· Original article ·

Preliminary evaluation of an algorithm to minimize the power error selection of an aspheric intraocular lens by optimizing the estimation of the corneal power and the effective lens position

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非球面人工晶状体度数计算的最优化

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摘要

目的：通过评价非球面人工晶状体（intraocular lens，IOL）屈光度的可预测性，初步开发一种计算屈光度（P_{IOL}）的优化算法。

方法：本研究纳入植入非球面 IOL（LENTIS L-313，Oculentis GmbH）65 眼，并分为 2 组：A 组 8 例 12 眼，$P_{IOL} \geqslant$ 23.0D；B 组 35 例 53 眼，$P_{IOL} < 23.0D$。术后 3mo 进行屈光度可预测性评价。参考角膜屈光力估计所致的可变性屈光指数计算出校正的 IOL 度数（P_{IOLadj}）及屈光结果，根据年龄和解剖学因素得出校正的有效晶状体位置（adjusted effective lens position，ELP_{adj}）。

结果：术后 A、B 两组等效球镜度数分别为-0.75 ~ +0.75D、-1.38 ~ +0.75D。A、B 两组的 P_{IOLadj} 和实际晶状体屈光度（$P_{IOLReal}$）之间无统计学差异（$P = 0.64$、0.82）。Bland-Altman 分析显示 A、B 两组 P_{IOLadj} 和 $P_{IOLReal}$ 之间的一致性区间分别为+1.11 ~ -0.96D 和+1.14 ~ -1.18D。Hoffer Q 公式和 Holladay I 公式计算 P_{IOLadj} 和 P_{IOL} 之间存在临床和统计学上的显著差异（$P < 0.01$）。

结论：植入非球面 IOL 白内障手术的屈光可预测性可通过平行轴光学联合线性法则使角膜屈光力及晶状体位置相关误差最小化。

Abstract

· **AIM**：To evaluate the refractive predictability achieved with an aspheric intraocular lens（IOL）and to develop a preliminary optimized algorithm for the calculation of its power（P_{IOL}）.

· **METHODS**：This study included 65 eyes implanted with the aspheric IOL LENTIS L-313（Oculentis GmbH）that were divided into 2 groups：12 eyes（8 patients）with $P_{IOL} \geqslant 23.0$ D（group A），and 53 eyes（35 patients）with $P_{IOL} < 23.0$ D（group B）. The refractive predictability was evaluated at 3mo postoperatively. An adjusted IOL power（P_{IOLadj}）was calculated considering a variable refractive index for corneal power estimation，the refractive outcome obtained，and an adjusted effective lens position（ELP_{adj}）according to age and anatomical factors.

· **RESULTS**：Postoperative spherical equivalent ranged from -0.75 to +0.75 D and from -1.38 to +0.75 D in groups A and B，respectively. No statistically significant differences were found in groups A（$P = 0.64$）and B（$P = 0.82$）between P_{IOLadj} and the IOL power implanted（$P_{IOLReal}$）. The Bland and Altman analysis showed ranges of agreement between P_{IOLadj} and $P_{IOLReal}$ of +1.11 to -0.96 D and +1.14 to -1.18 D in groups A and B，respectively. Clinically and statistically significant differences were found between P_{IOLadj} and P_{IOL} obtained with Hoffer Q and Holladay I formulas（$P < 0.01$）.

· **CONCLUSION**：The refractive predictability of cataract surgery with implantation of an aspheric IOL can be optimized using paraxial optics combined with linear algorithms to minimize the error associated to the estimation of corneal power and ELP.

· **KEYWORDS**：aspheric intraocular lens；intraocular lens power calculation；effective lens position

INTRODUCTION

The human eye is composed of two aspheric lenses, cornea and crystalline lens, which are the main ocular optical elements accounting for the final quality of the retinal image. The cornea is comprised of two prolate surfaces that induce positive spherical aberration that increases with age[1]. The crystalline lens is comprised of two aspheric surfaces that induce negative spherical aberration[2]. With age, the balance between the spherical aberration of the cornea and crystalline lens is progressively lost, leading to a reduction in the level of quality of the retinal image[3-6]. Aspheric intraocular lenses (IOLs) were developed with the aim of providing a compensation for the corneal positive spherical aberration and therefore to maintain the balance in terms of spherical aberration between cornea and IOL after cataract surgery[7]. An aspheric IOL may lead then to the achievement of better contrast sensitivity compared to a spherical IOL, especially under dim light conditions[7].

