Five Year Endothelial Cell Loss after Implantation with Artiflex Myopia and Artiflex Toric Phakic Intraocular Lenses

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Five-Year Endothelial Cell Loss After Implantation With Artiflex Myopia and Artiflex Toric Phakic Intraocular Lenses

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- **PURPOSE:** To evaluate the long-term changes in endothelial cell density (ECD) after the implantation of 2 types of foldable iris-fixated phakic intraocular lenses (pIOLs) for the treatment of myopia and astigmatism.
- **DESIGN:** Prospective clinical cohort study.
- **METHODS:** Two-hundred and ninety-three and 188 eyes implanted with, respectively, the Artiflex Myopia and Artiflex Toric (Ophtec B.V., Groningen, The Netherlands) iris-fixated pIOL for the treatment of myopia or astigmatism at the University Eye Clinic Maastricht as of January 2004. One-hundred and forty-six eyes from the myopic and 64 eyes from the toric groups completed a 5-year follow-up. Main outcome measures were chronic endothelial cell (EC) loss, percentage of eyes with a $\geq 25\%$ decrease in ECD, and the percentage of eyes with an ECD < 1500 cells/mm².
- **RESULTS:** Chronic EC loss showed an annual decline of 64 cells/mm² in the myopic ($P < .001$, standard error 3.58) and 62 cells/mm² in the toric ($P < .001$, standard error 3.77) groups. Total chronic EC loss from 6 months to 5 years postoperatively was 10.5% in the myopic and 10.2% in the toric groups. After 5 years, an ECD decrease of $\geq 25\%$ occurred in 4.4% and 4.3% of eyes, and an ECD < 1500 cells/mm² was reported in 3.0% and 0.0% of eyes, respectively. Explantation of a pIOL owing to EC loss was required in 3.1% and 0% of eyes.
- **CONCLUSION:** Chronic EC loss was around 10% over a 5-year period in eyes implanted with the foldable myopic (toric) pIOL. In up to 3.1% of eyes significant EC loss resulted in subsequent pIOL explantation. (Am J Ophthalmol 2018;194:110–119. © 2018 Elsevier Inc. All rights reserved.)

THE IRIS-FIXATED ARTIFLEX MYOPIA AND ARTIFLEX Toric phakic intraocular lenses (pIOLs) (Ophtec B.V., Groningen, The Netherlands) were introduced in 2005 and 2007, respectively, as an addition to the already

marketed rigid iris-fixated Artisan Myopia and Artisan Toric pIOLs (Ophtec B.V.). Owing to the configuration of the new lens, incorporating a foldable polysiloxane optic, incision size and surgically induced astigmatism (SIA) decreased significantly, and good results were obtained with respect to visual acuity (VA) and refractive correction.^{1–5} The lower refractive index of the polysiloxane material, 1.43 vs 1.49 in the rigid polymethyl methacrylate (PMMA) lens, results in a slightly thicker lens, bringing the peripheral edges of the optic closer to the corneal endothelium for a similar myopic correction.⁶ The importance of endothelial cell (EC) loss in reporting the safety of pIOLs was emphasized by guidelines formatted by the French Health Products and Safety Agency (AFSSAPS) and American Academy of Ophthalmology (AAO) in 2007 and 2016, respectively. The 2007 AFSSAPS statement regards an endothelial cell density (ECD) less than 1500 cells/mm² as a criterion for pIOL explantation.⁷ The AAO-defined endpoint refers to the percentage of eyes with a total EC loss of $\geq 25\%$ after 3 years as a safety parameter in studies on pIOLs.⁸ Currently there are no studies describing both the AFSSAPS- and AAO-defined endpoints or any data exceeding a 1- or 2-year follow-up in patients implanted with these foldable iris-fixated pIOLs.

This prospective study aims to report data on EC loss, the percentage of eyes with $\geq 25\%$ EC loss, and the percentage of eyes with an ECD < 1500 cells/mm² after a 5-year follow-up in myopic patients implanted with a foldable iris-fixated myopic or toric pIOL.

METHODS

- **DESIGN:** From January 1, 2004 to June 30, 2016, 479 eyes of 276 patients were implanted with a myopic or (myopic) toric iris-fixated pIOL at the University Eye Clinic Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands. Patients were prospectively evaluated preoperatively, and at 1 day, 1 week, and 1, 3, 6, and 12 months postoperatively in the first postoperative year. Regular follow-up continued with annual visits. The myopic pIOL was implanted in 293 eyes of 166 patients, and 137 eyes completed the 5-year follow-up. The toric pIOL was implanted in 188 eyes of 109 patients, and 63 eyes completed the 5-year follow-up.

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The current study was performed in adherence to the tenets of the Declaration of Helsinki; the Maastricht University Medical Center Institutional Review Board stated that approval was not required for this study.

• **IMPLANTATION CRITERIA:** Prior to pIOL implantation a patient had to be ≥ 18 years old and had to have a stable refraction for at least 2 years. Anterior chamber depth (ACD) from the corneal endothelium to the anterior plane of the crystalline lens had to be at least 2.8 mm with a maximal clear lens rise (CLR) of 600 μm before pIOL implantation was performed.^{9–11} Guidelines for phakic IOL implantation were formulated in 2006 by the Netherlands Society for Refractive Surgery (Nederlands Gezelschap voor Refractie Chirurgie [NGRC]). Based on this guideline, preoperative minimal ECD depended on age, with >2800 cells/ mm^2 required for patients from 21 to 25 years old, >2650 cells/ mm^2 for patients from 26 to 30 years old, >2400 cells/ mm^2 for patients from 31 to 35 years old, >2200 cells/ mm^2 for patients from 36 to 45 years old, and >2000 cells/ mm^2 in patients over 45 years old.^{9,12}

This article does not contain data of patients treated with iris-fixated pIOLs in cases of keratoconus or irregular astigmatism, or after corneal transplantation.

