Ophtec Iris Reconstruction Lens United States Clinical Trial Phase I

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Purpose: To determine the safety and efficacy of the Ophtec model 311 iris reconstruction lens for treatment of visual disturbances, such as glare or photophobia, related to partial or total absence of the human iris.

Design: Phase I multicenter, nonrandomized, investigational device study.

Participants: Ten iris reconstruction lenses were placed in 10 subjects at 6 sites.

Methods: Iris reconstruction lenses were placed in 9 patients who had lost all or part of their iris from trauma and in 1 patient who lacked iris pigmentation due to congenital albinism. Patients were examined preoperatively, intraoperatively, and postoperatively at day 1; week 1; and months 1, 3, 6, and 12.

Main Outcome Measures: Efficacy measures were uncorrected visual acuity (UCVA), glare, starbursts, and photophobia. Safety measures were best-corrected visual acuity (VA), surgical complications, and adverse events.

Results: Uncorrected VA improved in all eyes after implantation of the iris reconstruction lens. Best-corrected VA did not change significantly ($P = 0.24$). Postoperative photophobia was reduced in all 9 eyes that experienced moderate to severe preoperative photophobia. Likewise, postoperative glare was reduced in all 6 eyes with moderate to severe preoperative glare. There were no surgical complications. Adverse events included 2 cases of iritis and 1 case of macular edema.

Conclusions: Preliminary results suggest that the Ophtec model 311 iris reconstruction lens can improve UCVA and reduce glare and photophobia in patients with partial or total absence of the iris or iris pigmentation. *Ophthalmology 2004;111:1847–1852 © 2004 by the American Academy of Ophthalmology.*

Individuals who lack adequate iris tissue suffer from glare, photophobia, poor depth of field, and other visual disturbances that can cause social, mental, and/or economic problems. Artificial iris implants (Ophtec BV, Groningen, The Netherlands; Morcher, Stuttgart, Germany) have been used in Europe for over 10 years, and they have been available in the United States for approximately 5 years under special Compassionate Use Exemptions by the Food and Drug Administration.[1–14] These implants are designed to treat congenital or traumatic iris defects.

In 2002, Ophtec (Ophtec USA, Inc., Boca Raton, FL) initiated the first U.S. clinical trial of an artificial iris implant, the model 311 iris reconstruction lens (Fig 1), which is a single-piece implant made from clear and colored ultraviolet light–absorbing polymethyl methacrylate. It is designed for implantation into an aphakic or pseudophakic human eye for the correction of visual disturbances resulting from an incomplete or totally absent iris and the correction of spherical refractive error as necessary. The artificial irises are available in brown, blue, or green. Available powers range from +10.0 to +30.0 diopters (D) in 0.5-D increments. The lens is also available without power (plano). The opaque colored portion of the implant is 9.0 mm in diameter, whereas the central clear optic is 4.0 mm in diameter. The optic configuration is biconvex, and the anterior to posterior radius ratio depends on lens power. The implant has 2 C-loop haptics, each with an eyelet at the apex to provide the option to suture fixate the implant to the sclera. The uncompressed haptic diameter is 13.75 mm.

This is a report of 1-year follow-up data on the 10 eyes that were enrolled in the phase I iris reconstruction lens clinical trial. The phase I study eyes will continue to be followed for 3 years after lens implantation. Enrollment in a phase II clinical trial is currently underway.

Materials and Methods

This was a prospective, multicenter, nonrandomized, phase I U.S. Food and Drug Administration investigational device study to

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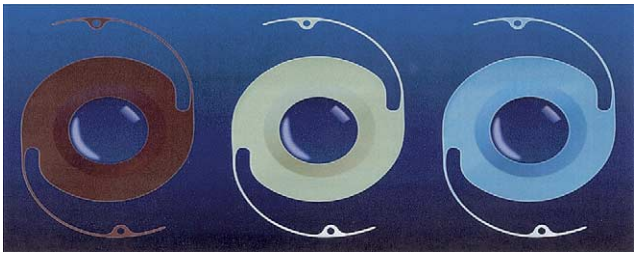

Figure 1. The Ophtec model 311 iris reconstruction lens is available in blue, brown, or green.

