Artigo Original

Pseudophakic anterior chamber depth measurement in second eye refinement cataract surgery

Pedro Gil[1], Rita Matos[1], Joana Pires[1], Mariana S. Cardoso[1], Filipa G. Rodrigues[1], Manuel Mariano[1]
[1]Centro Hospitalar Baixo Vouga, Portugal

RESUMO

Objectivo: Relacionar a simetria inter-ocular da posição efectiva da lente intra-ocular (LIO) com os resultados refractivos num modelo de cirurgia de catarata bilateral optimizado para o segundo olho.
Material e Métodos: Estudo retrospectivo em que se identificaram 112 doentes submetidos a cirurgia de catarata bilateral consecutiva. Erros de previsão para o primeiro e segundo olhos foram calculados para 3 fórmulas (HofferQ, SRK/T e Holladay 1). Um ajuste parcial de 50% do erro de previsão do primeiro olho foi usado na selecção da LIO do segundo olho. Os resultados refractivos foram analisados e comparados usando o erro médio absoluto (EMA). A profundidade de câmara anterior pseudofáquica (pACD) foi medida com Pentacam HR, e incrementos consecutivos de 50µm de assimetria inter-ocular foram usados para analisar os resultados refractivos.
Resultados: O EMA após ajuste de 50% foi significativamente inferior ($p<0.05$) nas 3 fórmulas comparado com um grupo de não ajuste (0.30D comparado com 0.36D para HofferQ, 0.26D comparado com 0.31D para SRK/T e 0.27D comparado com 0.33D para Holladay 1). A pACD correlacionou-se entre o primeiro e segundo olhos ($r=0.714$; $p<0.001$). Para as 3 fórmulas, quando a diferença inter-ocular de pACD foi ≥350µm (11.36% dos casos), o EMA foi significativamente superior e não diferente dos grupos de não ajuste e ajuste a 100%.
Conclusões: A optimização do cálculo do poder dióptrico da LIO do segundo olho baseada no primeiro olho é uma estratégia válida e promissora para melhorar os resultados refractivos do segundo olho em casos de assimetria inter-ocular de pACD até 350µm.

Palavras-chave
Optimização do segundo olho, biometria, cirurgia de catarata, erro médio absoluto, posição efectiva da lente.

ABSTRACT

Purpose: To study the effective lens position concept in second eye refinement (SER) cataract surgery, by relating inter-ocular symmetry of pseudophakic anterior chamber depth (pACD) and SER refractive outcomes.
Methods: One hundred and twelve patients were identified as having performed bilateral consecutive cataract surgery. Prediction errors for the first and second eyes were calculated for 3

formulae (HofferQ, SRK/T and Holladay 1). A 50% adjustment of the first eye prediction error was used in the intra-ocular lens (IOL) power selection of the second eye. Refractive outcomes were compared using the mean absolute error (MAE). Pentacam HR was used to measured pACD, and consecutive 50µm increments in inter-ocular asymmetry were used to assess refractive outcomes.

Results: The resulting MAE after the 50% SER was significantly lower in all formulas compared with no adjustment: 0.30D compared with 0.36D (p=0.009) for HofferQ, 0.26D compared with 0.31D (p=0.022) for SRK/T and 0.27D compared with 0.33D (p=0.012) for Holladay1. The pACD was significantly correlated between the first and second eyes (r=0.714; p<0.001). In all formulas, when the inter-ocular difference in pACD was higher than 350µm (11.36% of patients), the MAE resulting from SER was significantly higher and not different when comparing with the no adjustment group.

Conclusions: To our knowledge this is the first study to relate SER outcomes with the measured effective lens position. SER is a valid and promising strategy to improve cataract surgery refractive outcomes in cases of pACD inter-ocular asymmetry up to 350µm.

Keywords

Biometry, cataract surgery, effective lens position, mean absolute error, second eye refinement.

INTRODUCTION

The process of second eye refinement in bilateral cataract surgery is an adjustment in second eye intra-ocular lens (IOL) power calculation based on the first eye outcome. It was first tested by Jabbour et al in patients undergoing bilateral consecutive cataract surgery with implantation of one single IOL type[1], and further studies concluded that optimal refractive results were obtained using a partial 50% adjustment of the first eye prediction error[2-4].

