Three-Year Results of Artisan/Verisyse Phakic Intraocular Lens Implantation

Results of the United States Food and Drug Administration Clinical Trial

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Objective: To assess the safety and efficacy of the Artisan/Verisyse phakic intraocular lens (IOL) for the correction of high myopia.

Design: Prospective, open-label, noncomparative, multicenter clinical trial.

Participants: A total of 684 adults with axial myopia from −4.5 diopters (D) to −22 D were enrolled: 662 in the primary analysis group and 22 under compassionate use protocol expansion. Efficacy data are based on the 662 first eyes implanted.

Intervention: Implantation of the Artisan/Verisyse phakic intraocular lens.

Main Outcome Measures: Efficacy measures included uncorrected distance visual acuity (UCVA), refractive predictability and stability, patient satisfaction, and contrast sensitivity. Safety measures were best spectacle-corrected visual acuity (BSCVA), intraocular pressure, slit-lamp observations, endothelial cell density (ECD), complications, and adverse events.

Results: At 3 years, UCVA for first eyes were 20/40 or better in 84.0% (194/231) and 20/25 or better in 51.9% (120/231). Of first eyes, 71.7% to 76.7% were within 0.50 D of target refraction and 93.1% to 95.0% were within 1.0 D at 6 months and later. Best spectacle-corrected visual acuity was 20/40 or better for 99% to 100% of first eyes from the 1-month visit through 3 years. At 3 years, 54% of first eyes gained ≥1 lines of BSCVA, and 7.5% lost ≥1 lines of BSCVA. The mean change in ECD from baseline to 3 years was −4.8%±7.8%, with a 2.4% loss between 2 and 3 years. One site had a mean cell loss of −5.0% (P = 0.023), and the others combined had a mean cell loss of 1.7%±5.4%. For a cohort of 57 eyes with ECD data for all visits, the mean change from baseline was −3.8%±9.8% over 3 years. Approximately half (31/59) of the adverse events and preventative repositionings were among the first 10 cases performed by each investigator.

Conclusions: The Artisan/Verisyse phakic IOL provides excellent refractive outcomes; endothelial cell loss within a mean of 5.0% over 3 years, or 1.8% per year; and few complications. Ophthalmology 2008;115:464–472 © 2008 by the American Academy of Ophthalmology.

Patients with high myopia who have inadequate vision with spectacles and are contact lens intolerant have limited choices for surgical vision correction. LASIK achieves reasonably safe and predictable results in correcting myopia up to about −12 diopters (D) but is less satisfactory for higher degrees of myopia.1–4 Patients with high myopia may not be good candidates for LASIK because of the risk of corneal ectasia.5–7

Refractive lens exchange with intraocular lens (IOL) implantation can correct myopia, but lensectomy results in a complete loss of accommodation for pre-presbyopic pa-
tients and carries the risk of retinal detachment (RD) in patients with high myopia.

The iris-supported phakic IOL was developed by Ophtec BV (Groningen, Netherlands), who brought it to market in Europe as the Artisan phakic IOL (see “Appendix 2” [available at http://aaojournal.org]). Based on the results of international multicenter studies and phases I to III studies for submission to the United States Food and Drug Administration,8–10 the lens came to market in the U.S. as the Verisyse phakic IOL (Advanced Medical Optics, Inc., Santa Ana, CA) (hereinafter referred to as the Verisyse lens). It is available in powers up to −20 D and can correct refractive errors as great as −22 D. The crystalline lens remains intact, and accommodation is preserved.11

As shown in Video 1 (available at http://aaojournal.org), the surgeon inserts the Verisyse lens into the anterior chamber (AC), grasps a small fold of the relatively immobile midperipheral iris stroma, slips it through a gap in the first haptic, then repeats the process for the second haptic. This process of lens fixation is known as enclavation. An advantage of the lens design is its ease of attachment and detachment from the iris so that it can be repositioned during surgery or safely removed, if necessary. Figure 1 illustrates a cross-sectional view of the cornea and the implanted Verisyse lens.

The purpose of the current study was to determine the safety and effectiveness of the Verisyse lens for the treatment of axial myopia to meet Food and Drug Administration requirements for premarket approval in the U.S.

