Accuracy of five intraocular lens formulas in eyes with trifocal lens implant

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Abstract. Accuracy of intraocular lens (IOL) calculation formulas SRK/T, Hoffer Q, Holladay 1, Haigis and Barrett Universal II were compared in prediction of postoperative refraction for multifocal and implants using a single optical biometry device. The authors included 88 refractive lens exchange and cataract surgeries, with AcrySof IQ PanOptix implant (Alcon Laboratories, Inc.). All eyes were divided into three groups based on axial length (AL), group 1: <22 mm (14 eyes), group 2: 22-24.5 mm (68 eyes) and group 3: >24.5 mm (6 eyes). The refractive prediction error (RPE) and mean absolute error (MAE) were calculated for 5 different formulas: SRK/T, Hoffer Q, Holladay 1, Haigis and Barrett Universal II. For eyes with the AL between 22 mm and 24.5 mm the greatest percentage of eyes with RPEs within ±0.25 D was 32.4% for Haigis formula, followed by Barrett Universal II, Hoffer Q and Holladay 1 with 29.4%. The percentage of eyes with RPEs within ±0.50 D was 100% only for Barrett Universal II and Holladay 1, 94.1% for SRK/T and 91.2% for Haigis and Hoffer Q. The first and third group with AL <22 and >24.5 mm were too small to have statistical significance due to the reluctancy to use multifocal IOLs on extreme ALs. ANOVA test showed no statistical difference (P=0.166) between the RPEs measured for each formula in this cohort. This study showed no statistical difference between formulas for this trifocal lens implant. There was a tendency for the RPE to be within ±0.25 D for most of the eyes with the Haigis formula, and within ±0.50 D for all the eyes with the Barrett Universal II formula in the group with the AL between 22 and 24.5 mm.

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Introduction

With the progress of medical technology and better intraocular lens (IOL) quality, modern biometry with incorporated 4th generation formulas refractive outcome prediction accuracy has increased (1-3). Therewith, refractive expectations following cataract surgery are rising. More patients request refractive lens exchange hoping they can be free of spectacles, even for presbyopia. The demand and use of multifocal IOLs have risen and, thus, the need for modern calculation formulas with great refractive outcome prediction has increased as well.

AcrySof IQ PanOptix is a non-apodized diffractive hydrophobic monoblock IOL with an ultraviolet filter and a blue light filter (4). It has a 6.0 mm optical zone, consisting of a 4.5 mm central trifocal region with 15 diffraction rings and an external refractive rim (5,6). The 3 foci are for distance vision, for intermediary vision with an addition of +2.17 D, and for near vision with an addition of +3.25 D (7,8). The preferred focal point is at a distance of 60 cm (4,7). The light distribution within the lens is as follows: 50% for the distance vision, 25% for intermediary vision and 25% for near vision (9).

In Romania, older generation formulas like SRK/T, Hoffer Q and Holladay 1 are still popular, because ultrasound biometers, which include them, are still used. However, more modern formulas with greater accuracy are now available with the new optical biometers (1-3,7). Most of these 4th generation formulas are incorporated into a biometer software and have become more accessible. Calculation software and online calculators are also available, and most are free for use, but they are more prone to transcription errors and take more of the surgeons' time. However, not all surgeons trust these formulas, having greater experience and satisfactory results with the older ones.

Materials and methods

Patients. This study included consecutive patients who underwent uncomplicated cataract or refractive lens exchange surgery (88 eyes) with implantation of multifocal IOLs (AcrySof IQ PanOptix TFNT0) at our institution from January 1st, 2018 to December 31st, 2019.

The study was approved by the Ethics Committee of 'Prof. Dr. Agrippa Ionescu' Emergency Clinical Hospital in Bucharest (Romania) and all patients signed an informed consent after being informed about the benefits and risks of the procedure. The patients were followed-up prospectively at 1 week and 1 month, as scheduled.

Inclusion criteria for surgery were age ≥40, endothelial cell count >1,500 cells/mm^2, no corneal opacities, no ocular diseases, no previous ocular surgery or ocular trauma, normal central and peripheral retina, good general health. Exclusion criteria for surgery were patients who did not fulfill the inclusion criteria, irregular astigmatism (10-12), internal silicon oil tamponade, associated retinal pathology (13-22) and poor compliance.