With our current optic biometry methods, inaccurate pre-operative estimation of the final position of the IOL inside the capsular bag – the effective lens position (ELP) – has surpassed axial length (AL) measurement as the leading source of prediction error (35.5%) in IOL formulae[5]. Given the high inter-ocular symmetry between biometric measurements[1-4,6,7], it has been suggested that the factors contributing to inaccurate estimation of the IOL position (and inaccurate refractive predictions) are also related between both eyes. Second eye refinement would therefore benefit from the correlation between post-operative IOL position of first and second eyes, and its refractive improvements derived from accounting for these undetermined sources of error[2]. However, this theory has never been tested with data from pseudophakic anterior chamber depth (pACD) measurement in second eye refinement models.

This paper aims to study the importance of ELP in the particular context of second eye refinement cataract surgery. We sought to test if the refractive outcomes in a second eye refinement model can be related to inter-ocular symmetry of pACD measurement.

METHODS

Institutional review board approval was obtained and the clinical protocol was registered, reviewed and published on the National Institutes of Health public database (https://clinicaltrials.gov, NCT02423668). From the electronic database of medical records of a single ophthalmological centre, 112 patients were identified as having performed bilateral cataract surgery between 1st June 2013 and 24th July 2014. A total of 24 patients were excluded according to the considered criteria (table 1).

A retrospective chart review was conducted, including demographics (age and gender) and several parameters for both the first and second eyes: surgery date, AL, keratometric corneal power in 2 meridians, predicted IOL power recommended for plano target in each formulae (HofferQ, SRK/T and Holladay 1), implanted IOL power, predicted post-operative refraction for the implanted IOL for the 3 formulae, observed post-operative refraction in spherical equivalent and post-operative BCVA.

Keratometric corneal power in 2 meridians, AL and IOL power calculations were performed using a single calibrated instrument (IOL Master v.5, Carl Zeiss Meditec AG,

Table 1 | Exclusion criteria. Intra-ocular lens (IOL); Best-corrected visual acuity (BCVA).

Exclusion criteria	Number of excluded patients
Age < 18 years old	0
Inadequate follow-up	5
Incomplete medical records	5
Previous or combined ocular surgery	6
Manual extracapsular cataract extraction and not phacoemulsification	0
Corneal sutures	0
Implantation of any other IOL type	2
IOL implanted in the sulcus	1
Intra or postoperative complication	1
Post-operative BCVA worse than 5/10	2
Corneal astigmatism>3.00 D	1
Inadequate cooperation for Pentacam HR examination	1

Jena, Germany) by 2 trained ophthalmic technicians. In the presence of inter-ocular asymmetry, AL measurement was confirmed by ultrasound biometry, but in all cases the recorded value was the one given by IOL Master. Post-operative refraction and BCVA were evaluated 4 to 6 weeks after surgery. Surgery was performed by a group of 7 cataract surgeons, and in most cases the same surgeon performed both the first and second eyes. Lens power selection was at the discretion of the surgeon, and comprised in all cases calculations for the 3 formulae. The surgical technique was clear corneal phacoemulsification. The IOL model used was Abbott Tecnis® 1-piece acrylic IOL (Abbott Laboratories Inc., Illinois, USA), ZCB00, with a biconvex anterior aspheric surface and a square optic edge, 6mm optic diameter and 13mm haptic overall length, manufacturer's optical A-constant 119.3.

Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany, softwareversion 1.20r41) was used for pACD measurement. The exam was performed bilaterally at least 3 months after second eye surgery, and only exams classified as "OK" were used for grading. A total of 25 Scheimpflug images were obtained for each eye. Manual measurement was performed tracing a line between the anterior surface of the IOL and the central corneal epithelium apex. The value was averaged after 3 consecutive measurements. The Scheimpflug image selected for measurement was the one that provided visualization of the whole IOL optic. In cases where this was true for more than one image, only one was arbitrarily chosen and used (nevertheless, the other scans were also measured and a difference higher than 0.01mm was never observed). Manual measurement was performed by the same investigator in all cases.

First and second eyes were defined chronologically. The prediction error for the first (PE1) and second (PE2) eyes was calculated as the difference between the observed post-operative refraction in spherical equivalent and the predicted post-operative refraction by the IOL Master for the implanted IOL. This was obtained for the 3 formulae.

