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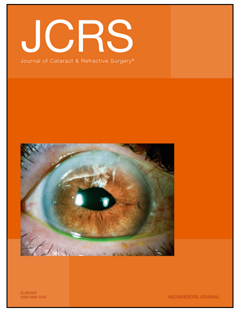


Predictive Value of Intracrystalline Interphase Point Measured by Low Coherence Reflectometry for the Estimation of the Anatomical Position of an Intraocular Lens After Cataract Surgery

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# PREDICTIVE VALUE OF INTRACRYSTALLINE INTERPHASE POINT MEASURED BY LOW COHERENCE REFLECTOMETRY FOR THE ESTIMATION OF THE ANATOMICAL POSITION OF AN INTRAOCULAR LENS AFTER CATARACT SURGERY

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## ABSTRACT

**Purpose:** To investigate the predictive value of the intracrystalline interphase point (ICIP) measured with optical low-coherence reflectometry (OCLR) to estimate the final position (FLP) of an intraocular lens (IOL) after cataract surgery.

**Setting:** Alcañiz Hospital, Teruel, Spain

**Design:** Single-center, retrospective, and descriptive study

**Methods:** 192 eyes of 174 patients (mean age: 76.4 years) undergoing cataract surgery were enrolled. According to the IOL implanted, the following groups were described: group 1, Acrysof IQ aspheric SN60WF (Alcon Laboratories) (77 eyes); group 2, enVista MX60 IOL (Bausch & Lomb) (71 eyes); group 3, CT Asphina 409 IOL (Carl Zeiss Meditec) (44 eyes). The Lenstar LS 900 system (Haag-Streit) was used for biometric measurements preoperatively and at 4-5 weeks postoperatively.

**Results:** 88.5% of eyes showed an absolute refractive prediction error (ARPE) <0.50 D. Mean ARPE was 0.25±0.21 D. Significantly higher values of FLP was found in group 2 compared to the other two groups ($p<0.001$). Significantly lower values of ICIP were found in those eyes with ARPE≥0.50 D compared to those with ARPE<0.50 D in groups 1 ($p=0.042$) and 2 ($p=0.023$). The correlation of FLP with ICIP was good in all three groups ($r\geq0.74$, $p<0.001$). Three linear expressions were obtained to predict FLP from ICIP and other preoperative data ($R^2$: 0.85, 0.69, and 0.49 in groups 1, 2 and 3, respectively).

**Conclusions**: The position of the intracrystalline interphase point (ICIP) measured with OCLR is correlated with the final position of the IOL after cataract surgery and may be used to optimize IOL power calculations.

**Keywords:** cataract surgery; optical biometry; optical low-coherence reflectometry; intraocular lens; intracrystalline interphase point; effective lens position

## Introduction

One of the most critical issues in cataract surgery, especially when implanting premium intraocular lenses (IOLs), is the correct determination of the optical power of the IOL implanted.[1] The objective is to minimize the postoperative residual refractive error, leading to an artificial emmetropia.[1] In clinical practice, the IOL power is determined by using mathematical formulas, most of them based on paraxial optics.[2,3] Some ocular parameters, such as axial length (AXL) or corneal power, as well as the intended postoperative refraction are necessary to perform a precise calculation of IOL power.[4] Considering that currently available biometry[5] and corneal topography devices[6] provide consistent and reliable measurements, the main source of potential bias in IOL power calculation is the estimation of the IOL position.[7,8] The parameter "effective lens position" (ELP), defined as the effective distance from the anterior surface of the cornea to the lens plane as if the lens was of infinite thinness, is used to optimize IOL power according to the IOL design and the formula used.[9] This parameter is formula-dependent and do not need to reflect the true postoperative anterior chamber depth (ACD) in the anatomical sense.[9] Specifically, 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[9] or the horizontal corneal diameter or white-to-white distance (WTW).[10]

The introduction of optical low-coherence reflectometry (OLCR) to perform non-contact optical biometry is one of the most relevant advances in cataract surgery and IOL power calculation in the last years.[11] This advanced technology is similar to temporal domain optical coherence tomography (OCT) and has been shown to provide very precise measurements, allowing the optimization of IOL power calculations in terms of the anatomical characterization of the eye.[12-16] The Lenstar LS 900 (Haag-Streit AG, Köniz, Switzerland) is an OCLR-based optical biometer providing a great variety of parameters with accuracy[17] as well as an echogram showing the different intraocular interphases found once the light is propagated into the eye.[18] In our experience, a point representing the interphase between the cortex-epinucleus complex and the nucleus of the crystalline lens can be always observed in all cataractous eyes explored with this OCLR system (Figure 1). The aim of the current study was to investigate the potential predictive value to estimate the final position of the IOL in eyes undergoing cataract surgery of this intracrystalline interphase point (ICIP) measured with OCLR optical biometry.

## Material and methods

### *Patients*

This single-center, retrospective, and descriptive study was conducted at the Department of Ophthalmology of Alcañiz Hospital (Teruel, Spain). It consisted on the recruitment of data from patients undergoing cataract surgery from October 2013 to January 2015. The study was carried out following the tenets of the Declaration of Helsinki and the Good Clinical Practices guidelines. Personal data was processed according to guidelines established by the Spanish Law of Data Protection (LOPD). The study was approved by the ethics committee CEICA (Comité Ético de Investigación de la Comunidad Autónoma de Aragón).

Inclusion criteria for the study were signed informed consent, patients of more than 18 years old, presence of visually significant cataract (decrease of CDVA or loss of visual quality), correct preoperative and postoperative optical biometry including all the parameters required for the study, and uncomplicated phacoemulsification cataract surgery performed by the same surgeon with implantation of monofocal IOL within the capsular bag. Exclusion criteria were impossibility of performing the biometric analysis with the Lenstar LS 900 (Haag-Stret, USA) system, mean corneal keratometric power over 46.5 D, active ocular pathology, amblyopia that may difficult fixation during biometric measurements, previous ocular surgery including trabeculectomy, vitrectomy and corneal surgery, corneal scar, irregular astigmatism, systemic diseases that may affect the cornea, astigmatisms over 2 D, phacoemulsification surgery with intraoperative events that may alter the stability of the IOL within the capsular bag (i.e., capsulorrhexis larger than the IOL optic size), and complicated cataract surgery (zonular disinsertion, capsular rupture, out-of-bag IOL implantation and others).

*Examination protocol*

A complete preoperative eye examination had been carried out in all patients enrolled in the study including the following tests: Uncorrected and Corrected Distance Visual Acuity (UDVA and CDVA, respectively), objective and subjective refraction, keratometry, ocular motility, anterior segment slit lamp biomicroscopy, Goldmann applanation tonometry, optical biometry with determination of ICIP, corneal endothelial analysis by specular microscopy, and dilated funduscopy. The optical biometry was conducted with the Lenstar LS 900 system before applying drops for other explorations (fluorescein, tropicamide) which uses a superluminiscent diode (SLD) of a wavelength of 820 nm. Measurements were always taken as quickly as possible, without patients withdrawing the head of the chin, being only encouraged to blink between them to lubricate the cornea. It has been described that the acquisition time of measurements with the Lenstar LS 900 system is longer than with other devices due to the alignment and focus methodology of the device that takes 5 consecutive measurements for the calculation of an average value, supposing a greater demand of fixation for the patient.[19] After each measurement, the patient moved backwards, and the device was realigned again to avoid the interdependence between successive captures. After this, the dioptric power of the IOL to be implanted was calculated using the own software of the biometer (Eyesuite), which incorporates the most usual formulas of third generation for IOL power calculation, as well as the formulas of Haigis, that consider preoperative anterior chamber depth (ACD), the Olsen formula for some types of IOLs that considers ACD as well as the crystalline lens thickness (LT), the Barrett Universal II formula that incorporates the white to white distance plus ACD and LT for its calculations, and the RBF-Hill method. For our study, all IOL power calculations were performed considering the SRK-T formula. ICIP measurements were performed manually by the same experienced examiner (FJCA) in all cases.

