Safety and Efficacy of Colored Iris Reconstruction Lens Implantation

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• PURPOSE: **We sought to evaluate the 1- to 9-year safety and efficacy of colored iris reconstruction lens implantation in eyes with visual disturbances caused by partial or complete aniridia.**

• DESIGN: **Prospective, interventional case series.**

• METHODS: **Thirty-eight patients were implanted with Ophtec 311 colored iris reconstruction lenses at the University of California, Los Angeles as part of a larger U.S. Food and Drug Administration clinical trial. Patients in group 1 lacked corneal pathology. Patients in group 2 patients had corneal pathology, such as endothelial failure, previous transplants, or scarring. Safety measures included loss of corrected distance visual acuity (CDVA), surgical complications, adverse events, secondary interventions, and corneal endothelial cell loss. Efficacy measures included improvement in uncorrected distance visual acuity (UDVA) and subjective visual disturbances.**

• RESULTS: **Groups 1 (n = 8) and 2 (n = 30) showed improvements in CDVA ($P = .155$ and .038), UDVA ($P = .002$ and $P < .001$), and subjective visual disturbance scores at year 3. Median CDVA and UDVA declined slightly for both groups after 1-2 years. Group 2 experienced more adverse events, surgical complications, and secondary interventions. Endothelial cell loss was greater for group 2 (19.7%) than group 1 (8.05%), although this difference was not statistically significant ($P = .067$).**

• CONCLUSIONS: **Colored iris reconstruction lens implantation improved CDVA, UDVA, and subjective visual disturbances 3 years postoperatively and beyond. Adverse events, complications, and subsequent declines in visual acuity were common, however, in these eyes with complex medical and surgical histories. (Am J Ophthalmol 2020;216:174–185.** © **2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)**

Accepted for publication Mar 24, 2020.

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PATIENTS WITH PARTIAL OR TOTAL ABSENCE OF IRIS tissue from trauma, surgery, severe inflammation, or congenital defects often suffer debilitating light and glare sensitivity. In addition, they experience reduced depth of field, reduced contrast sensitivity, and decreased overall visual quality and acuity.[1] These functional impairments, along with the cosmetic concerns of patients with light-colored irises, can lead to significant quality-of-life issues and numerous economic, social, and psychological consequences.[2]

In recent years, artificial iris implants have gained popularity for treating visual and cosmetic disturbances in these eyes. The first devices were designed by Peter Choyce in the 1950s. They are the forerunners of the devices reported herein.[3] In 1994, Sundmacher and associates[4,5] first described the implantation of a 2-piece black iris diaphragm intraocular lens (IOL), comprised of a clear polymethyl methacrylate (PMMA) IOL and a black PMMA annulus. A modified PMMA capsular tension ring with a black sectoral occluder was subsequently developed by Volker Rasch and Kenneth J. Rosenthal.[6] Various modifications have been made to these devices since the early years.[7,8] In the United States, artificial iris implants have been available through Compassionate Use Device Exemptions issued by the U.S. Food and Drug Administration (FDA) for several decades.[9–14] Morcher GmbH (Stuttgart, Germany) produces a variety of black iris diaphragm intraocular lenses with clear central optics of various diameters, a black iris diaphragm, and haptics with suture-fixation islets. HumanOptics AG (Erlangen, Germany) produces the CustomFlex artificial iris, which is the first artificial device to be approved by the FDA. Their device lacks a central optic. Reper (Nizhny Novgorod, Russia) also manufactures custom artificial irises.

The first clinical trial of an artificial iris in the United States was initiated by Ophtec USA (Boca Raton, Florida) in 2002. Its model 311 iris reconstruction lens is a rigid 2-piece device with an opaque, 9-mm colored outer ring, 2 integrated C-loop haptics, and a separate 4.0-mm clear central optic. The optic is available in a range of powers (Figure 1). The device is manufactured from clinical-grade, ultraviolet-absorbing PMMA and is available in brown, blue, and green. The dioptric powers include 0.0 diopter (D; Plano) and +10.0 D to +30.0 D in 0.5-D increments. This iris reconstruction lens can be suture-fixated to the sclera or passively fixated in the ciliary sulcus or capsular bag. The 1-year follow-up report from the phase

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0002-9394
https://doi.org/10.1016/j.ajo.2020.03.036

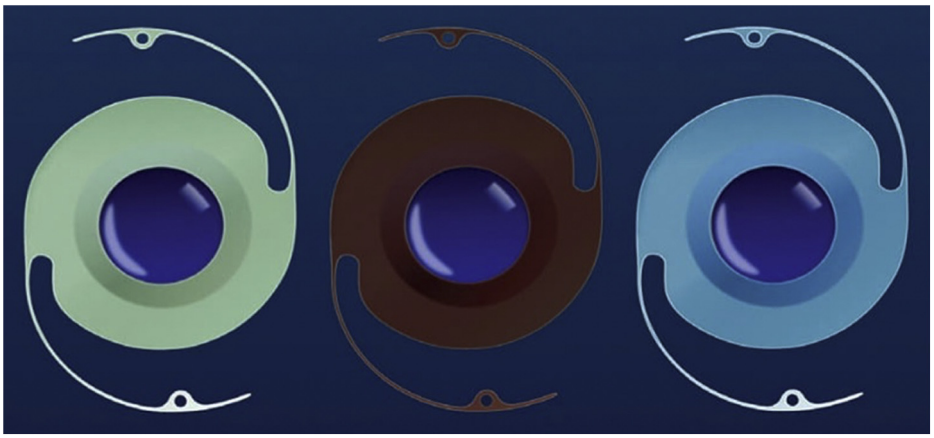

FIGURE 1. Ophtec model 311 colored iris reconstruction lenses.

1 trial of the Ophtec device showed significant improvements in both uncorrected distance visual acuity (UDVA) and subjective visual disturbances in 10 eyes with partial or total iris defects.[15] This phase had a limited patient enrollment and follow-up duration. The study was expanded shortly thereafter to include multiple investigators at multiple locations.

We aim to document the 1- to 9-year safety and efficacy of Ophtec 311 colored iris reconstruction lens implantation by evaluating the outcomes of 38 patients implanted at the University of California, Los Angeles (UCLA) during phase 3 of the trial and followed to their last recorded visit, with a focus on the effects of ocular comorbidities on the clinical course. Although this device was denied FDA approval for largely regulatory reasons, it remained available in Europe and elsewhere in the world. This report will provide valuable safety and efficacy information for current and future generations of surgeons who work with artificial irises and the device manufacturers who produce them.

