

Model to Predict Endothelial Cell Loss after Iris-Fixated Phakic Intraocular Lens Implantation

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PURPOSE. To describe a model predicting endothelial cell (EC) loss after iris-fixated phakic intraocular lens (pIOL) implantation, taking distance from the edge of the pIOL to the endothelium into account.

METHODS. This prospective observational study monitored long-term EC changes in 306 eyes after pIOL implantation. EC density (ECD) was determined before surgery, 6 months after surgery, and then annually up to 8 years after surgery. Mean follow-up was 31.7 ± 25.7 months. All eyes underwent anterior segment optical coherence tomography to determine minimum distance from the edge of the pIOL to the endothelium. Linear mixed-model analysis was performed to present a model that describes EC loss as a linear decrease and an additional decrease depending on the postoperative edge distance of the patient.

RESULTS. Mean minimum edge distance was 1.43 ± 0.23 mm (range, 0.70–2.21 mm). For this mean edge distance, the model predicted a yearly EC loss of 1.0%, whereas an edge distance of 1.20 mm resulted in a yearly EC loss of 1.7%, and an edge distance of 1.66 mm led to a yearly EC loss of only 0.2%. Furthermore, the model predicted that for patients with preoperative ECDs of 3000, 2500 or 2000 cells/mm², and edge distances of 1.43 mm, a critical ECD of 1500 cells/mm² (at which point pIOL explantation and cataract extraction can still safely be performed) will be reached at 56, 37, and 18 years after implantation.

CONCLUSIONS. The presented model predicts EC loss after iris-fixated pIOL implantation in relation to the measured edge distance, patient age, and preoperative ECD, which can assist ophthalmologists in patient selection and follow-up of pIOLs. (*Invest Ophthalmol Vis Sci.* 2010;51:811–815) DOI:10.1167/iops.09-3981

Since 1991, iris-fixated phakic intraocular lenses (pIOLs) have been successfully implanted in healthy eyes to correct myopia, hyperopia, and astigmatism. Previous studies have demonstrated that these pIOLs show stable and predictable visual results when strict inclusion criteria for implantation are applied.^{1–3} However, long-term endothelial cell (EC) loss remains a point of discussion. To investigate the effect of iris-fixated pIOLs on the corneal endothelium, several clinical trials studied EC loss after pIOL implantation, with variable results. Some investigators reported no statistically significant EC loss, whereas others found highly significant EC losses continuing

up to 5 years after pIOL implantation (9.0% at 5 years postoperatively).^{4,5} Furthermore, Saxena et al.⁶ reported a significant 12.6% EC loss 7 years after pIOL implantation and a significant negative correlation between anterior chamber depth (ACD) and EC loss after 3 years.

New noncontact imaging techniques have been extremely valuable in guaranteeing a safe distance from the pIOL to critical ocular tissues.⁷ Anterior segment optical coherence tomography (AS-OCT) has proven to be a good imaging tool to visualize the pIOL in the anterior chamber and to analyze its distance from the corneal endothelium and the crystalline lens.⁸ This has led to the development of new criteria to warrant the long-term safety of pIOLs. One of the mentioned criteria is a minimum distance from the edge of the pIOL to the corneal endothelium, which is the smallest distance (1.5 mm) from the pIOL to the endothelium because of its convex-concave shape.⁹ A new software update (Visante AS-OCT; Carl Zeiss Meditec Inc., Dublin, CA) has the ability to perform pIOL simulation and, consequently, can measure edge distance before surgery.

Recently, the importance of this edge distance has been demonstrated by Doors et al.¹⁰ They found that EC loss after pIOL implantation was associated with the distance from the edge of the pIOL to the corneal endothelium. An edge distance of 1.37 mm resulted in a yearly EC loss of 0.98%, whereas an edge distance of 1.15 mm predicted a yearly loss of 1.8%. Furthermore, the edge distance might not be constant with advancing age. Age-related changes to the crystalline lens cause a decrease in ACD of approximately 20 μ m per year.^{11,12} Guell et al.¹³ reported a stable distance between the pIOL and the crystalline lens during accommodation, which might suggest that the iris and the crystalline lens act as a unit and move forward. Consequently, if the iris and the crystalline lens move forward with an iris-fixated pIOL, the distance from the edges of the pIOL to the endothelium might decrease with increasing patient age.

