Follow-up Study of More Than 15 Years of an Angle-Supported Phakic Intraocular Lens Model (ZB5M) for High Myopia Outcomes and Complications

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In the last 2 decades, phakic intraocular lenses (PIOLs) have proven to be a safe and reliable method for correcting high myopia, hyperopia, and astigmatism when adequate inclusion criteria for implantation are applied.1-6 However, complications relating to PIOLs can be more severe and disabling than those of keratorefractive surgery. The first successful model distributed worldwide was the Baikoff ZB (Domilens) in 1986.7 Several studies8-10 have reported the refractive predictability and safety for these models; the longest reported follow-up periods were of 7 and 12 years.11,12 However, because available data concerning the long-term follow-up of eyes implanted with PIOLs remain limited, the stability in terms of efficacy, safety, and predictability has not yet been demonstrated for a period of more than 15 years. In this study, we report the results of a large, retrospective, nonrandomized, cumulative clinical study performed in a consecutive group of patients implanted with the ZB5M angle-supported PIOL. We describe the refractive status and the main parameters related to ocular safety evaluated 15 years and more after implantation.

Methods

Patients who were implanted with the Baikoff ZB at VISSUM Corporación Oftalmológica de Alicante between 1990 and 1996 were identified through surgical records (n = 123; 208 eyes).
From these, 44 patients could not be contacted by telephone, 3 had died, and 26 refused to be involved in the study; therefore, from the original group, 50 patients (97 eyes) had follow-up data available of more than 15 years. The ethical board committee of VISSUM Corporación Oftalmológica de Alicante approved the retrospective revision and analysis, for scientific purposes, of the ophthalmological data obtained from the patients included in the present investigation. Each patient gave oral informed consent for this research. The tenets of the Declaration of Helsinki (59th World Medical Association General Assembly, Seoul, Korea, October 2008) were followed for the analysis of cases. Inclusion criteria were age older than 20 years at the date of implantation, ZB5M PIOLs implanted, anterior chamber (AC) depth at the period of implantation of 3 mm or more from the corneal endothelium to the anterior capsule of the lens, and endothelial cell density of 2000 cells/mm² or more in patients 25 years or older and 2500 cells/mm² for younger patients. Exclusion criteria were different models of PIOLs implanted, uveitis, cataract, and glaucoma at presentation, anatomical alteration and previous surgery of the AC and angle, and follow-up of less than 15 years. For each patient, we considered the age at the first visit, the age at implantation, the age at explantation, and the date at onset of each complication (cornea decompensation, pupil ovalization, glaucoma, cataract, uveitis, and retinal detachment). To analyze the corneal endothelium, we used the Konan 5500 analyzer (Konan Camera Research Institute Inc). For follow-up performed after July 2000, a noncontact Topcon SP-2000P analyzer (Topcon) was used. A minimum of 50 cells were counted at the central corneal endothelium for determining the cellular density (number of cells per millimeter squared) and the coefficient of variation. To evaluate the amount of endothelial cell loss (ECL), we used this formula:

\[ \text{ECD}_i = \text{ECD}_0 \times (1 - \text{Percentage of Loss/100}) \times n, \]

where ECD\(_i\) is the current cell density estimated at any moment, ECD\(_0\) is the cell density at the first visit, and \(n\) is the number of years of follow-up.

Best-corrected visual acuity (BCVA), slitlamp microscopy, intraocular pressure (IOP), and fundus examinations were performed at all follow-up visits. A significant number of patients failed to attend some of the postoperative visits. To avoid bias, we analyzed the data at the first visit and the last follow-up. All data were tabulated and analyzed using the statistical package SPSS 17 for Windows (IBM SPSS). Incidence rates were calculated as the number of events or complications divided by the number of eyes at risk during the year (eye-year [EY]). Kaplan-Meier curves were used to compare eye complication rates. For the risk factor analyses, odds ratios (OR) were calculated using univariate logistic regression. Main outcomes were to evaluate the incidence and onset of each complication during the follow-up and risk factors and causes of loss of visual acuity.