Patients and Methods

Study Design and Subject Population

This was a prospective, open-label, noncomparative study sponsored by Ophtec USA (Boca Raton, FL), a subsidiary of Ophtec BV. The protocol was approved by the institutional review board at each study site. Study subjects were advised of the benefits and risks of lens implantation. Bilateral implantation was allowed after the first eye was stable, with no evidence of adverse events or loss of best spectacle-corrected visual acuity (BSCVA). A substudy was conducted at one site to evaluate contrast sensitivity.

Subjects were selected from the normal patient population seeking refractive surgery at each of the investigational sites. The original protocol allowed the enrollment of adults from 21 to 50 years old with visually disabling axial myopia between −4.5 D and −22 D who did not achieve satisfactory visual results with contact lenses or spectacles. Subjects were required to have stable manifest refraction (a change in mean manifest refractive spherical equivalent [MRSE] of no more than 0.50 D between 2 examinations performed 1 month apart), no more than 2.0 D of astigmatism at the spectacle plane, an AC depth (ACD) of ≥3.2 mm, a pupil size of ≤4.5 mm in ambient light, endothelial cell counts of ≥2,000 cells/mm², good general health, the ability to comply with the postoperative evaluation schedule, and consent to the procedure in writing. Potential subjects were excluded for the presence of cataract; an abnormal pupil, iris, or cornea; mesopic pupil size greater than lens optic size; an ocular disease or abnormality that would affect safety; or lack of vision or visual potential in the fellow eye.

The protocol was amended in November 2000 to allow for the inclusion of subjects with clinically insignificant and stable peripheral lens opacities, astigmatism of ≥2.5 D, ACD < 3.2 mm, age over 50, pupil size equal to or greater than the optic size, and preoperative BSCVA < 20/40.

All investigators underwent a prestudy training program on the surgical technique. One investigator had implanted the lens before commencement of the current study. With the exception of this investigator, this study represents the initial experience with the Verisyse lens.

Preoperative Examination

Subjects were required to discontinue contact lens wear for 1 week for hard lenses and 48 hours for soft lenses before their initial examination. They were evaluated preoperatively within 30 days of the planned operation and at 8 postoperative visits: days 1 to 6; weeks 2 and 3; months 1 and 2, 4 to 6, and 7 to 9; and years 1 to 3. The original study was planned as a 2-year follow-up but was extended to 3 years in 2001.

The preoperative evaluation included medical history, uncorrected distance visual acuity (UCVA), BSCVA, manifest and cycloplegic refractions, intraocular pressure (IOP), slit-lamp examination, mesopic pupil size, corneal status, and endothelial cell evaluation. Uncorrected distance visual acuity was measured using a Snellen chart, and BSCVA with an Early Treatment Diabetic Retinopathy Study chart. Preoperative testing was performed with the subject’s habitual correction. The same charts were used throughout the study. Biometry was performed to measure axial length, corneal curvature, and ACD. Contrast sensitivity was tested preoperatively and at 4 to 12 months postoperatively at one site. Photopic and mesopic testing were performed with and without glare at 1.5, 3.0, 6.0, 12.0, and 18.0 cycles per degree of visual angle using the Vision Contrast Test System (Vistech Consultants Inc., Dayton, OH). Photopic conditions of 25±3 foot-lamberts were produced with a combination of overhead fluorescent and incandescent lights. Mesopic conditions of 0.8±0.1 foot-lamberts were produced with dimmed overhead incandescent lights. Photopic glare was measured with the BAT brightness acuity tester (Marco Ophthalmic Inc., Jacksonville, FL) set at medium. Mesopic glare was produced with a light source of 5-foot-candles at eye level 1.0 m and 30° from the visual axis. Preoperative testing was performed with the subject’s habitual correction. Postoperative testing was performed with the subject’s best distance refraction in a trial frame.

The initial protocol permitted investigators to use the instruments available at each site to measure endothelial cell density (ECD) and to obtain one image per eye per visit. The protocol was amended in response to evolving American National Standards Institute and International Organization for Standardization guidelines, and sites were subsequently advised to use the Noncon Robo noncontact specular microscope (Konan Medical Inc., Hyogo, Japan) and to obtain 3 images of the central corneal endothelium per eye per visit.