In this study, we have extended our previous observations to an increased number of patients and assessed whether the endothelial cell density (ECD) changes conform to a mathematical model, taking the relationship between EC loss and edge distance into account. The main purpose was to design a model that can help physicians during the patient selection and follow-up process. It might be used to predict when a patient will reach a critical endothelial cell density level, such as an ECD of 1500 cells/mm²,^{14,15} at which point, in our opinion, pIOL explantation and cataract extraction can still safely be performed. To help ophthalmologists in patient selection, the model might be used to predict how long the pIOL can remain safely in the eye using the preoperative edge distance, measured with the pIOL simulation program (Visante AS-OCT; Carl Zeiss Meditec Inc.), and the preoperative ECD count.

METHODS

This prospective observational study included 306 consecutive eyes of 162 patients, who underwent pIOL implantation with Artisan or Arti-

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TABLE 1. ECD Changes after pIOL Implantation

Period	No. of Eyes	Mean ECD (cells/mm ²) ± SD	Preoperative Mean ECD (cells/mm ²) ± SD	Mean ECD Loss (%)	P*
Before surgery	306	2693 ± 347	—	—	—
6 months	181	2669 ± 354	2680 ± 343	0.40 ± 9.85	0.829
1 year	155	2660 ± 353	2692 ± 344	1.23 ± 9.52	0.742
2 years	147	2627 ± 349	2679 ± 363	2.03 ± 8.83	0.004
3 years	79	2562 ± 330	2673 ± 294	4.91 ± 12.64	<0.001
5 years	53	2576 ± 319	2659 ± 339	4.34 ± 8.92	0.011
7 years	20	2446 ± 278	2576 ± 248	5.41 ± 9.11	0.036

* Paired *t*-test between preoperative and postoperative ECD counts. *P* < 0.009 was considered significant (Bonferroni correction).

flex (Ophtec B.V., Groningen, The Netherlands) between 1998 and 2008 at the Academic Center for Refractive Surgery, University Eye Clinic Maastricht, for the correction of moderate to high myopia and astigmatism. Forty-eight men and 114 women were included in this study; mean patient age was 41.8 ± 10.6 years (range, 18–63 years) at the time of pIOL implantation. The study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all patients. Investigational review board approval was obtained from the Academic Hospital Maastricht.

The Artisan pIOL (Ophtec B.V.) is a rigid single-piece lens composed of polymethyl methacrylate (PMMA). It has a convex-concave shape with either a 6-mm (for intraocular lens powers up to −15.5 diopters [D]) or 5-mm (for intraocular lens powers from −16.0 to −24.0 D) optic. In contrast, the foldable Artiflex pIOL (Ophtec B.V.) is a three-piece lens that consists of a flexible optical part made of ultraviolet-absorbing silicone and two rigid haptics made of PMMA. Because of its foldable 6-mm silicone optic, this lens can be inserted through a smaller incision. The Artiflex pIOL is available in dioptric powers of −2.0 to −14.5. The surgical procedures were performed by the same surgeon (RN). The surgical technique of pIOL implantation and postoperative eyedrops regimen has been described elsewhere.^{10,16} The incision size for implantation of the rigid Artisan pIOL was 6.2 or 5.2 mm, depending on the size of the optic. For the foldable Artiflex pIOL, a 3.2-mm incision was used. The criteria for performing pIOL implantation in our institution are stable refractive error during the previous 2 years; central ACD of 2.8 mm or more (measured from the endothelium to the crystalline lens); pupil (in mesopic light conditions) < 6 mm; endothelial cell density ≥ 2000 cells/mm²; no corneal, pupil, or iris abnormalities; and no history of glaucoma or chronic or recurrent uveitis.

Before surgery, central ECD measurements were performed using a noncontact specular microscope (Noncon Robo SP-8000; Konan Medical Inc., Hyogo, Japan) and were repeated at 3 and 6 months and at 1,

2, 3, 4, 5, 6, 7, and 8 years after surgery. Follow-up ranged from 3 months to 8 years, with a mean follow-up of 31.7 ± 25.7 months per eye. Three consecutive endothelial images of the central cornea were obtained and analyzed using the dot method, in which the centers of 50 or more contiguous cells are marked. The average of these three measurements was used for the analysis. EC loss was defined as the decrease in cell density between the preoperative and postoperative examination expressed as a percentage of the preoperative cell density. Paired *t* tests were used to compare preoperative EC counts with postoperative EC counts for each follow-up visit. To correct for the multiple tests, we used a Bonferroni correction, which meant that a *P* < 0.009 was considered significant for the conducted paired *t*-tests (Table 1). During all follow-up examinations, patients were examined to detect complications, such as glaucoma or corneal edema.