Postoperatively, the following visits were scheduled: 24 hours (visit 1), 3-4 days (visit 2), 2 weeks (visit 3), and 4-5 weeks after surgery (visit 4). In the visit 1, a detailed examination of the anterior segment was performed with the slit lamp to confirm the absence of early complications as well as the measurement of the intraocular pressure (IOP). In visits 2 and 3, besides these two tests, the following measurements were performed: UDVA, CDVA, autorefraction, and manifest refraction. In the last visit (visit 4), all the previous mentioned tests were done as well as an analysis of the anterior and posterior segment under pupil dilation in order to evaluate the level of centration of the IOL, the level of covering of the IOL optic by the capsulorrhexis and the status of the fundus. Likewise, optical biometry (pseudophakic mode) was performed with measurement of the following variables:

-Postoperative ACD

-Thickness of the IOL

-Final lens position (FLP), calculated as the distance between corneal epithelium and anterior surface of the IOL

-Final lens position (FLP2), calculated as the distance between corneal epithelium and the central plane of the IOL

-The IOL position error (EPos), calculated as the difference between the effective lens position estimated with the SRK-T formula and FLP

-The IOL position error (EPos2), calculated as the difference between the effective lens position estimated with the SRK-T formula and FLP2.

*Surgical protocol*

All patients underwent phacoemulsification cataract surgery under topical anesthesia. All surgeries were performed by the same surgeon (FJCA) using the INFINITI® Vision System with the micro-coaxial system Intrepid® (Alcon Laboratories, Dallas, Texas, USA). The surgical procedure consisted on the following steps: creation of paracentesis and auto-sealing incision of 2.2 mm, generation of a continuous circular capsulotomy of approximately 4.5-5.5 mm, phacoemulsification using the torsional mode, micro-coaxial (MCCS) technique of irrigation/aspiration of the cortical material, and implantation of the IOL into the capsular bag. According to the monofocal IOL implanted, the following three groups were created: group 1 including eyes implanted with the Acrysof® IQ aspheric SN60WF IOL (Alcon Laboratories, Dallas, Texas, USA) (biconvex aspheric with C haptics, optical zone 6.0

mm, total diameter 13.0 mm, A-constant 118.7, refractive index 1.55), group 2 including eyes implanted with the IOL enVista® MX60 (Bausch & Lomb, Rochester, NY, USA) (biconvex aspheric with modified C haptics, optical zone 6.0 mm, total diameter 12.5 mm, A-constant 119.1, refractive index 1.53), and group 3 including eyes implanted with the IOL CT Asphina 409M (Carl Zeiss Meditec, Jena, Germany) (monofocal aspheric aberration-neutral with plate haptics, optical zone 6.0 mm, total diameter 11.0 mm, A-constant 117.7, refractive index 1.46).

*Statistical analysis*

SPSS statistics software package version 23.0 (IBM, Armonk, EEUU) was used for the statistical analysis. The qualitative variables were described by absolute frequencies (n) and relative frequencies expressed as percentages (%). In contrast, the quantitative variables were described by the mean, standard deviation (SD), and range. Normality of all data was checked by means of the Kolmogorov-Smirnov test. The association between variables was investigated by means of contrast of hypothesis with comparisons of means for quantitative variables (paired Student's t test with parametric statistics, U Mann-Whitney test with non-parametric statistics). Furthermore, the one-way analysis of variance (ANOVA) was used for the assessment of differences between IOL groups if variables were normally distributed, whereas the Kruskal-Wallis test was used if one or more variables were not normally distributed. The post-hoc comparative analysis for the ANOVA was performed with the Bonferroni test, while the Mann-Whitney tests with the Bonferroni´s adjustment was used for the post-hoc analysis of the Kruskal-Wallis test. Differences were considered as statistically significant when the associated p-value was <0.05. The analysis of interchangeability of ELP calculated preoperatively with the SRK-T formula and FLP was performed with the Bland and Altman method in each IOL group.

Pearson and Spearman correlation coefficients were used to assess the correlation between variables depending if the data samples were or not normally distributed. Simple linear regression analysis was performed with the purpose of obtaining a mathematical expression relating FLP and FLP2 with ICIP in each IOL group. Likewise, a multiple linear regression analysis based on the backward elimination method was used for obtaining a mathematical expression predicting FLP from different preoperative clinical data for each type of IOL. Concerning the models obtained, their assumptions were evaluated by analyzing residuals, the normality of unstandardized residuals (homoscedasticity), and the Cook's distance, to detect influential points or outliers. In addition, the lack of correlation between errors and multicollinearity was assessed by means of the Durbin-Watson test and the calculation of the collinearity tolerance and the variance inflation factor (VIF).

## Results

The sample included a total of 192 eyes of 174 patients of a mean age of 76.4 years (SD: 7.6, median; 78.0, range: 39 to 91 years). The gender distribution of the sample was as follows: 104 females (59.8%) and 70 males (40.2%). According to the IOL implanted, the following groups were described: group 1, 77 eyes implanted with the Acrysof IQ aspheric SN60WF IOL (40.1%); group 2, 71 eyes implanted with the enVista MX60 IOL (37.0%); and group 3, 44 eyes implanted with the CT Asphina 409 IOL (22.9%). Table 1 summarizes the main preoperative and postoperative clinical data. A total of 170 eyes (88.5%) showed a postoperative absolute refractive prediction error

(ARPE) (absolute value of the difference between postoperative spherical equivalent and that predicted preoperatively from IOL power calculations) of 0.50 D or below, and only 11.5% (22 eyes) showed ARPE values over 0.50 D. Mean refractive prediction error (RPE) in the sample evaluated was -0.06 D (SD: 0.33; median: -0.05; range: -1.24 to 0.94 D), with a mean absolute value of 0.25 D (SD: 0.21; median: 0.22; range: 0.00 to 1.24 D). In the whole sample, FLP was found to be significantly correlated with the following preoperative anatomical measurements: AXL ($r=0.541$, $p<0.001$), ACD ($r=0.689$, $p<0.001$), ICIP ($r=0.755$, $p<0.001$), and anterior segment depth (ACD + CCT + LT) ($r=0.665$, $p<0.001$). Likewise, FLP2 was found to be significantly correlated with AXL ($r=0.478$, $p<0.001$), ACD ($r=0.711$, $p<0.001$), ICIP ($r=0.781$, $p<0.001$) and anterior segment depth ($r=0.708$, $p<0.001$).