Verisyse Lens

The Verisyse IOL is a single-piece lens manufactured from Perspex CQ-UV, a clinical-quality ultraviolet light–absorbing polymethyl methacrylate material. The lens has a convex–concave optic incorporated into an 8.5-mm elliptical plate lens. It has a slight anterior vault to create space for aqueous flow and to avoid contact with the crystalline lens. Model 206 (5.0 mm diameter) was available in 1.0-D increments from −5.0 D to −20 D, and model 204 (6.0 mm diameter) was available in 1.0-D increments
Figure 1. Illustration of the implanted Verisyse lens, its attachment to the iris stroma, slight vaulting over the pupil, and position relative to the cornea.

Figure 2. Diagram of Verisyse models and appearance of the eye after implantation. D = diopter.
from −5.0 D to −15 D. Figure 2 shows a diagram of both lens models and the appearance of the eye after implantation.

Surgical Technique

Surgical preparation was the same as that for standard cataract surgery. A 5.2- or 6.2-mm incision was made for implantation of the 5.0- or 6.0-mm lens, respectively, and two 1.5-mm incisions were made at 2-o’clock and 10-o’clock to enable enclavation of the haptics. The surgeon injected a high-molecular weight cohesive viscoelastic, inserted the lens through the main incision, and rotated it perpendicular to the incision. A small fold of midperipheral iris was incorporated into a gap in the haptics using an enclavation tool designed for this purpose. A peripheral iridectomy or iridotomy was performed with a laser to reduce the risk of a pupillary block preoperatively or at the time of surgery. The viscoelastic was aspirated from the AC, the eye was patched, and postoperative medications were prescribed at the discretion of the surgeon.

Outcome Measures

The primary efficacy outcome measure was UCVA at 3 years. Secondary efficacy outcome measures were predictability and stability of manifest and cyclopegic refractions, patient satisfaction, and contrast sensitivity.

The primary safety outcome measure was BSCVA at 3 years. Secondary safety outcome measures were IOP, slit-lamp observations, ECD, operative complications, and postoperative adverse events.

The original analysis of ECD was performed using a single image obtained at each site on a variety of instruments, and the images were read by various site personnel. This method did not have the statistical power to rule out significant changes in ECD. A second analysis was therefore performed to increase the precision of the endothelial cell count. All readable and available images obtained at 12 sites with the Konan specular microscope were reexamined by 4 trained individuals at a central reading site who were masked as to the patient’s identity and whether the images were obtained preoperatively or postoperatively. A minimum of 100 cells in a contiguous area were counted, evaluated for hexagonality, and used to determine the coefficient of variation.

Statistical Analysis

Postoperative and operative data were tabulated to provide a descriptive profile of the study subjects and were summarized for different subgroups. Results were reported separately for all first eyes and for all second eyes. Postoperative UCVA and BSCVA were reported at each time point and were compared with preoperative values. Two-sided 95% confidence intervals (CIs) were used for specific study end point criteria (i.e., proportion of patients achieving 20/40 or better UCVA). Mean visual acuities (VAs) were reported using the logarithm of the minimum angle of resolution (logMAR) method for calculating means. Visual acuity was converted from Snellen to logMAR as 20/t = \log_{10} (x/20).

Differences in mean VA were evaluated for various subgroups using t tests and 95% CIs.

Spherical equivalent and cylinder values were reported as means and 95% CIs. Change in refractive cylinder was evaluated, as were the frequency and proportion of eyes within specific diopter amounts of their targeted refraction. The safety end points were defined a priori.

Special analyses were performed on endothelial cell count results. For each subject, endothelial cell counts were recorded 3 times at each visit and averaged.

The efficacy analysis included all first eyes of the 662 patients in the study, and the safety analysis included all eyes implanted: first eyes, second eyes of the same patient, and eyes implanted under the compassionate-use protocol expansion. Statistical significance was performed on the paired analyses using a 2-sided t test with α set at 0.05.

For the endothelial cell counts, α was set at 0.10, or 0.05 per side of the 2-sided t test. For the full population, using the method described by the International Standards Organization12 and an estimated standard deviation (SD) of 0.10, a sample of 300 subjects would ensure with 90% confidence that the true endothelial cell count decrease is ≤2% per year.