From 2006 to 2008, AS-OCT was performed once in all included patients to analyze the position of the iris-fixated pIOL using an OCT system (Visante; Carl Zeiss Meditec Inc.). All AS-OCT images were made on the horizontal meridian, in an unaccommodated state, and in the same light conditions (50 lux). Cross-sectional images were taken using the enhanced anterior segment single scan. One examiner analyzed the images and measured the distances from the edges of the pIOL to the corneal endothelium using the refractive tools provided by the manufacturer (Fig. 1). Of the two edge distances (nasal and temporal side), the smallest distance was used for statistical analysis.

Linear mixed-model analysis was applied to our data, with ECD as an independent variable and time as a covariate and assuming a random intercept per eye. This linear model is a useful test because it uses all available ECD data for each patient to fit the best linear model. To look for possible differences in EC loss for pIOLs with different distances between the edge of the pIOL and the corneal endothelium, we also included an interaction term “time” × “edge pIOL-corneal endothelium distance.” Our approach was to fit a linear mixed model using the following equation:



FIGURE 1. Anterior segment optical coherence tomography scan showing measured edge distances on the nasal (1.44-mm) and temporal (1.58-mm) side.

TABLE 2. Parameter Estimates of Linear Mixed-Model Analysis

Parameter	Estimate (cells/mm ²) ± SE	95% CI
Intercept α	2693 ± 18.5	2656-2729
Effect of time β	-12.95 ± 1.58	-16.05--9.85
Interaction effect γ	7.51 ± 1.06	5.44-9.58

$$y_i(t,d) = \alpha + \alpha_i + \beta t + \gamma(td) + \varepsilon_i \quad (1)$$

where $y_i(t,d)$ is the ECD count of an eye i after a follow-up of t months with edge distance d ; α represents the intercept; α_i represents the random intercept per eye; β is the effect of time after a follow-up of t months; γ is the interaction effect of time and edge distance with edge distance d and a follow-up of t months; and ε_i is the residual error.

RESULTS

Of the 306 included eyes, 186 eyes received an Artisan Myopia pIOL with a mean lens power of -12.91 ± 3.79 D (range, -5.00 to -23.50 D), 15 eyes were implanted with an Artisan Toric pIOL with a mean lens power of -7.77 ± 4.04 D (range, -2.00 to -15.00 D), 99 eyes received an Artiflex Myopia pIOL with a mean lens power of -10.06 ± 2.25 D (range, -4.00 to -14.50 D), and 6 eyes received an Artiflex Toric pIOL with a mean lens power of -8.33 ± 2.32 D (range, -5.00 to -10.50 D). The mean preoperative ECD count was 2693 ± 347 cells/mm² (range, 1588-3753 cells/mm²), and the mean minimum edge distance was 1.43 ± 0.23 mm (range, 0.70-2.21 mm). Artisan pIOLs showed a mean edge distance of 1.48 ± 0.23 mm and a mean preoperative ECD count of 2624 ± 355 cells/mm². The mean edge distance of the Artiflex pIOLs was 1.32 ± 0.20 mm, and the mean preoperative ECD count was 2775 ± 310 cells/mm². Eleven patients included in this study wanted the pIOL implantation despite an ECD <2000 cells/mm² and our warnings about possible complications; ECD in most of the patients ($n = 8$) was between 1950 and 2000 cells/mm². They underwent implantation because of complete contact lens intolerance and the inability to continue their occupations with spectacle correction. Mean EC losses at 6 months and 1 year after pIOL implantation were $0.40\% \pm 9.85\%$ and $1.23\% \pm 9.52\%$, respectively. To illustrate the ECD data used to compute the model, the changes in ECD at each follow-up visit compared with before surgery are shown in Table 1. All corneas of the included eyes stayed clear during follow-up.