Table 2 shows the results of the comparison of the preoperative and postoperative data between IOL groups. As shown, no statistically significant differences were found between IOL groups in any anatomical preoperative measurement ($p\geq0.088$), including ICIP ($p=0.840$). However, significantly lower values of ARPE were found in group 2 compared to groups 1 ($p=0.019$) and 3 ($p=0.048$). Likewise, there were statistically significant differences between IOL groups in FLP ($p<0.001$ for the comparisons groups 1-2 and groups 2-3), FLP2 ($p=0.001$ only for the comparison groups 1-2), EPos ($p\leq0.001$, all comparisons by pairs), and EPos2 ($p\leq0.008$, all comparisons by pairs). Furthermore, significant differences were found in ICIP between those eyes with ARPE≥0.50 D and those with ARPE<0.50 D in groups 1 ($p=0.043$) and 2 ($p=0.023$) (Figure 2). No significant positive correlations were found between ARPE and ICIP in any of the three IOL groups of the evaluated sample (group 1: $r=-0.135$, $p=0.243$; group 2: $r=-0.109$, $p=0.365$; group 3: $r=-0.041$, $p=0.793$) (Figure 3).

Figure 4 shows the Bland and Altman plot obtained in each IOL group to analyze graphically the potential proportional bias between the value of ELP obtained with the SRK-T formula and the FLP. As shown, in the three groups, the predicted value of ELP and FLP cannot be considered as interchangeable as the limits of agreement were large and showing a trend to overestimation of FLP considering ELP. Table 3 summarizes the correlation analysis of FLP (Figure 5) and FLP2 (Figure 6) with different clinical variables evaluated. As shown, statistically significant correlations were found with AXL, ACD, and anterior segment depth (ASD), although correlations were moderate in most of cases and became poorer in groups 2 and 3 compared to group 1. In contrast, the correlation of FLP and FLP2 with ICIP were good in the three IOL groups ($r \geq 0.722$, $p<0.001$) (Figure 5). The following linear expressions were obtained by means of linear regression analysis to estimate FLP and FLP2 as a function of ICIP in the three IOL groups analyzed:

Group 1 FLP=1.76 + 0.76*ICIP ($R^2$: 0.74) / FLP2=2.27 + 0.70*ICIP ($R^2$: 0.73)

Group 2 FLP=2.60 + 0.58*ICIP ($R^2$: 0.62) / FLP2=2.89 + 0.58*ICIP ($R^2$: 0.60)

Group 3 FLP=1.77 + 0.72*ICIP ($R^2$: 0.49) / FLP2=2.42 + 0.68*ICIP ($R^2$: 0.48)

The homoscedasticity of these models was confirmed by the normality of the unstandardized residuals distribution ($p>0.05$), the absence of influential points or outliers, and the independence of the residuals (Durbin-Watson ≈ 2 in all cases).

Finally, the following linear expressions were obtained by means of multiple regression analysis to estimate FLP and FLP2 as a function of the most predictive preoperative data in the three IOL groups analyzed:

Group 1: FLP=-4.86 + 0.20*WTW + 0.08*AXL + 0.002*CCT + 0.50*ICIP + 0.06*K1 ($R^2$: 0.85)

FLP2=-3.59 + 0.20*WTW + 0.05*AXL + 0.002*CCT + 0.51*ICIP + 0.05*K1 ($R^2$: 0.82)

Group 2: FLP=-1.64 + 0.20*WTW + 0.001*CCT + 0.47*ICIP + 0.04*K2 ($R^2$: 0.69)

FLP2=-1.41 + 0.21*WTW + 0.001*CCT + 0.46*ICIP + 0.04*K2 ($R^2$: 0.67)

Group 3: FLP=1.77 + 0.72*ICIP ($R^2$: 0.49)

FLP2=2.42 + 0.68*ICIP ($R^2$: 0.48)

,where WTW is the white-to-white corneal diameter, AXL is the axial length, CCT is the central corneal thickness expressed in micrometers, ICIP is the intracrystalline interphase point distance, K1 the flattest keratometric reading, and K2 the steepest keratometric reading.

The homoscedasticity of these models was also confirmed by the normality of the unstandardized residuals distribution ($p>0.200$), the absence of influential points or outliers, the absence of multicollinearity (tolerance below 1), and the independence of the residuals (Durbin-Watson ≈ 2 in all cases).

## Discussion

In the current study, a sample of eyes undergoing cataract surgery with implantation of one of three types of monofocal IOLs was evaluated. In all cases, the power of the IOL implanted was selected according to the SRK-T formula guidelines. ARPE was below 0.50 D in 88.5% of eyes from the whole sample and below 1 D in 99.50% of eyes. According to the European Registry of Quality Outcomes for Cataract and Refractive Surgery (EUREQUO), a total of 91% of eyes undergoing cataract surgery achieve a value of ARPE below 1 D.[20] Similarly, a registry in Sweden of more than 15,000 eyes undergoing cataract surgery showed that 71% of them had an associated RPE within ±0.50 D and 93% within ±1 D.[21] Recently, Sheard concluded that nowadays percentages of eyes with RPE within ±0.50 and ±1 D of 60% and 90% can be achieved, respectively.[5] Therefore, the global results of the current study are consistent with the quality standards defined in the peer-reviewed literature for cataract surgery. Likewise, the results were also consistent with the quality standards when were analyzed separately for the three different types of monofocal IOL implanted, with no significant differences between IOL groups. Mean APRE was 0.29, 0.20 and 0.28 D for the SN60WF, MX60 and CT Asphina IOLs, respectively. Similarly, Reitblat et al[22] obtained a mean value of ARPE of 0.20 ± 0.19 D in eyes undergoing cataract surgery with implantation of multifocal IOLs using the Lenstar system for obtaining the biometric measurements and IOL power calculations (SRK-T formula), as in the current study. Preussner et al[23] reported a mean RPE of 0.13 ± 0.59 D in a group of 1,121 eyes implanted with 13 different models of IOL and 0.13 ± 0.62 D in another group of 936 eyes undergoing cataract surgery, with ARPE of 0.44 and 0.50 D, respectively. It should be mentioned that in this study ultrasonic biometry was used and this may interfere in the outcomes reported by the authors.

Currently, one of the critical factors limiting the refractive precision in cataract surgery is the estimation of ELP for performing the calculation of IOL power,[7] contributing around 20-40% to postoperative residual refractive errors.[8] It should be considered that ELP is not exactly the anatomical position of the IOL and the different IOL power calculation formulas use different algorithms and consider different variables to estimate ELP. Third generation IOL power calculation formulas (Hoffer Q, Holladay 1 and SRK/T) use AXL and Km as variables to consider for the estimation of ELP.[24,25] However, a variability in the results is still present with these formulas due to the difference between the real position of the IOL that can be considered very similar to ELP in the "thin lens" approximation, and the ELP calculated.[24] An improvement has been achieved with the most recent formulas, such as Haigis, Holladay 2, Barret Universal II, and Olsen, including the measurement of ACD and LT in the estimation of ELP. Lam[26] compared the results obtained with the Holladay 2 formula incorporating the Lenstar measurement of LT in the estimation of ELP with those obtained incorporating a value of LT derived from an age-based calculation, obtaining mean ARPE values of 0.14 and 0.25 D, respectively. Likewise, new ray tracing-based methods have been developed that consider factors such as the anterior and posterior surfaces of the cornea and crystalline lens to predict the power of the IOL, as well as new constants to adjust the calculations and optimize the clinical outcomes (haptic plane, C-constant, H5 formula).[27,28] In the current study, the potential predictive value to estimate the final position of the IOL in eyes undergoing cataract surgery was investigated for a new variable, the preoperative intracrystalline interphase point (ICIP) measured with OCLR.