Traditional methods for estimating standard errors (SEs) assume that observations are independent. For patients implanted in both eyes, a within-subject correlation may exist. Treating correlated observations as if they were independent produces small SEs and increases the type 1 error rate for hypothesis testing. Therefore, we considered existing within-subject correlations in the analysis.

Methods for adjusting SEs for clustered (correlated) data were developed within the framework of the generalized linear model.13 This approach uses the method of scaling for adjusting SEs. The drawback of this method is that the adjustment is post hoc. It is performed after the model has been estimated and only adjusts the SEs. Liang and Zeger later extended the generalized linear model algorithm to calculate all the adjusted parameter estimates iteratively during model estimation. This method is known as the general estimating equations13–15 and is the one used here to adjust for within-subject correlation.

Results

Enrollment

Subjects were recruited from October 1997 through July 2003 at 22 investigational sites by 35 investigators in the U.S. A total of 684 subjects were enrolled: 662 in the primary analysis group and 22 under compassionate use. The efficacy results are based on the 662 first eyes enrolled.

Table 1. Subject Accountability

<table>
<thead>
<tr>
<th></th>
<th>Group A (First Eyes)</th>
<th>Group B (Second Eyes)</th>
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</thead>
<tbody>
<tr>
<td><strong>Subjects</strong></td>
<td>662 100.0</td>
<td>478 100.0</td>
</tr>
<tr>
<td><strong>Postoperative follow-up</strong></td>
<td></td>
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</tr>
<tr>
<td>3 yrs</td>
<td>232 35.0</td>
<td>154 32.2</td>
</tr>
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<td>2 yrs</td>
<td>357 53.9</td>
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<td>1 yr</td>
<td>493 74.5</td>
<td>349 73.0</td>
</tr>
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<td><strong>Ongoing subjects</strong></td>
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<td>313 65.5</td>
</tr>
<tr>
<td><strong>Discontinued subjects</strong></td>
<td>73 11.0</td>
<td>11 2.3</td>
</tr>
<tr>
<td><strong>Lens removed or exchanged</strong></td>
<td>18 2.7</td>
<td>5 1.0</td>
</tr>
<tr>
<td><strong>Died</strong></td>
<td>2 0.0</td>
<td>0 0.0</td>
</tr>
<tr>
<td><strong>Lost to follow-up</strong></td>
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<td>6 1.3</td>
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*Those who continue to be observed.

The efficacy analysis included all first eyes of the 662 patients in the study, and the safety analysis included all eyes implanted: first eyes, second eyes of the same patient, and eyes implanted under the compassionate-use protocol expansion. Statistical significance was performed on the paired analyses using a 2-sided t test with α set at 0.05.

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the mean age was 39.6 ± 7.8 years. The patient population was 85% white, 6.2% Asian, 4.1% Hispanic, 3.2% black, and 1.5% other. The predominant eye colors were brown (44.9% [297/662]) and blue (33.5% [222/662]).

The number of implants totaled 1140 in the primary analysis group (662 first eyes and 478 second eyes) and 39 for compassionate use (total N = 1179). At 3 years, 232 first eyes and 154 second eyes were available for analysis.

A number of subjects (26.9% [184/684]) were enrolled with protocol deviations. Of these, 73 had deviations in both eyes, 87 in the first eye only and 24 in the second eye only (total, 160 first eyes and 97 second eyes). Protocol deviations included patients over 50 years of age, patients with corneal disease, postop incisions were superior (68.3%; N = 203), limbal (34.4%; N = 228), and scleral (31.4%; N = 208), with a sclera tunnel in 3.5% (N = 23). Most incisions were superior (68.3%; N = 452), with temporal at 31.4% (N = 208) and inferior at 0.3% (N = 2).

Peripheral iridectomy or iridotomy was performed in all except 10 (1.5%) first eyes. Three had limbal relaxing incisions, and 1 had a punctual plug insertion. Seven (1.1%) had iris prolapse, and 1 each (0.2%) had a detached Descemet’s membrane or reaction to anesthesia or required lens repositioning intraoperatively.

## Efficacy Outcomes

### Uncorrected Distance Visual Acuity

Preoperative UCVA was 20/400 (Snellen) or worse in the majority of first eyes (92.0% [609/662]). Postoperative UCVs were 20/40 or better in 84.0% (194/231) and 20/25 or better in 51.9% (120/231) of the 3-year cohort (Table 2). Uncorrected VA was worse than 20/40 in 16.0% (37/231). One subject had missing VA data at the 3-year visit. Proportions of eyes achieving 20/40 or better UCVA were roughly equal for both models (82.2% [129/157] and 87.8% [65/74]).