Estimated parameters of the linear mixed model are listed in Table 2. When using these estimates in the described model, the following equation can be computed:

$$y_i(t,d) = 2693 + \alpha_i - 12.95t + 7.51(td) + \varepsilon_i \quad (2)$$

When applying this model to a patient with a preoperative ECD count of 2693 cells/mm² (i.e., mean ECD count of the investigated population) and a minimum edge distance of 1.43 mm (i.e., mean edge distance of the investigated population), the predicted ECD at 5 years after surgery would be $y(60,1.43) = 2693 - 12.95 \times 60 + 7.51 \times (60 \times 1.43) = 2560$ cells/mm². We can also calculate that after 44 years the patient will have enough endothelial cells (1525 cells/mm²)^{14,15} to undergo pIOL explantation and cataract extraction (Figs. 2, 3). The predictions of minimum edge distances of 1.66 mm and 1.20 mm (i.e., mean edge distance ± 1 SD) in the same patient are also shown in Figure 2 with the corresponding years of reaching ECD counts of 1500 cells/mm² in Table 3. For the mean edge distance of 1.43 mm, the model predicted a yearly EC loss of 1.0%, whereas an edge distance of 1.20 mm resulted

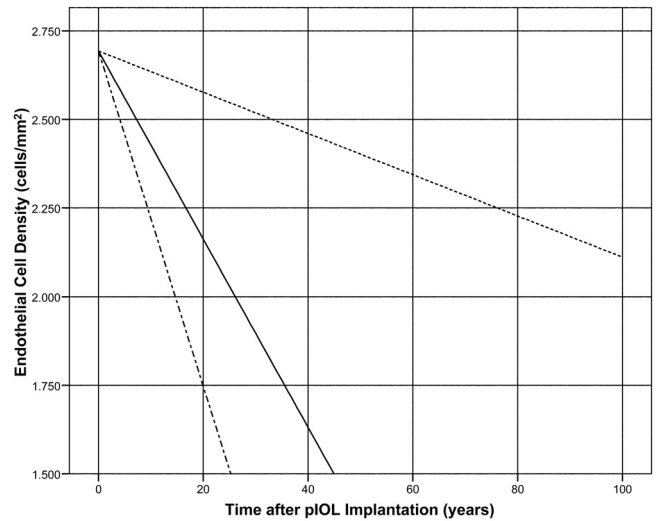


FIGURE 2. Linear mixed model applied to patient eligible for pIOL implantation with preoperative endothelial cell count of 2693 cells/mm² and edge distances of 1.20 mm (half dotted line), 1.43 mm (straight line), and 1.66 mm (dotted line).

in a yearly EC loss of 1.7%, and an edge distance of 1.66 mm led to a yearly EC loss of only 0.2%.

For patients with preoperative ECDs of 3000, 2500, or 2000 cells/mm² and edge distances of 1.43 mm, the model predicted that a critical ECD of 1500 cells/mm² will be reached at 56, 37, and 18 years after implantation, respectively.

DISCUSSION

In this study, we analyzed the data of 306 eyes after iris-fixed pIOL implantation and computed a linear mixed model to predict long-term EC loss in relation to the distance from the edge of the pIOL to the corneal endothelium. To our knowledge, this is the first attempt to describe such a model for patients after pIOL implantation. In the past, models predicting EC loss after cataract surgery and penetrating keratoplasty (PK) have been presented using exponential decay models.¹⁷⁻¹⁹

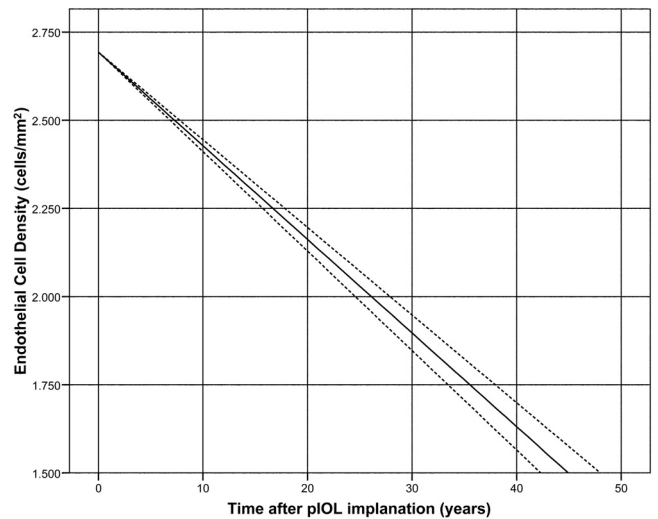


FIGURE 3. Linear mixed model applied to patient eligible for pIOL implantation with preoperative endothelial cell count of 2693 cells/mm² and edge distance of 1.43 mm (straight line) with the confidence intervals of the model (dotted lines).