Second eye refinement in the IOL power selection for the second eye was performed using a theoretical 50% partial adjustment of the PE1. Refractive outcomes were analysed and compared using the mean absolute error (MAE), the mean of the absolute value of the prediction error.

To relate refractive outcomes to pACD values, we performed subgroup analysis based on consecutive 50μm increments of inter-ocular asymmetry of pACD (50-600).

Normality was assessed using distribution plots and Shapiro-Wilk tests. All comparisons between eyes were performed either with Pearson Correlation Coefficient or paired-samples Student t-test. MAEs were compared with the paired-samples Student t-test.

Informed consent for cataract surgery was obtained from all patients. The study was designed and implemented with full accordance with the principles of the Declaration of Helsinki.

Data was analysed using Stata SE 13.0 (Stata Corp, TX, USA). Statistical significance was set at $p<0.05$.

RESULTS

Patient Characteristics

A total of 88 patients were included in the study, 29 male (32.95%) and 59 female (67.05%). Mean age at the time of the first eye surgery was 72.32±6.63 (54.00-84.00) and the mean time period between both surgeries was 5.04±6.11 (0.07-22.20) months.

The average AL for the first eye was 23.36±1.03 (21.90-27.92) mm and for the second eye was 23.38±1.03 (21.93-28.50) mm. The difference between average ALs was not statistically significant (p=0.605). Ninety five percent of patients had an inter-ocular difference of AL inferior to 0.42mm. There was a significant inter-ocular correlation between first and second eyes AL (Pearson correlation coefficient (r) = 0.979, p<0.001).

The average keratometric power for the first eye was 44.26±1.50 (40.91-48.18) D and for the second eye was 44.25±1.52 (40.42-48.17) D. This difference was not statistically significant (p=0.956). Ninety five percent of patients had an inter-ocular difference in average keratometric power inferior to 0.97 D. There was a significant inter-ocular correlation (r=0.953, p<0.001).

A high degree of correlation between the IOL power recommended for emmetropia in the first and second eyes was present for all formulae. The Pearson correlation coefficients were 0.951 (p<0.001) for the HofferQ, 0.958 (p<0.001) for the SRK/T and 0.952 (p<0.001) for the Holladay 1. The inter-ocular correlation was also present in terms of first and second eyes implanted IOL power with a Pearson correlation coefficient of 0.951 (p<0.001).

Prediction Error Statistics

Using the optimized IOL formulae, the first eye mean error of the sample was 0.055±0.501 D for the HofferQ, 0.028±0.449 D for the SRK/T and 0.050±0.474 D for the Holladay 1.

There was a significant correlation between PE1 and PE2 for all formulae. The Pearson correlation coefficient was 0.504 (p<0.001) for the HofferQ, 0.522 (p<0.001) for the SRK/T and 0.509 (p<0.001) for the Holladay 1.

Table 2 | Mean absolute errors with 50% partial adjustment (PA), no adjustment (NA) and full adjustment (FA) for each formula. *p<0.05 compared with both the full adjustment and the no adjustment groups, paired-samples Student t-test

	PA	NA	FA
HofferQ	0.30 D *	0.36 D	0.35 D
SRK/T	0.26 D *	0.31 D	0.31 D
Holladay 1	0.27 D *	0.33 D	0.32 D

The second eye refinement model with a 50% partial adjustment is represented in table 2. It includes the calculation of the MAE for all 3 formulae in 3 different settings: partial adjustment (PA), no adjustment (NA) and full adjustment (FA). The no adjustment group represents the observed prediction errors for the second eye without second eye refinement, while the full adjustment group represents a model where an adjustment in the IOL power selection for the second eye was done by the full amount of the PE1. The resulting MAE was statistically inferior in the PA group for all formula comparing with the NA and FA groups. There was no statistically significant difference between these last two groups in terms of resulting MAE.

Pseudophakic Anterior Chamber Depth Statistics

There was a significant correlation between the pACD for the first and second eyes (r=0.714, p<0.001).

The MAE after 50% partial adjustment in all formulae was not significantly different in all subgroups of 50µm increments in inter-ocular asymmetry of pACD up to 350µm. Above 350µm of pACD inter-ocular asymmetry, the MAE was significantly higher (table 3).