Of the 434/662 (65.0%) eyes for which emmetropia was the goal, 150 were evaluated 3 years postoperatively. Uncorrected VA of 20/40 or better was achieved in 88.0% (132/150), and 20/20 or better was achieved in 34.6% (52/150) of eyes. Twelve percent (18/150) had UCVA worse than 20/40, primarily due to refractive error and residual astigmatism. Among eyes targeted for emmetropia with preoperative BSCVA of 20/20 or better, 92% (81/88; 95% CI, 86.2%–97.9%) achieved UCVA of 20/40 or better and 44.3% (39/88; 95% CI, 28.7%–59.9%) achieved UCVA of 20/20 or better at 3 years.

The majority of eyes (71.7%) had an MRSE within 0.5 D of target, and nearly all (94.7%) were within 1.0 D of target refraction at 6 months and later. The mean change in MRSE between consecutive visits (6 months–1 year, 1–2 years, 2–3 years) was −4.6 to −21.9 D (N = 662). Most implants (80.0% [530/662]) were model 204 (6 mm optic), with a mean power of −11.9 ± 2.2 D and range of −5 to −15 D. Another 132 (20.0%) were implanted with the model 206 (5 mm optic), with a mean power of −15.9 ± 2.79 D and range of −8 to −20 D. Incision sizes were 6.2 ± 0.2 mm with the model 204 and 5.5 ± 0.5 mm with the model 206. Incision types were divided almost equally among corneal (30.2%; N = 203), limbal (34.4%; N = 228), and scleral (31.4%; N = 208), with a sclera tunnel in 3.5% (N = 23). Most incisions were superior (68.3%; N = 452), with temporal at 31.4% (N = 208) and inferior at 0.3% (N = 2).

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### Contrast Sensitivity

Contrast sensitivity data were obtained for 57 eyes of 31 subjects and were analyzed by eye. No contrast sensitivity decrease was seen under photopic conditions, photopic conditions with glare, and mesopic lighting conditions. Statistically significant differences, where present, showed better contrast
sensitivity postoperatively than preoperatively (Figs 3, 4), with the sole exception of mesopic contrast sensitivity with glare at 18 cycles per degree (not shown), for which preoperative contrast sensitivity was slightly better than it was postoperatively.

Safety

Best Spectacle-Corrected Distance Visual Acuity. All first eyes had BSCVA of 20/40 or better preoperatively, and 99% to 100% had 20/40 or better BSCVA postoperatively from the month 1 visit through 3 years. At 3 years, 54% of eyes gained and 7.5% lost lines of BSCVA (Table 3). Two eyes lost 2 lines of BSCVA—one due to RD and subsequent macular hole and the other due to posterior capsule haze developing after cataract surgery. The latter had BSCVA of 20/30 after neodymium:yttrium–aluminum–garnet (Nd:YAG) laser capsulotomy.

Induced Astigmatism. A change in refractive cylinder of $\geq 2.0$ D was seen in 2.4% (12/492) of first eyes at 1 year, 2.0% (7/355) at 2 years, and 3.5% (8/226) at 3 years.

Secondary refractive procedures were performed in 16 of 230 (6.9%) eyes: arcuate keratotomy (3 eyes), LASIK (11 eyes), limbal relaxing incisions (1 eye), and photorefractive keratectomy (1 eye). The result was UCVAs of 20/20 or better in 6 eyes, 20/25 to 20/40 in 6 eyes, and 20/50 to 20/100 in 4 eyes.

Intraocular Pressure. Mean preoperative IOP for all first implanted eyes was 14.6 mm Hg and was similar to baseline at most study examinations. Eighteen of 1140 eyes (1.6%) had IOPs $> 30$ mmHg, with most occurring 1 day postoperatively and none that persisted beyond 20 days after surgery. Most cases were attributed to retained viscoelastic or steroid response. One eye, in which a peripheral iridotomy was not performed, developed a pupillary block.

