Long-term endothelial changes in phakic eyes after Artisan intraocular lens implantation to correct myopia

Five-year study

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PURPOSE: To evaluate long-term endothelial cell changes in eyes that had implantation of an iris-fixated phakic Artisan intraocular lens (IOL) for moderate to high myopia.

SETTING: Casa di Cura Villa Igea, Ancona, Italy.

METHODS: Forty-nine eyes of 30 patients having implantation of Artisan IOL for moderate to high myopia were prospectively examined. Preoperative specular microscopy and serial postoperative specular microscopy (Noncon Robo SP 8000, Konan Medical) were performed to evaluate endothelial cell changes over 5 years. Endothelial cell images were collected in the central region of the cornea before surgery and 4, 12, 24, 36, 48, and 60 months after surgery. The endothelial cell density (ECD), coefficient of variation, and percentage of hexagonal cells were determined.

RESULTS: Preoperatively, the mean ECD was 2616 cells/mm^2 $\pm$ 347 (SD), the mean coefficient of variation was 39.6% $\pm$ 4.7%, and the mean percentage of hexagonal cells was 49.2% $\pm$ 6.7%. The mean endothelial cell loss from preoperatively was 2.3% at 4 months, 3.5% at 12 months, 4.7% at 24 months, 6.7% at 3 years, 8.3% at 4 years, and 9.0% at 5 years. Five years after surgery, the mean coefficient of variation was 35.9% $\pm$ 6.9% ($P = .1946$) and the percentage of hexagonal cells was significantly higher (mean 54.7% $\pm$ 10.3%) ($P = .087$).

CONCLUSIONS: Continuous endothelial cell loss was observed after surgery during a 5-year follow-up, especially during the first 2 years. A decrease in the coefficient of variation and an increase in the percentage of hexagonal cells were observed over time, reflecting the increasing stability and remodeling of the corneal endothelial cells 5 years postoperatively.

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Excimer laser refractive surgery has been successful in treating patients with mild to moderate ametropia. However, implantation of phakic intraocular lenses (pIOLs) was recently introduced as an alternative to corneal surgery for the correction of refractive errors,[1–3] especially in patients with severe ametropia. Implantation of pIOLs provides better quality of vision than excimer laser refractive surgery without the risk for haze or corneal ectasia.[4–7]

In 1978, Worst proposed the concept of iris-supported IOLs to correct aphakia during cataract surgery.[8] In the late 1980s, Worst and Fechner introduced refractive iris-supported IOLs.[9–14] Surgeons became hesitant to use these IOLs because the surgical techniques were difficult and invasive and the complications were severe,[15–19] especially those related to endothelial cell damage in eyes with biconcave model IOLs, determining corneal decompensation and bullous keratopathy.

Since 1991, improved designs, such as convex–concave pIOLs for iris fixation, have increased the

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safety and efficacy of these lenses in the correction of severe ametropia. Moreover, iris-supported pIOL implantation is considered a satisfactory and safe procedure to correct high myopia in phakic eyes, with predictable, accurate, and stable refractive results.[20–22] Nevertheless, long-term corneal endothelial cell loss remains a concern.

This prospective study evaluated the long-term (5-year) endothelial cell changes in eyes after implantation of iris-fixated pIOLs to correct high myopia.

PATIENTS AND METHODS

This study included 49 eyes of 30 patients that had Artisan pIOL implantation for moderate to high myopia. Before surgery, all patients provided written informed consent.

Inclusion criteria were older than 21 years, myopia greater than −6.00 diopters (D), stable myopia with a variation in spherical equivalent (SE) of less than −0.50 D over an 18-month preoperative period, best spectacle-corrected visual acuity (BSCVA) of at least 20/200, a normal anterior segment with an anterior chamber depth greater than 3.00 mm, an endothelial cell count of 2000 cells/mm^2 or greater, unsuccessful attempts to wear contact lenses, having contraindications to laser in situ keratomileusis on the basis of pachymetric data or other corneal shape characteristics (revealed through confocal microscopy), and intraocular pressure (IOP) of 20 mm Hg or less.