Data from a subset of these patients was reported in previous studies.^{1,3,6,13,14}

• **PHAKIC INTRAOCULAR LENSES AND SURGICAL TECHNIQUE:** The Artiflex Myopia pIOL is a 3-piece, polysiloxane and PMMA, foldable lens with a convex-concave optic. It consists of a 6.0 mm flexible optic, has a total diameter of 8.5 mm, and ranges from -2.0 to -14.5 diopters (D).

The Artiflex Toric pIOL is a 3-piece, polysiloxane and PMMA, foldable lens with a convex-concave optic. It consists of a 6.0 mm flexible optic and has a total diameter of 8.5 mm; it ranges from -1.0 to -13.5 D and has a cylindrical power of up to -5.0 D. Lens power calculations were performed by the manufacturer using the van der Heijde formula.¹⁵

One surgeon (R.N.) performed all pIOL implantations under general or local anesthesia at the University Eye Clinic Maastricht. Previous studies by our group have described the surgical procedure and postoperative medication regimen.^{6,13,16,17}

• **EVALUATION:** Preoperative examination consisted of subjective and cycloplegic refraction, Snellen uncorrected and corrected distance visual acuity (UDVA and CDVA) measurements, and slit-lamp examination, including Goldmann applanation tonometry and funduscopy. Additional measurements consisted of corneal topography (Orbscan [Bausch and Lomb, Rochester, New York, USA], Pentacam HR [OCULUS Optikgeräte GmbH, Wetzlar, Germany], Sirius [Schwind eye-tech-solutions GmbH & Co. KG, Kleinostheim, Germany]), biometry (A2500 [SonomedEscalon,

New Hyde Park, New York, USA], IOLMaster [Carl Zeiss AG, Oberkochen, Germany]), and specular microscopy (NONCON ROBO PACHY SP9000 S/N PK1-1137 [KONAN MEDICAL Inc, Nishinomiya, Japan], SP 3000 [Topcon Corporation, Tokyo, Japan]). All preoperative measurements were performed 1 week after removal of soft contact lenses and 2 weeks after removal of rigid gas-permeable contact lenses.

From 2006 onwards, the Visante OCT was used to perform preoperative pIOL simulation to measure the ACD, the vault between the pIOL and crystalline lens, the distance between the anterior pIOL and the endothelium, and CLR, as reported previously.^{6,9,11,18–20}

In respect of the known variation between specular microscopes and the influence of this variation on the correct calculation of endothelial cell loss, all eyes continued their follow-up measurements with the same specular microscope used during preoperative measurements. More specifically, patients measured preoperatively with the SP9000 specular microscope continued their follow-up with this device, whereas patients measured preoperatively with the SP 3000 continued their measurements with the SP 3000 specular microscope. Per protocol, the mean ECD in each eye was calculated by determining the mean of 3 consecutive measurements of 50 central endothelial cells using the manual center-to-center method.²¹

• **OUTCOME MEASURES:** The definitions of outcome measures were based on the recent guidelines of the AAO and AFSSAPS, describing the percentage of eyes reaching the AAO endpoint (ie, ECD decrease $\geq 25\%$ compared to the preoperative measurement) and AFSSAPS explantation criterion (ie, ECD < 1500 cells/ mm^2).^{7,8} We calculated the mean ECD 5 years after pIOL implantation, as well as the annual EC loss. To adhere to the AAO-defined guidelines, we not only presented the percentage of eyes meeting the AAO-defined endpoint after 5 years, but also added the percentage of eyes meeting this endpoint after 3 years.

• **STATISTICAL ANALYSIS:** Statistical analysis was performed using SPSS for Windows (version 23; IBM, Armonk, New York, USA). All visual acuity measurements were converted from Snellen VA to logarithm of the minimal angle of resolution (logMAR) prior to statistical analysis. Descriptive analyses were performed to compute mean and standard deviation (SD) in primary outcome measures and preoperative characteristics. Longitudinal changes over time were analyzed using a linear mixed-model analysis with an eye identification number as a grouping variable and time as a covariate. The best-fitted covariance structure was selected using the Bayesian information criterion. Similar to previous reports on EC loss, the effect of pIOL implantation on the endothelium was assessed from preoperatively until 6 months postoperatively (ie, acute EC loss), whereas chronic EC loss was

TABLE 1. Patient and Phakic Intraocular Lens Characteristics at Baseline

	Artiflex Myopia	Artiflex Toric
Age (y)	39.6 ± 10.6 (range 17.9 to 62.9)	40.1 ± 11.4 (range 19.4 to 63.4)
Ratio male/female (%)	35/65	38/62
Number of eyes	293	188
Number of patients	166	109
Refractive		
MRSE (D)	-9.09 ± 2.89 (range -20.5 to -1.25)	-9.22 ± 2.84 (range -15.25 to -2.50)
Cylinder (D)	-0.80 ± 0.51 (range -2.50 to 0.00)	-2.32 ± 0.88 (range -5.25 to -1.00)
Implanted lens		
Sphere (D)	-9.67 ± 2.59 (range -19.5 to -2.0)	-8.48 ± 2.83 (range -13.5 to -1.5)
Cylinder (D)	NA	-2.13 ± 0.87 (range -5.0 to -1.0)
CDVA (logMAR)	-0.007 ± 0.086 (range -0.18 to 0.52)	0.018 ± 0.117 (range -0.24 to 0.60)
IOP (mm Hg)	15.3 ± 2.9 (range 8.0 to 24.0)	15.6 ± 2.9 (range 10.0 to 23.0)
ACD (mm) ^a	3.27 ± 0.31 (range 2.75 to 3.96)	3.24 ± 0.35 (range 2.68 to 4.47)
AXL (mm) ^a	26.78 ± 1.27 (range 23.88 to 30.21)	26.92 ± 1.37 (range 23.48 to 31.03)

ACD = anterior chamber depth; AXL = axial length; CDVA = corrected distance visual acuity; D = diopters; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; MRSE = manifest refractive spherical equivalent; NA = not applicable.

Results are mean ± standard deviation unless indicated.