PATIENTS AND METHODS

THIS PROSPECTIVE INTERVENTIONAL CASE SERIES WAS approved by the UCLA Institutional Review Board. Chart review and data collection were conducted in compliance with the Health Insurance Portability and Accountability Act of 1996. Written informed consent for participation in the clinical trial, surgical management, and publication of medical information including photographs was obtained from all participants.

UCLA was 1 study site in a larger, multicenter FDA investigational device trial. The larger study did not publish its final findings, so we decided to publish ours separately because the data are clinically relevant to the general topic of artificial iris implantation. The original study was scheduled for 1-year follow-up and excluded eyes with corneal pathology. After the study commenced, the majority of patients presenting to study sites had corneal pathology, so the study was amended to include corneal pathology and the FDA extended the follow-up interval to 3 years.

At UCLA, we recruited 40 patients who underwent surgical implantation of an Ophtec model 311 iris reconstruction lens between December 2002 and December 2009. Two patients were excluded, 1 who was lost to follow-up after 3 months and another who died 1 month after surgery from leukemia that had not been diagnosed before surgery. The remaining 38 patients (38 eyes) completed ≥1 year of follow-up. The patients were divided into 2 groups by study design as mentioned previously based on pre-existing corneal comorbidity. Patients in group 1 ($n = 8$) had clear corneas, while patients in group 2 ($n = 30$) had corneal pathologies, such as corneal endothelial failure, previous corneal transplantation, or visually significant scarring. Patients who were enrolled before the study was opened to subjects with corneal pathology were followed for 1 year. All other patients were followed for 3 years. No attempt was made to segregate groups based on comorbidities other than corneal pathology.

Patients were examined preoperatively, intraoperatively, and postoperatively at day 1; week 1; months 1, 3, and 6; years 1, 2, and 3; and at the last recorded visit. At each visit up to year 3, patients completed a survey grading the severity of their visual disturbances including daytime and nighttime glare, starbursts, and photophobia, scoring 0 = none, 1 = mild, 2 = moderate, or 3 = severe. In addition to demographic information, recorded data included the operated eye, ocular comorbidities, cause of the iris defect, and extent of the iris defect as 0-24%, 25-49%, 50-74%, or 75-100%. Postoperative data collection included UDVA, corrected distance visual acuity (CDVA), intraocular pressure (IOP), endothelial microscopy, surgical complications, adverse events, and

secondary interventions. Safety was assessed by loss of CDVA, surgical complications, adverse events, secondary interventions, and reduction in corneal endothelial cell count (ECC) as assessed by a Konan CellChek XL (Konan Medical USA, Irvine, California, USA) specular microscope. Cell counts could not always be obtained, especially in group 2. Efficacy was assessed by improvement in UDVA and subjective visual disturbance scores.

Details of the surgeries varied considerably from patient to patient based on pre-existing ocular pathologies. General anesthesia was administered most of the time, but local anesthesia with a retrobulbar block was administered occasionally. Scleral pockets were fashioned as needed. Cataract, if present, was removed by the phacoemulsification technique. Anterior or pars plana vitrectomy was performed as needed. Corneal trephination was performed when corneal scarring was significant. Otherwise, an 11-mm limbal incision was fashioned to accommodate the nonfolding Ophtec 311 implant. IOL removal was performed, as needed. The Ophtec 311 was passively fixated in the ciliary sulcus if there was adequate capsule and zonular support; otherwise, it was fixated to the sclera with 9-0 Prolene sutures. Gore-Tex sutures (W. L. Gore & Associates, Elkton, Maryland, USA) were not available at this time. Finally, a replacement corneal graft was sutured in place, if planned, or the limbal incision was closed with interrupted 10-0 nylon sutures.

For statistical analyses, Snellen acuities were converted to logarithm of minimal angle of resolution (logMAR) values. The following logMAR conversions were used for nonnumeric visual acuity values: count fingers (CF) = 1.7, hand motion (HM) = 2.0, light perception (LP) = 2.3, and no light perception (NLP) = 3.0. Visual acuity medians and means were calculated from logMAR values. Results were graphed as median ± the 25th-75th interquartile range. Changes in the visual acuity and ECC were analyzed using the Student *t* test. *P* values < .05 were considered statistically significant.

RESULTS

THE STUDY ANALYZED OUTCOMES FROM 38 PATIENTS, including 29 men and 9 women, who ranged in age from 26 to 79 years. Table 1 shows demographic information. The minimum follow-up was 1 year. The mean follow-up interval, defined as the interval between surgery and the last recorded visit, was 5.0 ± 2.0 years. Several patients were followed many years after the conclusion of the formal study.

Table 2 shows the preoperative condition of the study eyes. All 8 eyes in group 1 had iris defects measuring <50%, whereas nearly half of the eyes in group 2 (46.7%) had defects involving >50% of the iris. The most common cause of iris defect for group 1 was surgical trauma (62.5%), whereas the most common cause for group 2 was blunt or penetrating trauma (73.3%). Group 2 had significantly more preoperative ocular comorbidity, including previous corneal transplantation (43.3%), previous retinal detachment repair (36.7%), and glaucoma (30.0%). There was no view of the fundus for 10 eyes in group 2 secondary to ocular pathologies, such as dense corneal scars and corneal edema. Thirteen eyes in group 2 required concurrent penetrating keratoplasty.

TABLE 1. Demographic Information and Length of Follow-Up

	Group 1	Group 2	Total
n (%)	8 (21.1)	30 (78.9)	38 (100)
Age (y)			
Mean ± SD	66.8 ± 14.6	55.5 ± 13.2	57.9 ± 14.2
Median (range)	70 (29-78)	54 (26-79)	56 (26-79)
Sex, n (%)			
Male	8 (100)	21 (70.0)	29 (76.3)
Female	0 (0)	9 (30.0)	9 (23.7)
Race/ethnicity, n (%)			
White	8 (100)	18 (60.0)	26 (68.4)
Hispanic	0 (0)	5 (16.7)	5 (13.2)
Asian	0 (0)	3 (10.0)	3 (7.9)
Other	0 (0)	4 (13.3)	4 (10.5)
Follow-up (y), n (%)			
1	8 (100)	30 (100)	38 (100)
3	7 (87.5)	26 (86.7)	33 (86.8)
6	3 (37.5)	18 (60.0)	21 (55.3)
9	1 (12.5)	5 (16.7)	6 (15.8)
Mean ± SD	4.2 ± 1.9	5.2 ± 2.0	5.0 ± 2.0

SD = standard deviation.