In our sample, the mean final position of the IOL (FLP), defined as the distance between corneal epithelium and anterior surface of the IOL, was 4.55 ± 0.32 mm, which is consistent with the data previously reported by other authors evaluating the same distance (4.47 ± 0.32 mm) using optical biometry,[29] or even Scheimpflug imaging technology (4.58 ±0.34,[30] 4.82 ±0.32).[31] In addition, statistically significant differences in FLP were found in the current series when comparing the three different types of IOL (SN60WF: 4.50 mm; MX60: 4.70 mm; CT Asphina: 4.40 mm), leading to significant differences in EPos. Besides FLP, another anatomical parameter was measured, FLP2, which was calculated as the distance between corneal epithelium and the central plane of the IOL. In this case, only statistically significant differences were found between MX60 (4.99 mm) and SN60WF IOLs (4.81 mm), although significant differences between all pairs were found for EPos2, which was the difference between FLP2 and the value of ELP estimated preoperatively. FLP2 has been calculated considering that previous authors have observed that the center of the IOL is a point associated to lower variability.[32] Likewise, this point shows less changes when different types of IOL are compared.[32] Olsen[27] introduced in his algorithm the new constant C that defined the position of the IOL as postoperative ACD (distance between corneal vertex and anterior surface of the IOL + half of the thickness of the IOL). In the current series, the MX60 IOL has shown a more posterior position of the IOL within the eye possibly due to the geometric characteristics of the IOL as well as to its lower mean thickness (Mean values obtained from optical biometry measurements: MX60: 0.58 ± 0.05 mm, SN60WF: 0.63 ± 0.08 mm, CT Asphina: 1.03 ± 0.07 mm). However, no more significant trend to hyperopia was found with the MX60 IOL. This may be due to the compensation achieved with the adjustment introduced by the constant of the IOL in the IOL power calculation formulas that theoretically would account for the more posterior position of this IOL.

As previously mentioned, it should be remarked again that ELP is not exactly the anatomical position of the IOL as it is a virtual distance resulting from a calculation. However, they are considered as coincident or almost coincident in a great number of cases because the IOL is considered as an extremely thin optical biconvex element and some mathematical simplifications can be assumed. However, in our sample, the value of ELP estimated and FLP could not be considered as interchangeable according to the large limits of agreement found for the three IOLs evaluated. Larger values of ELP compared to FLP were obtained in almost all cases of all three groups, with only group 1 showing a trend to an increased difference between parameters for increasing ELP values. In the whole sample, FLP was found to be correlated with preoperative anatomical parameters, such as AXL, ACD or ICIP, with the stronger correlation corresponding to ICIP. However, when this analysis of correlations was done separately in each IOL group, poorer correlations were found in eyes implanted with the CT Asphina IOL. Considering that the sample of eyes implanted with each type of IOL did not differ significantly preoperatively, this finding suggests a less predictable position of this specific type of IOL, being the characteristics of the haptics, the optical configuration of IOL surfaces, IOL thickness, IOL diameter and the lower refractive index of the IOL potential factors accounting for this. Whang et al[33] demonstrated that the corrective effect of the aspheric IOL CT Asphina 509M was influenced by preoperative axial length and postoperative anterior chamber depth. It should be also considered that some errors can be present in extreme cases (very short or long eyes requiring extreme values of IOL power and therefore IOLs with very specific optical configurations) or in cases with wrong estimations of the real corneal power.[27] Recently, the difference between ELP and the anatomical position of the IOL has been shown to depend primarily on IOL power, thickness, and shape factor.[34]

A mean value of 3.63 ± 0.35 mm of the new parameter defined, ICIP, was obtained in the population evaluated, with no significant differences between IOL groups. This value is lower than that obtained by Yoo et al[35] for a parameter called crystalline lens equatorial plane (LEP) and presented recently as a new parameter for predicting the postoperative IOL position. Therefore, the point corresponding to the intracrystalline lens interphase is located anterior to the LEP. In the current study, ICIP was found to be significantly correlated with FLP and FLP2 for the three IOLs evaluated. FLP and FLP2 have been also found to be significantly correlated with AXL and ACD, although these correlations were poorer, especially for the IOL CT Asphina. In contrast, no correlation was found between the anatomical position of the lens and LT or Km, suggesting that the most relevant factor for the final position of the IOL is the anterior chamber and not the thickness of the crystalline lens. The potential association between ELP and LT has not been considered as relevant for most of IOL power calculation formulas, except for Olsen and Holladay formulas. Olsen described the influence of LT on ELP, considering its impact more relevant than that corresponding to corneal curvature.[9] The authors proposing the use of LT to improve the estimations of ELP are based on the natural correlation between ACD and crystalline lens, but there is an age-related shortening of the ACD because of the age-related thickening of the crystalline lens. Hirnschall et al[36] proposed by the first time the use of the intraoperative anatomical position of the crystalline lens capsules as a predicting factor of ELP. These authors concluded that the best predictor of ELP in eyes undergoing cataract surgery with implantation of an IOL was the intraoperative position of the anterior capsule of the crystalline lens after inserting a capsular tension ring. Likewise, these authors concluded that the position of the posterior capsule and LT were weak predictors of ELP.[36] Other authors have attempted to determine if there was any differential aspect in the preoperative echogram-A obtained with the Lenstar system allowing a better prediction of the final position of the IOL.[37] They concluded that variations in the range from 0.40 to -0.44 mm of the position of the IOL may condition the presence of a refractive error of 0.5 D.[37] In the current study, the use of preoperative ICIP is proposed for the prediction of ELP due to the good levels of correlation between ICIP and FLP independently of the type of IOL. This use should be investigated further in the more extreme cases, very short and long eyes. In a 2-part retrospective observational study followed by a prospective evaluation, the postoperative ACD was found to be correlated with the ante-nucleus distance (AND), the nucleus thickness (NT) of the cataractous lens, and the axial length measured with the Lenstar system.[38] An estimated ACD (EACD) equation was established and used prospectively in a new formula on eyes scheduled for cataract surgery.[38] Using the IOL power formula considering the equation to estimate postoperative ACD, the median absolute error was 0.28 D, with 82.7% of the eyes within ±0.50 D and 100% within ±1.00 D.[38]

Finally, three linear equations were obtained for the prediction of FLP and FLP2 from ICIP as well as from a set of predictive preoperative data. The predictability associated to the linear equations obtained for the SN60WF and MX60 IOLs was good, although more limited for the IOL CT Asphina. This finding is consistent with the lower correlation of FLP and FLP2 with AXL and ACD obtained for this specific IOL. Specifically, only ICIP was found to be a predictive factor of the FLP of this specific IOL, with no significant contributions of AXL, keratometry or CCT, as happened with the other two IOLs evaluated. The configuration and behaviour of the haptics and the variation of the shape factor of the IOL with AXL and/or ACD may account for this. Savini et al[39] concluded that an early forward shift of a 3-piece design IOL may be the consequence of the haptic-compression force decay typical of these IOLs, with their rigid haptics exerting more pressure against the capsular bag than the haptics of 1-piece IOLs.