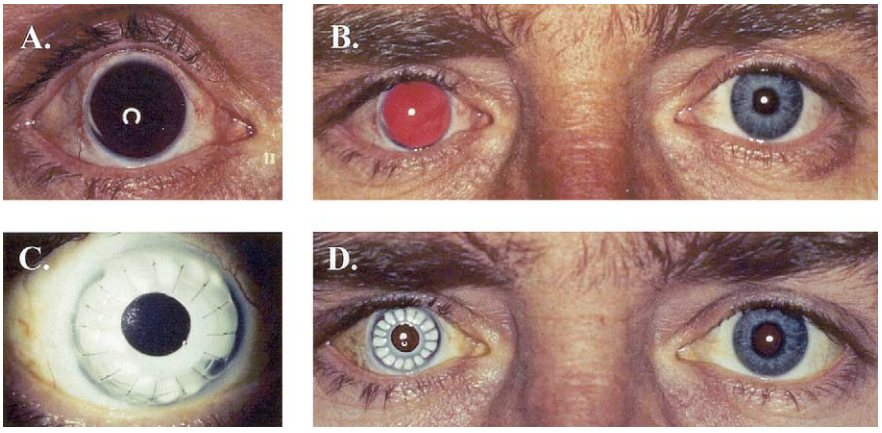

Figure 2. A, B, In case 7, 75% of the iris was missing as a result of blunt trauma, and the cornea had decompensated. **C, D**, A blue model 311 lens was suture fixated to the sclera, and a penetrating keratoplasty was performed. The radial lines are sutures in the corneal graft.

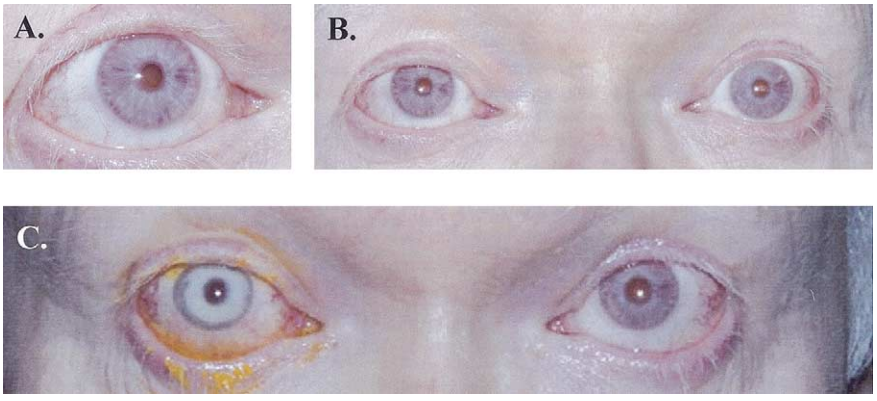

Figure 3. A, B, In case 5, there was lack of iris pigmentation due to congenital albinism. **C**, A blue model 311 lens was suture fixated to the sclera. The lens is visible through the patient's translucent iris.

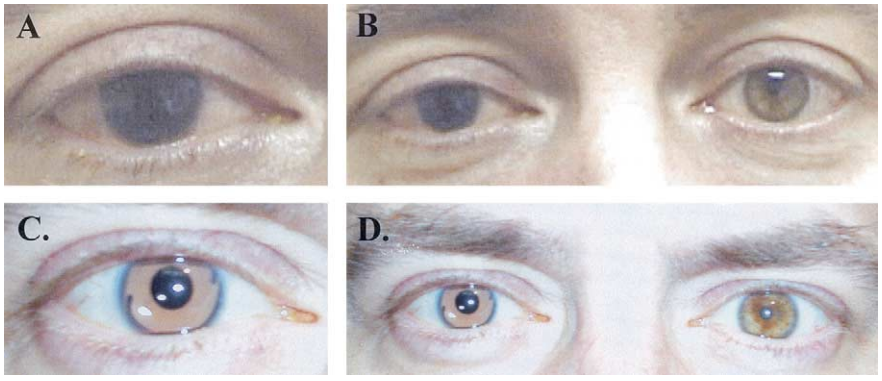

Figure 4. A, B, In case 3, over 75% of the iris was missing as a result of blunt trauma. **C, D**, A brown iris reconstruction lens was suture fixated to the sclera.

Table 1. Preoperative Pathology and Operative Data

Case	% Iris Missing	Lens Power	Lens Color	Lens Placement	Preoperative Pathology
1	75	21	Blue	Sulcus, sutured	Glaucoma Linear corneal scar Scleral buckle
2	75	22.5	Brown	Sulcus, sutured	Dense cataract, partial zonular dehiscence Traumatic mydriasis
3	>75	18	Brown	Sulcus, sutured*	Atrophic temporal scar in retina
4	50	23	Blue	Sulcus, sutured	Cornea transplant Glaucoma controlled with medication
5	<25	0	Blue	Sulcus, sutured	Ocular albinism Macular atrophy Nystagmus
6	25	24	Brown	Capsular bag	Nystagmus Full-thickness corneal scleral scar Posterior ectasia Chemical burns
7	75	19.5	Blue	Sulcus, sutured	Corneal decompensation Moderate stromal edema Moderate superficial punctate keratitis Temporal macular scar Scleral buckle
8	25	0	Brown	Sulcus	Partial iris loss during phacoemulsification Cornea transplant Posterior chamber intraocular lens
9	75	17.5	Green	Sulcus, sutured*	Scleral buckle
10	75	24.5	Brown	Sulcus, sutured†	Glaucoma Cornea transplant Scleral buckle