Changes in median CDVA after surgery are graphed in Figure 2. The error bars represent the 25th and 75th percentiles. Error bars were not plotted for the total. Loss of CDVA was the primary safety outcome of the study. Over 3 years, group 1 experienced a 27.6% improvement in logMAR CDVA ($P = .155$) and group 2 experienced a 35.7% improvement ($P = .038$). The overall improvement for both groups was 34.1% ($P = .027$). The greatest improvement occurred between postoperative months 3 and 6 for group 1 and between postoperative months 1 and 3 for group 2. Both groups experienced a slight worsening of CDVA after years 1 and 2, respectively. At the last visit, no patient in group 1 experienced a decrease in CDVA of ≥2 lines compared with baseline and 1 patient experienced an improvement from 20/80 at baseline to 20/25 at 8.5 years postoperatively. In group 2, 7 patients experienced a decrease in CDVA of ≥2 lines at their last visit 3-8.5 years postoperatively and all but 1 was a result of corneal graft failure or rejection. For the 1 patient who was the exception, the loss of CDVA from CF at baseline to NLP at the 2-year follow-up examination was caused by protracted intraocular inflammation and end-stage glaucoma. By

TABLE 2. Preoperative Information

	Group 1 (n = 8)	Group 2 (n = 30)	Total (N = 38)
Operative eye, n (%)			
Right	4 (50.0)	13 (43.3)	17 (44.7)
Left	4 (50.0)	17 (56.7)	21 (55.3)
Extent of iris defect, n (%)			
0-24%	7 (87.5)	6 (20.0)	13 (34.2)
25-49%	1 (12.5)	10 (33.3)	11 (28.9)
50-74%	0 (0)	9 (30.0)	9 (23.7)
75-100%	0 (0)	5 (16.7)	5 (13.2)
Etiology of iris defect, n (%)			
Blunt or penetrating trauma	3 (37.5)	22 (73.3)	25 (65.8)
Surgical trauma	5 (62.5)	6 (20.0)	11 (28.9)
Congenital	0 (0)	1 (3.3)	1 (2.6)
Other	0 (0)	1 (3.3)	1 (2.6)
Lens status, n (%)			
Aphakic	4 (50.0)	23 (76.6)	27 (71.1)
Pseudophakic	3 (37.5)	5 (16.7)	8 (21.1)
Cataract	1 (12.5)	2 (6.6)	3 (7.9)
Corneal pathologies, n (%)			
Previous corneal transplant	0 (0)	13 (43.3)	13 (34.2)
Epithelial abnormality	0 (0)	6 (20.0)	6 (15.8)
Corneal edema	0 (0)	4 (13.3)	4 (10.5)
Stromal anomaly	0 (0)	3 (10.0)	3 (7.9)
Endothelial defect	0 (0)	2 (6.6)	2 (5.3)
Keratopathy	0 (0)	1 (3.3)	1 (2.6)
Corneal decompensation	0 (0)	1 (3.3)	1 (2.6)
Other ocular comorbidities, n (%)			
Previous retinal detachment	1 (12.5)	11 (36.7)	12 (31.6)
Glaucoma	1 (12.5)	9 (30.0)	10 (26.3)
Maculopathy	1 (12.5)	7 (23.3)	8 (21.1)
Synechiae	0 (0)	3 (10.0)	3 (7.9)
Iritis	1 (12.5)	0 (0)	1 (2.6)
Nystagmus	0 (0)	1 (3.3)	1 (2.6)
Other	0 (0)	3 (10.0)	3 (7.9)

comparison, 9 patients in group 2 experienced an improvement in CDVA of ≥2 lines at the last examination 3-6 years postoperatively, with the greatest changes being seen in 3 patients whose CDVAs improved from CF at baseline to 20/20, 20/30, and 20/50, respectively.

Figure 3 and Table 3 show how mean IOP varied over time. Table 3 contains the *P* values associated with IOP changes at each postoperative time point. The mean preoperative IOP was 14.0 ± 3.1 mm Hg and 14.3 ± 4.4 mm Hg for groups 1 and 2, respectively. At the last visit, the mean IOP was 12.3 ± 1.1 mm Hg for group 1 (a 12.9% reduction compared with the preoperative baseline, $P = .15$) and 12.6 ± 4.5 mm Hg for group 2 (an 11.9% reduction, $P = .18$). There was no obvious trend toward higher pressures during the study in either group, but several patients were under treatment with pressure-lowering medications during the study. One patient in group 1 was started on timolol at the 1-month postoperative visit because of an IOP increase from 15 to 22 mm Hg and was maintained on the drop with excellent IOP control. Two patients in group 2 were started on timolol and dorzolamide, and another 3 patients were started on timolol, dorzolamide, and brimonidine; all but 2 of them were eventually taken off drops. One patient in group 2 began timolol at postoperative day 1 with good IOP control, was then monitored off the drop, but experienced a spike in IOP to 35 mm Hg. The patient was started on travoprost, timolol, dorzolamide, and brimonidine at this time and eventually required tube shunt placement. Two other patients in group 2 underwent tube shunt placement. One patient, also in group 2, experienced hypotony with an IOP of 2 mm Hg with positive Seidel sign caused by loose sutures in the corneal graft. The patient underwent reoperation to resuture the graft with an eventual return of IOP back to baseline.