According to some optical simulations, a real benefit can be obtained with aspheric IOLs in corneas of a moderate prolate aspheric shape with a negative asphericity (Q) value of -0.22 or below[8]. In spite of the potential benefit of aspheric IOLs over conventional spherical IOLs, it should be mentioned that the outcomes obtained with aspheric IOLs are more susceptible to misalignments or decentrations[9] as well as to residual optical errors[10]. Furthermore, the potential benefit of aspheric IOLs has been suggested to be more limited in longer eyes than in short eyes[8]. This may be due to some inaccuracies in IOL power calculations in such cases. Hoffmann and Lindeman[11] demonstrated that ray tracing based on biometry data improved IOL prediction accuracy over conventional formulas in normal eyes implanted with aspheric IOLs. The aim of the current study was to evaluate the predictability of the refractive correction achieved with a specific model of aspheric IOL and to develop a preliminary algorithm for IOL power calculation to optimize the refractive predictability with this IOL by minimizing the error associated to the keratometric estimation of the corneal power and by developing a predictive formula for the estimation of the effective lens position. This study was planned as a preliminary evaluation of the possibility of a further optimization of IOL power calculation using paraxial optics.

SUBJECTS AND METHODS

Patients　A total of 65 eyes of 43 patients ranging in age from 56 to 92 years old were included retrospectively in this study. All these eyes underwent cataract surgery with implantation of the aspheric IOL LENTIS L-313 (Oculentis GmbH, Berlin, Germany). As will be explained later, two groups of eyes were differentiated according to the power of the IOL implanted: group A, including 12 eyes of 8 patients implanted with an IOL ≥23.0 D, and group B, including 53 eyes of 35 patients with an IOL <23.0 D of power. The inclusion criteria of this study were patients with visually significant cataract or presbyopic/pre-presbyopic patients suitable for refractive lens exchange. The exclusion criteria were patients with active ocular diseases, illiteracy and topographic astigmatisms >1.5 D. All volunteers were adequately informed and signed a consent form. The study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of the University of Alicante (Alicante, Spain).

Intraocular Lens　The LENTIS L-313 is an acrylic one-piece IOL with a hydrophobic surface and ultraviolet-filtering components. It has biconvex design with a 6.0-mm optic, an overall length of 11.0 mm, and a C-loop haptic design with 0-degree angulation. The posterior surface of the IOL is aspheric and provides some level of negative spherical aberration aimed at compensating for the positive spherical aberration of the cornea. It is available in powers from 10 to 30 D in 0.5-D steps and from 0 to 10 D and from 30 to 35 D in 1.0-D steps.

Surgical Technique　All surgeries were performed by one experienced surgeon (Ramón ML) using a standard technique of phacoemulsification. In all cases, topical anesthesia was administered and pupillary dilation was induced with a combination of tropicamide and phenylephrine 10% every 15min half an hour previous to the procedure. Iodine solution 5% was instilled on the eye 10min before the operation. A 2.75-mm clear incision was made with a diamond knife on the steepest meridian to minimize post-surgical astigmatism. A paracentesis was made 60°-90° clockwise from the main incision and the anterior chamber was filled with viscoelastic material. After the crystalline lens removal, the IOL was implanted through the incision into the capsular bag using a specific injector developed by the manufacturer for such purpose. Finally, the surgeon proceeded to retrieve the viscoelastic material using the irrigation-aspiration system. A combination of topical steroid and antibiotic (Tobradex, Alcon, Fort Worth, TX, USA) as well as a non-steroidal anti-inflammatory drops (Dicloabak, Laboratorios Thea, Barcelona, Spain) were prescribed to be applied 4 times daily for 1wk after the surgery and 3 times daily the second postoperative week. In addition, the non-steroidal anti-inflammatory drops were also prescribed to be applied 3 times daily during 2wk more after surgery.

Preoperative and Postoperative Examinations　Preoperatively, all patients had a full ophthalmologic examination including the evaluation of the refractive status, distance and near visual acuities, slit lamp examination, optical biometry (IOL-Master, Carl Zeiss Meditec, Jena, Germany), tonometry and funduscopy. Postoperatively, patients were evaluated at 1d, 1wk, 1 and 3mo after surgery. In all visits, visual acuity, refraction and the integrity of the anterior segment were evaluated. Funduscopy was also performed in the postoperative revision at 3mo.

Calculation of the Adjusted IOL Power   Almost all theoretical formulas for IOL power calculation are based on the use of a simplified eye model, with thin cornea and lens models[12]. According to such approach, the power of the IOL (P_{IOL}) can be easily calculated using the Gauss equations in paraxial optics[13]:

$$P_{IOL} = \left(\frac{n_{hv}}{(AL - ELP)} \right) - \left(\frac{n_{ha}}{\left(\frac{n_{ha}}{R_{des} + P_c} - ELP \right)} \right) \qquad (1)$$

where P_c is the total corneal power, ELP is the effective lens plane, AL is the axial length of the eye, n_{ha} is the aqueous humour refractive index, n_{hv} is the vitreous humour refractive index and R_{des} represents the postoperative desired refraction calculated at corneal vertex.