^aMeasured from the corneal epithelium.

TABLE 2. Mean Endothelial Cell Density in Eyes Implanted With a Rigid Iris-Fixated Myopic or Toric Phakic Intraocular Lens

Time Period	Artiflex Myopia		Artiflex Toric	
	Number of Eyes	Cells/mm ² , Mean ± SD (Range)	Number of Eyes	Cells/mm ² , Mean ± SD (Range)
Preoperatively	293	2739 ± 286 (1915-3531)	188	2769 ± 370 (1643-3871)
Acute: 6 months	206	2680 ± 336 (943-3445)	140	2697 ± 418 (1644-3813)
Chronic: 1 year	202	2657 ± 352 (1227-3447)	131	2669 ± 426 (1641-3588)
Chronic: 5 years	137	2480 ± 369 (1138-3423)	63	2488 ± 360 (1840-3399)

assessed from 6 months postoperatively until the end of follow-up. Kaplan-Meier and multivariate Cox regression analyses were performed to assess survival from implantation to the occurrence of the AAO-defined endpoint (ie, total EC loss ≥ 25%) and the AFSSAPS explantation criterion (ie, ECD < 1500 cells/mm²). *P* values were considered significant if *P* < .05.

RESULTS

BETWEEN JANUARY 2004 AND JUNE 2016, 293 EYES OF 166 PATIENTS AND 188 EYES OF 109 PATIENTS WERE IMPLANTED WITH THE IRIS-FIXATED MYOPIC AND TORIC pIOL, RESPECTIVELY. BASELINE CHARACTERISTICS OF BOTH GROUPS ARE DEPICTED IN [Table 1](#). Mean duration of follow-up was 56.9 ± 39.8 months in the myopic and 42.5 ± 31.1 months in the toric group.

In 3 eyes of 2 patients, aged 48 and 52 years, the preoperative ECD was between 1900 and 2000 cells/mm². In the toric

group 5 eyes of 4 patients had an ECD < 2000 cells/mm²; their mean preoperative age was 52 ± 4 years and their mean preoperative ECD was 1817.3 ± 112.8 cells/mm². All patients with a preoperative ECD < 2000 cells/mm² were informed on the risks of pIOL implantation in case of lower preoperative ECD counts, before opting for surgery.

• **ENDOTHELIAL CELL DENSITY:** Mean preoperative, 6-month, and 5-year ECD of the myopic and toric group are reported in [Table 2](#) and [Figure 1](#). From preoperatively to 6 months postoperatively, we found a significant acute ECD decline of 51 cells/mm² (*P* = .001, standard error [SE] 15.59) in the myopic group and a significant 6-month ECD decline of 55 cells/mm² (*P* = .007, SE 19.97) in the toric group.

In order to separate the effect of surgical trauma on ECD, chronic EC loss was measured from 6 months until the end of follow-up. Longitudinally, using linear mixed-model analysis, we found a significant annual ECD decline of 64 cells/mm² (*P* < .001, SE 3.58) in the myopic group and a significant annual ECD decline of 62 cells/mm² (*P* < .001, SE

FIGURE 1. Mean endothelial cell density from preoperatively to 10 years postoperatively in patients implanted with foldable myopic (n = 293) and toric (n = 188) phakic intraocular lenses (mean ± standard deviation).

3.77) in the toric group. The total loss from 6 months to 5 years postoperatively was 10.5% in the myopic and 10.2% in the toric group. When correcting for an annual physiological EC loss of 0.6%,^{22,23} our results show a pIOL-related total EC loss of 7.4% in the myopic and 7.5% in the toric group from 6 months to 5 years postoperatively.

Three years after implantation 2.9% of the myopic pIOL-implanted and 1.6% of the toric pIOL-implanted eyes met the AAO-defined endpoint (ie, a decrease in ECD ≥ 25%). After 5 years a decrease in ECD ≥ 25% was seen in 4.4% and 4.3% of eyes, whereas an ECD < 1500 cells/mm² (ie, AFSSAPS explantation criterion) was reported in 3.0% and 0.0% of eyes in the myopic and toric groups, respectively. None of the eyes with a preoperative ECD < 2000 cells/mm² lost 120 cells/mm² or more in the first year after pIOL implantation. Furthermore, none of these eyes suffered a ≥25% decrease in ECD, reached an ECD < 1500 cells/mm², or required explantation of their pIOL at any time during follow-up. Median survival time (ie, until 50% reached the AAO endpoint or AFSSAPS explantation criterion) was 120 months in the myopic group. Survival time could not be calculated in the toric group (Figure 2), since too few eyes had reached the defined clinical endpoints.

EC loss resulted in pIOL explantation in 9 eyes of 5 patients (3.1%) implanted with a myopic pIOL at 86 ± 26 months (range 42-127 months), postoperatively. Three out of 4 patients with bilateral explantation were prone to eye rubbing because of severe pollen allergy (1 patient), chronic irritation related to topical glaucoma therapy (1 patient), and a medical history reporting suspected Sjögren disease that was ruled out after a salivary gland biopsy (1 patient). In 2 eyes of 2 patients from the myopic group pIOL explantation owing to EC

loss had to be performed after a follow-up of less than 5 years. No explantations were performed in the toric group (Table 3). Unfortunately, it was not possible to compute a median survival time (ie, time until 50% of eyes require explantation), because of the small number of explantations.

• **RISK FACTORS:** Possible predictive factors for EC loss included preoperative ACD, distance from the central pIOL edge to the endothelium, distance from the peripheral pIOL edge to the endothelium, preoperative age, preoperative ECD, preoperative AXL, and pIOL type. Additional univariate linear mixed-model analyses were performed, but no significant predictive factors were identified ($P > .05$).

Similarly, additional univariate Cox regression analyses evaluating survival until reaching the AAO endpoint or AFSSAPS explantation criterion (ie, ≥25% EC loss or ECD < 1500 cells/mm²), as well as survival until pIOL explantation owing to EC loss, did not identify any significant influencing factors. Preoperative ACD, distance from the central pIOL edge to the endothelium, distance from the peripheral pIOL edge to the endothelium, preoperative age, preoperative ECD, preoperative AXL, and pIOL type were all analyzed and deemed insignificant ($P > .05$).