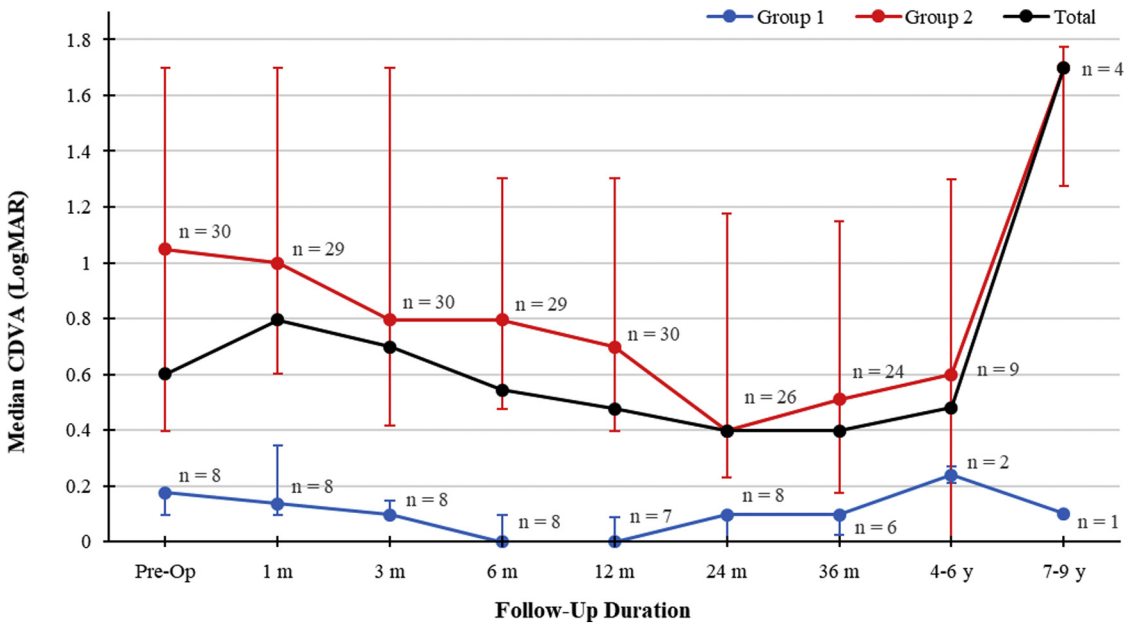

FIGURE 2. Changes in median corrected distance visual acuity after surgery. Error bars were not added to the total group. CDVA = corrected distance visual acuity; m = month; y = year.

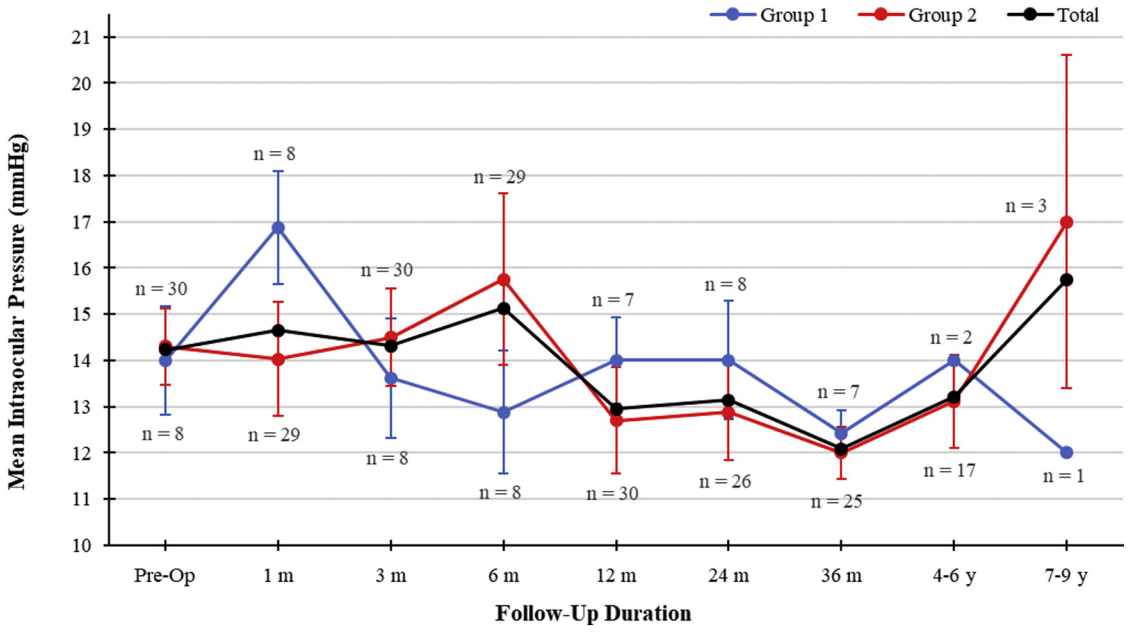

FIGURE 3. Changes in intraocular pressure after surgery. The error bars represent standard deviations. Error bars were not added to the total group.

Table 4 shows additional safety outcomes. Fifteen adverse events were reported in 14 patients during the formal 3-year study (3 in group 1 and 12 in group 2). Only 1 was considered to be device related. Six months after surgery, 1 patient in group 1 presented with a slight inferior displacement of the device in the absence of antecedent trauma because of zonular dehiscence. A reoperation was performed to suture fixate the device to the sclera and it remained centered for the duration of the study. Another patient in group 1 died of pneumonia between the second- and third-year follow-up examinations.

During the 3-year formal study, there were 4 intraoperative complications and 21 postoperative complications. All of the intraoperative complications occurred in group 2

TABLE 3. Mean Intraocular Pressure in mm Hg at Each Study Visit

Group	Preoperatively	No. of Months			No. of Years					Last Visit
		1	3	6	1	2	3	4-6	7-9	
1	14.0 (n = 8)	16.9 (P = .13, n = 8)	13.6 (P = .83, n = 8)	12.9 (P = .60, n = 8)	14.0 (P = .66, n = 7)	14.0 (P = 1.0, n = 8)	12.4 (P = .25, n = 7)	14.0 (P = .70, n = 2)	N/A (n = 1)	12.3 (P = .15, n = 8)
2	14.3 (n = 30)	14.0 (P = .87, n = 29)	14.5 (P = .88, n = 30)	15.8 (P = .50, n = 29)	12.7 (P = .21, n = 30)	12.9 (P = .29, n = 26)	12.0 (P = .019, n = 25)	13.1 (P = .34, n = 17)	17.0 (P = .63, n = 3)	12.6 (P = .18, n = 30)

N/A = not applicable.

eyes. In 2 instances, pre-existing Ahmed glaucoma valves impeded proper positioning of the iris reconstruction lens. There was 1 instance of scleral in-folding, which made suture closure of the surgical wound difficult. Finally, 1 eye with an opaque cornea was found to have a retinal detachment that had not been present on ultrasound examination several weeks earlier. The detachment was treated by intraocular gas tamponade and scleral buckling. The most common postoperative complications during the formal study were corneal edema (7 eyes), followed by increased IOP (5 eyes), iritis (4 eyes), and posterior capsular opacification (3 eyes).