Our research group proposed in 2012 the use of a variable keratometric index (n_{kadj}) depending on the radius of the anterior corneal surface (r_{1c}) expressed in millimetres for minimizing the error associated to the keratometric approach for corneal power calculation[14]. Specifically, the following expression was defined according to the Gullstrand eye model:

$$n_{kadj} = -0.0064286r_{1c} + 1.37688 \qquad (2)$$

Using this algorithm, a new keratometric corneal power, named adjusted keratometric corneal power (P_{kadj}), can be calculated using the classical keratometric approach for corneal power estimation without clinically relevant error[15].

In the current study, an adjusted IOL power (P_{IOLadj}) was calculated, which was defined as the IOL power calculated from the equation 1 using the n_{kadj} value for the estimation of the corneal power (P_{kadj}), as well as the n_{ha} and n_{hv} values corresponding to the Gullstrand eye model (1. 336). In such calculation, the postoperative spherical equivalent at corneal vertex was considered as the desired refraction ($R_{des} = SE_{post}$). This adjusted IOL power (P_{IOLadj}) was compared with the real power of the IOL implanted ($P_{IOLReal}$). The P_{IOLadj} calculation was performed after estimating the ELP(effective lens plane) using two different approaches: ELP calculation following the SRK/T formula guidelines (named $P_{IOLadjSRK/T}$) and ELP calculation using a mathematical expression obtained by multiple regression analysis (named ELP_{adj}), as explained carefully in the next section.

Furthermore, the P_{IOL} was also calculated using three conventional formulas (Haigis, Hoffer Q and Holladay I) considering the ELP defined by each formula and that $R_{des} = SE_{post}$. A comparative analysis was done between these values of P_{IOL} and P_{IOLadj} and $P_{IOLReal}$. All the formulas were implemented in Excel version 14. 0. 0 for Mac (Microsoft, Irvine, CA, USA).

Estimation of Adjusted ELP by Multiple Regression Analysis   Considering in each case the equation 1, the values of $P_{IOLreal}$ and P_{kadj}, and that $R_{des} = SE_{post}$, the real ELP

was obtained. A multiple regression analysis was then performed to obtain a mathematical expression predicting the best as possible the real ELP corresponding to each case. This ELP was named adjusted effective lens position (ELP_{adj}). An initial estimation of ELP_{adj} was obtained considering the whole sample of 65 eyes, but the results were inconsistent leading to clinically relevant errors in the calculation of the P_{IOLadj}. As we realized that the calculation of ELP_{adj} was dependent on the IOL power implanted and consequently of the IOL geometry, two groups were differentiated according to this parameter, groups A and B, as previously mentioned. In group A, this effective lens position was named $ELP_{adj \geq 23}$, whereas in group B it was named $ELP_{adj<23}$.

Statistical Analysis   The statistical analysis was performed using the SPSS statistics software package version 21. 0 for Mac (IBM, Armonk, NY, USA). Normality of data samples was evaluated by means of the Kolmogorov – Smirnov test. When parametric analysis was possible, the Student's t – test for paired data was used for comparing the different approaches for P_{IOL} calculation. When parametric analysis was not possible, the Wilcoxon rank sum test was applied to assess the significance of such comparisons. Differences were considered to be statistically significant when the associated P – value was less than 0. 05. Regarding the interchangeability between pairs of methods used for obtaining P_{IOL}, the Bland – Altman analysis was used[16].

A multiple regression analysis was used for predicting the real ELP from different preoperative anatomical and clinical parameters (ELP_{adj}). Model assumptions were evaluated by analysing residuals, the normality of non – standardized residuals (homoscedasticity), and the Cook's distance to detect influential points or outliers. In addition, the lack of correlation between errors and multicolinearity was assessed using the Durbin – Watson test, the calculation of the colinearity tolerance, and the variance inflation factor.