*Pars plana vitrectomy was performed at time of iris lens placement.
†Glaucoma surgery was performed at the time of iris lens placement.

evaluate the safety and efficacy of the model 311 iris reconstruction lens. The study was conducted with institutional review board approval. All subjects read and signed an informed consent form, and the work was compliant with the Health Insurance Portability and Accountability Act of 1996. The investigators who implanted lenses in the phase I study included the authors F. Price, Chang, and Miller and Michael E. Snyder, MD (Cincinnati Eye Institute, Cincinnati, Ohio), Kenneth J. Rosenthal, MD (Rosenthal Eye and Facial Plastic Surgery, New York, New York), and R. Gale Martin, MD (Carolina Eye Associates, Greenville, North Carolina).

Before the clinical trial, toxicity testing was performed in accordance with American National Standards Institute standards for intraocular lens (IOL) implants. The testing included but was not limited to intraocular implants and histology in rabbits, muscle implants in rabbits, accelerated leaching tests, yttrium–aluminum–garnet laser tests, and photostability. The lens pigment composition is proprietary (ICI Chemical, London, United Kingdom).

Between August 2002 and January 2003, 10 iris reconstruction lenses were placed in 10 subjects who had a partially or totally missing iris (coloboma/aniridia/trauma) or other significant iris defect (i.e., absence of iris pigmentation). To be enrolled in the study, subjects were required to have clinically significant and measurable iris defect–related visual disturbances, such as glare, halos, starbursts, or photophobia. Also, for inclusion, the expected best-corrected visual acuity (BCVA) after lens implantation had to be 20/60 or better in the treated eye and at least 20/200 in the contralateral eye. At the preoperative visit, the surgeon made a drawing of the functional iris defect and estimated whether it comprised <25%, 25% to 49%, 50% to 74%, or 75% to 100% of the iris. A fixed and dilated pupil was treated as a functional iris defect.

Subjects were examined preoperatively, intraoperatively, and postoperatively at day 1; week 1; and months 1, 3, 6, and 12 after surgery. Subjects will be examined again at 24 and 36 months after surgery before exiting the study. Efficacy measures included uncorrected visual acuity (UCVA) and reduction of glare and photophobia. Safety measures included BCVA, surgical complications, and adverse events. The assessments made at postoperative visits included UCVA; manifest refraction; BCVA; intraocular pressure; specular microscopy of the corneal endothelium; and slit-lamp evaluation of the cornea, anterior chamber, lens position, and fundus. Patients were questioned regarding their use of systemic and topical medications, and they were asked to grade the degree of visual disturbances they experienced with day vision and night vision.

Statistical Analysis

Results are reported as mean ± standard deviation (SD). Changes in visual acuity (VA) were analyzed using the paired-difference *t* test. Mean manifest cylinders before and after lens implantation were compared using the 2-sample *t* test. *P* values of <0.05 were considered significant.

Results

During the study, 10 iris reconstruction lenses were placed in 10 subjects, 3 female and 7 male. The subjects ranged in age from 27 to 70 years (mean, 45; standard deviation, 15).

Seven of the 10 study eyes had suffered blunt trauma, 2 had sustained surgical trauma, and 1 lacked iris pigmentation due to congenital albinism. All 10 eyes exhibited significant preoperative

Table 2. Comparison of Preoperative and Postoperative Uncorrected Visual Acuity (UCVA), Best-Corrected Visual Acuity (BCVA), Daytime Glare, and Photophobia

Case	UCVA		BCVA		Glare		Photophobia	
	Preoperative	*Postoperative*	*Preoperative*	*Postoperative*	*Preoperative*	*Postoperative*	*Preoperative*	*Postoperative*
1	20/400	20/200	20/60	20/60	0	0	++	0
2	20/400	20/50	20/400	20/25	Dense cataract	0	Dense cataract	0
3	20/400	20/100	20/30	20/25	0	0	+++	0
4	20/400	20/50	20/40	20/25	++	0	+++	+
5	20/400	20/400	20/400	20/400	+++	0	+++	+
6	20/100	20/60	20/100	20/40	+++	+	+++	0
7	20/400	20/60	20/50	20/30	+++	+	++	+
8	20/400	20/300	20/30	20/50	++	0	++	0
9	20/400	20/70	20/30	20/20	+++	0	+++	0
10	20/400	20/125	20/25	20/70	+++	+	+++	++

+++, severe; ++, moderate; +, mild; 0, none.

ocular pathology in addition to the iris defect (Table 1). Functionally, at least 75% of the iris was missing in 6 cases, 50% was missing in 1 case, ≤25% was missing in 2 cases, and there was 1 albino eye (Table 1).