DISCUSSION

DESPITE THE MULTITUDE OF ANTERIOR CHAMBER PIOLs taken off the market owing to excessive EC loss in the past, no guidelines existed on management of corneal

FIGURE 2. Survival curve for reaching the American Academy of Ophthalmology (AAO) endpoint (ie, $\geq 25\%$ total endothelial cell loss) or French Health Products and Safety Agency explantation criterion (ie, endothelial cell density < 1500 cells/mm²), in eyes implanted with foldable myopic ($n = 293$) and toric ($n = 188$) phakic intraocular lenses.

safety in patients implanted with pIOLs until the recent publication of the AAO Task Force and AFSSAPS criteria.^{7–9,24}

The current study is the first to apply the AAO and AFSSAPS criteria over a 5-year follow-up period in eyes implanted with foldable myopic or toric pIOLs. This study stands out from previous papers on the foldable iris-fixated myopic and toric pIOLs because all surgeries were performed by the same surgeon (R.N.), all measurements were performed with the same specular microscope used prior to implantation, and all measurements were performed using the same protocol, cutting out most variation that can be induced by changing surgeons or measurement methods.^{25–28}

- **ENDOTHELIAL CELL DENSITY:** We calculated the percentage of total EC loss and the percentage of total EC loss corrected for an annual physiological loss of 0.6% by using the results of the mixed-model linear regression analyses.^{22,23} After 6 months, the acute EC loss in the myopic and toric groups was similar to the 0.05% to 4.3% short-term EC loss after 6 months reported in the literature,^{1,3,29} with 0.7% and 1.6% of eyes showing a decrease in ECD $\geq 25\%$ after uncomplicated surgery, respectively

(data on file). From 6 months to 5 years postoperatively, we found a chronic total EC loss of 10.5% and 10.2% in the myopic and toric groups, respectively. No published study has reported 5-year follow-up data, but studies with a shorter follow-up showed a total EC loss of 9.0% and 9.4% after 1 year, and 1.1% and 7.4% after 2 years.^{2,3,5,30} In over half of all cited articles the groups were relatively small^{2,5,29,30} and all papers discussed the results after a relatively short follow-up.^{1–3,5,29,30} The results of the current study show similar or lower EC loss than the results of most previous papers,^{1,2,5,29,30} with the exception of 1 study published in 2009.³ The latter reported a total EC loss of 1.07% with a high standard deviation of 16.35% after 2 years, which might be explained by the study being a multicenter study. Patients were included in 12 countries, resulting in more than 12 different surgeons and sites. In that study, neither the method nor the specular microscope used to measure endothelial cell density was described. Variable and insufficiently specified measurement methods, as well as the use of different specular microscopes in multiple clinics, may lead to a high variability and a large standard deviation, as well as less reliable outcomes. Additionally, all previously mentioned studies relied on comparing means (ie, *t* test), using nonparametric tests or

TABLE 3. Incidence and Indications of Phakic Intraocular Lens Explantations in Patients Implanted With Foldable Iris-Fixated Myopic and Toric Phakic Intraocular Lenses

	Artiflex Myopia (N = 293)			Artiflex Toric (N = 188)		
	No. Eyes [Patients]	Ratio (%)	Time (mo)	No. Eyes [Patients]	Ratio (%)	Time (mo)
Cataract	14 [11]	4.78	75.4 ± 34.2 (4.7–130.7) ^a	1 [1]	0.53	7.8
EC loss	9 [5]	3.07	85.6 ± 25.7 (42.5–126.6) ^a	NA	NA	NA
Cataract after retinal surgery	2 [2]	0.68	21.0 and 18.0	2 [2]	1.06	15.0 and 23.0
EC loss after retinal surgery	1 [1]	0.34	23.4	NA	NA	NA
High IOP	1 [1]	0.34	15.4	NA	NA	NA
Excessive pigment on pIOL	NA	NA	NA	1 [1]	0.53	6.4

EC = endothelial cell; IOP = intraocular pressure; NA = not applicable; pIOL = phakic intraocular lens; VA = visual acuity.

^aMean ± SD (range).

descriptive statistics to present their work.^{1–3,5,29,30} However, when testing for a longitudinal change during a follow-up period with multiple visits, mixed-linear regression analyses are preferred.

Additional outcome parameters were added based on guidelines published by the AAO Task Force and AFSSAPS.^{7,8} As previously mentioned, prior to the January 2017 publication by the AAO Task Force, no guidelines existed on standardized reporting of ECD after refractive surgery.⁸ The AAO guideline focuses on reporting the percentage of eyes that had lost ≥25% of ECD after 3 years with a pIOL present. Application and interpretation of this guideline is complicated by the fact that no cutoff points are reported with respect to the percentage of eyes that are allowed to experience an EC loss ≥ 25% before a pIOL is deemed unsafe and should be taken off the market, nor does it specify whether a ≥25% EC loss requires pIOL explantation in an individual patient. Contrary to the AAO Task Force, the AFSSAPS did report either an ECD < 1500 cells/mm² or ≥30% EC loss as reasons for explantation in an individual patient but also failed to supply criteria that should indicate when the pIOL should be taken off the market.⁷ Because pIOL explantation will have an enormous impact on young, highly myopic patients who want to remain spectacle independent, the decision to explant a pIOL should be very well substantiated and preferably based on a global consensus.