Exclusion criteria were systemic disease, corneal pathology, iris abnormalities, previous corneal or intraocular surgery, glaucoma, intraocular inflammation, and preexisting macular degeneration or high risk for retinal degeneration.

Artisan Myopia Intraocular Lens

The Artisan pIOLs used in the study (models 206 and 204, Ophtec BV) are convex–concave iris-fixated lenses. The biomaterial of the single-piece compression-molded IOLs is CQ-ultraviolet absorbing poly(methyl methacrylate). Both models have an overall length of 8.5 mm; the thickness depends on the refractive power, increasing with the negative power. Model 204, available in powers from −3.00 to −15.50 D, and has a 6.0 mm diameter optic. Model 206, available in powers from −3.00 to −23.50 D, and has a 5.0 mm diameter optic.

Preoperative Examination

The preoperative examination included uncorrected visual acuity (UCVA), BSCVA, manifest and cycloplegic refractions, slitlamp examination, tonometry (Topcon CT 80 computerized tonometer), keratometry (Nidek ARK-700), scotopic and mesopic pupillary diameters (Procyon Pupillometer, Procyon Instruments Ltd.), videokeratography (Keratron, Optikon), elevation and curvature corneal maps (Orbscan II, version 3.0, Bausch & Lomb), central corneal ultrasound pachymetry (DGH-500), axial length and anterior chamber depth measurement by ultrasonic biometry (Humphrey, model 820), confocal microscopy (Confoscan II, Nidek Technologies), iris evaluation (vaulting, position, color, and thickness), and indirect ophthalmoscopy.

Surgical Technique

All procedures were performed by the same surgeon (S.B.) between May 1999 and December 2000 using the same surgical protocol in all cases.[21] The power of the pIOL to be implanted was calculated using van der Heijde's formula[23] based on the refractive power of the cornea (mean corneal curvature (K), adjusted anterior chamber depth (0.8 mm), and the SE refractive error (spectacle correction at a 12.0 mm vertex). An Artisan model 204 IOL was implanted in patients with myopia from −6.75 to −15.50 D (SE) and model 206, in patients with myopia from −16.00 to −23.00 D (SE).

Two days before surgery, norfloxacin 0.3%, dexamethasone 0.2%, diclofenac 0.1%, and gentamicin 0.3% were administered topically 4 times a day. All procedures were done using peribulbar anesthesia comprising 6 mL of a proportional combination of lidocaine 2%, mepivacaine 1%, and mucopolysaccharidase. A scleral tunnel incision was made at 12 o'clock with a 5.5 or 6.5 mm width depending on the IOL diameter. Two lateral paracenteses were created in the cornea at 10 o'clock and 2 o'clock with a 1.5 mm width.

Acetylcholine was injected, and the anterior chamber was filled with a cohesive ophthalmic viscosurgical device (OVD) (sodium hyaluronate 1.4% [Healon GV]). The IOL was inserted from the 12 o'clock position and rotated into a horizontal position. The lens haptic was enclavated to a fold of midperipheral iris stroma using an enclavation needle at the 3 o'clock and 9 o'clock meridians to achieve perfect IOL centration. A peripheral surgical iridotomy was made at the 12 o'clock meridian. All OVD material was carefully removed by manual irrigation to avoid postoperative ocular hypertension, and the incision was closed with continuous 10-0 nylon suture. All patients received a subconjunctival injection of betamethasone and gentamicin at the end of the procedure.

Postoperative treatment included topical betamethasone 0.2% and chloramphenicol 0.5% (Betabioptal) every 4 hours for 1 week and then tapered over 4 weeks.

Endothelial Study

Endothelial images were taken at the center of the cornea using the Noncon Robo SP 8000 noncontact specular microscope (Konan Medical). The cells were analyzed using the dot method, in which the centers of approximately 80 to 100 contiguous cells are marked. The mean endothelial cell density (ECD), percentage of hexagonal cells, polymorphism, coefficient of variation, and polymegethism were also evaluated. Examinations were repeated 4 months and 1, 2, 3, 4, and 5 years after surgery.

