







Endothelial Cell Loss in Anterior Chamber Phakic Intraocular Lenses: The Role of Critical Distance at Different Meridians

Perda de Células Endoteliais nas Lentes Intraoculares Fáquicas de Câmara Anterior: O Papel da Distância Crítica em Diferentes Meridianos

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ABSTRACT

INTRODUCTION: Our aim was to assess the influence of minimum distance from the edge of the anterior chamber phakic intraocular lens (iris-fixated pIOL) to the corneal endothelium (critical distance; CD) measured at four different points using high-resolution swept-source optical coherence tomography (ANTERION® Heidelberg Engineering) on endothelial cells density (ECD).

METHODS: A cross-sectional study was performed on patients who underwent Artiflex® implantation between 2003 and 2022. Eyes submitted to iris-fixated pIOL explantation or lost to follow-up were excluded. All eyes underwent CD evaluation with ANTERION® in 2023 at four evaluation points: nasal (N), superior (S), temporal (T) and inferior (I). ECD and anterior chamber depth were also evaluated. A mixed-effects linear regression was performed to assess the effect of CD on annual ECD loss, adjusting for age. Receiver operating characteristic (ROC) curves were used to assess the discriminative ability of CD at each location.

RESULTS: Sixty-three patients (108 eyes) were included in this study. The mean±SD age was 31.3±5.4 years. The median (IQR) follow-up was 12.67 (11.75 – 15.38) years. The mean±SD CD at N, T, S and I points were 1.47±0.24, 1.54±0.24, 1.64±0.27 mm and 1.49±0.34, with significant differences between locations (N vs S points and S vs I, both $p<0.001$). The mean±SD minimum CD at any point was 1.33±0.25 mm. The mixed-effect linear analysis revealed a significant effect of CD at all locations on annual ECD percentual loss with N location presenting the highest coefficient. Using a mean distance of 1.5 mm in the linear model, an annual ECD loss of 1.38%, 1.38%, 1.50% and 1.52% was predicted for N, T, S and I points, respectively. Using annual ECD loss of 1% as cut-off, the S distance presented the highest AUROC.

CONCLUSION: The evaluation of critical distances at the 4 different points seems to be relevant in the follow-up of patients with iris-fixated pIOL. In addition to ECD, the annual follow-

up visits of patients with iris-fixated pIOL should include the measurement of critical distance by points and not only on the horizontal meridian.

KEYWORDS: Anterior Chamber; Corneal Endothelial Cell Loss; Endothelium, Corneal; Myopia/surgery; Phakic Intraocular Lenses.

RESUMO

INTRODUÇÃO: O nosso objetivo foi avaliar a influência da distância mínima entre o bordo da lente intraocular fática de câmara anterior (*iris-fixated* pIOL) ao endotélio corneano (distância crítica; CD) medida em quatro pontos diferentes usando tomografia de coerência ótica de *swept-source* de alta resolução (ANTERION® Heidelberg Engineering) na densidade de células endoteliais (ECD).

MÉTODOS: Foi realizado um estudo transversal com pacientes submetidos a implante de Artiflex® entre 2003 e 2022. Foram excluídos olhos submetidos a explante da *iris-fixated* pIOL ou com perda de seguimento. Todos os olhos foram submetidos à avaliação da CD com ANTERION® em 2023 em quatro pontos: nasal (N), superior (S), temporal (T) e inferior (I). A ECD e a profundidade da câmara anterior também foram avaliados. Usou-se uma regressão linear de efeitos mistos para avaliar o efeito da CD na perda anual de ECD, ajustando para a idade. Usaram-se curvas *receiver operating characteristic* (ROC) para avaliar a capacidade discriminativa da CD em cada local.

RESULTADOS: Sessenta e três pacientes (108 olhos) foram incluídos no estudo. A média±DP de idade foi 31,3±5,4 anos. A mediana (IQR) do tempo de seguimento foi de 12,67 (11,75 – 15,38) anos. As médias±DP da CD nos pontos N, T, S e I foram 1,47±0,24, 1,54±0,24, 1,64±0,27 mm e 1,49±0,34, com diferenças significativas entre os locais (pontos N vs S e S vs I, ambos $p < 0,001$). A média±DP da CD mínima em qualquer ponto foi de 1,33±0,25 mm. A regressão linear de efeito misto mostrou um efeito significativo da CD em todos os locais na perda percentual anual de ECD, com a localização nasal apresentando o maior coeficiente. Utilizando uma distância média de 1,5 mm no modelo linear, obteve-se uma perda ECD anual de 1,38%, 1,38%, 1,50% e 1,52% para os pontos N, T, S e I, respetivamente. Utilizando como ponto de corte a perda anual de ECD de 1%, a distância S apresentou a maior AUROC.