Adhering to the AAO guidelines 2.9% and 4.4% of eyes in the myopic group reached an endpoint of ≥25% EC loss after 3 and 5 years, respectively. Similarly, the toric group showed 1.6% and 4.3% of eyes with ≥25% EC loss. The only other study reporting the AAO endpoint focused on rigid myopic and toric iris-fixated pIOLs and reported a lower percentage of eyes with ≥25% EC loss after 5 years (ie, 1.8% and 3.2%, respectively).³¹ In line with the above-mentioned study on rigid pIOLs, we reported an ECD < 1500 cells/mm² after 5 years in up to 3.0% of eyes, as well as EC loss related pIOL explantations in up

to 0.7% of eyes after 5 years.³¹ Comparison of the total explantation rate and mean time until explantation between foldable and rigid pIOLs is complicated by the large difference in mean follow-up between pIOLs types, because the rigid pIOLs were launched prior to 2001, as opposed to the foldable pIOLs, which were launched after 2003. As a result of the differences in follow-up, mean time to EC loss–related explantation was 7.2 years in the foldable myopic group (3.1% explantations), as opposed to 11.9 years in the rigid myopic group (6.0% explantations). No pIOL was explanted owing to EC loss in the foldable toric group, as opposed to 4.8% of rigid toric pIOLs after 7.4 years.³¹ Survival analyses would normally enable a reliable comparison of the foldable and rigid lens types because they function by reporting a median survival, defined as the time until 50% of eyes are expected to reach a previously defined endpoint. Unfortunately, because of the small number of events, median survival until EC loss–related explantation could not be computed in any of the foldable or rigid, myopic or toric groups, and median survival until reaching either the AAO or AFSSAPS criterion could only be computed in the myopic groups.³¹ Median survival until reaching the AAO or AFSSAPS criterion differed by 5 years, with a longer median survival in the rigid myopic group that can be explained by the longer mean follow-up as well as the slower ECD decline in the rigid myopic group.

- **RISK FACTORS:** Based on the design of the foldable pIOL described in this study, there are 2 possible optic-related explanations for the reported increased EC loss in the foldable pIOL type. Because of a smaller refractive index of the polysiloxane material, the foldable optic is slightly thicker than the rigid PMMA optic, which could result in a smaller distance between the central and peripheral pIOL edge and the corneal endothelium.⁶ Despite the fact that ACD decreased significantly in the myopic ($P = .029$) and toric ($P = .001$) groups (data on file), and although previous studies have shown increased EC loss in eyes with a smaller

ACD as well as a smaller distance between the central and peripheral pIOL edge and corneal endothelium, we did not find similar results in the current study.^{6,14,31–33} Similarly, neither ACD nor central or peripheral distance from the pIOL to the endothelium influenced the time between pIOL implantation and losing $\geq 25\%$ of ECD (ie, AAO endpoint) or reaching an ECD < 1500 cells/mm² (ie, AFSSAPS explantation criterion), nor did it influence the time until EC-related pIOL explantation. Furthermore, no significant differences were reported when comparing central and peripheral pIOL edge to the endothelium distance between eyes implanted with the foldable or rigid pIOL ($P > .05$, data on file). Additional analyses did show a significant difference in EC loss between foldable and rigid pIOLs ($P = .034$, data on file), that could not be explained by differences in lens position between the 2 lens types. Looking closer at the data, a smaller pIOL edge to the endothelium distance was associated with a statistically insignificant increased EC loss in the foldable group, but this effect was much larger—and only significant—in the rigid group (data on file). It should be noted that when the foldable pIOL was first introduced in a clinical trial in 2003, the optic-haptic junction and the vault between this junction and the iris plane was shaped differently than the finally marketed type 2 iris-fixated pIOL.^{1,3} During the clinical trial with the first pIOL model, a higher incidence of iris pigment (4.8%) and giant cell (1.4%) precipitates was reported, which were believed to be caused by compression of the iris between the pIOL and the crystalline lens.^{3,34,35} This compression was most likely caused by the lower vault between optic-haptic junction and iris in the first foldable model (0.13 mm), as compared to the rigid pIOL (0.20 mm), resulting in an alteration of the optic-haptic junction to create a higher, 0.20 mm vault between junction and iris. As a result, the marketed type 2 iris-fixated pIOL has a vault height similar to the rigid iris-fixated pIOL.^{1,3} Because lens type (1 or 2) did not significantly influence EC loss in the current study, all 27 eyes of the 14 patients implanted with the first foldable model were combined with the 454 eyes of the 261 patients implanted with the second foldable model (data on file).

Lens precipitates developed in the first postoperative year in 40.6% and 23.4% of eyes in the foldable myopic and toric groups, respectively, whereas these numbers were only 0.3% and 1.6% in the respective rigid groups (data on file). Precipitates were transient in most cases, with some cases requiring additional application of topical anti-inflammatory drops before clearing up. The higher rates of iris pigment and giant cell precipitates in the foldable group serve as an indicator for inflammation, and pose the question whether the increased EC loss in the foldable pIOL type could be attributed to an inflammatory response induced by the foldable polysiloxane material.³⁶ One previous study evaluated EC loss in a randomized paired eye comparison and showed similar EC loss in rigid and foldable pIOLs, but did not investigate long-term changes or objectively test the inflammatory response.²

Previous studies assessing the role of the IOL material on inflammation have mainly been conducted on eyes with cataract and a history of uveitis.^{37,38} Eyes with a history of uveitis are especially suitable for evaluation of the inflammatory response because their chronic—disease specific—inflammation induces a weakened blood-aqueous barrier, resulting in an intensified cellular response that is easier to detect in a clinical setting. The results of these studies point toward a higher inflammatory response in eyes implanted with a silicone material, whereas PMMA and hydrophobic acrylic seem to result in less pigment and giant cell precipitates on the IOL.^{37,38} Unfortunately not all pIOL- or IOL-oriented studies objectively quantified the inflammatory responses, and all studies showed a high degree of variation in inflammation between different durations of follow-up.^{2,37–39} Despite the fact that combined evidence is leaning somewhat toward a silicone material as a risk factor for inflammation, we must conclude that more research should be conducted directly comparing rigid and foldable pIOLs in a larger number of eyes to take a closer look at the influence of the optic material on long-term EC loss. Further research on the intraocular inflammatory response after implantation with both optic materials is required to provide a more definitive answer to this problem.