The method of implantation was the same for all 208 cases. After local peribulbar anesthesia, a valved limbal incision was created with a 45° superblade (Alcon), without entering the AC. Then, a 1-mm paracentesis was performed with irrigation of the AC with acetylcysteine, 1% (Alcon Cusi). The AC was filled with hydroxypropyl methylcellulose, 2% (Alcon Cusi), and the incision was enlarged to 6 mm with a level-up crescent knife (Alcon). A 5-mm silicone slide sheet was introduced into the AC down to the 6-o’clock position, and viscoelastic was again injected over the slide sheet. The PIOL was then introduced toward the 6-o’clock position and the slide was withdrawn. The PIOL was then rotated using a Lester lens dialer (Katena Instrument) to the meridian in which the pupil was best centered in relation to the PIOL optic. A peripheral iridotomy was performed in all cases using Gill scissors (Katena Instruments). A 3-bite, 10-0 running nylon suture was used to close the wound, and the viscoelastic was removed. The suture was then knotted and a deep sub-Tenon injection of gentamicin (Gevramycin; Schering-Plough SA) was administered.

Postoperative care included the instillation of dexamethasone with polymyxin B and neomycin (Maxitrol; Alcon) drops 3 times a day for 1 month, and topical diclofenac (Voltaren; Ciba Vision) was instilled 3 times daily for 3 months.

### Results

The characteristics of the study population and visual outcomes are summarized in Table 1. The mean (SD) preoperative spherical equivalent refraction was −19.36 (6.7) diopters (Δ) (range, −10 to −38Δ) and at the end of follow-up, it was −1.4 (2.6) Δ (range, −11.7 to −1.75Δ) (Wilcoxon test, \(P < .001\)). The mean (SD) BCVA at the preoperative visit was 0.35 (0.2) decimal (d) (range, 0.05 to 0.8 d) and at the end of follow-up, 0.56 (0.3) d (range, 0.01 to 1 d) (Wilcoxon test, \(P < .01\)). Thirty percent of eyes lost lines of BCVA during the follow-up. In this group, 13.4% (13 eyes) had a small decrease in visual acuity with no change in Snellen visual acuity and 17.5% (17 eyes) lost lines of BCVA. Of 97 eyes, 8.2% (8 eyes) lost 1 line of BCVA; 6.1% (6 eyes), 2 lines; 1% (1 eye), 3 lines; and 2.1% (2 eyes), 4 lines. Among these, 6 had myopic maculopathy; 5, elevated IOP with visual field defect; and 6, secondary posterior capsule opacification. The median of visual lines lost was −0.1 (range, −0.5 to −0.1) from the preoperative examination to the end of the follow-up. Seventy percent of eyes gained lines of BCVA. The median improvement was 0.4 (range, 0.1 to 0.7). Ten (10%) of 97 eyes gained 1 line of BCVA; 5 (5%), 2 lines; 6 (6%), 3 lines; 15 (12%), 4 lines; 9 (9%), 5 lines; and 6 (6%), more than 6 lines at

### Table 1. Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>50</td>
</tr>
<tr>
<td>No. of eyes</td>
<td>97</td>
</tr>
<tr>
<td>Age at surgery, y</td>
<td>35.9 (12.6)</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>33 (66)</td>
</tr>
<tr>
<td>Duration of follow-up, y</td>
<td>18.1 (1.9)</td>
</tr>
<tr>
<td>BCVA before the surgery, decimal</td>
<td>0.35 (0.2)</td>
</tr>
<tr>
<td>BCVA at the end of follow-up, decimal</td>
<td>0.56 (0.3)</td>
</tr>
<tr>
<td>Endothelial cell count before the surgery, cells/mm²</td>
<td>2873 (555)</td>
</tr>
<tr>
<td>Endothelial cell count at the end of follow-up, cells/mm², mean (SD)</td>
<td>1966 (439)</td>
</tr>
</tbody>
</table>