TABLE 3. Linear Mixed Model Applied to Patient with Preoperative ECD Count of 2693 Cells/mm² and Different Edge Distances, with Corresponding Years of Reaching ECD Levels of 1500 Cells/mm²

Edge distance (mm)	Estimate ECD (cells/mm ²)	Years after pIOL Implantation
1.20	1511	25
1.43	1525	44
1.66	1500	205

Patel et al.¹⁹ and Armitage et al.¹⁷ both described a biexponential model of EC loss after PK. Single exponential decay models have been shown to underestimate the early EC loss and to overestimate late EC loss after PK. Other possibilities include an exponential followed by a linear decrease or a two-phased linear decrease with a rapid linear decrease in the early postoperative period.²⁰ We used a single linear model because it was the best fit to our data. Our EC loss results showed that we did not find a large EC loss shortly after pIOL implantation, which is the case after cataract surgery and penetrating keratoplasty and thus follows an exponential decay model. An explanation for this stable ECD in the first months after pIOL implantation might be the redistribution of endothelial cells from the periphery to the center after the discontinuation of contact lens wear. Peripheral corneal ECD seems to be significantly higher than central corneal ECD and functions as a physiologic reserve for endothelial cells.²¹ Similar to our results, most studies investigating EC loss after pIOL implantation did not report a rapid loss in the first 6 months after surgery.^{1,3,4,22,23} In these studies, short-term EC losses varied from 0.09% at 6 months to 3.3% at 1 year after surgery. Our reported mean EC losses of 4.3% at 5 years and 5.4% at 7 years after pIOL implantation are in accordance with the recent literature. Three years after pIOL implantation, Stulting et al.³ reported an EC loss of 4.8%, and Benedetti et al.⁵ found an EC loss of 9.0% at 5 years after surgery.

The aim of our study was to describe a model to assist ophthalmologists in their decision to implant iris-fixated pIOLs into healthy eyes. The presented model uses preoperative ECD and the minimum edge distance to estimate ECD counts during follow-up. To build the described model, the edge distance was measured postoperatively because AS-OCT has only been available in our institution since 2006. A new software update of the OCT (Visante; Carl Zeiss Meditec Inc.) system now has the possibility to assess the edge distance in the preoperative setting using a pIOL simulation program. Recently, we tested this pIOL simulation tool and found small mean differences between preoperative simulation and actual postoperative measurements.²⁴ Therefore, this preoperative simulation is a useful tool in determining edge distance in the preoperative patient, which can be used in the presented model.

However, as we mentioned before, it is known that ACD decreases with age, which might result in a decrease in the minimum edge distance over time. In our opinion, all patients should be monitored using AS-OCT during long-term follow-up to investigate the effect of age on the minimum edge distance. For example, when presuming a yearly ACD decrease of 20 μ m, which, in a worst-case scenario, will result in a decreasing edge distance of 0.02 mm per year, the presented patient with a preoperative ECD count of 2693 cells/mm² and a minimum edge distance of 1.43 mm, will reach an ECD count of 1500 cells/mm² 42 years after pIOL implantation (Fig. 4). This is 2 years sooner than predicted without taking this decrease of ACD into account. As more data become available during long-term follow-up of pIOLs using AS-OCT, we hope this leads to the development of a good mathematical description of the

postoperative EC loss with an accurate estimation of the decrease in edge distance over time.

We tried to evaluate our model using studies reporting EC loss after iris-fixated pIOL implantation.^{1-6,23,25-28} However, the main problem of previously reported studies was the unavailability of measured edge distances, which can be expected because the Visante OCT (Carl Zeiss Meditec Inc.) has only been on the market since 2006. Computing an estimated mean edge distance for all available data was difficult because edge distance is related to ACD but also to the power and design of the pIOL. Furthermore, some studies did not report mean ACD or did not describe the measurement device, which makes it difficult to assess whether ACD was measured from the crystalline lens to the endothelium or epithelium. Our suggestion would be to perform AS-OCT before surgery and to use the pIOL simulation program to estimate edge distance but also to continue the evaluation of this edge distance during long-term follow-up.