Eight aphakic eyes received lenses with power, and 1 pseudophakic eye received a plano lens (Table 1). The remaining patient had a mild cataract removed, with implantation of a low power IOL in the capsular bag and placement of a plano artificial iris in the sulcus over the intact bag. Four subjects chose the blue iris, 5 chose the brown, and 1 chose the green.

Lens implantation was performed at the time of penetrating keratoplasty in 1 eye and through a limbal incision in 6 eyes, a scleral incision in 2 eyes, and a corneal incision in 1 eye. The mean incision length was 9.45 mm. The lens was placed in the sulcus in 9 eyes and in the capsular bag in 1 eye (Table 1). Seven of the IOLs were secured to the sclera with 9-0 Prolene (Ethicon Inc., Somerville, NJ) anchor sutures.

Uncorrected VAs before iris implantation were 20/400 in 9 eyes and 20/100 in 1 eye (Table 2). After iris implantation, UCVA significantly improved ($P = 0.002$), with a mean improvement of 4 lines. Central vision was limited in case 5 by macular atrophy due to macular degeneration/macular hypoplasia. The patient reported significant improvement in overall vision after lens implantation, although this was not measurable with the Snellen acuity chart. There was no significant change in BCVA after iris implantation ($P = 0.24$). Preoperative and postoperative manifest refractions are shown in Table 3. The mean preoperative cylinder was 2.4±2.1 D, and the mean postoperative cylinder was 1.3±1.1 D, not a significant difference ($P = 0.18$).

Moderate to severe photophobia was reported by 9 of the 10 subjects before treatment; the remaining patient had a dense cataract. Implantation of the iris lens reduced photophobia in all 9 symptomatic eyes (Table 2). Likewise, 6 of the 10 subjects experienced moderate to severe preoperative glare, and all 6 symptomatic subjects reported reduced glare after implantation of the artificial iris.

There were no surgical complications. As of the most recent visit, all 10 lenses were centered, and all anterior chambers were clear. Reported adverse events included iritis (cases 2 and 10) and macular edema (case 10). In case 2, the iritis was noted 1 day after surgery, and it resolved with corticosteroid therapy by the 1-week visit; iritis is a common occurrence at the 1-day postoperative visit with any type of lens implantation. In case 10, iritis was noted at the 6-month visit and treated with corticosteroids. Cases 1, 4, and 10 had preexisting glaucoma; no new cases of glaucoma developed after lens implantation.

All 10 patients reported satisfaction with lens aesthetics and the improvement in their cosmetic appearance. Figures 2 to 5 show the preoperative and postoperative appearance of 4 study eyes.

Discussion

This study is the first U.S. multicenter study of an implantable artificial iris. Patients with partial or total aniridia are often desperate for improved vision and relief from light

Table 3. Manifest Refraction before and after Lens Implantation

Case	Preoperative			Postoperative		
	Sphere	*Cylinder*	*Axis*	*Sphere*	*Cylinder*	*Axis*
1	9.00	3.00	65	−2.75	1.75	106
2		Dense cataract		−1.50	1.00	162
3	14.25	0.25	90	−3.00	0.50	180
4	12.50	2.50	145	−3.00	2.75	120
5	10.00	0	0	−1.00	0.00	0
6	−1.75	6.00	80	−1.25	1.50	115
7	9.00	1.25	70	−1.00	3.25	94
8	−7.50	5.00	15	−2.50	2.00	137
9	9.50	1.00	95	−1.5	0.00	0
10	−19.75	2.25	98	−1.00	0.50	105