Preoperative assessment. The preoperative ocular examination included: best corrected distance visual acuity (BCVA), manifest refraction, keratometry, tonometry, corneal pachymetry, corneal topography, corneal endothelial cell count, optical coherence biometry, anterior segment slit-lamp biomicroscopy, mydriatic fundoscopy and optical coherence tomography. The refraction, keratometry, non-contact tonometry and optical pachymetry were measured with the autorefracto/kerato/tono/pahimeter Tonoref III (Nidek Co., Ltd.). The corneal endothelial cells were evaluated with the SP 3000P Specular Microscope (Topcon). The optical coherence biometry was measured with the Aladdin HW3.0 (Topcon) (6). This biometer obtains several measures using laser interferometry: axial length (AL), anterior chamber depth, lens thickness, central corneal thickness (6). The keratometry performed with the Aladdin, which scans with Placido disc technology was correlated with the keratometry obtained by the Tonoref III, a device that measures via the double mire ring method. An optical coherence tomography of the macula was performed for each patient with the Cirrus HD-OCT 4000 (Carl Zeiss Meditec AG), in order to rule out potential retinal pathologies that could interfere with the postoperative visual acuity.

Formula calculations. Spherical equivalent formula predictions and lens constant optimizations were performed with the Topcon Aladdin biometer, which has the following on-board calculation formulas: SRKII and SRK/T, Hoffer Q, Holladay 1, Haigis, Barrett Universal II and Olsen IOL formulas for untouched corneas, and Camellin Calossi and Shammas no history, Olsen and Barrett True K formulas for post refractive surgery IOL calculations.

For this study, the authors focused on the comparison between SRK/T, Hoffer Q, Holladay 1, Haigis and Barrett Universal II. The formulas had the following constants: SRK/T A-constant of 119.100, Hoffer Q pACD of 5.630, Holladay 1 surgeon factor of 1.830, Haigis' a-constants of 1.390 for a0, 0.400 for a1 and 0.100 for a2 and Barrett lens factor of 1.936. All formulas, including Haigis' a0 constant and Barrett's lens factor were optimized in collaboration with the lens manufacturer for this specific trifocal lens, before starting the study.

The Barrett Formula Suite, Barrett Rx, Barrett Toric Calculator Formula, Barrett True K and Barrett Universal II take into account the posterior cornea, calculate the lens position for each individual patient including consideration of the measured lens thickness rather than an estimation based on patient's age (23). The Barrett Universal II formula predicts IOL power based on Gaussian optics and utilizes this information to calculate the effect of the cylinder power at the cornea (7). Therefore, it needs the following parameters: anterior chamber depth (ACD), AL and keratometry, measured by the optic biometer, as well as 2 constants - Lens Factor and A Constant - available in the biometer software.

The Haigis formula recommends an IOL power based on a three-variable (a0, a1 and a2) function. The a1 constant is tied to the measured ACD, while the a2 constant is tied to the measured AL. This allows all three constants to be optimized for a wide range of ALs and ACDs using double-regression analysis (24).

Surgical procedure. All surgeries were performed by the same surgeon (H.T.S.) using the same surgical protocol and technique, under local peribulbar anesthesia with 2.5 ml Xiline 4% and 2.5 ml Marcaine 0.5%. The phacoaspiration (72 eyes)/phacoemulsification (16 eyes) was performed using the INFINITI® Vision System phacoemulsifier (Alcon).

Postoperative treatment and evaluation. Immediately after surgery, the authors prescribed topical eye drops: Moxifloxacin 0.5%, q.d.s. for 1 week, Tobramycin/Dexamethasone 0.3%/0.1% for 6 weeks (p.d.s. then q.d.s. 1 week each, then t.d.s for 3 weeks), Tropicamide 0.5% q.d. for 3 weeks and Dexpantenol 5% gel t.d.s. for 4 weeks.

The first examination was in the first postoperative day, when, after the removal of the bandage, slit lamp examination and mydriatic fundoscopy were performed. The second examination, 1 week after surgery, consisted in the uncorrected distance visual acuity (UDVA), manifest refraction, keratometry, tonometry, corneal pachymetry, anterior segment slit-lamp biomicroscopy and mydriatic fundoscopy.