RESULTS

Group A included 12 eyes of 8 patients [11 eyes in males (91. 7%)], with a mean age of 68. 2±9. 4y (range: 56. 0 to 80. 0y). In this group, mean preoperative keratometry ($P_{k1.3375}$), axial length (AL) and anterior chamber depth (ACD) were 44. 79±1. 44 D (range: 42. 92 to 47. 34 D), 22. 33±0. 55 mm (range: 21. 30 to 23. 09 mm), and 2. 95± 0. 33 mm (range: 2. 41 to 3. 35 mm), respectively. According to all these data and using the SRK – T formula, mean IOL power implanted ($P_{IOLReal}$) was 23. 75 ± 0. 69 D (range: 23. 00 to 25. 00 D). Group B included 53 eyes of 35 patients [24 eyes in males (45. 3%)], with a mean age of 72. 2±7. 1y (range: 57. 0 to 92. 0y). Mean $P_{k1.3375}$, AL and ACD were 44. 37±1. 35 D (range: 41. 09 to 47. 28 D), 23. 70±1. 13 mm (range: 22. 20 to 28. 33 mm), and 3. 32±0. 34 mm (range: 2. 48 to 4. 15 mm), respectively. According to all these data and using the SRK–T formula, mean IOL power implanted was 19. 72±3. 10 D (range: 7. 50 to 22. 50 D). All these data are summarized in Table 1.

Table 1　Mean visual, refractive, biometric and IOL power calculation data

Parameter	$P_{IOLReal} \geqslant 23.0D$		$P_{IOLReal} < 23.0D$	
	Mean±SD	Range	Mean±SD	Range
SE_{pre} (D)	1.04±1.64	−2.38 to 2.75	−0.84±3.05	−12.38 to 3.38
SE_{post} (D)	−0.20±0.40	−0.75 to 0.75	−0.25±0.44	−1.38 to 0.75
r_{1c} (mm)	7.54±0.24	7.13 to 7.86	7.61±1.13	7.14 to 8.21
ACD (mm)	2.95±0.33	2.41 to 3.35	3.32±0.34	2.48 to 4.15
AL (mm)	22.33±0.55	21.30 to 23.09	23.70±1.13	22.20 to 28.33
$ELP_{adjSRK/T}$ (mm)	4.60±0.13	4.37 to 4.86	5.17±0.78	4.65 to 9.24
ELP_{adj} (mm)	4.44±0.31	3.93 to 5.01	4.59±0.50	3.90 to 6.16
ELP_{Haigis} (mm)	4.75±0.14	4.54 to 4.90	5.04±0.21	4.66 to 5.65
$ELP_{HofferQ}$ (mm)	4.68±0.08	4.59 to 4.88	5.06±0.33	4.74 to 6.42
$ELP_{Holladay}$ (mm)	3.77±0.42	3.08 to 4.29	4.24±0.43	3.17 to 5.31
n_{kadj}	1.328±0.002	1.326 to 1.331	1.328±0.002	1.324 to 1.331
$P_{k1.3375}$ (D)	44.79±1.44	42.92 to 47.34	44.37±1.35	41.09 to 47.28
$P_{cHaigis}$ (D)	43.99±1.41	42.16 to 46.50	43.58±1.33	40.35 to 46.43
P_{kadj} (D)	43.58±1.61	41.50 to 46.44	43.11±1.51	39.45 to 46.36
$P_{IOLReal}$ (D)	23.75±0.69	23.00 to 25.00	19.72±3.10	7.50 to 22.50
$P_{IOLadjSRK/T}$ (D)	24.18±0.99	21.85 to 25.87	20.69±3.00	9.81 to 24.31
P_{IOLadj} (D)	23.82±1.02	22.16 to 25.76	19.70±3.13	7.41 to 23.08
$P_{IOLHaigis}$ (D)	23.95±1.16	21.25 to 26.14	19.95±3.58	6.35 to 24.05
$P_{IOLHofferQ}$ (D)	22.68±1.47	20.24 to 25.07	17.93±4.15	4.55 to 22.47
$P_{IOLHolladay}$ (D)	22.90±1.00	20.51 to 24.61	19.19±3.37	5.58 to 23.01

SE_{pre}: Preoperative spherical equivalent; SE_{post}: Postoperative spherical equivalent; r_{1c}: Radius of curvature of the anterior corneal surface; ACD: Anterior chamber depth; AL: Axial length; $ELP_{SRK/T}$: Effective lens position for the SRK/T formula; ELP_{adj}: Effective lens position for the adjusted formula; ELP_{Haigis}: Effective lens position for the Haigis formula; $ELP_{HofferQ}$: Effective lens position for the Hoffer Q formula; $ELP_{Holladay}$: Effective lens position for the Holladay formula; n_{kadj}: Adjusted keratometric index; $P_{k1.3375}$: Corneal power obtained using IOL-Master or keratometric power; $P_{cHaigis}$: Corneal power obtained for the Haigis formula; P_{kadj}: Corneal power obtained using the adjusted keratometric index; $P_{IOLReal}$: Power of the intraocular lens implanted which was calculated using the SRK/T formula; $P_{IOLadj-SRK/T}$: Power of the intraocular lens obtained using adjusted formula and ELP calculated with the SRK/T formula; P_{IOLadj}: Intraocular lens power obtained using the adjusted formula and ELP_{adj}; $P_{IOLHaigis}$: Intraocular lens power obtained using the Haigis formula; $P_{IOLHofferQ}$: Intraocular lens power obtained using the Hoffer Q formula; $P_{IOLHolladay}$: Intraocular lens power obtained using the Holladay formula.