In the pACD inter-ocular asymmetry <350µm subgroup, the MAE after 50% partial adjustment was significantly inferior when comparing to the no adjustment and full adjustment groups. In the pACD inter-ocular asymmetry ≥350µm subgroup (11.36% of patients), there was no significant difference between the MAE after 50% partial adjustment

Table 3 | Ocular parameters according to the stage of ROP.

	pACD inter-ocular asymmetry < 350 µm			pACD inter-ocular asymmetry ≥ 350 µm (11.36% of patients)		
	PA	NA	FA	PA	NA	*FA*
HofferQ	0.27 D *	0.34 D	0.33 D	0.49 D	0.51 D	0.50 D
SRK/T	0.24 D *	0.29 D	0.29 D	0.42 D	0.45 D	0.44 D
Holladay 1	0.25 D *	0.31 D	0.30 D	0.45 D	0.47 D	0.46 D

andthe no adjustment and full adjustment groups. There was no difference in terms of MAE between the no adjustment and full adjustment groups, for any subgroup of inter-ocular pACD asymmetry. This was true for all formulae (table 3).

DISCUSSION

With our current standard of care, it is estimated that the lowest MAE achievable is between 0.36 D and 0.40 D[5]. This means that there are still theoretical limits to biometry accuracy even in the presence of 3rd or 4th generation optical biometry formulas and an uneventful IOL-in-the-bag cataract surgery. Second eye refinement represents one of the most promising and exciting ways to overcome those limits.

Like in previous papers, our results show that there is a high degree of inter-ocular symmetry between biometric measurements[1-4,6,7]. This is evident in terms of mean anterior keratometry, AL, implanted IOL dioptric power and, most importantly, prediction errors between both eyes, which are significantly correlated in all formulae. These premises make second eye refinement not only possible, but also logical. In fact, by adjusting the second eye IOL power selection by half of the prediction error of the first eye, the resulting MAE is significantly decreased in all formulae. This had been previously shown by similar works[2-4]. By reporting the numerical mean error of the sample (which is close to zero in all formulas), we can consider the MAE as a valid representative of the accuracy of the predictions. Therefore, the observed reduction of the MAE can be attributed to the refractive improvement after second eye refinement, and not due to correction of non-optimized IOL formulas.

To our knowledge, this is the first study to relate second eye refinement refractive outcomes with the measured IOL position. There is extensive literature regarding different methods to measure ACD but there have been contradictory results regarding the direct comparison between them. In phakic eyes, most studies have shown a consistent agreementbetween non-contact methods, including partial coherence interferometry (PCI)[8,9], Pentacam (rotating Scheimpflug camera)[8,10-12], Orbscan (scanning-slit topography; Orbtek Inc, Salt Lake City, Utah, USA)[8,11] and IOL Master (PCI-based but uses a slit beam photographic technique for measuring ACD; Carl Zeiss Meditec, Jena, Germany)[9,10,12]. Most authors have reported that contact A-scan methods result in shallower ACD measurements due to unintentional indentation of the cornea and off-axis measurement[9,12,13]. However, in other papers the results have been comparable to non-contactoptical methods[14]. Regarding immersion ultrasound, there is less consistent data. The results have been compared to Orbscan with high correlation between measurements[15]. When comparing to anterior segment OCT (Visante, Carl Zeiss, Meditec), immersion US resulted in ACD measurements significantly lower[16].

Regarding pseudophakic eyes, the limitations inherent to contact ultrasound are still true, but even between non--contact optical methods there is less agreement than in phakic eyes. Su *et al* reported that Pentacam measurements had a larger standard deviation than IOL Master and ultrasound, and that automatic Pentacam examination failed to correctly identify the anterior IOL surface in a significant proportion of patients[12]. Nemeth *et al* reported a surprisingly lower ACD value with automatic Pentacam measurement than with contact ultrasound[14]. Another paper by Kriechbaum *et al* showed an absence of correlation in ACD measurements between IOL Master and a laboratory prototype version of PCI[9], while Koranyi *et al* reported a good agreement between optical methods in pseudophakic eyes, unlike contact ultrasound[13]. The lack of agreement between optical methods might be mainly IOL-related and not equipment-related. The reflecting properties of an IOL interfere with the determination of its anterior surface in a way that acrylic IOLs blur the lens edge during the Pentacam or IOL Master examination[9]. IOLs that have a UV-absorbing chromophore to protect the retina might also partially absorb the blue slit light produced by some optic methods (including Pentacam), leading to erroneous IOL surface recognition[12]. In miotic pupils, the iris can also be misidentified as the IOL anterior surface[12].