CONCLUSÃO: A avaliação das distâncias críticas nos 4 diferentes pontos parece ser relevante no seguimento de pacientes com *iris-fixated* pIOL. Além do ECD, as consultas anuais de acompanhamento dos pacientes com *iris-fixated* pIOL devem incluir a medição da distância crítica em diferentes pontos e não apenas no meridiano horizontal.

PALAVRAS-CHAVE: Câmara Anterior; Endotélio Corneano; Lentes Intraoculares Fáticas; Miopia/cirurgia; Perda de Células Endoteliais da Córnea.

INTRODUCTION

Iris-fixated phakic intraocular lenses (pIOLs) have been used worldwide to correct high myopia, hyperopia, and astigmatism since their first implantation in 1986.¹ The Artiflex® Myopia and Artiflex® Toric lenses (Ophtec B.V., Groningen, The Netherlands) are foldable iris-fixated pIOLs which allows their implantation through a sutureless corneal incision with less surgically-induced astigmatism.² Due to the lower refractive index of the silicone material used, Artiflex® pIOL is thicker than the rigid Artisan® pIOL, resulting in closer proximity to corneal endothelium, which can decrease the endothelial cell density (ECD).³ Therefore,

ECD and anterior chamber morphometrics need to be regularly assessed for surveillance.

The American Academy of Ophthalmology recommends the performance of specular microscopy preoperatively and at the 6-, 12-, 24-, and 36-month postoperative intervals.⁴ In addition, close monitoring (every 4-6 months) of eyes with >20% endothelial cell loss or an endothelial cell count of <1500 cells/mm² is advised.⁴ Concerning the anterior chamber morphometrics, the critical distance (CD) is defined as the distance between the iris-fixated pIOL and the corneal endothelium. Güell *et al*⁵ suggested a safety CD of 2.0 mm for the center of the iris-fixated pIOL whereas Baikoff⁶ recommended 1.5 mm for the edges. The latter

distance is usually measured at nasal and temporal edges. Although, it has been demonstrated that age-dependent decline of iridocorneal angle is greater in the superior location⁷ suggesting that superior ACD also decreases more than the other regions. Thus, it is paramount to assess the distance between the endothelium and the edge of the iris-fixated pIOL at other location than the horizontal meridian and determine its influence on ECD loss.

In this study, we sought to assess the association between CD measured at horizontal and vertical meridians and the ECD loss as well as to determine the discrimination performance of CD at those locations.

METHODS

This is a cross-sectional study that enrolled consecutive adult patients submitted to phakic foldable iris-fixated Artiflex® (Ophtec B.V., Groningen, The Netherlands) IOL implantation at the Department of Ophthalmology of Centro Hospitalar Universitário de Santo António, Porto, Portugal, between 2003 and 2022. This study was conducted following the tenets of the Declaration of Helsinki⁸ and complied with the requirements of the institute's committee on human research. Patients' anonymity was carefully protected. Informed consent was signed for all procedures, following the guidelines required by the institution with which all the authors are affiliated.

PATIENT POPULATION

The inclusion criteria, surgical technique and postoperative care for iris-fixated pIOL implantation in our center have been described elsewhere.⁹ In short, currently these criteria select healthy patients aged ≥ 21 years with stable refraction for at least 1 years, normal age-adjusted endothelial cell density, no history or observation of ocular diseases, an aqueous depth (AQD) of at least 3.2 mm, a pupil < 6.0 mm under mesopic conditions and a refractive error or corneal abnormalities precluding laser vision correction. This study did not include patients with keratoconus, irregular astigmatism, or previous corneal transplantation.