Agreement of $P_{IOLReal}$ and $P_{IOLadj-SRK/T}$　　In group A, no statistically significant differences were found between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ when ELP was calculated with the SRK/T formula guidelines and $R_{des} = SE_{post}$ ($P = 0.06$, paired Student's t-test). The correlation between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ was statistically significant ($r = 0.680$, $P < 0.01$) (Figure 1A). According to the Bland and Altman analysis, mean difference between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ was 0.43 D, with limits of agreement of +1.84 and −0.98 D. Figure 2A shows the Bland and Altman plot corresponding to this agreement analysis.

In group B, statistically significant differences were found between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ when ELP was calculated with the SRK/T formula guidelines and $R_{des} = SE_{post}$ ($P < 0.01$, Wilcoxon test). A very strong and statistically significant correlation was found between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ ($r = 0.898$, $P < 0.01$) (Figure 1B). The Bland and Altman analysis showed a mean difference between $P_{IOLadj-SRK/T}$ and $P_{IOLReal}$ of 0.97 D, with limits of agreement of +2.24 and −0.30 D (Figure 2B).

Estimation of ELP_{adj}　　The multiple regression analysis revealed that the ELP_{adj} was significantly correlated with age

and corneal astigmatism (CA) ($P < 0.01$) in group A:

$$ELP_{adj \geqslant 23} = 5.983 - 0.015 Age - 0.460 CA \qquad (3)$$

The homoscedasticity of the model was confirmed by the normality of the non-standardized residuals distribution ($P = 0.20$) and the absence of influential points or outliers (mean Cook's distance: 0.146±0.259). With this model, 58.33% of non-standardized residuals were 0.20 or lower. The poor correlation between residuals (Durbin-Watson test: 2.320) and the lack of multicolinearity (tolerance 0.971 to 0.971; variance inflation factors 1.029 to 1.029) was also confirmed.

No statistically significant differences were found between ELP calculated with the SRK/T formula guidelines and the $ELP_{adj \geqslant 23}$ ($P = 0.07$, Student's t-test).

In group B, the $ELP_{adj < 23}$ was found to be significantly correlated with age, ACD, AL and r_{1c} ($P < 0.01$):

$$ELP_{adj < 23} = 5.327 + 0.015 Age + 0.346 ACD + 0.334 AL - 1.430 r_{1c} \qquad (4)$$
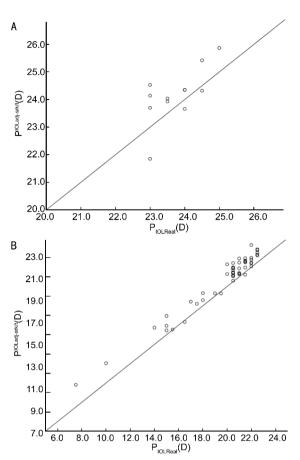
Figure 1 Scattergram showing the relation between the adjusted IOL power using the ELP estimated using the SRK-T formula guidelines ($P_{IOLadj-SRK/T}$) and the real power of the IOL implanted ($P_{IOLReal}$) A: Results in group A; B: Results in group B.
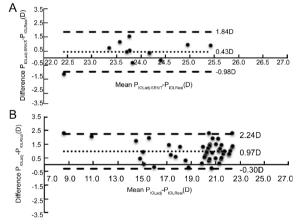

Figure 2 Bland-Altman plots for the comparison between the adjusted IOL power using the ELP estimated using the SRK-T formula guidelines ($P_{IOLadj-SRK/T}$) and the real power of the IOL implanted ($P_{IOLReal}$) The dotted lines show the limits of agreement ($\pm 1.96SD$). A: Results in group A; B: Results in group B.

The homoscedasticity of the model was also confirmed by the normality of the non-standardized residuals distribution ($P = 0.20$) and the absence of influential points or outliers (mean Cook's distance: 0.04 ± 0.13). With this model, 84.91% of non-standardized residuals were 0.50. The poor correlation between residuals (Durbin-Watson test: 2.208) and the lack
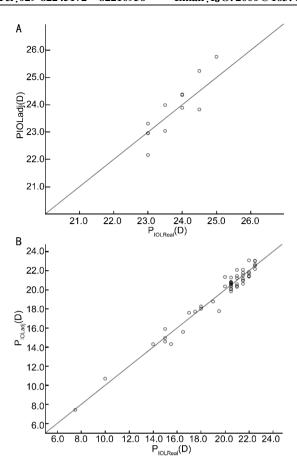

Figure 3 Scattergram showing the relation between the adjusted IOL power using the regression analysis adjusted ELP (P_{IOLadj}) and the real power of the IOL implanted ($P_{IOLReal}$) A: Results in group A; B: Results in group B.

of multicolinearity (tolerance 0.733 to 0.926; variance inflation factors 1.080 to 1.364) was also confirmed.

