm or more (20/30 versus 20/48). This is potentially due to the effect of increasing corneal aberrations that can negatively impact vision in the presence of a larger pupil. Further, both this substudy and that of Superstein et al.²⁷ confirmed that mean contrast sensitivity in pseudophakic eyes does not, in general, increase in the presence of a glare source, contrary to observed results in the 7 standard IOL patients. Therefore, the authors believe the difference in contrast sensitivity between Crystalens AT-45 and standard lens patients with pupil diameters of 5.5 mm or greater at 6 cpd with the glare source was due to the exceptional results achieved by the 7 standard IOL patients and not due to reduced performance among Crystalens AT-45 IOL patients. With only 7 standard IOL patients available for comparison, this effect is likely to be a sampling error.

The excellent uncorrected acuity results in this study at all distances and the absence of any serious lens-related safety concerns establish the safety and effectiveness of the Crystalens AT-45 accommodating IOL. The Crystalens AT-45 appears to provide accommodation, as characterized by the near acuities through the distance correction, without reducing contrast sensitivity. Particularly noteworthy are the combined uncorrected distance, near, and intermediate results achieved binocularly when biometry is accurate (ie, eyes refract within 0.5 D of plano). In that situation, nearly 100% eyes achieved 20/32 at distance and 20/32 (J2) or better at intermediate and near. These superior functional visual results suggest that this IOL is a viable alternative to multifocal designs in treating presbyopia in cataract patients.

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