SURGICAL TECHNIQUE AND POSTOPERATIVE CARE

IOL power calculations were performed by the manufacturer using the van der Heijde formula. All surgeries were performed under general anesthesia after pharmacologic miosis induction with pilocarpine 2%. For toric iris-fixated pIOL implantation, limbal reference marks were placed in the horizontal meridian with a needle at slit-lamp and used to mark the alignment axis with a Mendez ring intraoperatively until 2020 and assisted by Verion Digital Marker (Alcon Laboratories, Inc.) since 2021. The iris-fixated pIOL was introduced through a 3.2 mm superior corneoscleral incision using a purposely-designed spatula and fixated with a disposable enclavation needle (Ophtec BV). A cohesive ophthalmic viscosurgical device was inserted through the paracen-

teses to fill the anterior chamber, protect the endothelium, and facilitate adjustments of the iris-fixated pIOL within the eye during fixation. A 12 o'clock iridectomy was performed to avoid pupillary block glaucoma.

After surgery, all patients were prescribed with topical ofloxacin 3 mg/mL 5 times a day for 2 weeks, prednisolone acetate 10 mg/mL 5 times a day for 3 weeks, and flurbiprofen sodium 0.3 mg/mL 5 times a day for 4 weeks. Oral prednisolone 1 mg/kg/d was also used on all patients on a tapered schedule.

PREOPERATIVE ASSESSMENT

Preoperative examination consisted of subjective refraction, cycloplegic refraction, when necessary, Snellen uncorrected and corrected distance visual acuity (UDVA and CDVA) assessment, biomicroscopy, Goldmann application tonometry, funduscopy under pharmacological mydriasis, corneal tomography (Orbscan® (Bausch & Lomb, Inc.) or Pentacam® HR (Oculus Optikgerate GmbH)) and specular microscopy (KSS-300® (Konan Medical Inc.), and EM 4000® (Tomey GmbH)).

ENDOTHELIAL CELL DENSITY AND ANTERIOR CHAMBER MORPHOMETRICS

From February 2023 to August 2023 all eyes were assessed for endothelial cells density and anterior chamber measurements. Central ECD counts were performed with specular microscopy (EM 4000® (Tomey GmbH)). The anterior chamber morphometrics were assessed using Pentacam® HR (Oculus Optikgerate GmbH) for AQD measurement and an anterior-segment ocular coherence tomography (AS-OCT; ANTERION®, Heidelberg Engineering) for evaluation of the CD between the edge of the iris-fixated pIOL and the corneal endothelium (Fig. 1). One examiner (JL) analyzed all images and measured the distance between the iris-fixated pIOL edge and the corneal endothelium at vertical and horizontal meridians, to retrieve the values for nasal (N), superior (S), temporal (T) and inferior (I) points. Pupil center was retrieved from Pen-

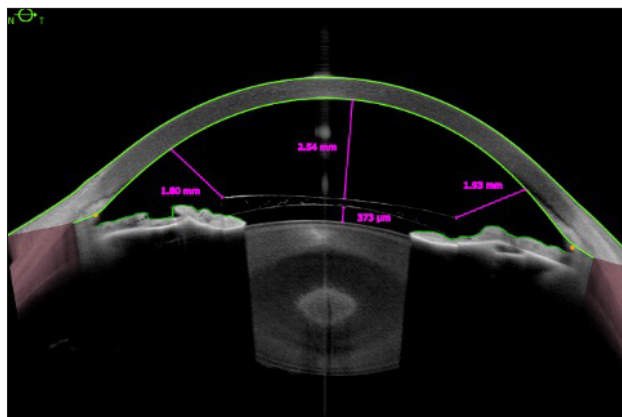


Figure 1. Representation of critical distance measurement with Anterior Segment-Optical Coherence Tomography (ANTERION®, Heidelberg Engineering).

tacam® HR (for reference, positive values in x and y axis represent temporal and superior displacement, respectively, of the pupil center relatively to the corneal vertex). All AS-OCT and Pentacam® images were taken in an unaccommodated state and under mesopic conditions.

OUTCOMES

Our main outcome is the association between annual ECD percentual loss and CD at four points overmentioned. As secondary objectives, we aim to assess the discrimination ability of CD at each location for annual ECD percentual loss using 1%, the sample mean and 1SD above the sample mean as cut-offs.

STATISTICAL ANALYSIS

All statistical analyses were performed using Stata software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Continuous variables are presented through means and standard deviations (SD) or 95% confidence interval (CI) for data with Gaussian distribution, or medians and interquartile ranges (IQR) for variables with a skewed distribution. Categorical variables are described as absolute and relative frequencies. Parametric or nonparametric tests were used for continuous variables comparison between groups according to the normality of data. A mixed-effects linear regression was performed to assess the effect of CD on annual endothelial cell loss, adjusting for age and using patient identification number as a random effect to correct for the inclusion of both eyes. To assess the discriminative ability of CD at each location, we performed receiver operating characteristic (ROC) curves and calculated the area under the curve (AUC) and the ideal cut-off points for annual ECD loss of 1% and the calculated mean of the sample.