In conclusion, the final position of an IOL after cataract surgery is strongly correlated with the depth of the anterior chamber and of the anterior segment, but not with the thickness of the crystalline lens. A new anatomical variable is proposed as a predictor of the final position of an IOL, the position of the intracrystalline interphase point (ICIP) measured with OCLR optical biometry, due to its acceptable correlation with this final position for three different types of IOL, which was better than that corresponding to anterior segment depth and ACD. Factors such as IOL thickness and refractive index may contribute to this better predictability of ICIP, considering that the distance between ELP and anterior IOL vertex position has been shown to depend primarily on IOL power, thickness, and shape-factor.[34] Future studies should be conducted to confirm this in prospective randomized studies evaluating the potential benefit on refractive predictability of considering this new factor.

WHAT WAS KNOWN

- The main source of potential bias in IOL power calculation is the estimation of the IOL position considering that currently available biometry and corneal topography devices that provide consistent and reliable measurements.

- The parameter “effective lens position” (ELP) is used to optimize IOL power according to the IOL design and the formula used. 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 or the horizontal corneal diameter or white-to-white distance (WTW).

- Optical low-coherence reflectometry (OLCR) has been shown to provide very precise measurements, allowing the optimization of IOL power calculations in terms of the anatomical characterization of the eye.

WHAT THIS PAPER ADDS

- The final position of an IOL after cataract surgery is strongly correlated with the depth of the anterior chamber and of the anterior segment, but not with the thickness of the crystalline lens

- A new anatomical variable is proposed as a predictor of the final position of an IOL, the position of the intracrystalline interphase point (ICIP) measured with OCLR optical biometry, due to its acceptable correlation with this final position for three different types of IOL. This point represents the interphase between the cortex-epinucleus complex and the nucleus of the crystalline lens.

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**Figure legends**

Figure 1.- Echogram obtained with the Lenstar LS 900 system showing the detection of the intracrystalline interphase point (ICIP) (blue arrow).

Figure 2.- Values of the distance from corneal endothelium to the position of the peak corresponding to the intracrystalline lens point interphase (ICIP) in eyes with absolute refractive prediction error (ARPE) ≥ 0.50 D and eyes with ARPE < 0.50 D in the three IOL groups evaluated in the current study.

Figure 3.- Scattergrams showing the relationship of the intracrystalline lens point interphase (ICIP) and the absolute refractive prediction error (ARPE) in the three IOL groups of the sample evaluated (up: group 1, middle: group 2, down: group 3).

Figure 4.- Bland and Altman plot showing the potential proportional bias between the value of ELP obtained with the SRK-T formula and the FLP in the three IOL groups of the sample evaluated (up: group 1, middle: group 2, down: group 3).

Figure 5.- Scattergrams showing the relationship of the final lens position calculated as the distance between corneal epithelium and anterior surface of the IOL (FLP) and the following preoperative anatomical parameters in the three IOL groups of the current study (group 1: grey dots; group 2: orange dots; group 3: blue dots): axial length (AXL), anterior chamber depth (ACD), anterior segment depth (ASD) and the distance from corneal endothelium to the position of the point corresponding to the intracrystalline lens interphase (ICIP).

Figure 6.- Scattergrams showing the relationship of the final lens position calculated as the distance between corneal epithelium and the central plane of the IOL (FLP2) and the following preoperative anatomical parameters in the three IOL groups of the current study (group 1: grey dots; group 2: orange dots; group 3: blue dots): axial length (AXL),

anterior chamber depth (ACD), anterior segment depth (ASD) and the distance from corneal endothelium to the position of the point corresponding to the intracrystalline lens interphase (ICIP).

**Synopsis**

The final position of the IOL after cataract surgery can be predicted with accuracy using a new anatomical parameter measured by optical low-coherence reflectometry, the position of the intracrystalline interphase point.

| **Mean (SD) Range** | **Preoperative** | **Postoperative** | **p-value** |
|---|---|---|---|
| Astigmatism (D) | 0.79 (0.44)<br>0.79 (0.00 to 2.08) | 0.81 (0.43)<br>0.75 (0.00 to 2.00) | 0.319* |
| SE (D) | --- | -0.13 (0.26)<br>-0.12 (-1.25 to 0.63) | --- |
| LogMAR UDVA | --- | 0.12 (0.20)<br>0.05 (0.00 to 1.30) | --- |
| LogMAR CDVA | 0.75 (0.42)<br>0.70 (0.15 to 2.00) | 0.07 (0.14)<br>0.00 (0.00 to 0.92) | <0.001* |
| AXL (mm) | 23.29 (1.02)<br>23.22 (21.15 to 27.45) | 23.21 (1.02)<br>23.18 (21.12 to 27.36) | <0.001* |
| ACD (mm) | 2.54 (0.42)<br>2.55 (1.58 to 3.90) | 4.01 (0.32)<br>4.03 (3.25 to 4.75) | <0.001† |
| LT (mm) | 4.65 (0.40)<br>4.68 (3.57 to 5.68) | --- | --- |
| CCT ($\mu$m) | 537.48 (34.87)<br>540.00 (456 to 630) | 541.05 (35.76)<br>543.00 (447 to 651) | <0.001† |
| Km (D) | 44.12 (1.32)<br>44.15 (40.90 to 46.46) | 44.03 (1.34)<br>44.01 (40.74 to 47.07) | 0.003* |
| WTW (mm) | 11.86 (0.41)<br>11.81 (10.78 to 12.79) | 11.86 (0.42)<br>11.81 (10.75 to 12.80) | 0.018* |
| ICIP (mm) | 3.63 (0.35)<br>3.67 (2.82 to 4.41) | --- | --- |
| Implanted IOL (D) | 21.34 (2.93)<br>21.50 (10.00 to 30.00) | | |
| FLP (mm) | --- | 4.55 (0.32)<br>4.58 (3.77 to 5.30) | --- |
| IOL thickness (mm) | --- | 0.70 (0.19)<br>0.63 (0.40 to 1.10) | --- |
| FLP2 (mm) | --- | 4.90 (0.30)<br>4.93 (4.24 to 5.79) | --- |