During the 3-year formal study, there were 11 secondary surgical interventions including repeat corneal transplantation (4 eyes), glaucoma tube shunt placement (2 eyes) or removal (1 eye), Ophtec 311 repositioning (1 eye), laser capsulotomy (2 eyes), and anterior chamber washout (1 eye). There were also 11 nonsurgical interventions, all of which consisted of the administration of additional eye drops. One patient in group 1 developed iritis, an epiretinal membrane, and macular edema 1 year postoperatively. The cause was felt to be uveal irritation and the eye was treated with corticosteroid eyedrops, resulting in complete remission of the iritis and edema. One patient in group 2 developed idiopathic iritis with vitreous hemorrhage at postoperative week 2. Symptoms completely resolved after 2 months with continued use of postoperative medications.

After the formal study there were another 20 late complications and an additional 15 late surgical interventions. Seven patients experienced 10 graft failures (1 patient had multiple repeat grafts) from 4-6.5 years after device implantation, 2 of which were caused by allograft rejection. During this time period, 4 patients underwent a total of 6 procedures, including 4 penetrating keratoplasties and 2 Descemet stripping endothelial keratoplasties. These events occurred beyond the final 3-year study visit, and therefore they were not reported to the IRB. No patient in group 1 experienced corneal complications requiring additional surgery during the study.

Specular endothelial microscopy images were obtained when corneal visibility permitted at the preoperative visit and following surgery at months 6, 12, 24, and 36. A total of 21 patients (7 in group 1 and 14 in group 2) had ≥2 reliable specular microscopy images. Figure 4 shows the changes in mean ECC over the duration of follow up. On average, there was a 27.7% reduction in ECC per eye between the first and final specular microscopy measurements. The mean decrease in ECC per year was 8.05% for group 1 ($P = .047$), 19.7% for group 2 ($P < .001$), and 16.8% overall ($P < .001$). The difference in mean percent decrease in ECC per year between groups I and II was not statistically significant ($P = .067$).

Changes in median UDVA over time are plotted in Figure 5. Visits occurring after 3 years fell outside the formal study and were not subject to the rigorous data collection protocol used during the study. Thus, there is

TABLE 4. Secondary Safety Outcomes of Colored Iris Reconstruction Lens Implantation

		Complications			Secondary Interventions			
	Adverse Events[a]	Intraoperatively[a]	Postoperatively[a]	Late[b]	Surgical[a]	Nonsurgical[a]	Late Surgical[b]	Decrease in ECC/Year[a]
Group 1 (n = 8)	3	0	4	1	1	2	1	8.05% ($P = .047$)
Group 2 (n = 30)	12	4	17	19	10	9	14	19.7% ($P < .001$)
Total (N = 38)	15	4	21	20	11	11	15	16.8% ($P < .001$)

ECC = endothelial cell count.
[a]Collected prospectively during the U.S. Food and Drug Administration clinical trial.
[b]Collected retrospectively after patients exited the clinical trial.

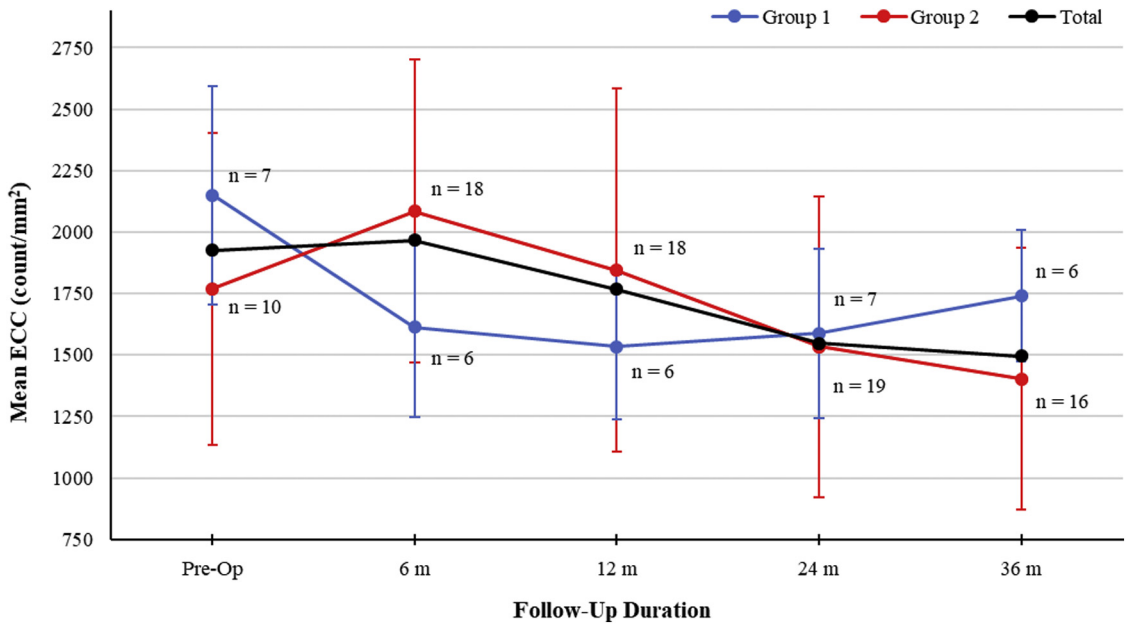

FIGURE 4. Changes in mean endothelial cell count after surgery. Error bars were not added to the total group. ECC = endothelial cell count; m = month.

discrepancy between the number of UDVAs and CDVAs reported at the 4- to 6-year and 7 to 9-year time points.

Other efficacy measures are tabulated in Table 5. The improvement in mean UDVA after 3 years was 54.1% for group 1 ($P = .002$), 36.3% for group 2 ($P < .001$), and 40.2% overall ($P < .0001$). For both groups, there was an improvement in all subjective visual disturbance scores compared with preoperative values. No patient reported worsening of daytime glare, daytime or nighttime starbursts, or daytime photophobia. Two patients reported an increase in nighttime glare, which changed from mild to moderate in both cases. Three patients reported increased nighttime photophobia by 1 scale point.

• **CASE EXAMPLES:** The following 3 case examples were selected to highlight typical preoperative presentations and postoperative clinical courses of patients in groups I and II.

Patient T.M. was 29 years of age at the time of colored iris reconstruction lens implantation. He was assigned to group 1. The photographs shown in Figure 6A were taken preoperatively. His ocular history was notable for blunt trauma to the right cheek from a golf club 5 years earlier. He underwent immediate repair of cheek fractures, followed 6 months later by a lensectomy and evacuation of intraocular clot. Three subsequent strabismus operations were performed. At the time of study surgery, he was aphakic and he had a markedly deformed iris and pupil. Under our care, he underwent anterior vitrectomy, implantation of a green iris reconstruction lens, and partial iridodialysis repair. The photographs in Figure 6B were taken 3 months after surgery. Three years after surgery, his UDVA was 20/50 and his CDVA with spectacles was 20/20 −2.