RESULTS

Sixty-three patients (108 eyes) were included in this study with a mean±SD age of 31.3±5.4 years at time of surgery. For 18 patients, only one eye met the inclusion criteria as the fellow eye was implanted with Artisan® model or submitted to laser vision correction. Table 1 presents the patients' demographics and ophthalmological characteristics at baseline. The median (IQR) follow-up was 12.67 (11.75 – 15.38) years. No difference was found in preoperative parameters according to Artiflex model.

During the follow-up, the mean±SD annual ECD absolute and percentual losses were 45.10±31.01 cells/mm² and 1.53%±0.99%. There was a significant decrease of AQD ($\Delta=-0.20\pm0.02$, $p<0.001$) and ECD ($\Delta=-593.75\pm37.94$, $p<0.001$). No difference was found for the reduction of both parameters according to the iris-fixated pIOL model.

The mean±SD CD at N, T, S and I points were 1.47±0.24, 1.54±0.24, 1.64±0.27 mm and 1.49±0.34, with significant differences between locations (N vs S points and S vs I, both $p<0.001$). The mean±SD minimum CD at any point was

Table 1. Demographic and ophthalmological characteristics of population at baseline.

Characteristic	Value
Number of patients / eyes	63 / 108
Age, years	31.26 ± 5.40
Female sex	41 (65.1%)
Right eyes	52 (48.1%)
Sphere, D	
Mean ± SD	-7.94 ± 2.72
Range	-0.5 to -13.5
Cylinder, D	
Mean ± SD	-1.71 ± 1.56
Range	0.0 to -6.5
AQD, mm	
Mean ± SD	3.22 ± 0.24
Range	2.74 to 3.83
ECD, cells/mm ²	
Mean ± SD	2867.94 ± 363.24
Range	2179 to 3831
Artiflex model	
Myopia (model 401)	71 (65.7%)
Toric (model 4A/4C)	37 (34.3%)
Horizontal position	19 (48.6%)
Oblique position	18 (51.4%)

Data shown as number (percentage) and mean ± standard deviation (SD). D, diopters; AQD, aqueous depth; ECD, endothelial cell density.

1.33±0.25 mm. When considering the meridians separately, the minimum CD was 1.39±0.27 and 1.42±0.23 for vertical and horizontal meridians, respectively; the difference was not statistically significant ($p=0.090$) but both values were significantly higher than the minimum CD at any point. Eyes implanted with the toric model had a significantly higher CD at inferior location ($\beta=0.24$; $p=0.003$), adjusted for spherical equivalent and iris-fixated pIOL position (horizontal vs oblique). The mean±SD values of pupil center position in the x and y axes were -0.03±0.016 and -0.02±0.16 µm, respectively. The x-axis but not y-axis position presented a trend ($p=0.06$) for being significantly different than zero (i.e., a significant nasal displacement considering the corneal vertex). No difference was found between Artiflex models for pupil center position.

The mixed-effect linear analysis revealed a significant effect of CD at all locations on annual ECD percentual loss with nasal location presenting the highest coefficient (Table 2). The inclusion of the Artiflex model in the regression was not significant for any location and thus was not considered. An annual ECD loss of 1.38%, 1.38%, 1.50% and 1.52% was calculated from the models of N, T, S and I locations, respectively, by using a mean distance of 1.5 mm. Table 3 presents the calculated annual ECD loss using as mean distance the minimum CD±1SD of this sample. Nasal location presented the highest variation of ECD loss, ranging

Table 2. Mixed-effects linear models for assessment of the effect of CD on yearly ECD percentual loss.

Variable	Nasal		Temporal		Superior		Inferior	
	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value
CD	1.45 (0.60-2.30)	0.001	0.87 (0.03-1.71)	0.041	0.80 (0.04-1.55)	0.038	0.62 (0.05-1.19)	0.034
Age	0.02 (-0.01-0.05)	0.279	0.01 (-0.03-0.04)	0.722	0.01 (-0.02-0.04)	0.671	0.003 (-0.03-0.35)	0.845
Constant	-4.46 (-6.70 - -2.23)	<0.001	-3.14 (-5.37 - -0.92)	0.006	-3.15 (-5.37 - -0.94)	0.005	-2.59 (-4.41 - -0.78)	0.005

Table 3. Annual ECD loss as calculated from the mixed-effects models.