A third theory of EC loss has been suggested in one previous report that showed that intraocular presence of an iris-fixated pIOL changed the aqueous flow pattern.⁴⁰ The authors assumed that the altered aqueous flow would result in an insufficient distribution of nutrients over the corneal endothelial cells, as well as insufficient drainage of waste, eventually resulting in endothelial cell death. No other study has been conducted to test this hypothesis and there is no reason to assume a different aqueous flow, shear stress, and nutrient distribution in eyes implanted with the foldable vs in eyes implanted with a rigid pIOL.

• **OTHER PHAKIC INTRAOCULAR LENSES:** Other types of pIOLs that have been implanted over recent years are the anterior chamber, angle supported, Cachet pIOL (Alcon, Fort Worth, Texas, USA), and several types of the posterior chamber Visian Implantable Collamer Lens pIOL (ICL; STAAR Surgical, Nidau, Switzerland). The single-piece foldable angle supported pIOL is made of a cross-linked acrylate and methacrylate copolymer, and has recently been taken of the market owing to excessive EC loss in some patients.^{41–43} Two recent studies reported the 5-year results with these pIOLs in a nonrandomized setting, and showed a mean total EC loss of 8.9% and 13.7% from preoperatively to 5 years postoperatively that was similar to—or only slightly higher than—the results with the iris-fixated pIOLs described in the current paper.^{42,43} The 2016 article described the results of 1087 eyes and reported a decrease in ECD $> 30\%$ in 8.0% and an ECD ≤ 1500 cells/mm² in 2.7% of eyes.⁴³ Both studies emphasized the importance of sufficient distance between both central and peripheral

pIOL and endothelium, but no study assessed the effect of these distances on EC loss.^{42,43}

No previous study reported data on inflammatory responses after implantation with the foldable angle-supported pIOL, so it remains unclear if accelerated EC loss in this group of patients is caused by differences in design of the pIOL—with the haptics touching the peripheral endothelium or bringing the optic closer to the endothelium—or might be caused by an increased inflammatory response induced by the pIOL material. Studies assessing the inflammatory response of different IOL materials in patients with a history of uveitis reported the lowest rate of inflammation in eyes implanted with a foldable hydrophobic acrylic material, a material similar to that of the foldable angle-supported pIOL.³⁷ This could imply that the higher rates of EC loss in the angle-supported pIOL are caused by a closer proximity between pIOL and endothelium—attributed to a different lens design—rather than an enhanced inflammatory response. Alterations in aqueous humor circulation have not been investigated yet, but the position of the pIOL in front of the pupil, as well as the absence of a peripheral iridectomy, will result in an altered flow pattern.

The abovementioned foldable hydrophilic porcine collagen (0.1%)/hydroxyethyl copolymer (ie, collamer) posterior chamber pIOLs have been hypothesized to cause less EC loss owing to their position away from the endothelium, while this same—retropupillary—position has been reported to result in contact between pIOL and crystalline lens, thus inducing cataract.^{44,45} This adverse effect has resulted in several alterations in lens design, creating a larger lens vault to prevent touch between the phakic and crystalline lens, as well as additional—central—holes in the optic to change the direction of aqueous flow.^{45–47} Almost all ICL papers report ECD data by comparing means (ie, *t* test) or by using descriptive statistics. In a sub-study of the FDA trial a total EC loss after 3 and 4 years of 8.9% and 9.4% was described, which was in line with EC loss both in the current study and in previous studies on iris-fixated pIOLs with a similar follow-up.^{31,48} The main idea of posterior chamber pIOLs is that their position induces less EC loss, but since the additional holes in the optic

are unlikely to result in a major change in pIOL position, one should wonder if EC loss is not just caused by chronic—subclinical—inflammation related to the presence of any type of pIOL in the eye. Previous research assessing inflammation in eyes implanted with the ICL looked at clinical signs of inflammation as well as signs of inflammation using a flare cell meter, and showed a minor increase in inflammation that was similar to the increase in inflammation after cataract surgery, as reported in studies from the early 1990s.^{49–51} However, since all studies reported data on a small number of patients, no study reported the effect of the collamer material in eyes with uveitis, and both surgical technique and measurements have evolved since the early 1990s, we feel that revisiting the inflammatory response in eyes implanted with collamer posterior chamber pIOLs is required to assess inflammation as well as the influence of inflammation on EC loss.

One study simulated aqueous humor flow in eyes implanted with an ICL with a central hole with a peripheral iridectomy, and in eyes with an ICL with a central hole but without a peripheral iridectomy. Their results showed that aqueous humor flow is likely sufficient to prevent an increase in intraocular pressure in eyes without a peripheral iridectomy, but they did not specify if these changes in might increase shear stress on the endothelial cells or alter the nutrient distribution in the anterior chamber.⁵²

• **RECOMMENDATIONS:** In contrast to previous studies, a smaller ACD or a crowded anterior chamber did not significantly affect EC loss or EC loss–related outcome measures in the current study. The results of both the current study and previous literature give reason to believe that the silicone optic material might cause subclinical inflammation, probably serving as a risk-factor for EC loss. Research on iris-fixated pIOLs should focus on evaluating the effects of different materials (eg, silicone vs acrylic polymers) on EC loss and subclinical inflammation, in order to evaluate if development of new materials is required to safeguard the corneal endothelium.