Endothelial cell count data were based on the average of 3 measurements obtained during each visit, including preoperative and all postoperative examinations.

Follow-up

All patients were examined on the first postoperative day and 1, 3, and 6 weeks after surgery. Subsequent examinations were performed at 4 and 12 months and 2, 3, 4, and 5 years. Each postoperative examination included visual acuity, manifest and cycloplegic refractions, tonometry, slitlamp examination, endothelial specular microscopy, and indirect ophthalmoscopy.

Statistical Analysis

Microsoft Excel was used to compile the data. Statistical analysis was performed with GraphPad InStat 3 for Windows to compute descriptive statistics and 95% confidence intervals (CIs) for ECD, coefficient of variation, and percentage of hexagonal cells. A repeated-measures analysis of variance was used to compare differences between examinations. When a statistically significant difference was found, the differences between time points were further compared using the Tukey-Kramer multiple comparison test. Differences with a P value less than 0.05 were considered statistically significant. The results are given as the mean ± SD.

RESULTS

The study comprised 49 eyes of 30 patients (13 men, 17 women); 19 patients had surgery in both eyes. The mean age of the patients was 36.2 ± 7.3 years (range 22 to 52 years).

Table 1 shows the visual acuity and refractive data of patients. The mean attempted correction was −13.60 ± 4.26 diopters (D) (range −6.50 to −23.50 D). Twenty-four patients (80%) had a history of contact lens wear (16 patients for more than 20 years). The mean power of the pIOLs implanted was −13.90 ± 3.50 D (range −7.50 to −21.00 D). Of the eyes, 33 had a model 294 pIOL implanted and 16, a model 206 pIOL.

Intraoperative and Postoperative Complications

Table 2 shows the intraoperative and postoperative complications. There were no intraoperative complications in 34 eyes (69.4%). In 2 eyes (4.1%), intraoperative bleeding into the anterior chamber occurred at the time of iridectomy, in 12 eyes (24.5%) centering the lens was difficult, and in 5 eyes (10.2%) iris prolapse occurred. The IOL was damaged during the lens manipulation in 1 case, but the damage was not clinically significant.

Table 1. Visual acuity and refractive data of patients.

Parameter	Mean ± SD	Range
Preoperative		
UCVA	0.02 ± 0.1	0.01 to 0.07
BSCVA	0.8 ± 0.2	0.20 to 1.00
SE refraction (D)	−13.60 ± 4.26	−6.50 to −23.50
Cylinder (D)	−1.20 ± 1.10	0.00 to −4.00
Postoperative		
UCVA	0.56 ± 0.3	0.10 to 1.00
BSCVA	0.86 ± 0.20	0.40 to 1.00
SE refraction (D)	−1.32 ± 1.20	0.00 to −4.75
Cylinder (D)	−0.60 ± 0.70	0.00 to −3.00
IOL power (D)	−13.90 ± 3.50	−7.50 to −21.00

BSCVA = best spectacle-corrected visual acuity; IOL = intraocular lens; SE = spherical equivalent; UCVA = uncorrected visual acuity

Table 2. Intraoperative and postoperative complications.

Complication	Number of Eyes	(%)
Intraoperative		
Hypema/bleeding	2	(4.1)
Iris prolapse	5	(10.2)
IOL damage	1	(2.0)
Difficult IOL centering or enclavation	12	(24.5)
Postoperative		
Iris atrophy	8	(16.3)
Iris pigment precipitates	4	(8.2)
Ocular hypertension	4	(8.2)
Wound infection	1	(2.0)
Glare/halos	4	(8.2)
Diplopia	1	(2.0)
IOL not centered	4	(8.2)

IOL = intraocular lens

Postoperatively, 33 eyes (67.3%) had no complications. Various grades of iris atrophy (Figure 1) were observed at the site of the IOL implantation in 8 eyes (16.3%). Decentration of the pIOL optic of less than 1.0 mm (Figure 2) was present in 4 eyes (8.2%). There were no cases of pupillary block or synechia formation. Late elevated IOP not associated with pupillary block, which was observed in 4 eyes (8.2%), was probably related to the steroid treatment. No eye required explantation or repositioning of the pIOL.