Patient P.H. was 48 years of age at the time of colored iris reconstruction lens implantation. He was assigned to group

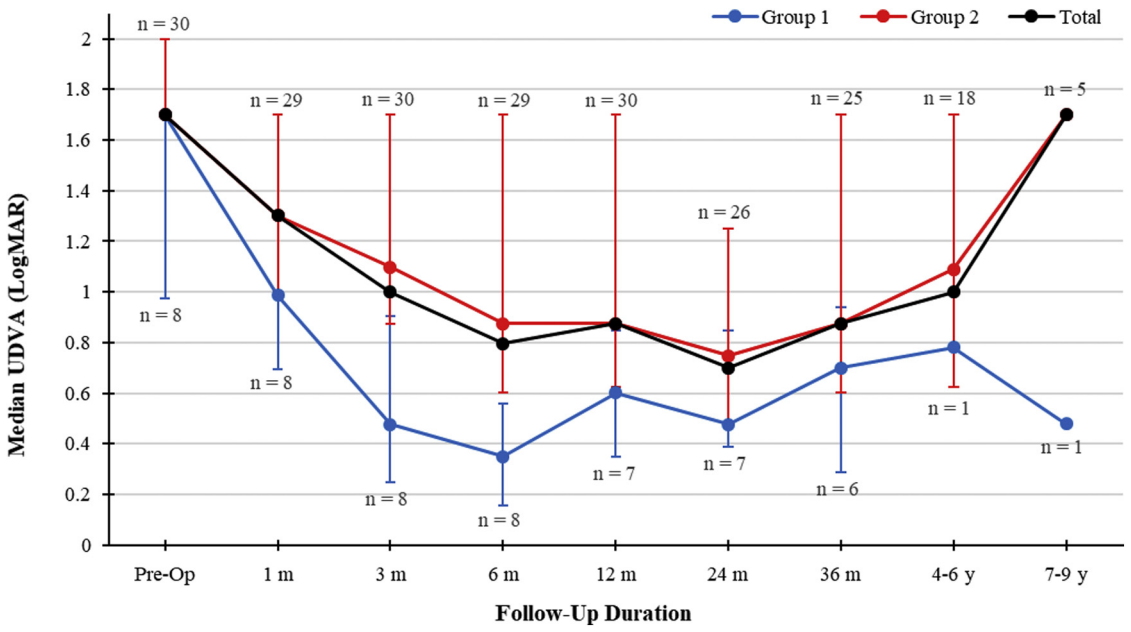

FIGURE 5. Changes in median uncorrected distance visual acuity after surgery. Error bars were not added to the total group. m = month; UDVA = uncorrected distance visual acuity; y = year.

TABLE 5. Mean Subjective Visual Disturbance Scores

	Preoperative	3 Months	1 Year	3 Years
Glare (day)				
Group 1	2.4 ± 0.70	1.5 ± 0.50	1.0 ± 0.76	1.7 ± 0.94
Group 2	2.6 ± 0.55	1.5 ± 0.67	1.3 ± 0.70	1.3 ± 0.67
Total	2.6 ± 0.59	1.5 ± 0.64	1.3 ± 0.74	1.3 ± 0.76
Glare (night)				
Group 1	2.5 ± 0.71	1.5 ± 0.50	1.0 ± 0.53	1.2 ± 0.37
Group 2	2.1 ± 0.85	1.0 ± 0.66	0.9 ± 0.68	1.0 ± 0.69
Total	2.2 ± 0.84	1.1 ± 0.66	0.9 ± 0.67	1.1 ± 0.64
Starbursts (day)				
Group 1	1.6 ± 1.22	0.6 ± 0.70	0.3 ± 0.45	0.7 ± 0.75
Group 2	1.9 ± 1.14	1.0 ± 0.89	0.8 ± 0.87	0.8 ± 0.78
Total	1.8 ± 1.16	0.9 ± 0.87	0.7 ± 0.85	0.8 ± 0.77
Starbursts (night)				
Group 1	2.3 ± 1.30	1.3 ± 0.97	0.9 ± 0.99	1.2 ± 0.90
Group 2	2.2 ± 1.08	1.1 ± 0.88	1.0 ± 0.93	0.9 ± 0.78
Total	2.2 ± 1.13	1.2 ± 0.90	1.0 ± 0.94	1.0 ± 0.81
Photophobia (day)				
Group 1	2.8 ± 0.43	1.3 ± 0.66	1.4 ± 0.73	1.8 ± 0.90
Group 2	2.7 ± 0.60	1.4 ± 0.76	1.3 ± 0.77	1.1 ± 0.80
Total	2.7 ± 0.57	1.4 ± 0.74	1.3 ± 0.78	1.3 ± 0.87
Photophobia (night)				
Group 1	2.0 ± 0.87	1.3 ± 0.66	1.4 ± 0.73	0.8 ± 0.90
Group 2	1.9 ± 0.92	1.0 ± 0.68	0.8 ± 0.65	1.0 ± 0.78
Total	1.9 ± 0.91	1.1 ± 0.69	0.9 ± 0.71	1.0 ± 0.81

2. The photographs shown in Figure 7A were taken preoperatively. His ocular history was notable for a nail injury to the left eye 35 years earlier. The nail penetrated the cornea and went through his eye, traumatizing the retina in the temporal macula. He lost his iris and lens in the process. He underwent primary repair of the globe injury followed