Abbreviation: BCVA, best-corrected visual acuity.
the end of the follow-up. Risk factors and causes for loss of visual acuity of −0.2 line are shown in Table 2. Weak associations with a loss of BCVA were found with cataract (OR, 0.2; 95% CI, 0.08-0.7; \(P < .006\)), elevated IOP (OR, 0.7; 95% CI, 0.2-2.25; \(P < .50\)), oval pupil (OR, 0.27; 95% CI, 0.1-0.74; \(P < .008\)), uveitis (OR, 0.6; 95% CI, 0.6-6.06; \(P < .60\)), and ECL coefficient greater than 40% (OR, 0.2; 95% CI, 0.03-2.16; \(P < .60\)), and a strong association was found with retinal detachment (OR, 2; 95% CI, 0.25-14.8; \(P < .40\)). Mean (SD) endothelial cell density preoperatively and at the end of the follow-up was 2783 (787) cells/mm² and 1921 (672) cells/mm², respectively (Wilcoxon, \(P < .01\)). The median coefficient of ECL was 17.5% (minimum, 5.2%; maximum, 72.7%). The incidence of cataract during the follow-up was 0.010 EY among eyes with ZB5M implanted and free of cataract at the first visit; cornea decompensation, 0.001 EY; ocular hypertension, 0.008 EY; pupil ovalization, 0.020 EY; uveitis, 0.001 EY; and retinal detachment, 0.002 EY. These data are shown in Table 2. Intraocular pressure elevation was observed in 15% of eyes at the end of the follow-up. The median (SE) time of onset during the follow-up was 18.8 (0.5) years (95% CI, 17.6-20.4) (Figure, A). Cataract complication was found in 38% of eyes. The median (SE) onset was at 20.5 (0.5) years (95% CI, 16.7-18.7) (Figure, B). Uveitis occurred in 3% of eyes. All the observations were at the beginning of the follow-up and 1 year after the surgery (Figure, C). Pupil ovalization occurred in 36% of eyes during the follow-up. The median (SE) onset was 16.5 (0.6) years (95% CI, 15.2-17.8) (Figure, D). Retinal detachment was diagnosed in 4 eyes.

Table 2. Complications During Follow-up

<table>
<thead>
<tr>
<th>Complication</th>
<th>No./Total No. (%)</th>
<th>95% CI</th>
<th>Incidence Rate, Eye-year(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>33/97 (34)</td>
<td>0.25-0.43</td>
<td>0.010</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>15/97 (15)</td>
<td>0.09-0.23</td>
<td>0.008</td>
</tr>
<tr>
<td>Pupil ovalization</td>
<td>35/97 (36)</td>
<td>0.27-0.46</td>
<td>0.020</td>
</tr>
<tr>
<td>Uveitis</td>
<td>3/97 (3)</td>
<td>0.01-0.08</td>
<td>0.001</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>4/97 (4)</td>
<td>0.01-0.10</td>
<td>0.002</td>
</tr>
<tr>
<td>Cornea decompensation</td>
<td>1/97 (1)</td>
<td>0.001-0.05</td>
<td>0.001</td>
</tr>
</tbody>
</table>

\(^a\) Number of events/number of affected eyes at risk.

\(^b\) Calculated as the number of events divided by the number of affected eyes at risk during the year (eye-year).

Figure. Kaplan-Meier Curve

Elevated intraocular pressure (IOP) (A), cataract (B), uveitis (C), oval pupil (D), retinal detachment (E), and endothelial cell loss (F) among patients without these complications at the first visit.

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The median (SE) onset was 18 (0.1) years (95% CI, 18.4-21) (Figure, E). Corneal decompensation was found only in 1 eye at 19 years of follow-up. During the follow-up, PIOLs in 29 eyes (29.8%) were explanted. The median (SE) time to explantation was 12.3 (0.5) years (95% CI, 11.2-13.3).

Discussion

Angle-supported PIOLs have been used for more than 2 decades for treating high refractive errors, with their main advantage being easy anterior segment insertion. The long-term complications for eyes implanted with PIOLs have been reported in several articles.10-15

Pupil Ovalization

Our study showed a prevalence of pupil ovalization in 36% of eyes implanted with the ZB5M, with an incidence of 0.020 EY. Pupil ovalization is the most frequent complication of PIOLs and the most difficult to avoid.10,14-16 It occurs as a consequence of PIOLs oversizing, causing compression and ischemia of the iris root. In the French Multicenter Study, an overall incidence of 22.6% was reported. In 5.8% of the cases, pupil ovalization developed at 1 month; 9.9%, at 1 year; 16.7%, at 2 years; and 27.5%, at 3 years.13 The reason for this is probably the difficulty of adapting the 3 lens sizes available to all possible diameters of the AC in addition to the imprecise measurement methods used at the moment of implantation. For adequate sizing of the PIOL implanted, Kiraly and Duncker17 identified the IOL Master 500 (Carl Zeiss Meditec) as the easiest and most precise instrument to measure the AC depth and diameter. On the contrary, Reinstein et al18 reported the Visante OCT (Carl Zeiss Meditec) as the best instrument able to provide the data directly on request, without performing a prospective study. The models implanted in our group had 3 different diameters (12.5, 13, and 13.5 mm). Severe pupil ovalization with symptoms such as glare and halos was found in 2 cases, and in both cases, the lenses were explanted and replaced with lenses of a smaller diameter.