Endothelial Changes

Table 3 shows the cumulative endothelial cell loss from preoperatively and at each postoperative visit. The mean postoperative cell loss was −2.3% at 4 months, −3.5% at 12 months, −4.7% at 2 years, −6.7%

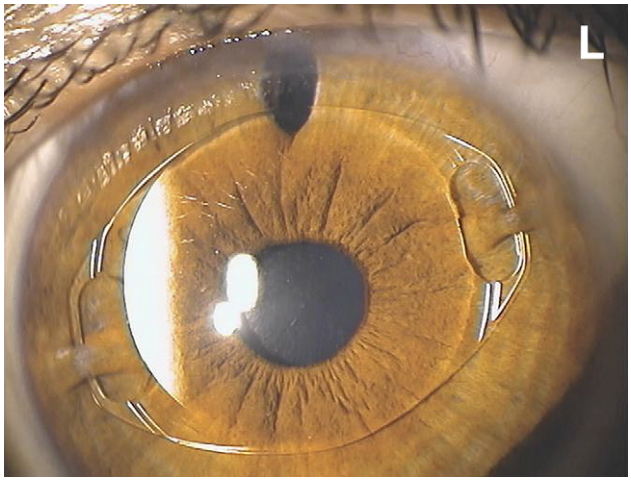


Figure 1. Iris atrophy in the fixation area due to repetuted enclavation.

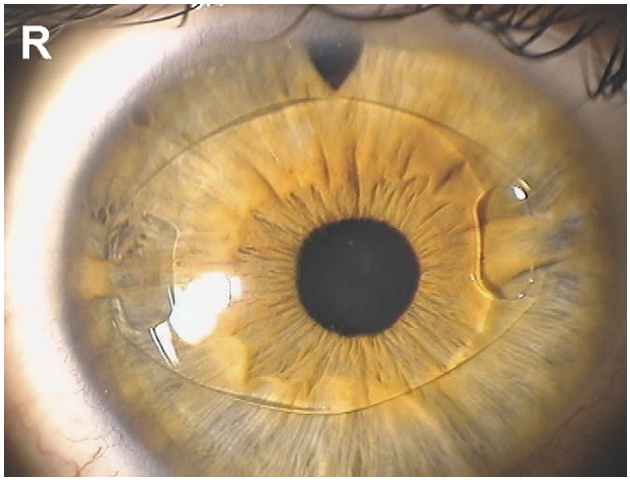


Figure 2. An example of slight IOL decentration that was not clinically significant.

at 3 years, −8.3% at 4 years, and −9.0% at 5 years. Differences in mean ECD were statistically significant at every consecutive visit ($P<.0001$).

Table 4 shows the coefficient of variation over the course of the study. The mean coefficient of variation in cell size was 37.4 ± 6.2 at 4 months, 37.6 ± 6.3 at 12 months, 36.6 ± 4.5 at 2 years, 35.8 ± 6.6 at 3 years, 36.2 ± 6.9 at 4 years, and 35.9 ± 6.9 at 5 years. A decrease in the coefficient of variation was observed over time, although the differences between the preoperative and 5-year values were not statistically significant ($P = .1946$).

The percentage of hexagonal cells increased over the course of the study (Table 5). The mean percentage of hexagonal cells was 51.1% ± 10.8% at 4 months, 52.3% ± 11.0% at 12 months, 52.4% ± 8.9% at 2 years, 55.7% ± 9.2% at 3 years, 54.7% ± 10.3% at 4 years, and 54.7% ± 10.3% at 5 years. The difference between the preoperative and 5-year percentage of hexagonal cells was statistically significant ($P = .0087$).

Figure 3 shows the ECD before and 5 years after Artisan pIOL implantation in 1 eye.