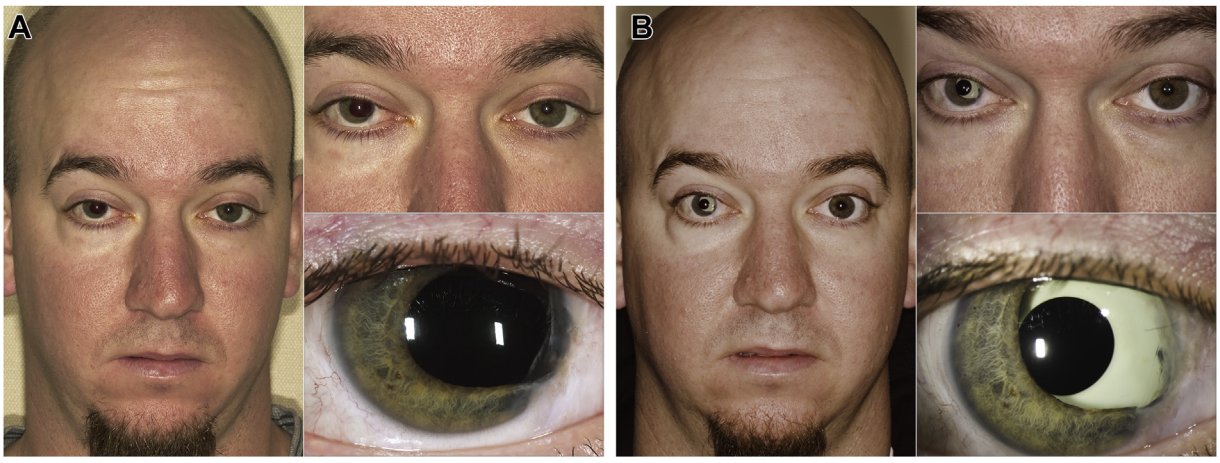

FIGURE 6. (A) Preoperative and (B) 3-month postoperative composite photographs of a 29-year-old man with a history of blunt trauma to his right cheek 5 years earlier from a golf club.

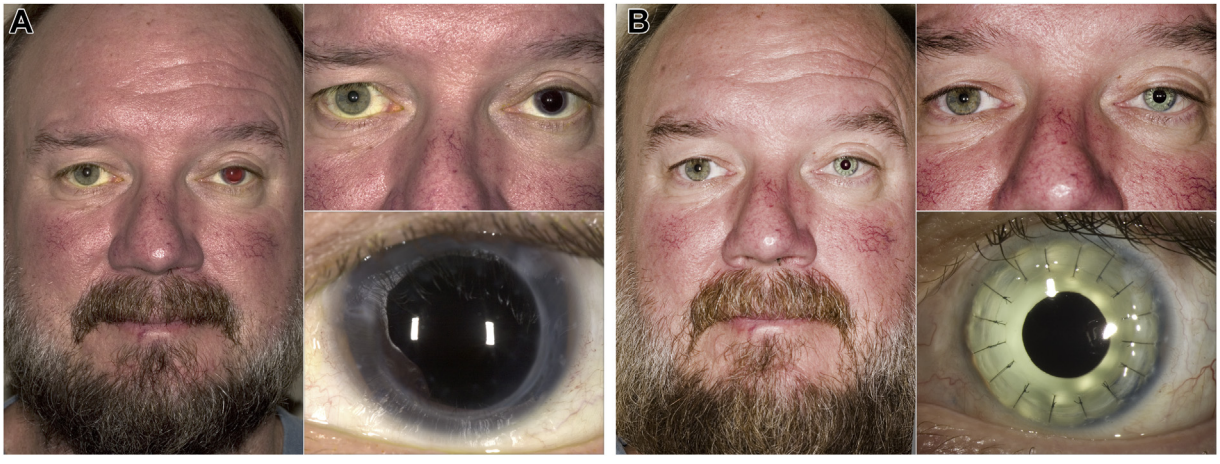

FIGURE 7. (A) Preoperative and (B) 3-month postoperative composite photographs of a 48-year-old man who suffered a nail injury to the left eye 35 years earlier.

by corneal transplantation 20 years later. He had strabismus surgery subsequently and an unrelated operation for a right cholesteatoma, which left him with a partial right VII cranial nerve paresis and poor orbicularis oculi tone. Under our care, he underwent repeat penetrating keratoplasty and scleral suture fixation of a green iris reconstruction lens. The photographs in Figure 7B were taken 3 months after surgery. Three years after surgery, his UDVA was 20/50 and his CDVA with spectacles was 20/20 −2.

Patient K.G. was 35 years of age at the time of colored iris reconstruction lens implantation. He was assigned to group 2. The photographs shown in Figure 8A were taken preoperatively. His ocular history was notable for radial and astigmatic keratotomy in the left eye. He had been assaulted 4 years earlier. The blunt injury to his left globe resulted in globe rupture and expulsion of intraocular contents including the iris and lens. He also suffered several left orbital fractures. After primary repair of the rupture and fractures, his examination was notable for aphakia with some retained lens capsule, nearly complete aniridia, and corneal scarring. Under our care, he underwent penetrating keratoplasty, residual lensectomy, anterior vitrectomy, and scleral suture fixation of a brown iris reconstruction lens. The photographs in Figure 8B were taken 3 months after surgery. Three years after surgery, his UDVA was 20/60 −1 and his CDVA with spectacles was 20/50 +1. The remaining corneal sutures were removed and he was referred for rigid contact lens fitting.

DISCUSSION

THE OPHTEC 311 COLORED IRIS RECONSTRUCTION LENS IS A 2-piece implant that is designed to correct visual

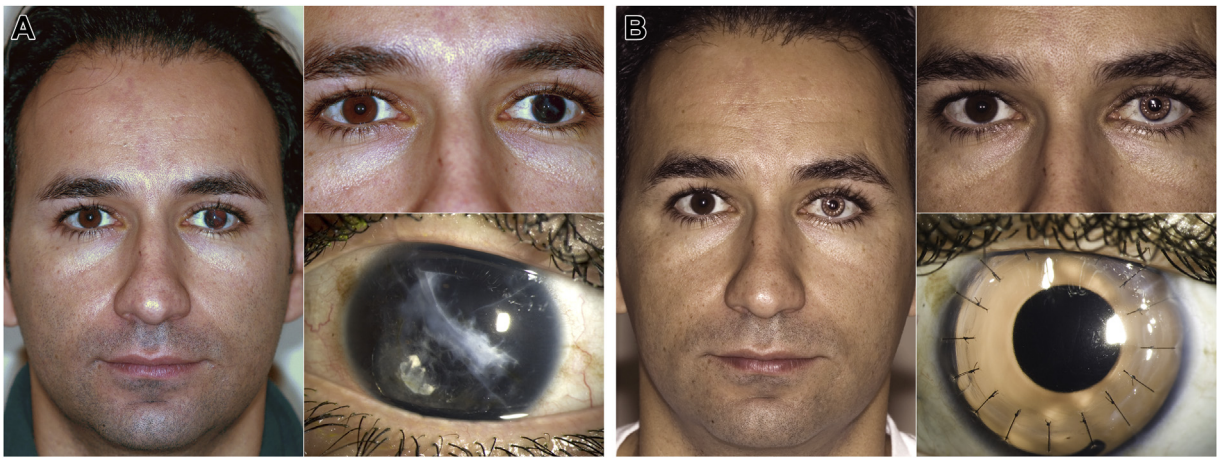

FIGURE 8. (A) Preoperative and (B) 3-month postoperative composite photographs of a 35-year-old man who was assaulted 4 years earlier. The blunt injury to his left globe resulted in globe rupture and expulsion of intraocular contents including the iris and lens.