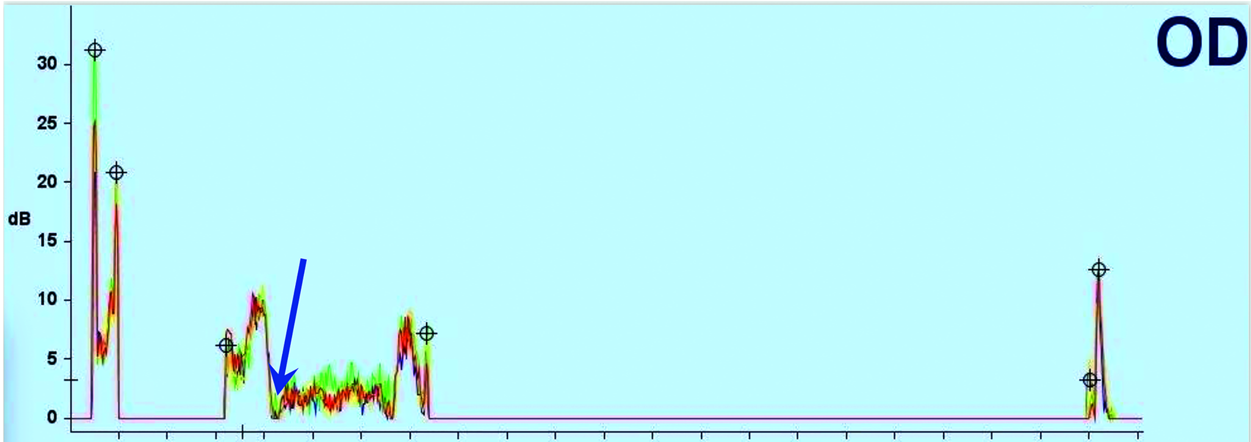
Table 1.- Summary of the outcomes obtained in the sample evaluated. Abbreviations: SD, standard deviation; D, diopter; SE, spherical equivalent; UDVA, uncorrected distance visual acuity; CDVA, corrected distance visual acuity; AXL, axial length; ACD, anterior chamber depth; LT, lens thickness; CCT, central corneal thickness; Km, mean keratometry; WTW, white-to-white corneal diameter; IOL, intraocular lens; FLP, final lens position calculated as the distance between corneal epithelium and anterior surface of the IOL; FLP2, final lens position calculated as the distance between corneal epithelium and the central plane of the IOL (FLP + half of the thickness of the IOL); ICIP, distance from corneal endothelium to the position of the point corresponding to the intracrystalline lens interphase. Non-parametrical and parametrical tests were indicated with the symbols * and †.

| Mean (SD)<br>Range | Group 1 | Group 2 | Group 3 | P-value (mean difference) |
|---|---|---|---|---|
| Age (years) | 75.0 (8.5)<br>77.0 (39 to 91) | 76.7 (7.3)<br>78.5 (52 to 89) | 77.9 (6.4)<br>78.5 (62 to 89) | 0.191* |
| Preoperative AXL (mm) | 23.45 (1.31)<br>23.21 (21.15 to 27.45) | 23.25 (0.78)<br>23.25 (21.39 to 25.04) | 23.06 (0.70)<br>23.10 (21.63 to 24.32) | 0.438* |
| Preoperative ACD (mm) | 2.56 (0.44)<br>2.51 (1.58 to 3.90) | 2.52 (0.43)<br>2.54 (1.58 to 3.31) | 2.53 (0.37)<br>2.56 (1.60 to 3.23) | 0.823† |
| Preoperative Km (D) | 44.06 (1.25)<br>44.09 (40.90 to 46.46) | 44.11 (1.32)<br>44.18 (41.31 to 46.33) | 44.24 (1.45)<br>44.21 (41.51 to 46.41) | 0.781† |
| Preoperative LT (mm) | 4.57 (0.38)<br>4.62 (3.57 to 5.68) | 4.70 (0.40)<br>4.76 (3.93 to 5.59) | 4.70 (0.40)<br>4.69 (3.88 to 5.60) | 0.088† |
| Preoperative anterior segment depth (mm): CCT+ACD+LT | 7.66 (0.41)<br>7.68 (6.88 to 8.46) | 7.75 (0.35)<br>7.74 (6.79 to 8.69) | 7.77 (0.33)<br>7.74 (7.10 to 8.46) | 0.207† |
| RPE (D) | -0.04 (0.37)<br>-0.05 (-1.24 to 0.82) | -0.07 (0.26)<br>-0.05 (-0.77 to 0.60) | -0.05 (0.36)<br>-0.09 (-0.69 to 0.94) | 0.868† |
| ARPE (D) | 0.29 (0.23)<br>0.24 (0.00 to 1.24) | 0.20 (0.18)<br>0.14 (0.00 to 0.77) | 0.28 (0.22)<br>0.24 (0.01 to 0.94) | 0.036*<br>Groups 1-2, 0.019 (0.09 D)<br>Groups 1-3, 0.999 (0.01 D)<br>Groups 2-3, 0.048 (-0.08 D) |
| FLP (mm) | 4.50 (0.33)<br>4.46 (3.85 to 5.15) | 4.70 (0.26)<br>4.73 (4.10 to 5.20) | 4.40 (0.30)<br>4.48 (3.77 to 5.30) | <0.001*<br>Groups 1-2, <0.001 (-0.20 mm)<br>Groups 1-3, 0.183 (0.10 mm)<br>Groups 2-3, <0.001 (0.30 mm) |
| FLP2 (mm) | 4.81 (0.31)<br>4.78 (4.24 to 5.42) | 4.99 (0.26)<br>5.01 (4.38 to 5.51) | 4.91 (0.29)<br>4.98 (4.30 to 5.79) | 0.003*<br>Groups 1-2, 0.001 (-0.18 mm)<br>Groups 1-3, 0.079 (-0.10 mm)<br>Groups 2-3, 0.272 (0.08 mm) |
| EPos (mm) | 1.04 (0.33)<br>0.96 (0.31 to 2.33) | 0.86 (0.27)<br>0.84 (0.31 to 1.49) | 0.61 (0.30)<br>0.59 (-0.04 to 1.20) | <0.001*<br>Groups 1-2, 0.001 (0.18 mm)<br>Groups 1-3, <0.001 (0.43 mm)<br>Groups 2-3, <0.001 (0.25 mm) |
| EPos2 (mm) | 0.73 (0.35)<br>0.65 (-0.04 to 2.11) | 0.57 (0.28)<br>0.57 (0.03 to 1.19) | 0.10 (0.31)<br>0.12 (-0.56 to 0.77) | <0.001†<br>Groups 1-2, 0.008 (0.16 mm)<br>Groups 1-3, <0.001 (0.63 mm)<br>Groups 2-3, <0.001 (0.47 mm) |
| ICIP (mm) | 3.61 (0.37)<br>3.61 (2.82 to 4.33) | 3.64 (0.36)<br>3.71 (2.88 to 4.41) | 3.66 (0.30)<br>3.65 (3.11 to 4.24) | 0.840* |

Table 2.- Comparison of the preoperative and postoperative data between IOL groups. Abbreviations: SD, standard deviation; D, diopter; AXL, axial length; ACD, anterior chamber depth; LT, lens thickness; CCT, central corneal thickness; IOL, intraocular lens; RPE, refractive prediction error; ARPE, absolute refractive prediction error; FLP, final lens position calculated as the distance between corneal epithelium and anterior surface of the IOL; FLP2, final lens position calculated as the distance between corneal epithelium and the central plane of the IOL (FLP + half of the thickness of the IOL); EPos, IOL position error defined as the difference between the effective lens position estimated with the SRK-T formula and FLP; EPos2, IOL position error defined as the difference between the effective lens position estimated with the SRK-T formula and FLP2; ICIP, distance from corneal endothelium to the position of the point corresponding to the intracrystalline lens interphase. Non-parametrical and parametrical tests were indicated with the symbols * and †.