DISCUSSION

The corneal endothelium is the single cell layer that forms a physical barrier between the corneal stroma and aqueous humor. The barrier and ionic pump functions of corneal endothelial cells are essential in maintaining stromal transparency. The human corneal endothelium has a limited proliferative capacity in vivo[24] but responds by spreading out in the process of wound healing.[25] Loss of endothelial cells from increasing age, trauma, disease, or corneal surgery can reduce the density of endothelial cells and affect the ability of the endothelium to maintain its primary function.[25]

Although implantation of pIOLs is an effective and predictable method of correcting high myopia, the main problem is retaining the long-term tolerance of the corneal endothelium to the IOL. Alterations in the corneal endothelium depend on surgical technique and style; although endothelial cell loss is mainly the result of surgical trauma, continuous endothelial cell loss can occur. Endothelial cells can be injured by direct contact with surgical instruments or the IOL during surgery. Late corneal decompensation often occurs in the absence of direct intraoperative endothelial trauma. These complications can be explained by the toxic effect of inflammatory mediators on the corneal endothelium.[26]

Analysis of ECD is a simple procedure that provides important information on the corneal endothelium; however, endothelial cell morphometry is the most sensible index of corneal endothelial functional reserve.[26,27] Endothelial cell damage not only diminishes cell density, it also alters the normal morphometric endothelial pattern. The coefficient of variation in cell size, measure of cell-size variation (polymegethism), percentage of hexagonal cells, and measure of cell pleomorphism are independent of cell density. In fact, they offer a more sensitive indication of endothelial cell damage and functional reserve than cell density alone.

Table 3. Descriptive statistics and 95% CIs for ECD.

		Postoperative					
	Preoperative	4 Months	1 Year	2 Years	3 Years	4 Years	5 Years
Median	2616	2554	2523	2493	2441	2398	2379
Standard deviation	347	407	287	277	349	347	344
Standard error of mean	48.59	56.991	40.188	38.788	48,87	48,59	48.17
95% CI							
Lower limit	2518.3	2439.4	2442.2	2415	2342.7	2300.3	2282.2
Upper limit	2713.7	2668.6	2603.8	2571	2539.3	2495.7	2475.8
Cumulative cell loss (%)	—	−2.3	−3.5	−4.7	−6.7	−8.3	−9.0

CI = confidence interval

Table 4. Descriptive statistics and 95% CIs for coefficient of variation.

		Postoperative					
Parameter	Preoperative	4 Months	1 Year	2 Years	3 Years	4 Years	5 Years
Median	39.6	37.4	37.6	36.6	35.8	36.2	35.9
Standard deviation	4.7	6.2	6.3	4.5	6.6	6.9	6.9
Standard error of mean	1.086	0.8848	0.8944	0.6402	1.040	0.9823	0.9804
95% CI							
Lower limit	36.876	35.587	35.833	35.303	34.642	34.207	33.925
Upper limit	41.246	39.148	39.433	37.880	38.828	38.161	37.871

CI = confidence interval

An inverse correlation exists between the number of 6-sided cells and the coefficient of variation of cell area.[26,27] The percentage of hexagonal cells is an expression of the degree of polymorphism. The coefficient of variation is an index of variability in cell size and the mean cell size. A high coefficient of variation of cell area may be an early sign of continuing endothelial cell loss.

Several studies of Artisan iris-fixated IOL implantation report endothelial damage and cell loss[28–33]; the first studies were retrospective and did not analyze endothelial changes in detail. Previous reports of the Artisan pIOL in myopic eyes found larger endothelial cell loss, especially with biconcave model IOLs.[14,28,32]

Pérez-Santonja et al.[34] found significantly greater endothelial cell loss after pIOL implantation than after cataract surgery in 13% of eyes and 17.6% of eyes 12 months and 24 months after surgery, respectively. Menezo et al.[35] report a mean postoperative cell loss of 3.85% at 6 months, 6.59% at 12 months, 9.22% at 2 years, 11.68% at 3 years, and 13.42% at 4 years.