One of the limitations of a prediction model in general is the uncertainty of extrapolation of the data outside the ranges of the estimated values. The minimum edge distances of the eyes included in our study ranged between 0.70 and 2.21 mm. Therefore, in patients with minimum edge distances lower than 0.70 mm, the model should not be used since this could lead to inaccurate ECD estimates. Our maximum follow-up period was 8 years with a limited number of eyes. Therefore, extrapolation after our 8 years of follow-up could become more unreliable. We will continue to monitor our ECD data in the coming years and hope to provide more accurate values beyond 8 years of follow-up with a larger number of eyes in the future. Furthermore, to increase the validity of the presented model, it should be applied to a second independent population for validation. In our model we included both eyes of a large number of patients, which can cause bias in the statistical analysis. However, when repeating the analysis using only right or left eyes, the results were not very different from the presented model; therefore, we believe that the inclusion of both eyes did not lead to severe bias.

Our decrease in ECD is described as an absolute decrease in endothelial cells, which is actually a worst-case scenario. When using a relative decrease, which is usually reported in articles about EC loss, the decrease in ECD would be not as fast as the

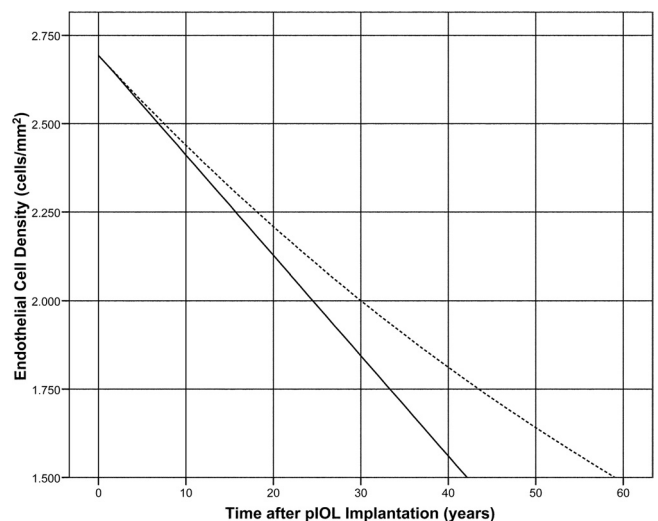


FIGURE 4. Linear mixed model with decreasing edge distance because of aging (*straight line*) and relative endothelial cell loss (*dotted line*) applied to patient eligible for pIOL implantation, with preoperative endothelial cell count of 2693 cells/mm² and edge distance of 1.43 mm.

absolute decrease. An example of a relative decrease is visualized for the presented patient in Figure 4. During the first 15 years of follow-up, the relative and absolute EC losses are almost identical. After this period, the difference between the models becomes evident. The patient will reach our critical ECD count of 1500 cells/mm² 70 years after implantation, which is 14 years later when compared with the absolute decrease in ECD. When follow-up periods of 15 years and longer become available in the future, the choice between a relative and an absolute decrease will be more reliable.

In conclusion, a linear mixed-model analysis was used to describe a linear model that predicts ECD counts after iris-fixed pIOL implantation in relation to the measured minimum edge distance using AS-OCT. Longer follow-up with AS-OCT will be needed to evaluate the effect of age-related changes of the natural lens on the distance from the edge of the pIOL to the endothelium.