| Coefficient of correlation (p-value) | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| FLP vs. AXL | 0.683 (p<0.001) | 0.476 (p<0.001) | 0.363 (p=0.015) |
| FLP2 vs. AXL | 0.618 (p<0.001) | 0.461 (p<0.001) | 0.264 (p=0.083) |
| FLP vs. ACD | 0.819 (p<0.001) | 0.735 (p<0.001) | 0.631 (p<0.001) |
| FLP2 vs. ACD | 0.818 (p<0.001) | 0.728 (p<0.001) | 0.585 (p<0.001) |
| FLP vs. LT | -0.109 (p=0.344) | -0.193 (p=0.107) | 0.001 (p=0.993) |
| FLP2 vs. LT | -0.107 (p=0.355) | -0.185 (p=0.123) | 0.041 (p=0.789) |
| FLP vs. ASD | 0.782 (p<0.001) | 0.673 (p<0.001) | 0.621 (p<0.001) |
| FLP2 vs. ASD | 0.784 (p<0.001) | 0.677 (p<0.001) | 0.617 (p<0.001) |
| FLP vs. Km | -0.083 (p=0.471) | 0.012 (p=0.919) | 0.054 (p=0.727) |
| FLP2 vs. Km | -0.084 (p=0.467) | -0.004 (p=0.975) | 0.038 (p=0.806) |
| FLP vs. ICIP | 0.859 (<0.001) | 0.788 (p<0.001) | 0.739 (p<0.001) |
| FLP2 vs. ICIP | 0.852 (p<0.001) | 0.774 (p<0.001) | 0.722 (p<0.001) |

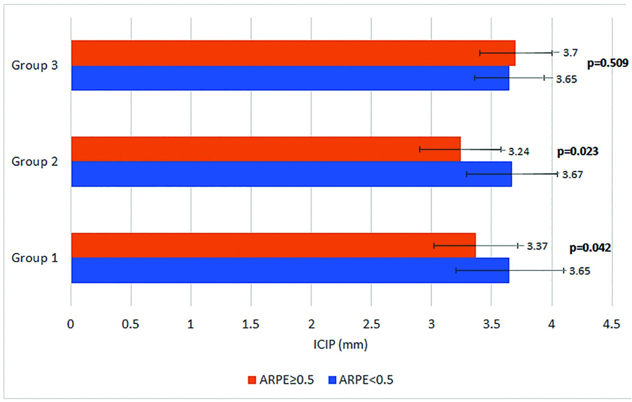
Table 3.- Summary of the correlations of FLP (final lens position calculated as the distance between corneal epithelium and anterior surface of the IOL) and FLP2 (final lens position calculated as the distance between corneal epithelium and the central plane of the IOL) with the following variables in the three IOL groups evaluated: AXL, axial length; ACD, anterior chamber depth; LT, lens thickness; ASD, anterior segment depth (corneal thickness + ACD + LT); Km, mean keratometry; and ICIP, distance from corneal endothelium to the position of the point corresponding to the intracrystalline lens interphase.

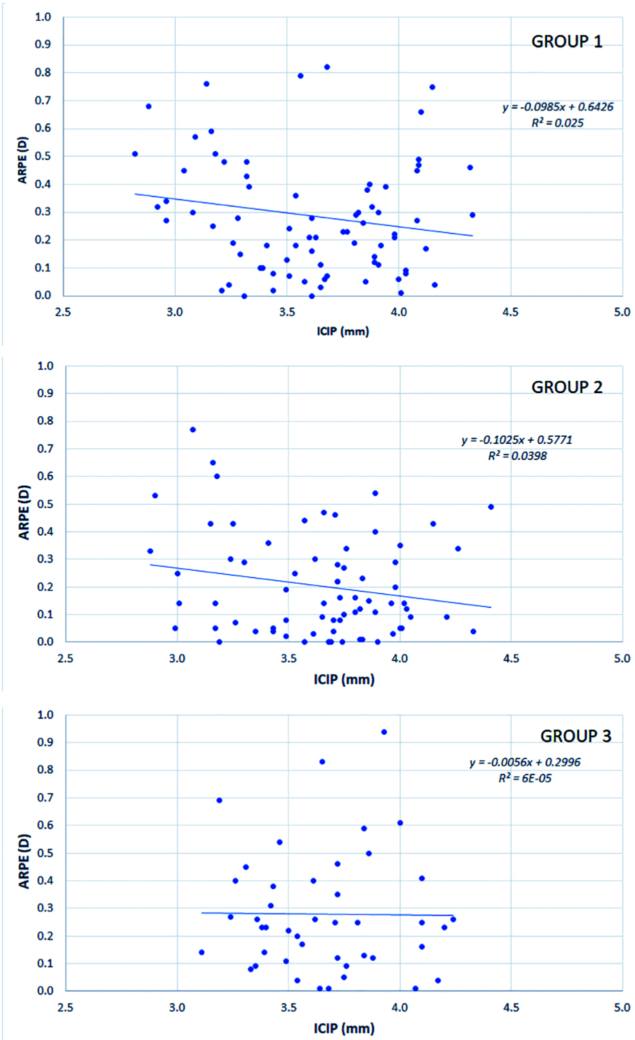


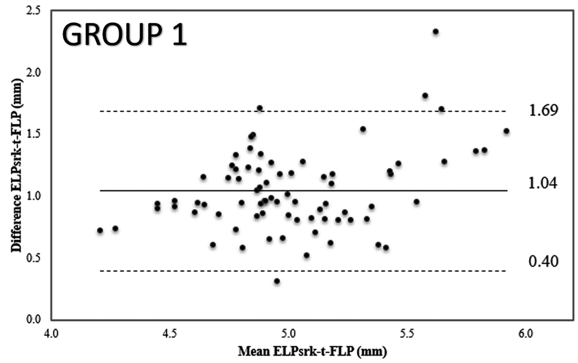

| | Measurement | CCT [µm] | AD [mm] | LT [mm] | RT [µm] | AL [mm] | |
|---|---|---|---|---|---|---|---|
| 1 | | 534 | 2.61 | 4.65 | 200 | 24.21 | ☑ |
| 2 | | 535 | 2.60 | 4.66 | 200 | 24.22 | ☑ |
| 3 | | 535 | 2.59 | 4.65 | 200 | 24.20 | ☑ |
| 4 | | 536 | 2.58 | 4.68 | 200 | 24.22 | ☑ |
| 5 | | 536 | 2.60 | 4.66 | 200 | 24.22 | ☑ |
| | **Average** | **535 µm** | **2.60 mm** | **4.66 mm** | **200 µm** | **24.21 mm** | |
| | Standard dev. | 1.0 | 0.012 | 0.014 | 0.0 | 0.007 | |

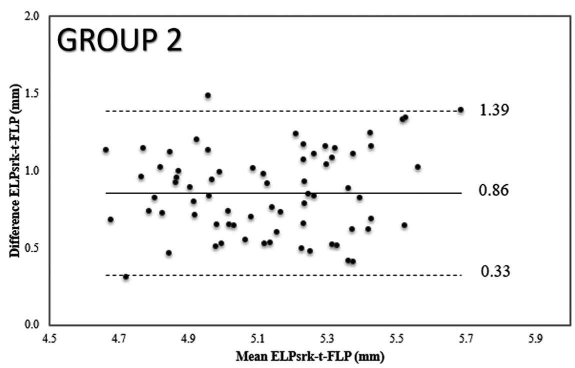
CCT Cornea thickness
AD Aqueous depth
LT Lens thickness
RT Retina thickness
AL Axial length