Landesz et al.[36] found a mean endothelial cell loss of 5.5% after 6 months, 7.21% after 12 months, 9.1% at 24 months, and 10.9% at 36 months. However, in a subsequent study,[37] they noted no significant change in ECD from baseline after 24 months. Pop and Payette[38] found no statistically significant postoperative endothelial cell loss up to 2 years after implantation of the myopic Artisan pIOL.

Bourne et al.[39] report a mean cell loss of 0.6% $\pm$ 0.5% per year over 10 years in a longitudinal study of normal unoperated eyes, correlated with the values found in previous studies conducted over shorter periods. Unfortunately, to our knowledge, published studies of endothelial morphometric data over the decades of life of subjects with high myopia have not been reported.

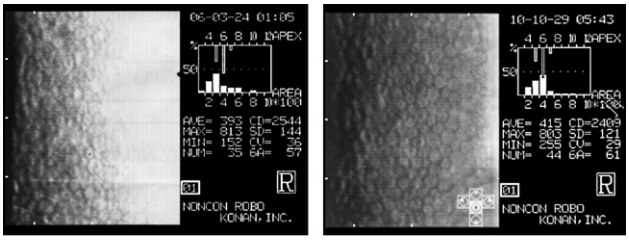
Our study showed a continual decrease in ECD after pIOL implantation that was significantly greater than in unoperated eyes. The endothelial cell loss was 2.3% at 4 months, 3.5% at 12 months, 4.7% at 24 months, 6.7% at 3 years, 8.3% at 4 years, and 9.0% at 5 years. Our results show that the latest generation of Artisan pIOLs induces less mean endothelial cell loss than that previously reported.

In our study, we also evaluated other possible reasons for endothelial cell loss. We have been concerned that contact lens wearers who have polymegethism would be predisposed to further endothelial cell changes after pIOL implantation. However, reversal of distribution between central and peripheral density of endothelial cells has been observed after contact

Table 5. Descriptive statistics and 95% CIs for percentage of hexagonal cells.

		Postoperative					
	Preoperative	4 Months	1 Year	2 Years	3 Years	4 Years	5 Years
Median	49.2	51.1	52.3	52.4	55.7	54.7	54.7
Standard deviation	6.7	10.8	11.0	8.9	9.2	10.3	10.3
Standard error of mean	1.103	1.546	1.574	1.273	1.414	1.476	1.467
95% CI							
Lower limit	46.983	47.990	49.117	49.806	51.072	51.743	51.742
Upper limit	51.425	54.214	55.454	54.929	56.765	57.685	57.646

CI = confidence interval



A B

Figure 3. The eye of a 24-year-old patient preoperatively (*A*) and 5 years postoperatively (*B*), at which time endothelial cell loss was −5%.

lens removal, and redistribution phenomenon may mask cell loss resulting from surgically induced endothelial trauma.[40] In this study, 80% of patients were long-term contact lens wearers, with 53.3% wearing them for more than 20 years. Our results suggest that contact lens wear does not predispose the cornea to further endothelial cell damage by an iris-claw pIOL.

In our series, the largest reduction in ECD occurred during the first 4 months postoperatively. The rate of cell loss diminished by the 4-year and 5-year follow-ups.

Moreover, although endothelial cell loss continued over the 5 years of follow-up, a decrease in the coefficient of variation and an increase of percentage of hexagonal cells were observed. This reflects the increasing stability of corneal endothelial cells over time. This pattern is more compatible with corneal remodeling than with chronic cell loss, which is characterized by coefficient of variation increases and hexagonality decreases over time. These results indicate that endothelial remodeling had already taken place and that endothelial cell loss was primarily caused by mechanical trauma to the endothelium at the time of surgery.

Further studies with a larger number of patients and a longer follow-up are needed to determine the long-term effects of Artisan pIOLs. Endothelial specular microscopy examinations before surgery and during regular intervals during the follow-up period are mandatory when using this type of pIOL.

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