A statistically significant difference was found between ELP calculated with the SRK/T formula guidelines and the $ELP_{adj<23}$ ($P<0.01$, Wilcoxon test), with a lower value with our adjustment (Table 1).

Agreement between $P_{IOLReal}$ and P_{IOLadj} No statistically significant differences were found in any group between P_{IOLadj} and $P_{IOLReal}$ when ELP_{adj} and $R_{des} = SE_{post}$ were considered for P_{IOLadj} calculation (Group A: $P=0.64$, unpaired Student's t-test; Group B: $P=0.82$, Wilcoxon test). A strong and statistically significant correlation was found between P_{IOLadj} and $P_{IOLReal}$ in both groups (Group A: $r=0.88$, $P<0.01$; Group B: $r=0.91$, $P<0.01$) (Figure 3). In group A, the Bland and Altman analysis showed a mean difference between P_{IOLadj} and $P_{IOLReal}$ of 0.08 D, with limits of agreement of +1.11 and -0.96 D (Figure 4A). In group B, the mean difference between P_{IOLadj} and $P_{IOLReal}$ was -0.02 D, with limits of agreement of +1.14 and -1.18 D (Figure 4B).

Agreement of P_{IOLadj} and P_{IOL} with Other Formulas The ELP values corresponding to different available IOL power formulas were calculated and afterwards an estimation of P_{IOL} was performed with each of these formulas (Table 1). In group A, statistically significant differences were found in all comparisons ($P<0.01$, paired Student's t-test) except for the

Table 2　Bland & Altman analysis outcomes of the comparison between P_{IOLadj} and the IOL power obtained with other commonly used formulas

Formulas	Group A			Group B		
	$\Delta P_{IOL} \pm SD$（D）	LoA（D）	P	$\Delta P_{IOL} \pm SD$（D）	LoA（D）	P
Haigis	0.13±0.69	1.47 to −1.22	=0.53	0.25±0.50	1.24 to −0.73	<0.01
Hoffer Q	−1.14±1.15	1.11 to −3.40	<0.01	−1.76±1.84	1.84 to −5.36	<0.01
Holladay 1	−0.93±0.61	0.26 to −2.12	<0.01	−0.50±0.36	0.20 to −1.20	<0.01

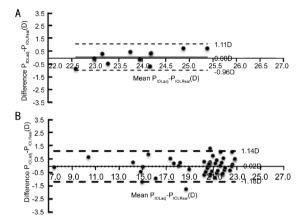ΔP_{IOL}: Difference in intraocular lens power; LoA: Limits of agreement; SD: Standard deviation.

Figure 4　Bland−Altman plots for the comparison between the adjusted IOL power using the regression analysis adjusted ELP (P_{IOLadj}) and the real power of the IOL implanted ($P_{IOLReal}$) The dotted lines show the limits of agreement（±1.96SD）; A: Results in group A; B: Results in group B.

comparison of P_{IOLadj} and $P_{IOLHaigis}$（$P=0.53$ paired Student's $t-$test）. A strong and statistically significant correlation was found between $P_{IOLHaigis}$ and P_{IOLadj}（$r=0.81$, $P<0.01$）, and between $P_{IOLHolladay}$ and P_{IOLadj}（$r=0.82$, $P<0.01$）. Also, a statistically significant correlation but of moderate strength was found between $P_{IOLHofferQ}$ and P_{IOLadj}（$r=0.63$, $P=0.03$）. In group B, statistically significant differences were found between P_{IOLadj} and all formulas analysed（$P<0.01$, Wilcoxon test）. A strong and statistically significant correlation was found between $P_{IOLHaigis}$ and P_{IOLadj}（$r=0.99$, $P<0.01$）, between $P_{IOLHofferQ}$ and P_{IOLadj}（$r=0.66$, $P<0.01$）and between $P_{IOLHolladay}$ and P_{IOLadj}（$r=0.98$, $P<0.01$）. Table 2 summarizes the outcomes of the Bland and Altman analysis when comparing P_{IOLadj} with the rest of formulas.