Slit-Lamp Findings. Transient postoperative inflammation, as evidenced by cells and flare, was 40.3% at day 1 (266/660)—of which 30.6% (202) was mild, 8.5% (56) was moderate, 0.3% (2) was severe, and 0.9% (6) was not rated—and decreased to 8.3% at weeks 2 and 3 (52/630) and 3.6% at months 1 and 2.

Iris pigment was often noted adherent to the corneal endothelium or to the IOL and was asymptomatic. Iris pigment precipitates, likely caused by surgery and iris manipulation at the attachment sites, also decreased over time. Iris pigment precipitates were seen in 6.8% (45/660) of first eyes at the days 1 and 2 visit, 9.0% (57/630) at the weeks 1 and 2 visit, 9.4% (61/645) at the months 1 and 2, 6.9% (40/581) at months 4 to 6, then progressively lower, with no reports at year 3.

Corneal edema was noted in 19.4% (128/660) of first eyes on postoperative day 1. Most occurrences were recorded as mild, and very few were rated moderate or severe. By 2 weeks, the prevalence dropped to 2.2% (14/630), and most were mild.

The most common pupil-related report was of an asymptomatic oval pupil. The incidence decreased considerably from 13.0% (86/660) at day 1 to 1.7% (10/581) at the 4- to 6-month visit. One subject (0.4%) was reported to have an oval pupil at 3 years. Progressive distortion of the pupil was not reported.

Endothelial Cell Counts

The original analysis of the endothelial cell counts did not provide good statistical power to rule out significant changes in ECD. The mean change from baseline at 3 years was $0.4\% \pm 24.5\%$, and SDs ranged from 17.5% to 24.5%. The original protocol allowed the gathering of data with various instruments. As technology improved, the protocol was changed, but it was not possible to reacquire preoperative data.

As a result, a post hoc analysis was conducted on a subset of patients for whom 3 Konan specular microscopy images were available. The best of the 3 images was analyzed for this group of 353 eyes of 215 subjects (Table 4). The mean percent change from baseline at 3 years was $4.8\% \pm 7.8\%$ (90% CI, $-6.0\%$ to $-3.5\%$), with a change of $-2.4\% \pm 6.3\%$ between 2 and 3 years (90% CI, $-6.0\%$ to $-3.5\%$).

Figure 3. Contrast sensitivity under photopic conditions without glare preoperatively and within 1 year of Verisyse implantation (n = 31). Contrast sensitivity was significantly better postoperatively at 1.5 and 6 cycles per degree of visual angle.

Figure 4. Contrast sensitivity under photopic conditions with glare preoperatively and within 1 year of Verisyse implantation (n = 31).
Secondary surgical interventions are shown in Table 6. These

Adverse Events

We further analyzed a consistent cohort of 57 eyes with endo-
thelial cell counts for all visits. The mean change from baseline
ECD was $-3.8\% \pm 9.8\%$ at 3 years (Table 5). The estimated
change over the entire study was $-1.7\% \pm 5.4\%$ (90% CI, $-2.3\%$
to $1.1\%$).

There was no change in the percent of hexagonal cells or the
coefficient of variation after surgery.

Adverse Events

Secondary surgical interventions are shown in Table 6. These
included inadequate lens fixation resulting in IOL dislocation (5
cases). Twenty preventative repositioning procedures were also
performed in cases in which the original IOL fixation was deemed
insufficient. Approximately half (31/61) of the adverse events and
repositionings were seen in the first 10 cases performed by each
surgeon.

Retinal detachments occurred in 0.51% (6/1179) of eyes, or a
rate of approximately 0.3% per eye per year. All were in subjects
with an MRSE between $-11.50$ D and $-18.6$ D. Three of 1179
(0.25%) subjects developed significant lens opacities that required
cataract extraction (CE). These subjects were 47, 50, and 56 years
old, and the lens opacities were reported as nuclear sclerosis. Two
were in the protocol deviation substudy, and both had family
histories of early cataract development. The 47-year-old had an
initial complication of elevated IOP attributed by the investigator
to retained viscoelastic.