Location	1.58 mm	1.33 mm	1.08 mm
	mean+1SD	mean	mean+1SD
Nasal	1.27	1.63	1.99
Temporal	1.31	1.53	1.75
Superior	1.44	1.64	1.84
Inferior	1.48	1.63	1.79

Table 4. Performance of CD for discrimination of eyes according to ECD loss.

Location	Optimal cut-off point	Sensitivity (%)	Specificity (%)	AUC
Nasal	1.58	51	75	0.615
Temporal	1.50	66	58	0.609
Superior	1.73	57	73	0.663
Inferior	1.45	57	56	0.524
Annual ECD loss of 1.53% (sample mean)				
Nasal	1.57	45	80	0.655
Temporal	1.50	54	56	0.554
Superior	1.65	52	61	0.571
Inferior	1.44	60	63	0.588
Annual ECD loss of 2.52% (sample mean+1SD)				
Nasal	1.38	72	60	0.704
Temporal	1.44	64	70	0.668
Superior	1.45	81	55	0.668
Inferior	1.44	57	75	0.675

between 1.27% and 1.99%. The highest values of ECD loss were predicted by the nasal and superior locations models for the CD-1SD distance (1.08 mm).

Table 4 presents the discriminative ability of CD according to the annual ECD loss rates. Using an annual ECD loss of 1% as cut-off, the superior distance presented the highest AUROC (0.663) and the highest value of optimal cut-off point (1.73 mm). The optimal cut-off point at nasal locations (1.58 mm) was also above the Baikoff’s recommendation. Both locations had a specificity above 70%. Using this sample mean as cut-off (1.53%), the nasal location had the highest AUROC (0.652) and the highest specificity (80%). Of note, optimal cut-off for each location but superiorly did not change significantly with the modification of criteria. For an annual ECD loss equal to this sample mean+1SD (2.52%), the higher AUC was found for the nasal distance and all optimal cut-off points were below 1.5 mm.

DISCUSSION

Long-term surveillance of iris-fixated pIOL is warranted to prevent endothelial damage. Myopic iris-fixated pIOL has a convex shape, which means the edges are closer to the endothelium than the center. Studies assessing the distance between the iris-fixated pIOL edge to the endothelium use a horizontal scan for measuring nasal and temporal distances.¹⁰⁻¹² Although, a greater age-dependent decline of superior iridocorneal has been demonstrated⁷ suggesting that superior ACD may also suffer a greater narrowing. The main aim of this study was to assess the potential role of the vertical meridian to predict ECD loss in the follow-up of patients implanted with iris-fixated pIOL. In this study, we found a significant association between the CD and the annual ECD loss at all four locations. Of those, the nasal location seemed to have a higher influence on the endothe-

lial loss. In addition, we found that for nasal and superior locations the optimal distances are higher than the recommended by Baikoff⁶ when considering ECD loss cut-offs of 1% and 1.53%. To our best knowledge, this is the first study evaluating the vertical meridian in this context.

The models hereby described aim to predict the annual ECD loss using the CD at each point. However, the CD was only measured postoperatively years after the surgery; for a true prediction model, CD would need to be assessed right after the procedure. The assumption is that CD will remain stable or decrease with age and thus the CD as measured years after the procedure is equal or inferior to the CD right after the surgery. As the postoperative AQD was significantly lower than the preoperative, CD most certainly follows this trend which means that annual ECD loss will be overestimated for the measured CD, leading to more conservative results. In a translation to the clinical practice, our models would predict a higher ECD loss and could lead to closer surveillance of endothelium. This assumption seems adequate for a first cross-sectional study on the topic and does not thwart the conclusions. Prospective research exploring the anterior chamber morphometrics for iris-fixated pIOL follow-up is warranted as AS-OCT is becoming widespread as this technology allows a more comprehensive and thorough assessment of anterior segment.

In this study, the nasal location presented the lower mean CD, the higher coefficient in the linear model and the highest ECD loss prediction when using a CD of 1.08 mm in the model. These facts highlight the relevance of this location that may be attributed to a slight nasal decentration of the iris-fixated pIOL in relation to the cornea apex, aiming to center it with the pupil axis. In fact, the pupil center of our sample was displaced nasally, justifying this value. In addition, we found that CD at inferior location was higher in patient with Artiflex toric. The study by Doors *et al*¹⁰ also reported a higher minimum CD for the toric model, despite only considering the horizontal meridian. Pupil positioning or axis of implantation do not justify this result.