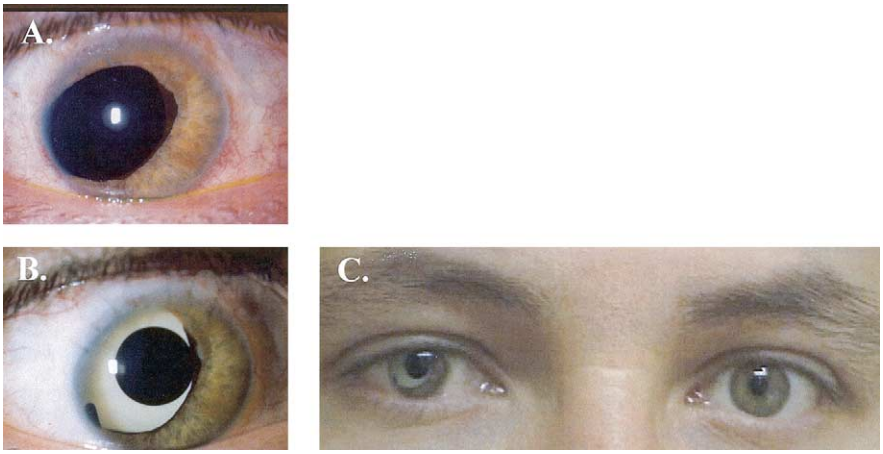

Figure 5. A, In case 9, approximately 75% of the functional iris was missing due to blunt trauma. **B, C**, A green model 311 lens was suture fixated to the sclera.

sensitivity. However, the relatively low incidence of congenital or traumatic aniridia has provided little incentive for major ophthalmic companies to seek approval of artificial iris devices in the United States due to the high costs associated with the approval process. Artificial iris implants have been available in Europe for over 10 years, but they have previously only been available in the U.S. on a compassionate use basis. The authors acknowledge the willingness on the part of both Ophtec and the Food and Drug Administration to proceed with this study, especially because many of the eyes that would benefit from this implant have significant preexisting ocular pathology that falls outside the typical guidelines for IOL studies. There were no congenitally aniridic patients enrolled in the phase I study because most could not meet the minimum VA inclusion criteria. However, patients with congenital aniridia have received treatment under exemptions to the study, and they are included in a phase II substudy.

Total or partial aniridia is disabling for most patients. Aniridic patients routinely experience what normal individuals notice when they leave a dark movie matinee and go out into bright sunshine. The lack of effective iris tissue or pigmentation allows too much light into the eye, causing not just photophobia, but also an inability to open the eye normally. Aniridic patients also lose the depth of field normally provided by a small or medium pupil (similar to the aperture effect in a camera). Moreover, these patients suffer from image degradation due to an increase in higher order aberrations in the human optical system with increased pupil size.[15] The Ophtec model 311 lens corrects these visual disabilities by providing a fixed 4-mm pupil size, which limits the amount of light entering the eye, increases depth of field, and minimizes higher order aberrations associated with larger pupil sizes. The 4-mm pupil size is a compromise between normal pupil sizes for scotopic and photopic conditions, and we have found it to be adequate for examination of the peripheral retina.

In addition to significant visual disabilities, patients with total or partial aniridia suffer many of the same psychologic and social disabilities as those with heterotropias because they often have a grossly disfigured eye. It has long been accepted that correcting heterotropias provides significant psychosocial benefit for patients, and the medical necessity of providing this improvement has long been recognized by third party medical insurance providers. Now it is possible for aniridic patients to receive comparable psychosocial benefits from an iris reconstruction lens. The model 311 lens comes in 3 colors: blue, brown, and green. These colors approximate normal iris colors and give patients an improved cosmetic appearance, as shown in Figures 2 to 5. The availability of colored implants represents a significant aesthetic improvement over earlier artificial iris implants that were only available in black.

The opaque portion of the model 311 lens has a 9-mm outer diameter, whereas the black Morcher lens designs have an outer diameter of at least 10 mm. Also, the model 311 clear optic diameter is 4 mm, compared with the Morcher lens's 5 mm. The choice of clear optic diameter and outer opaque diameter involves tradeoffs between pupil size, implant size, and the amount of opaque area blocking out excess light. The model 311 lens size seems to be a reasonable compromise. In this study, the Ophtec lens sufficiently blocked excess incident light to reduce photophobia and/or glare in all eyes that previously experienced these visual disturbances, including eyes that were missing iris tissue peripheral to the 9-mm lens diameter. Furthermore, all patients were pleased with the cosmetic results. The model 311 lens was typically implanted through a 9.5-mm incision, which could potentially induce astigmatism. Nine of the 10 study eyes had preoperative astigmatism, and overall, there was no significant change in the mean manifest cylinder postoperatively.

The phase I study has shown that the model 311 iris reconstruction lens can improve UCVA and reduce visual disturbances, such as photophobia and glare, caused by the absence of all or part of the human iris or by lack of iris pigmentation. In addition, the study subjects were uniformly pleased with the improvement in their cosmetic appearance after lens implantation.

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