We built our study based on the findings by Savini *et al*[17]. The authors reported that a manual measurement of the pACD using Pentacam was a reliable method in pseudophakic eyes, while preserving adequate repeatability and reproducibility. Like in previous studies, the authors confirmed that an automatic measurement provided some erroneous measurements, in which the iris or the posterior capsule were mistaken for the anterior surface of the IOL. Using the Scheimpflug images provided by the Pentacam, the observer can directly identify the correct anterior surface of the IOL and manually measure the true pACD. In the case of our study, the inter-observer reproducibility was nulled by the fact that only one investigator performed all manual measurements. In this context, Pentacam provides a valuable advantage over other optical methods such as IOL Master, in which the measure is obtained from an automatic photographic capture and analysis without the possibility of visual confirmation of the correct identification of the IOL anterior surface. The same is true for A-scan ultrasound, for which in some cases can be difficult to identify the exact spike corresponding to the IOL.

The refractive improvement after second eye refinement has soon been linked to an attempt to account for prediction errors in biometric formulas due to incorrect estimation of ELP in symmetrical pairs of eyes[2].The negative results first reported by Jabbour *et al* evidenced that a full adjustment is not appropriate, as it will account for other systematic errors in IOL calculation (including anterior keratometry and AL measurements)[1]. The partial 50% adjustment is an attempt to solely address the errors attributable to the empirical inter-ocular correlation of IOL position, first reported by Olsen[7]. The authors also showed that the refractive improvements after a 50% partial adjustment are similar to the effect of using the measured pACD of the first eye in the calculation of the second eye IOL power using the Olsen formula, a finding recently confirmed by Muthappan *et al*[18].

Like previous studies, our results confirm the significant inter-ocular correlation of IOL position, as measured by pACD[7,18]. By being the first to relate refractive outcomes in a second eye refinement model to inter-ocular symmetry of pACD measurement, this paper highlights the fact that the added improvement is dependent on the expected symmetry in terms of IOL position between symmetrical eyes. The 50µm increments in inter-ocular asymmetry of pACD allow us to conclude that in cases where the IOL position of the first eye is not a good predictor of the IOL position of the second eye (inter-ocular asymmetry of pACD≥350µm), the resulting MAE after second eye refinement is higher. Not only that, but it is also not significantly different from the MAE after no adjustment or full adjustment. This novel data further confirms that the refractive improvement after second eye refinement is in fact due to a correction of estimated IOL position, and not due to correction of anterior keratometry or AL measurements or other systematic errors in IOL power calculation formulas. The fact that the inter-ocular asymmetry of pACD cut-off was the same for all formulas (≥350µm) should not be regarded as a mere coincidence, but an evidence of the consistency of the data and, most importantly, the result of using three 3rd generation formulae, with similar designs and prediction accuracies. This cut-off might be different for other formulas (such as the SRK II and Olsen formulas), a topic that may be addressed in further studies.

Limitations to this study include its moderate sample size, although comparable to others such as Jabbour *et al*[1]or Muthappan *et al*[18]. Although the refractive improvement of second eye refinement has been confirmed across the majority of our currently used IOL formulas (including HofferQ[2], Holladay 1[2,3], SRK/T[1,2,7], Haigis[4] or Olsen[7,18]), we cannot make any definite considerations regarding the validity of the main findings of this article in other IOL formulas. Like all previous studies on the topic of second eye refinement, except for Jivrajka *et al*[4], our is a retrospective study based on theoretical corrections. Therefore, precaution is still warranted when commenting on refractive outcomes, particularly in cases of biometric inter-ocular asymmetry.

In conclusion, this is the first study to relate refractive outcomes to pACD inter-ocular asymmetry in a second eye refinement model. Our results confirm that the refractive improvement after a 50% partial adjustment is dependent on the expected symmetry in terms of IOL position between symmetrical eyes. The observed reduction of the MAE is due to a correctionof second eye estimated IOL position when the inter-ocular asymmetry of pACD is less than 350µm.

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CONTACTO
Pedro Gil
Serviço de Oftalmologia
Centro Hospitalar Baixo Vouga
Avenida Artur Ravara
3814-501 Aveiro
e-mail: pedroqgil@gmail.com