When using annual ECD loss of 1% and 1.53% as threshold, nasal and superior location presented cut-offs points higher than the Baikoff's recommendation.⁶ Rather than a change in the recommended safety limit of CD, this fact may point out for the relative relevance of each location with nasal and superior locations assuming a particular role. The reasoning for the nasal relevance has been described. Considering the superior location, the higher age-dependent decline in anterior chamber angle may explain the results. For clinical practice, these results altogether seem to suggest that a CD approaching the threshold of 1.5 mm proposed by Baikoff⁶ may lead to a closer surveillance if detected in superior or nasal locations. When considering higher values of ECD loss, all locations had optimal cut-off points below 1.5 mm, which strengthens the use of this value. In addition, AUROC was quite similar for all locations, implying that any location suits for detection of higher rates of endothelial reduction. In agreement with previous suggestions of other authors,^{10,11} we strongly recommend the assessment of anterior chamber morphomet-

rics and the use of preoperative simulation to determine the safest approach for each patient.

The minimum CD of this sample using any location was 1.33 mm. When meridians were considered separately, the horizontal one had a higher value than the vertical one and both meridians had a CD higher than the minimum CD at any point. Thus, if only one meridian is considered, the CD is overestimated. In a sample of 306 implanted with iris-fixated pIOL, both Artisan and Artiflex, Doors *et al*¹⁰ reported a minimum CD of 1.43 ± 0.23 for the whole sample, 1.48 ± 0.23 for the Artisan group and 1.32 ± 0.20 for the Artiflex group. Another study by Doors *et al*¹² reported a CD of 1.25 ± 0.15 and 1.31 ± 0.22 for Artiflex myopia and Artiflex toric respectively. Our follow-up period (for comparison, mean \pm SD of 13.2 ± 2.9 years) was significantly higher when compared with both studies by Doors *et al* (mean follow-up of 34.1 ± 24.712 and 31.7 ± 25.7 10 months and ranges of 3 months to 7¹² and 8⁰ years). Due to expected reduction of ACD with age and the longer follow-up period in our study, one would expect lower CD values in the present study compared with the ones by Doors *et al*.^{10,12} Although, CD values are significantly higher in our sample if we considered that Doors *et al*^{10,12} only assessed the horizontal meridian. Differences in preoperative ACD do not seem to explain this finding as the study by Doors *et al*¹² reported a higher values than ours (3.65 ± 0.34 vs 3.22 ± 0.24 ; ACD not reported in their 2010 study¹⁰). The explanation for the CD difference might be related with the follow-up period as most of our patients were submitted to surgery more than 10 years ago. Thus, our sample represents long-term stable patients without losses to follow-up whereas the studies by Doors *et al*^{10,12} presented a wide variety of follow-up periods, enrolling eyes that possibly will be needing explant in the first decade after surgery and some that may still be missing surveillance appointments. This fact reinforces the role of selection criteria for iris-fixated pIOL implant, including not only morphometric parameters but also the psychological profile and patients' commitment with surveillance.

This study has some limitations. Preoperative and postoperative ECD was measured with different devices for patients with long follow-up. In addition, coefficient of variation and percentage of hexagonal cells were not assessed. Regarding the anterior chamber morphometrics, measurements were manually retrieved by a single investigator, which may come with some inherent variability, despite the experience of the investigator. Additionally, other metrics could have been explored, namely lens rise and the distance between the iris-fixated pIOL center and the endothelium. We only used preoperative and last postoperative ECD to calculate the annual ECD loss ratio. Longitudinal data analysis would allow to analyze trends according to the different periods. That approach would give more information but possibly without changing our conclusions. As mentioned, CD measured years after the surgery was used as surrogate of the CD in the early postoperative period however this approach does not jeopardize the study objectives. Several strengths of this study can be mentioned. We used the same iris-fixated pIOL and tech-

nique for all patients and this sample is large and has a long follow-up. The CD distance of all patients was measured by the same investigator. Our option for mixed-effects models allowed to include both eyes of the same patient, increasing the sample size.