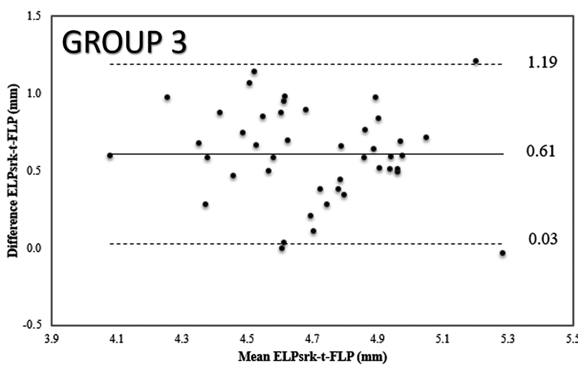
* Value user-defined
** System constant

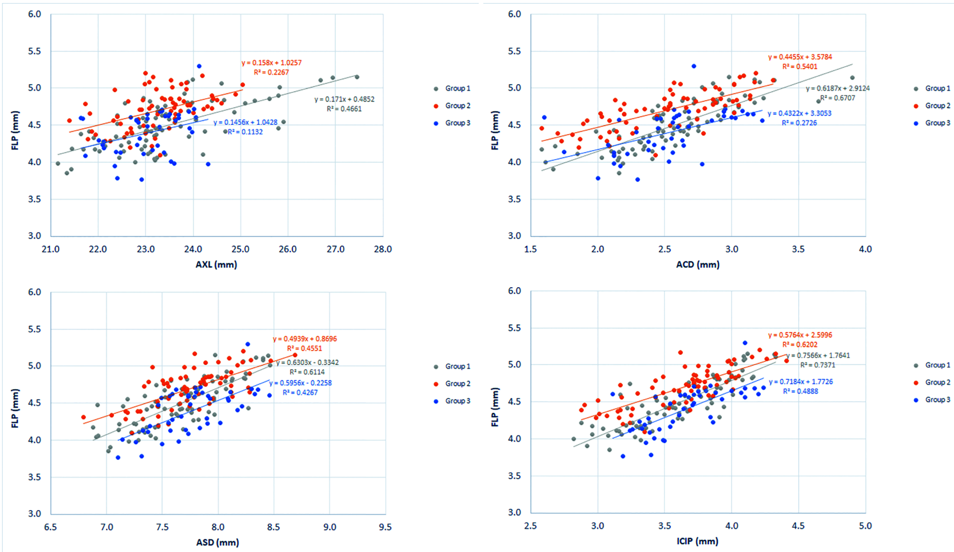

Group 3
Group 2
Group 1
3.7
3.65
p=0.509
3.24
3.67
p=0.023
3.37
3.65
p=0.042
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
ICIP (mm)
ARPE≥0.5
ARPE<0.5


GROUP 1
y = -0.0985x + 0.6426
R² = 0.025
ARPE (D)
ICIP (mm)
GROUP 2
y = -0.1025x + 0.5771
R² = 0.0398
ARPE (D)
ICIP (mm)
GROUP 3
y = -0.0056x + 0.2996
R² = 6E-05
ARPE (D)
ICIP (mm)

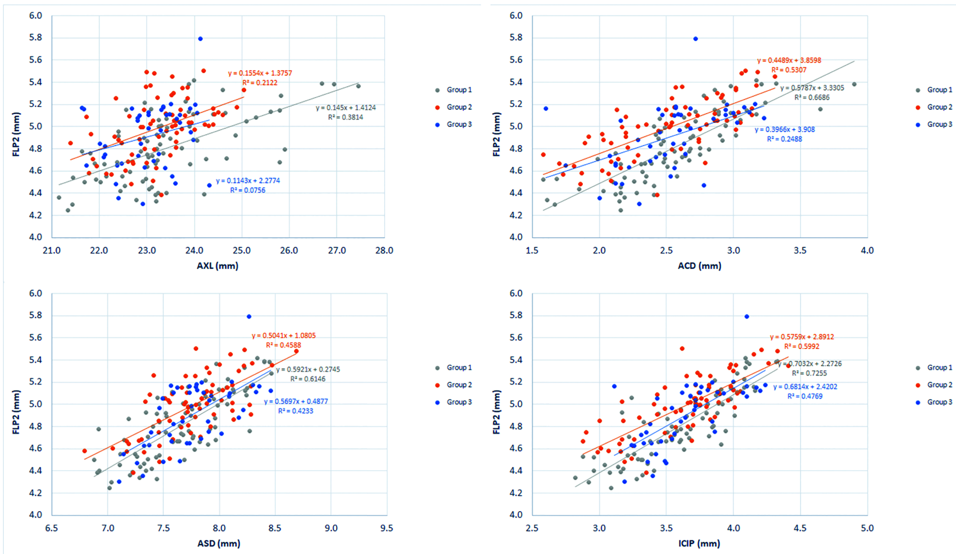

GROUP 1
Difference ELPsrk-t-FLP (mm)
Mean ELPsrk-t-FLP (mm)
1.69
1.04
0.40
2.5
2.0
1.5
1.0
0.5
0.0
4.0
4.5
5.0
5.5
6.0


GROUP 2
Difference ELPsrk-t-FLP (mm)
Mean ELPsrk-t-FLP (mm)
1.39
0.86
0.33
2.0
1.5
1.0
0.5
0.0
4.5
4.7
4.9
5.1
5.3
5.5
5.7
5.9


GROUP 3
Difference ELPsrk-t-FLP (mm)
Mean ELPsrk-t-FLP (mm)
1.19
0.61
0.03
1.5
1.0
0.5
0.0
-0.5
3.9
4.1
4.3
4.5
4.7
4.9
5.1
5.3
5.5



FLP (mm)
AXL (mm)
y = 0.158x + 1.0257
R² = 0.2267
y = 0.171x + 0.4852
R² = 0.4661
y = 0.1456x + 1.0428
R² = 0.1132
ACD (mm)
y = 0.4455x + 3.5784
R² = 0.5401
y = 0.6187x + 2.9124
R² = 0.6707
y = 0.4322x + 3.3053
R² = 0.2726
ASD (mm)
y = 0.4939x + 0.8696
R² = 0.4551
y = 0.6303x - 0.3342
R² = 0.6114
y = 0.5956x - 0.2258
R² = 0.4267
ICIP (mm)
y = 0.5764x + 2.5996
R² = 0.6202
y = 0.7566x + 1.7641
R² = 0.7371
y = 0.7184x + 1.7726
R² = 0.4888
Group 1
Group 2
Group 3


FLP2 (mm)
AXL (mm)
y = 0.1554x + 1.3757
R² = 0.2122
y = 0.145x + 1.4124
R² = 0.3814
y = 0.1143x + 2.2774
R² = 0.0756
Group 1
Group 2
Group 3
ACD (mm)
y = 0.4489x + 3.8598
R² = 0.5307
y = 0.5787x + 3.3305
R² = 0.6686
y = 0.3966x + 3.908
R² = 0.2488
ASD (mm)
y = 0.5041x + 1.0805
R² = 0.4588
y = 0.5921x + 0.2745
R² = 0.6146
y = 0.5697x + 0.4877
R² = 0.4233
ICIP (mm)
y = 0.5759x + 2.8912
R² = 0.5992
y = 0.7032x + 2.2726
R² = 0.7255
y = 0.6814x + 2.4202
R² = 0.4769