Discussion

The results of this study indicate that the Verisyse phakic IOL corrects the refractive error in patients with high myopia with a high degree of predictability, long-term stability, and improvement in contrast sensitivity. Uncorrected distance VA was excellent, despite the fact that only 1.0-D lens power increments were available, patients with preoperative astigmatism were included, and postoperative refractive surgery was not allowed by the protocol. Adverse events were infrequent and occurred more often during early cases, when surgeons were relatively inexperienced. It is impor-
tant to note that the decision as to whether to perform surgery in the second eye may have been related to the success of the first eye, and for this group, we analyzed the data accordingly.

Unlike IOLs for aphakia, phakic lenses are implanted in a relatively young population, and the possibility of progressive endothelial cell loss over a lifetime is a concern.

Obtaining accurate endothelial cell counts was a chal-
lege in the current study due to poor reproducibility from
multiple observers, multiple methods of measuring the cell
counts, lack of consistent training, and machine-related is-
issues, but these inconsistencies were typical of clinical pro-
tocols that were written at the time this study was designed. As

technology improved, the protocol was modified, but it
was not possible to recapture preoperative endothelial cell
images.

Landesz et al reported a similar difficulty.15 Small
changes could not be measured accurately using the Topcon
2000 specular microscope (Topcon Corp., Tokyo, Japan),

Table 5. Changes in Endothelial Cell Density for Consistent Cohort

<table>
<thead>
<tr>
<th>Baseline to</th>
<th>N</th>
<th>Mean Change from Baseline (Paired Analysis) (% ± SD)</th>
<th>Equivalent Yearly Rate (%)</th>
<th>P Value between Consecutive Periods</th>
<th>90% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>6 mos</td>
<td>57</td>
<td>0.52±9.0</td>
<td>-1.04</td>
<td>NA</td>
<td>-1.44</td>
</tr>
<tr>
<td>1 yr</td>
<td>57</td>
<td>-1.09±8.7</td>
<td>-1.09</td>
<td>0.331</td>
<td>-2.99</td>
</tr>
<tr>
<td>2 yrs</td>
<td>57</td>
<td>-1.43±9.5</td>
<td>-0.71</td>
<td>0.842</td>
<td>-3.50</td>
</tr>
<tr>
<td>3 yrs</td>
<td>57</td>
<td>-3.80±9.8</td>
<td>-1.27</td>
<td>0.189</td>
<td>-5.94</td>
</tr>
</tbody>
</table>

NA = not applicable; SD = standard deviation
resulting in a significant and clinically unlikely gain in ECD of >10% in 17 of the 78 eyes in their study.

The endothelial cell counts reported by Budo et al in the 3-year multicenter study of the Artisan/Verisyse phakic lens in Europe showed cell density decreases of 4.8% at 6 months, 2.4% at 1 year, 1.7% at 2 years, and 0.7% at 3 years from a mean baseline of 2876±410 cells/mm² in 129 eyes (method not reported).8

Pop and Payette reported 2-year endothelial cell densities in the first 765 eyes enrolled at 25 North American sites in the clinical trial for the U.S. Food and Drug Administration.17 The mean preoperative endothelial cell count was 2631±442 cells/mm². Most of the measurements (98.4% of eyes) were made with noncontact specular microscopy. None of the changes from baseline was statistically significant.

In the current study, the reanalyzed equivalent yearly rate of change in ECD over the entire study was −1.7% per year. The stability of the percent of hexagonal cells indicates that the implanted lens does not continue to stress the endothelium.

The current study showed some induced astigmatism, as expected due to the large incision. The impact on postoperative UCVA was minimized by selective incision placement and selective suture removal. Intraocular pressure rises occurred in the early postoperative period and were largely attributed to retained viscoelastic, which can be prevented by more vigorous removal during surgery. There was a case of pupillary block, IOL removal, and cataract in a patient who did not have an iridotomy. The pupillary block resolved as soon as an iridotomy was performed, emphasizing the necessity of performing the procedure before lens implantation.

Half of the adverse events occurred in the first 10 subjects implanted by each investigator, most due to improper lens fixation. Many of the subjects of this study are high myopes who are at increased risk for RD and cataracts. The RD rate in this study represents an incidence of 0.3% per eye per year in a population of eyes with an MRSE between −11.5 and −18.6 D, similar to RD rates reported for highly myopic individuals who do not undergo refractive surgery.18–21

Most lens opacities were nuclear, which are unlikely to be related to an implanted lens. A very few were anterior subcapsular opacities, which might be expected from surgical trauma. Three subjects required CE: 1 after removal of the lens for high IOP (pupillary block on the first postoperative day when no iridotomy had been performed) and 2 in the patients with a family history of cataracts.