Endothelial Cell Loss

Another potential risk is ECL. We found the median coefficient of ECL as 17.5%, with a rate of 0.97% every year. A previous study12 in patients with PIOLs implanted reported an average rate of ECL as 1.78% every year. The relationship between ECL and age has been described. Laule et al19 reported a sharp decline in cell count up to the age of 25 years followed by a more gradual decline. Other studies20,21 showed a reduction of endothelial cells until the fifth decade but no subsequent fall. Yee et al22 estimated a physiological rate of decrease in the endothelial cell density of 0.56% per year in a healthy eye. In 1998, Baikoff et al15 suggested that the new models of angle-supported PIOL were well tolerated by the corneal endothelium because of the substantial improvements in their design and probably in the quality of surgery. Anterior chamber inflammation was usually mild and subclinical without severe complications. A risk factor for ECL and cataract (OR, 2.04; 95% CI, 0.66-6.32; P < .20) showed a strong association but it was not statistically significant. The strong association and statistical significance were found with elevated IOP (OR, 3.45; 95% CI, 0.98-12.19; P < .04). Two different mechanisms have been proposed to explain the deterioration of endothelial cell density: the excessive proximity of the PIOL parts to the corneal endothelium, which may intermittently or permanently be in contact with the posterior part of the cornea,9,10,23 or the presence of inflammatory mediators in the aqueous humor produced by any kind of trauma to uveal structures.24,25 The Kaplan-Meier curve for ECL showed that a loss of 20% of endothelial cells occurred in all patients (median [SE], 19 [0.3] years; 95% CI, 18.4-19.7) after PIOL implantation (Figure, F).

Cataract

In our series, the prevalence of cataract 15 years after surgery was found in 37 eyes (38%) with an incidence of 0.010 EY. Among these, subcapsular cataract was found in 41%; nuclear cataract was found in 38%; cortical, in 11%; and cortical and nuclear, in 11%. The mean (SD) age at diagnosis of cataract was 47.3 (5.3) years (range, 35.5-61.8 years). In 22 cases, cataract surgery was required. In all these patients, the BCVA was affected. Twelve cases had nuclear cataract, and among these, 8 cases had a reduction of the safety zone of 1.5 mm between the endothelium and the lens. A very young woman developed nuclear cataract in both eyes 9 years after implantation. Her visual defect before the surgery was −29 diopters of myopia in both eyes. The visual outcome after the bilensectomy (PIOL explantation followed by phacoemulsification of the crystalline lens) was very good, gaining 2 lines and 1 line of BCVA, respectively. The long-term risk of developing cataracts after PIOL implantation is still controversial.26 Prevalence of cataract among those with high myopia is 4 times more common than in nonmyopic patients,27,28 and nuclear cataract is the most frequent type (54.7%). The incidence of age-related cataract becomes significant in the 40- to 50-year age group of the population, ranging from 3.7% to 7.6%.29 Subclinical degrees of inflammation at the AC could explain the high incidence of nuclear cataracts in this group of patients.14

Elevated IOP

Fifteen of the 97 eyes with follow-up of more than 15 years had an IOP more than 21 mm Hg in the absence of treatment. We found an incidence rate of 0.008 EY with a median (SE) onset at 18.8 (0.5) years of follow-up. Thirteen of these patients also had cataract. A strong and significant correlation was found between cataract and elevated IOP (Pearson χ² = 0.4; P < .001). The high IOP would be more related to cataract and angle dimension change than PIOL. Furthermore, the median time of onset of elevated IOP was observed to be quite similar to the age at onset of cataract. The mean (SD) age of the patient when cataracts appeared was 48.5 (6.5) years (range, 35.5-64.5 years) and elevated IOP was found at the mean (SD) age of 42.6 (8 years) range, 33.6-61.5 years). No correlation was found between the postoperative elevation of IOP and the presence of ovalization or postoperative elevation of IOP and the development of postoperative acute anterior uveitis. A previous study23 reports a low cumulative risk predicted by the Kaplan-Meier curves for developing chronic IOP elevation.
Retinal Detachment