DISCUSSION

The selection of the IOL power to implant in cataract surgery is a critical step for obtaining an optimized outcome[17−18]. This power is determined by using mathematical formulas based most of them on paraxial optics[17−18]. In these formulas, some ocular parameters are required as well as the intended target refraction[17−18]. The AL and corneal power are always necessary for IOL power calculation and the accuracy of the measurement of these parameters is considered as the first potential source of inaccuracy in the determination of the IOL power to implant. Another source of potential bias is the estimation of the IOL position that is required for the optical calculations. Specifically, the "effective lens position" (ELP) is estimated which is defined as the effective distance from the anterior surface of the cornea to the lens plane as if the lens was of infinite thinness[19]. This parameter is formula−dependent and do not need to reflect the true postoperative ACD in the anatomical sense[19]. Indeed, each formula for IOL power calculation has its own algorithm to estimate the ELP that is based on different anatomical parameters, such as corneal power, preoperative ACD[19] or the horizontal corneal diameter or white−to−white distance（WTW）[20]. In the current study, a preliminary algorithm based on paraxial optics was developed to calculate the power to implant of a specific model of aspheric IOL. This algorithm was optimized by minimizing the error associated to the keratometric estimation of the corneal power as well as by obtaining a consistent predictive formula for the estimation of the ELP. As previously commented, the visual outcomes obtained with aspheric IOLs are especially worsened when refractive residual errors are present due to inaccurate IOL power calculations[10].

In our series, the refractive outcomes obtained with the aspheric IOL evaluated were less predictable for those eyes implanted with IOLs of powers of less than 23 D. Specifically, the postoperative SE ranged from −0.75 to +0.75 D in eyes implanted with $P_{IOL} \geqslant 23$ D and from −1.38 to +0.75 D in eyes implanted with $P_{IOL} < 23$ D. Therefore, there was a slight trend to residual myopia in those eyes implanted with lower IOL power values and consequently longer AL. This is consistent with the results of previous studies reporting myopic residual refractive errors in myopic eyes implanted with aspheric IOLs, especially in those with extreme preoperative myopia[21]. The results of the study of Eldaly and Mansour[22] suggested that AL−adjusted A−constants might be used for IOL power calculations. Indeed, these authors found different trends for a personal A−constant with different aspheric IOLs even for the same range of axial length[22]. In our series, in spite of the acceptable predictability achieved with the specific model of aspheric IOL evaluated, an attempt of optimization has been done by using an optimized model for corneal power calculation and an equation to estimate ELP based on a retrospective regression analysis of the postoperative outcomes obtained. As the behaviour of this regression model was very dependent on the IOL power, two groups were differentiated, as previously mentioned.

A limitation of the predictability of the refractive correction with the evaluated aspheric IOL may be attributable to the bias

associated to the use of the keratometric approach for the calculation of the corneal power, errors in the determination of the axial length or inaccuracy in the estimation of the ELP for this specific IOL. However, the errors in the estimation of AL with optical biometry have been shown to be minimal and with a very limited impact on the refractive predictability[23]. For this reason, the current study was aimed at analysing the potential contribution of the corneal power and ELP factors to the limitation of the refractive predictability with the aspheric IOL evaluated. The potential impact of the keratometric error was first evaluated by calculating the corneal power using an adjusted keratometric index aimed at minimizing the clinical error in the estimation of the corneal power[13-15]. This adjusted corneal power was used to obtain an estimation of the IOL power considering the AL, $R_{des} = SE_{post}$ and an ELP estimated with the algorithm established for the SRK – T formula ($P_{IOLadj-SRK/T}$)[24]. Thus, the ability of this approach to reproduce the real clinical outcome was evaluated. In the two groups of our study, eyes implanted with $P_{IOL} \geqslant 23$ D and eyes implanted with $P_{IOL} < 23$ D, clinically relevant differences were found between $P_{IOLadjSRK/T}$ and $P_{IOLReal}$ which demonstrated that the correction of this factor had a minimal effect on the outcomes achievable with the aspheric IOL evaluated. Likewise, statistically significant differences were found between $P_{IOLadjSRK/T}$ and $P_{IOLReal}$ in those eyes implanted with lower IOL powers. The reason for not finding statistically significant differences in group A may be the smaller number of patients included in this group.