CONCLUSION

In summary, the evaluation of critical distances at the 4 different points seems to be relevant in the follow-up of patients with iris-fixated pIOL as the nasal and superior locations present the highest AUROC and cut-off points superior to the recommended when more strict rates of annual ECD loss are considered. This study reinforces the idea that annual follow-up visits of patients with iris-fixated pIOL should include anterior chamber morphometrics by points and not only in the horizontal meridian.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

AF: Data analysis, drafting and revising the manuscript.

JL, BCV: Collection and interpretation of data, drafting and revising the manuscript.

ACA, SM and MCP: Study design, data interpretation, drafting and revising the manuscript.

All authors approved the final version to be published.

AF: Análise dos dados, redação e revisão do manuscrito.

JL, BCV: Colheita e interpretação dos dados, redação e revisão do manuscrito.

ACA, SM e MCP: Desenho de estudo, interpretação dos dados, redação e revisão do manuscrito.

Todos os autores aprovaram a versão final a ser publicada.

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Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

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REFERENCES

1. Fechner PU, van der Heijde GL, Worst JG. The correction of myopia by lens implantation into phakic eyes. *Am J Ophthalmol.* 1989;107:659-63. doi:10.1016/0002-9394(89)90264-x
2. Doors M, Budo CJ, Christiaans BJ, Luger M, Marinho AA, Dick HB, et al. Artiflex Toric foldable phakic intraocular lens: short-term results of a prospective European multicenter study. *Am J Ophthalmol.* 2012;154:730-9 e2. doi:10.1016/j.ajo.2012.04.006
3. Jonker SM, Berendschot T, Ronden AE, Saelens IE, Bauer NJ, Nuijts R. Five-year endothelial cell loss after implantation with artiflex myopia and artiflex toric phakic intraocular lenses. *Am J Ophthalmol.* 2018;194:110-9. doi:10.1016/j.ajo.2018.07.015
4. MacRae S, Holladay JT, Hilmantel G, Calogero D, Masket S, Stark W, et al. Special Report: American Academy of Ophthalmology Task Force Recommendations for Specular Microscopy for Phakic Intraocular Lenses. *Ophthalmology.* 2017;124:141-2. doi:10.1016/j.ophtha.2016.09.034
5. Guell JL, Morral M, Gris O, Gaytan J, Sisquella M, Manero F. Evaluation of Verisyse and Artiflex phakic intraocular lenses during accommodation using Visante optical coherence tomography. *J Cataract Refract Surg.* 2007;33:1398-404. doi:10.1016/j.jcrs.2007.04.026
6. Baikoff G. Anterior segment OCT and phakic intraocular lenses: a perspective. *J Cataract Refract Surg.* 2006;32:1827-35. doi:10.1016/j.jcrs.2006.08.025
7. Rufer F, Schroder A, Klettner A, Frimpong-Boateng A, Roeder JB, Erb C. Anterior chamber depth and iridocorneal angle in healthy White subjects: effects of age, gender and refraction. *Acta Ophthalmol.* 2010;88:885-90. doi:10.1111/j.1755-3768.2009.01588.x
8. Carlson RV, Boyd KM, Webb DJ. The revision of the Declaration of Helsinki: past, present and future. *Br J Clin Pharmacol.* 2004;57:695-713. doi:10.1111/j.1365-2125.2004.02103.x
9. Marta A, Leite J, Abreu AC, Monteiro S, Pinto C. Long-term results in patients with iris-fixated foldable phakic intraocular lenses for myopia and astigmatism. *J Cataract Refract Surg.* 2022;48:993-8. doi:10.1097/j.jcrs.0000000000000914
10. Doors M, Berendschot TT, Webers CA, Nuijts RM. Model to predict endothelial cell loss after iris-fixated phakic intraocular lens implantation. *Invest Ophthalmol Vis Sci.* 2010;51:811-

5. doi:10.1167/iovs.09-3981

11. Ferreira TB, Portelinha J. Endothelial distance after phakic iris-fixated intraocular lens implantation: a new safety reference. *Clin Ophthalmol.* 2014;8:255-61. doi:10.2147/OPHT.S56484
12. Doors M, Cals DW, Berendschot TT, de Brabander J, Hendrikse F, Webers CA, et al. Influence of anterior chamber morphometrics on endothelial cell changes after phakic intraocular lens implantation. *J Cataract Refract Surg.* 2008;34:2110-8. doi:10.1016/j.jcrs.2008.08.023



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