The Verisyse lens had a low rate of cataract formation compared with the 44.1% (26/59) and 9.5% (2/21) reported by Menezo et al for the Adatomed 094M-1 (not commercially available) and Staar ICL (Staar Surgical, Monrovia, CA).22–24 Nuclear cataract developed in 1.5% (2/137) of eyes implanted with the Artisan lens, at a mean of 54.8±22.1 months after implantation.

In the group of eyes that underwent secondary surgical interventions after Verisyse lens implantation, more eyes gained than lost BSCVA. Two eyes lost ≥2 lines, 1 due to an RD and subsequent macular hole and 1 due to posterior capsular haze after IOL implantation. Best spectacle-corrected VA in the latter eye returned to 20/30 after Nd:YAG laser capsulotomy.

We conclude that implantation of the Verisyse phakic IOL is a safe and effective method for the surgical correction of high myopia in patients who are poor candidates for LASIK. Complications are uncommon and rarely cause loss of BSCVA. Adverse events tend to occur when surgeons are relatively inexperienced with the lens.

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References


Errata

With apologies from the authors, in the Ophthalmic Technology Assessment entitled “Optic Nerve Head and Retinal Nerve Fiber Layer Analysis” (Ophthalmology 2007;114:1937–49) line 14 (second column) of page 1938 should read “Other CSLO devices, such as the TOPCON (Topcon Corporation, Tokyo, Japan), have not been evaluated due to current unavailability of the device and limited published peer-reviewed evidence on the technology.”

With apologies from the authors of “Determinants of Normal Retinal Nerve Fiber Layer Thickness Measured by Stratus OCT” (Ophthalmology 2007;114:1046–52), an incorrect citation number was used in “Discussion.” The fifth line up from the bottom of the second column of page 1051 should cite reference 22 (Varma R, Skaf M, Barron E. Retinal nerve fiber layer thickness in normal human eyes. Ophthalmology 1996;103:2114–9) and not reference 18.
Appendix 1: The U.S. Verisyse Study Group

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Appendix 2: Brief History of the Iris-Supported Phakic Intraocular Lens

This iris-supported IOL was conceived by Prof Jan G. F. Worst in the Netherlands and first introduced by Ophtec in 1978 for the correction of aphakia after cataract surgery. More than 400,000 Worst lenses have been implanted in aphakic eyes. The lens was redesigned for implantation in phakic eyes and marketed in 1986 as the Worst–Fechner iris claw lens. More than 300 lenses were implanted before it was discontinued. The lens underwent further design changes by Ophtec and entered the market as the Worst myopia claw lens in 1991. Today, Ophtec markets the lens as the Artisan phakic IOL, and Advanced Medical Optics markets it as the Verisyse phakic IOL. The current phakic IOL design has been in use since 1991, with more than 100,000 myopic, hyperopic, and toric lenses implanted by more than 5000 surgeons worldwide. International multicenter studies and phases I, III, and interim III results of the Food and Drug Administration studies showed the lens to be a safe, effective, predictable method of correcting high myopia.8–10

Initial work on implanting a concave lens into the AC without removing the crystalline lens was performed in the 1950s and 1960s by Kelman,25 Ridley,25 Strampelli,26 Barraquer,27 and Choyce.28 Kelman and Ridley introduced tripod AC implants. Choyce developed the first quadrupedal AC lens in response to problems with the tripod implants, which had a tendency to work loose and move around the AC.25 Kelman designed an early angle-supported implant, and Baïkoff developed the ZB5M lens in the late 1980s.29 The lens significantly reduced myopia, but residual refractive error, loss of refractive stability, endothelial cell loss, and creation of oval pupils were problematic for early models. Fyodorov developed the first posterior chamber lens, but early designs were associated with a high incidence of cataract formation.30 Posterior chamber implants came to market as the Visian Implantable Collamer Lens (Staar Surgical, Monrovia, CA) and Chiron-Adatomed lens (Chiron-Adatomed GmbH, Munich, Germany). Angle-supported lenses came to market but were withdrawn due to concerns over endothelial cell loss.