According to these first outcomes, the estimation of ELP seemed to be the most critical factor accounting for the presence of a relatively limited predictability with the aspheric IOL, especially in eyes with shorter AL. In order to confirm this, an analysis was performed to obtain an expression for estimating an optimized ELP (ELP_{adj}). As a result, two different expressions were obtained by means of multiple linear regression analysis according to the power of the IOL implanted, one expression for $P_{IOL} < 23$ D ($ELP_{adj<23}$) and another for $P_{IOL} \geqslant 23$ D ($ELP_{adj \geqslant 23}$). This confirms the relevance of the geometric factor of the IOL in the estimation of ELP. The adjusted ELP was used to recalculate the IOL power considering that $R_{des} = SE_{post}$ (P_{IOLadj}) with the aim of checking if this new estimation was able to reproduce the real clinical outcome. An initial expression for ELP_{adj} considering the whole sample of 65 eyes was obtained, but the ELP_{adj} values obtained led to inconsistent values of $P_{IOL adj}$. However, when the two differentiated groups of eyes were considered, and two different expressions for ELP_{adj} were obtained ($ELP_{adj<23D}$ and $ELP_{adj \geqslant 23D}$), no statistically significant and clinically acceptable differences between P_{IOLadj} and $P_{IOLReal}$ were found. Indeed, mean differences between simulated and clinical outcomes were practically zero in groups A and B, with limits of agreement around 1 D, which is the manufacturer tolerance for extreme IOL powers (IOLs with powers from 0 to 10 D and from 30 to 35 D).

In our linear regression analyses, ELP_{adj} was found to be related to different factors in groups A and B. Age is the only factor shared by both models. This may be in relation with the age – dependence of the capsular behaviour after cataract surgery. A retrospective cohort study conducted on 801 patients in a Spanish hospital revealed that age could be associated with capsular bag distension syndrome[25]. Vass et al[26] confirmed that the capsular bag diameter was correlated with age, among other factors such as AL, corneal power or lens thickness. In group B that included eyes with longer AL, the anatomical factors were crucial determinants of the ELP of the IOL evaluated. Specifically, ELP_{adj} was higher in those eyes with longer AL and ACD, which is consistent with the linear dependence of the final position of the IOL on the AL reported by previous authors[27]. Besides the AL and ACD anatomical factors in group B, a corneal factor was included in the ELP models obtained in groups A and B in terms of corneal astigmatism magnitude and radius of curvature of the first corneal surface, respectively. This may be expected as some level of anatomical correlation between the corneal geometry and intraocular dimensions has been described in the human eye[28].

Finally, commonly used IOL power formulas were compared with our P_{IOLadj}. In both groups, according to the Bland and Altman analysis, clinically relevant differences were found between P_{IOLadj} and the IOL power values obtained with the Haigis, Hoffer Q, and Holladay I formulas. Likewise, these differences were also statistically significant. Only the difference between P_{IOLadj} and the IOL power calculated with the Haigis formula in group A did not reach statistical significance possibly due to the limitation in the sample size of this group. These differences between formulas seem to be in relation with the different estimations of ELP provided by each of them, with the most accurate outcome for ELP_{adj}. P_{IOLadj} was able to reproduce more accurately the real value of the power of the IOL implanted and therefore the refractive outcome. This suggests that our approach may be a useful method for IOL power calculation with the aspheric IOL evaluated. This should be corroborated in future prospective studies.

There are several limitations in the currentstudy, such as the limited sample size, the use in some cases of both eyes of the same subject or the short follow-up. It should be considered that, although rare, changes in IOL position has been described more than 3mo after surgery, especially after Nd：YAG capsulotomy[29]. Another potential limitation is that the Holladay II formula was not used in our comparison as it was not available in our clinic. Possibly, our approach may be more similar to the results of the Holladay II formula as both types of calculation use an optimized algorithm for the estimation of ELP, but this should be confirmed in future studies. This study was planned as a preliminary experience to evaluate the possibility of optimizing further the widely used approaches for IOL power calculation based on paraxial optics. For this reason, a retrospective study with a limited sample size was conducted. According to the positive findings

obtained, a prospective study with a large sample size is being conducted currently, including eyes implanted with different types of IOL. Finally, it should be mentioned that only one surgeon performed all the surgeries and therefore the algorithm developed could be somewhat imprecise for some surgeons. In future studies, this algorithm will be validated for different surgeons and the clinical relevance of differences will be evaluated. Furthermore, an analysis similar to that performed in the current study could be used to define a personalized algorithm for IOL power calculation for each specific surgeon. In conclusion, the refractive outcomes after cataract surgery with implantation of aspheric IOLs can be optimized by minimizing the keratometric error using a variable keratometric index for corneal power estimation and by estimating ELP using a mathematical expression dependent on the geometric factor of the IOL, age and anatomical factors. Therefore, optimizations of paraxial models for IOL power calculations can be performed to improve the clinical outcomes obtained with currently available IOL models without the need for ray tracing simulations. Jin et al[30] confirmed in a simulation study that theoretical thin-lens formulas were as accurate as the ray-tracing method in IOL power calculations in normal eyes and even in eyes after refractive surgery. Future prospective studies should be performed to validate this model of IOL power calculation for the evaluated aspheric IOL and other models with larger sample of sizes including more extreme cases (long and short AL).

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