References

1. 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;114:1133-1142.
2. Budo C, Hessloehl JC, Izak M, et al. Multicenter study of the Artisan phakic intraocular lens. *J Cataract Refract Surg*. 2000;26:1163-1171.
3. Stulting RD, John ME, Maloney RK, Assil KK, Arrowsmith PN, Thompson VM. Three-year results of Artisan/Verisyse phakic intraocular lens implantation: results of the United States Food and Drug Administration clinical trial. *Ophthalmology*. 2008;115:464-472, e461.
4. Pop M, Payette Y. Initial results of endothelial cell counts after Artisan lens for phakic eyes: an evaluation of the United States Food and Drug Administration Ophtec Study. *Ophthalmology*. 2004;111:309-317.
5. Benedetti S, Casamenti V, Benedetti M. Long-term endothelial changes in phakic eyes after Artisan intraocular lens implantation to correct myopia: five-year study. *J Cataract Refract Surg*. 2007;33:784-790.
6. 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;115:608-613, e601.
7. Kohnen T, Cichocki M, Koss MJ. Position of rigid and foldable iris-fixed myopic phakic intraocular lenses evaluated by Scheimpflug photography. *J Cataract Refract Surg*. 2008;34:114-120.
8. 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;30:1843-1850.
9. Baikoff G. Anterior segment OCT and phakic intraocular lenses: a perspective. *J Cataract Refract Surg*. 2006;32:1827-1835.
10. 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;34:2110-2118.
11. Baikoff G, Bourgeon G, Jodai HJ, Fontaine A, Lellis FV, Trinquet L. Pigment dispersion and Artisan phakic intraocular lenses: crystal-line lens rise as a safety criterion. *J Cataract Refract Surg*. 2005;31:674-680.
12. Atchison D, Markwell E, Kasthurirangan S, Pope J, Smith G, Swann P. Age-related changes in optical and biometric characteristics of emmetropic eyes. *J Vis*. 2008;8:29:21-20.
13. 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;33:1398-1404.
14. Baradaran-Rafii A, Rahmati-Kamel M, Eslani M, Kiavash V, Karimian F. Effect of hydrodynamic parameters on corneal endothelial cell loss after phacoemulsification. *J Cataract Refract Surg*. 2009;35:732-737.
15. Storr-Paulsen A, Norregaard JC, Ahmed S, Storr-Paulsen T, Pedersen TH. Endothelial cell damage after cataract surgery: divide-and-conquer versus phaco-chop technique. *J Cataract Refract Surg*. 2008;34:996-1000.
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;142:31-39.
17. Armitage WJ, Dick AD, Bourne WM. Predicting endothelial cell loss and long-term corneal graft survival. *Invest Ophthalmol Vis Sci*. 2003;44:3326-3331.
18. Bates AK, Hiorns RW, Cheng H. Modelling of changes in the corneal endothelium after cataract surgery and penetrating keratoplasty. *Br J Ophthalmol*. 1992;76:32-35.
19. Patel SV, Hodge DO, Bourne WM. Corneal endothelium and post-operative outcomes 15 years after penetrating keratoplasty. *Am J Ophthalmol*. 2005;139:311-319.
20. Moller-Pedersen T. A comparative study of human corneal keratocyte and endothelial cell density during aging. *Cornea*. 1997;16:333-338.
21. Odenthal MT, Gan IM, Oosting J, Kijlstra A, Beekhuis WH. Long-term changes in corneal endothelial morphology after discontinuation of low gas-permeable contact lens wear. *Cornea*. 2005;24:32-38.
22. Maloney RK, Nguyen LH, John ME. Artisan phakic intraocular lens for myopia: short-term results of a prospective, multicenter study. *Ophthalmology*. 2002;109:1631-1641.
23. Moshirfar M, Holz HA, Davis DK. Two-year follow-up of the Artisan/Verisyse iris-supported phakic intraocular lens for the correction of high myopia. *J Cataract Refract Surg*. 2007;33:1392-1397.
24. Doors M, Berendschot TT, Hendrikse F, Webers CA, Nuijts RM. Value of preoperative phakic intraocular lens simulation using optical coherence tomography. *J Cataract Refract Surg*. 2009;35:438-443.
25. Menezo JL, Cisneros AL, Rodriguez Salvador V. Endothelial study of iris-claw phakic lens: four year follow-up. *J Cataract Refract Surg*. 1998;24:1039-1049.
26. Landesz M, van Rij G, Luyten G. Iris-claw phakic intraocular lens for high myopia. *J Refract Surg*. 2001;17:634-640.
27. Silva RA, Jain A, Manche EE. Prospective long-term evaluation of the efficacy, safety, and stability of the phakic intraocular lens for high myopia. *Arch Ophthalmol*. 2008;126:775-781.
28. Guell JL, Morral M, Gris O, Gaytan J, Sisquella M, Manero F. Five-year follow-up of 399 phakic Artisan-Verisyse implantation for myopia, hyperopia, and/or astigmatism. *Ophthalmology*. 2008;115:1002-1012.