disabilities associated with partial or complete aniridia. It consists of an opaque 9.0-mm diaphragm and a central, fixed 4.0-mm optic, which blocks excess light from entering the eye while allowing for examination of the peripheral retina via indirect ophthalmoscopy. The 2004 paper by Price and associates,[15] which reported 1-year outcomes of a phase I clinical trial of the Ophtec device in the United States, showed improvements in UDVA, visual disturbances, and cosmetic appearance after device implantation. In 2007, Miller and associates[16] confirmed those results in a 3-year follow-up study of 9 eyes that underwent combined penetrating keratoplasty and Ophtec 311 implantation. All of the patients in the 2007 report are included in this long-term follow-up study.

Two other sets of artificial iris devices are similar to the Ophtec 311. One is a series of black iris diaphragm IOLs manufactured by Morcher GmbH. Only 1 prospective study has been published on these devices to date, specifically the model 67B. The authors of the study found that black iris diaphragm IOL implantation in aphakic eyes with large iris defects was relatively safe and effective at improving CDVA and reducing light and glare sensitivity.[17] That study had a follow-up interval of 1 year. The results of the current study are similar in terms of overall outcomes at 1 year. The other is a series of acrylic artificial iris devices with integrated optics made by Reper. There are only anecdotal reports of this device in the published literature.

The current report focuses on 1- to 9-year outcomes of 38 patients who underwent implantation of the Ophtec 311 device at the Stein Eye Institute between 2002 and 2009. These patients were part of a larger US FDA clinical trial. The patients were divided into 2 groups based on the presence of preoperative corneal pathology. Group 2 patients (n = 30), who had pre-existing corneal pathology, had significantly greater iris involvement and a higher incidence of other ocular comorbidities than those in group 1 (n = 8). This discrepancy is related to the higher prevalence of uncontrolled blunt or penetrating injury in group 2 as compared with the surgical trauma sustained by most patients in group 1.

The primary safety measure of the study was loss of CDVA. Patients in both groups showed improvements in mean CDVA 3 years postoperatively compared with baseline, although only group 2 patients achieved statistical significance. The worsening of CDVA observed in both groups at 1 and 2 years, respectively, represented progression of ocular comorbidities. Group 2 patients showed a relatively greater loss. Eleven patients experienced corneal decompensation and 1 patient with advanced retinitis pigmentosa developed cystoid macular edema. Progression of glaucoma may have played a partial role in 3 patients. It is possible that device implantation accelerated these changes, but there is no way to know from the study design because there was no control group. Despite the overall improvement in CDVA experienced by patients as a whole, 2 patients (5.26%) lost CDVA compared with their preoperative status by 3 years. This is a low number given the trauma history and comorbidity load observed in the study population. Other safety measures, including surgical complications, adverse events, and secondary interventions, were more prevalent in group 2, as expected.

Efficacy measures included improvements in UDVA and subjective visual disturbance scores. By 3 years postoperatively, both groups achieved a statistically significant improvement in UDVA with group 1 showing a greater improvement than group 2. Unlike CDVA, the inflection in the graph of median UDVA over time was seen much earlier and to a greater degree than in group 1. This may be attributable in part to fluctuations in regular and irregular corneal astigmatism, which ranged from +0.25 D to +10.50 D. Another efficacy measure, the subjective visual disturbance score, showed an overall improvement in

daytime and nighttime glare, starbursts, and photophobia for both groups 3 years postoperatively.

Although cosmesis was not evaluated as part of this study, it should be noted that 1 patient in group 2 requested explantation of his colored iris reconstruction lens 1 year postoperatively because of cosmetic concerns. As previously described, this device is only available as a flat, untextured diaphragm in 1 of 3 colors: brown, blue, or green. This necessarily limits the extent to which the device can match the natural color and texture of the iris in the fellow eye. Other concerns with the implant are its relatively small outer diameter of 9 mm and relatively large pupil diameter. Recently, the CustomFlex, a custom-printed artificial iris prosthesis developed by HumanOptics AG (Erlangen, Germany), received FDA premarket approval (PMA).[18] While the CustomFlex device is foldable and offers a more natural and aesthetic alternative to the Ophtec model 311, factors such as cost and the lack of a built-in IOL need to be considered when comparing and contrasting different types of iris implants. With the HumanOptics device, a lens must be implanted separately or sutured to the iris if the eye to be implanted will be aphakic at the time of implantation. In addition, the HumanOptics device has been implicated in residual iris retraction syndrome if a fiber-containing model is trephined and contacts uveal tissue.[19]

Data from the 3-year Ophtec 311 clinical trial were presented to the FDA in a PMA application. As part of the process, the FDA asked to inspect the facility where the raw materials were manufactured. That facility was closed years earlier, but considerable material was warehoused for future device manufacture. Because the FDA was unable to inspect the manufacturing facility, the Ophtec PMA application request was denied. The device remained CE marked. Ophtec BV more recently announced at the 2019 meeting of the European Society of Cataract and Refractive Surgeons that they would discontinue sales of the Ophtec 311 on December 31, 2019 and begin sales of the Reper acrylic artificial iris instead on January 1, 2020. Despite the cessation of future sales, lessons learned from this clinical trial should benefit patients already implanted and provide guidance and benchmarking data against which to compare future artificial iris designs.

In summary, the Ophtec model 311 colored iris reconstruction lens was found to be relatively safe and effective at improving visual acuity and subjective visual disturbances caused by partial or total iris defects. As evidenced by the modest percentage of eyes that experienced adverse safety events, the risk of performing complicated surgery on eyes with significant comorbidities must be thoroughly assessed. The potential benefits of iris reconstruction lens implantation should be carefully weighed against the possibility of complications and loss of CDVA.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST. Funding/Support: The authors indicate no financial support. Financial Disclosures: Dr Miller is a consultant for Alcon Research and Johnson & Johnson Vision. All other authors indicate no financial conflict of interest. All authors attest that they meet the current ICMJE criteria for authorship.

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