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REFERENCES

1. Doors M, Budo CJ, Christiaans BJ, et al. Artiflex Toric foldable phakic intraocular lens: short-term results of a prospective European multicenter study. *Am J Ophthalmol* 2012;154(4):730–739.e732.
2. Couillet J, Guell JL, Fournie P, et al. Iris-supported phakic lenses (rigid vs foldable version) for treating moderately high myopia: randomized paired eye comparison. *Am J Ophthalmol* 2006;142(6):909–916.
3. Dick HB, Budo C, Maleceze F, et al. Foldable Artiflex phakic intraocular lens for the correction of myopia: two-year

- follow-up results of a prospective European multicenter study. *Ophthalmology* 2009;116(4):671–677.
4. Hashemi H, Taherzadeh M, Khabazkhoob M. Correction of high myopia with foldable Artiflex phakic intraocular lenses: 1 year follow-up results. *Acta Med Iran* 2013;51(9):620–625.
 5. Ozerturk Y, Kubaloglu A, Sari ES, et al. Foldable iris-fixated phakic intraocular lens implantation for the correction of myopia: two years of follow-up. *Indian J Ophthalmol* 2012; 60(1):23–28.
 6. Doors M, Cals DW, Berendschot TT, et al. Influence of anterior chamber morphometrics on endothelial cell changes after phakic intraocular lens implantation. *J Cataract Refract Surg* 2008;34(12):2110–2118.
 7. Bernard P, Fournier M. Definitive stop of marketing, product recall and follow-up of implanted patients. Presbyopic intraocular lenses NEWLIFE/VIVARTE PRESBYOPIC. Available at: ; 2007. <http://ansm.sante.fr/S-informer/Informations-de-securite-Retraits-de-lots-et-de-produits/Lentilles-intra-oculaires-NEWLIFE-VIVARTE-PRESBYOPIC-GBR-VIVARTE-MYOPIC-de-IOLTECH>; Accessed October 31, 2016.
 8. MacRae S, Holladay JT, Hilmantel G, et al. Special report: American Academy of Ophthalmology Task Force recommendations for specular microscopy for phakic intraocular lenses. *Ophthalmology* 2017;124(1):141–142.
 9. Guell JL, Morral M, Kook D, Kohner T. Phakic intraocular lenses part 1: historical overview, current models, selection criteria, and surgical techniques. *J Cataract Refract Surg* 2010;36(11):1976–1993.
 10. Baikoff G. Anterior segment OCT and phakic intraocular lenses: a perspective. *J Cataract Refract Surg* 2006;32(11): 1827–1835.
 11. Baikoff G, Lutun E, Ferraz C, Wei J. Static and dynamic analysis of the anterior segment with optical coherence tomography. *J Cataract Refract Surg* 2004;30(9):1843–1850.
 12. Aalders-Deenstra V, Bartels M, Beerthuisen J, et al. Consensus Refractie Chirurgie. 3rd ed. Nederlands Gezelschap voor Refractie Chirurgie (NGRC); 2013. Available at: <http://www.ooglaseraadvies.org/wp-content/uploads/2013/12/ConsensusRC2013.pdf>. Accessed August 2016.
 13. Visser N, Berendschot TT, Bauer NJ, Nuijts RM. Vector analysis of corneal and refractive astigmatism changes following toric pseudophakic and toric phakic IOL implantation. *Invest Ophthalmol Vis Sci* 2012;53(4):1865–1873.
 14. Doors M, Berendschot TT, Webers CA, Nuijts RM. Model to predict endothelial cell loss after iris-fixated phakic intraocular lens implantation. *Invest Ophthalmol Vis Sci* 2010;51(2): 811–815.
 15. van der Heijde GL, Fechner PU, Worst JG. [Optical consequences of implantation of a negative intraocular lens in myopic patients]. *Klin Monbl Augenheilkd* 1988;193(1):99–102.
 16. Tahzib NG, Bootsma SJ, Eggink FA, Nuijts RM. Functional outcome and patient satisfaction after Artisan phakic intraocular lens implantation for the correction of myopia. *Am J Ophthalmol* 2006;142(1):31–39.
 17. Doors M, Eggink FA, Webers CA, Nuijts RM. Late-onset decentration of iris-fixated phakic intraocular lenses: a case series. *Am J Ophthalmol* 2009;147(6):997–1003. 1003.e1-2.
 18. Guell JL, Morral M, Gris O, Gaytan J, Sisquella M, Manero F. Evaluation of Verisyse and Artiflex phakic intraocular lenses during accommodation using Visante optical coherence tomography. *J Cataract Refract Surg* 2007;33(8):1398–1404.
 19. Baumeister M, Bühren J, Kohner T. Position of angle-supported, iris-fixated, and ciliary sulcus-implanted myopic phakic intraocular lenses evaluated by Scheimpflug photography. *Am J Ophthalmol* 2004;138(5):723–731.
 20. Baikoff G, Bourgeon G, Jodai HJ, Fontaine A, Lellis FV, Trinquet L. Pigment dispersion and Artisan phakic intraocular lenses: crystalline lens rise as a safety criterion. *J Cataract Refract Surg* 2005;31(4):674–680.
 21. McCarey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices, and new intraocular drugs and solutions. *Cornea* 2008;27(1):1–16.
 22. Tahzib NG, Nuijts RM, Wu WY, Budo CJ. Long-term study of Artisan phakic intraocular lens implantation for the correction of moderate to high myopia: ten-year follow-up results. *Ophthalmology* 2007;114(6):1133–1142.
 23. Bourne WM, Nelson LR, Hodge DO. Central corneal endothelial cell changes over a ten-year period. *Invest Ophthalmol Vis Sci* 1997;38(3):779–782.
 24. Kohner T, Kook D, Morral M, Guell JL. Phakic intraocular lenses: part 2: results and complications. *J Cataract Refract Surg* 2010;36(12):2168–2194.
 25. Cheung SW, Cho P. Endothelial cells analysis with the TOPCON specular microscope SP-2000P and IMAGENet system. *Curr Eye Res* 2000;21(4):788–798.
 26. Ding X, Huang Q, Zheng Y, Jiang Y, Huang S, He M. Measurement area and repeatability of semiautomated assessment of corneal endothelium in the Topcon specular microscope SP-2000P and IMAGENet system. *Cornea* 2012;31(10): 1111–1118.
 27. Prinz A, Varga J, Findl O. Reliability of a video-based noncontact specular microscope for assessing the corneal endothelium. *Cornea* 2007;26(8):924–929.
 28. van Schaick W, van Dooren BT, Mulder PG, Volker-Dieben HJ. Validity of endothelial cell analysis methods and recommendations for calibration in Topcon SP-2000P specular microscopy. *Cornea* 2005;24(5):538–544.
 29. Ruckhofer J, Seyeddain O, Dextl AK, Grabner G, Stoiber J. Correction of myopic astigmatism with a foldable iris-claw toric phakic intraocular lens: short-term follow-up. *J Cataract Refract Surg* 2012;38(4):582–588.
 30. Munoz G, Cardoner A, Albarran-Diego C, Ferrer-Blasco T, Belda-Salmeron L. Iris-fixated toric phakic intraocular lens for myopic astigmatism. *J Cataract Refract Surg* 2012;38(7): 1166–1175.
 31. Jonker SMR, Berendschot T, Ronden AE, Saelens IEY, Bauer NJC, Nuijts R. Long-term endothelial cell loss in patients with Artisan Myopia and Artisan Toric phakic intraocular lenses: 5- and 10-year results. *Ophthalmology* 2018; 125(4):486–494.
 32. Saxena R, Boekhoorn SS, Mulder PG, Noordzij B, van Rij G, Luyten GP. Long-term follow-up of endothelial cell change after Artisan phakic intraocular lens implantation. *Ophthalmology* 2008;115(4):608–613.e601.
 33. Shajari M, Scheffel M, Koss MJ, Kohner T. Dependency of endothelial cell loss on anterior chamber depth within first 4 years after implantation of iris-supported phakic intraocular lenses to treat high myopia. *J Cataract Refract Surg* 2016; 42(11):1562–1569.
 34. Tahzib NG, Eggink FA, Frederik PM, Nuijts RM. Recurrent intraocular inflammation after implantation of the Artiflex