Retinal detachment occurred in 4 eyes (4.1%). The mean (SD) age of the patients in the retinal detachment group was 47.5 (6) years. The median (SE) time between implantation and retinal detachment was 18 (0.1) years (95% CI, 18.4-21). In all cases, retinal detachment was spontaneous; it was related to flap tear in 1 eye, an atrophic hole in 1 eye, and flap tear with holes in 2 eyes. Two of these 4 eyes had undergone treatment by argon laser on the peripheral retina for lattice degeneration in 1 eye and atrophic hole in 1 eye. In these 2 eyes, retinal detachment appeared through new lesions unrelated to previously treated lesions. In all cases, the retina was reattached successfully with the first retinal detachment surgery. A clear relationship between severe myopia and retinal detachment has been reported. The surgical trauma of intraocular lens implantation is also a risk factor for retinal detachment. Initial studies reported a low incidence of 0.84% to 0.61%, while in a long-term follow-up study, the incidence was slightly higher at 4.8%.

Uveitis

Iridocyclitis can occur months or years after the implantation of angle-supported PIOLs. In our group, 3 eyes (3%) developed this complication. All the observations were within 1 year of the surgery. All patients had blurred vision, redness, and pain. Posterior synechiae was detected in 1 patient and IOL precipitates in 2 cases. After topical steroid therapy, all patients fully recovered and there were no recurrences during the follow-up. In our group, this complication did not lead to PIOL explantation. Another study reported an incidence between 3.1% and 4.5%. The haptic-angle interaction has been proposed as a possible mechanism for inflammation except in cases of bacterial endophthalmitis and in the uncommon case of undersized and movable PIOLs.

Criteria Followed for PIOL Explantation

Cataract was described as the most frequent indication for PIOL removal. In our group of patients, PIOLs in 29 eyes (29.8%) were explanted. The explantation was related to cataract in 22 eyes, significant ECL in 4 eyes, retinal detachment in 2 eyes (in these 2 patients, bisectionomy was chosen because they presented with signs of cataract onset), and corneal decompensation in 1 eye. The median (SE) time to explantation was 12.3 (0.5) years (95% CI, 11.2-13.3).

The criteria we followed for explantation were:

1. Cases with cataract: Patients with PIOL and a decrease in BCVA of at least 3 lines since PIOL implantation and related to evident lens sclerosis or cataract. Potential visual acuity measurements confirming the potential for sight improvement after cataract surgery were obtained prospectively in most cases with the Guyton-Minkowski potential acuity meter or Retinal Acuity Meter (RAM; AMA Optics Inc). Cataract type and morphology were evaluated using the Lens Opacities Classification System III.
2. Cases with ECL: PIOLs were explanted in these patients when:
   A. The endothelial cell count decreased markedly, approaching 1500 cells/mm², with evidence of progressive deterioration in their endothelial cell count over 6 months.
   B. Progressive ECL of more than 20% per year for 2 years regardless of the number of cells.
   C. The PIOL was incorrectly sized and/or significant progressive ECL was occurring related to the PIOL.
3. Cases with other serious complications secondary to PIOLs such as endothelial decompensation, pupil ovalization, (symptomatic) iris atrophy, ocular hypertension, lens vaulting, and retinal detachment.
4. Cases where the AC morphology was modified and the safety zone of 1.5 mm between the endothelium and PIOL was no longer respected.

Conclusions

In summary, this study reports for the first time, to our knowledge, the long-term outcomes and complications of the ZB5M PIOL for high myopia. The data related to cataract, elevated IOP, and ECL complications suggest the need for carrying out an evaluation of AC and angle depth in patients older than 40 years with PIOL to verify the possible modification in the AC related to the lens thickness. The lens thickness increases from 18 to 20 µm every year. The increase in lens thickness corresponds to an AC reduction of approximately 18, 3 µm per year. Suggested that if the edge of the haptic is less than 1.50 mm from the endothelium, the corneal distortions that occur during eye rubbing can give rise to endothelial alterations by contact with the edge of the PIOL, with the consequence of endothelial change. Explantation of PIOLs should be considered when the safety zone between the PIOL and endothelium is not respected.