- phakic intraocular lens for the correction of high myopia. *J Cataract Refract Surg* 2006;32(8):1388–1391.
35. Koss MJ, Cichocki M, Kohnen T. Posterior synechias following implantation of a foldable silicone iris-fixated phakic intraocular lens for the correction of myopia. *J Cataract Refract Surg* 2007;33(5):905–909.
 36. Kohnen T, Cichocki M, Koss MJ. Position of rigid and foldable iris-fixated myopic phakic intraocular lenses evaluated by Scheimpflug photography. *J Cataract Refract Surg* 2008;34(1):114–120.
 37. Alio JL, Chipont E, BenEzra D, Fakhry MA. Comparative performance of intraocular lenses in eyes with cataract and uveitis. *J Cataract Refract Surg* 2002;28(12):2096–2108.
 38. Abela-Formanek C, Amon M, Schauersberger J, Kruger A, Nepp J, Schild G. Results of hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses in uveitic eyes with cataract: comparison to a control group. *J Cataract Refract Surg* 2002;28(7):1141–1152.
 39. Braga-Mele R, Cohen S, Rootman DS. Foldable silicone versus poly(methyl methacrylate) intraocular lenses in combined phacoemulsification and trabeculectomy. *J Cataract Refract Surg* 2000;26(10):1517–1522.
 40. Repetto R, Pralits JO, Siggers JH, Soleri P. Phakic iris-fixated intraocular lens placement in the anterior chamber: effects on aqueous flow. *Invest Ophthalmol Vis Sci* 2015;56(5):3061–3068.
 41. Aerts AA, Jonker SM, Wielders LH, et al. Phakic intraocular lens: two-year results and comparison of endothelial cell loss with iris-fixated intraocular lenses. *J Cataract Refract Surg* 2015;41(10):2258–2265.
 42. Alio JL, Plaza-Puche AB, Cavas F, Yebana Rubio P, Sala E. An angle-supported foldable phakic intraocular lens for correction of myopia: a five-year follow-up. *Arch Soc Esp Ophthalmol* 2017;92(1):4–11.
 43. Kohnen T, Maxwell WA, Holland S. Correction of moderate to high myopia with a foldable, angle-supported phakic intraocular lens: results from a 5-year open-label trial. *Ophthalmology* 2016;123(5):1027–1035.
 44. Bleckmann H, Keuch RJ. Results of cataract extraction after implantable contact lens removal. *J Cataract Refract Surg* 2005;31(12):2329–2333.
 45. Lindland A, Heger H, Kugelberg M, Zetterstrom C. Vaulting of myopic and toric Implantable Collamer Lenses during accommodation measured with Visante optical coherence tomography. *Ophthalmology* 2010;117(6):1245–1250.
 46. Fernandes P, Gonzalez-Meijome JM, Madrid-Costa D, Ferrer-Blasco T, Jorge J, Montes-Mico R. Implantable collamer posterior chamber intraocular lenses: a review of potential complications. *J Refract Surg* 2011;27(10):765–776.
 47. Shimizu K, Kamiya K, Igarashi A, Shiratani T. Early clinical outcomes of implantation of posterior chamber phakic intraocular lens with a central hole (Hole ICL) for moderate to high myopia. *Br J Ophthalmol* 2012;96(3):409–412.
 48. Edelhauser HF, Sanders DR, Azar R, Lamielle H. Corneal endothelial assessment after ICL implantation. *J Cataract Refract Surg* 2004;30(3):576–583.
 49. Sanders DR. Postoperative inflammation after implantation of the implantable contact lens. *Ophthalmology* 2003;110(12):2335–2341.
 50. el-Maghraby A, Marzouki A, Matheen TM, Soucek J, Van der Karr M. Reproducibility and validity of laser flare/cell meter measurements of intraocular inflammation. *J Cataract Refract Surg* 1993;19(1):52–55.
 51. Shah SM, Spalton DJ, Taylor JC. Correlations between laser flare measurements and anterior chamber protein concentrations. *Invest Ophthalmol Vis Sci* 1992;33(10):2878–2884.
 52. Kawamorita T, Shimizu K, Shoji N. Theoretical study on the need for laser iridotomy in an implantable collamer lens with a hole using computational fluid dynamics. *Eye (Lond)* 2017;31(5):795–801.