The third postoperative examination was carried out after a month, when the UDVA, the uncorrected intermediary visual acuity (UIVA), the uncorrected near visual acuity (UNVA), manifest refraction, keratometry, tonometry and pachymetry were measured and also slit-lamp examination was performed and measured. All measurements were performed by the same technician on the same devices, which were calibrated before each measurement.

Data analysis and statistics. Patient data were collected and centralized in an Excel® database (ver. 1902, Microsoft Office 365 ProPlus. Microsoft Corp.) for further analysis. Data analysis was performed on Statistical Package for the Social Sciences (SPSS) software (ver. 24, IBM® SPSS® Statistics, IBM Corp.).

The final postoperative manifest refraction was measured by the same technician, on the same auto-kerato-refractometer 1 month after surgery and it was converted into its spherical equivalent. For the statistical analysis of the postoperative refractive data, the 1-month manifest refraction was analyzed.

All eyes were divided into three groups based on the AL, group 1: <22 mm (14 eyes), group 2: 22-24.5 mm (68 eyes) and group 3: >24.5 mm (6 eyes). The refractive prediction error (RPE) and the mean absolute error (MAE) were calculated for 5 different formulas: 3 third generation formulas: SRK-T, Hoffer Q and Holladay 1, and 2 fourth generation formulas: Haigis and Barrett Universal II.

Table I. Descriptive data of all patients.

Parameter	Age (years)	ACD (mm)	AL (mm)	IOL diopter
Mean ± SD	62.090±10.742	3.236±0.384	23.207±0.920	22.440±3.119
Range	32	1.49	3.95	15
Minimum	45	2.51	21.57	17
Maximum	77	4	25.50	32

ACD, anterior chamber depth; AL, axial length; IOL, intraocular lens.

Table II. Descriptive data of each group.

Parameter	Age (years)	ACD (mm)	AL (mm)	IOL diopter
Group 1 (AL <22 mm, n=14)				
Mean ± SD	65.142±12.871	2.995±0.14	21.842±0.139	26.36±3.134
Range	29	0.35	0.39	8
Minimum	48	2.86	21.57	24
Maximum	77	3.21	21.96	32
Group 2 (AL 22-24.5 mm, n=68)				
Mean ± SD	61.5±10.453	3.247±0.392	23.325±0.612	22.03±2.359
Range	31	1.49	2.28	10
Minimum	45	2.51	22.09	17
Maximum	76	4	24.27	27
Group 3 (AL >24.5 mm, n=6)				
Mean ± SD	61.666±9.048	3.68±0.226	25.05±0.431	18±0.447
Range	18	0.47	0.96	1
Minimum	50	3.39	24.54	18
Maximum	68	3.86	25.5	19

ACD, anterior chamber depth; AL, axial length; IOL, intraocular lens.

The mean numerical error or RPE represents the difference between the postoperative spherical equivalent at the 1-month follow-up and the predicted postoperative spherical equivalent, chosen by the surgeon from a list generated by the optical coherence biometer (25). A negative predictive error indicates more myopic results, a tendency towards overcorrection, while a positive predictive error indicates more hyperopic results, a tendency towards undercorrection (25). The MAE was calculated as the magnitude of the prediction error, regardless of the sign (25). The proportion of eyes within ±0.25 D, ±0.50 D, ±1.00 D, and ±2.00 D of the predicted refraction was also calculated in all three groups.

The statistical analysis followed a descriptive stage, which were performed for all cohorts, as well as an inferential stage, which was performed for cohorts with an eye number >30. After checking the normality of the distribution of continuous variables by Shapiro-Wilk test, the authors aimed to evaluate the refractive results. The small number of eyes in the first and third group did not allow inferential analysis. The descriptive statistics were reported for each group and outcomes evaluated postoperative for the second group using ANOVA test, analyzing the differences among the five formulas.

The third group of eyes with AL >24.5 mm is small, because the authors were still reluctant in using multifocal IOLs, considering the unpredictability factor for myopic eyes, i.e. fundus pathology, ACD variability and capsular bag size with effective lens position instability (26). The first group of eyes with AL <22 mm is also reduced, because in hyperopes, the ideal centration axis for devices that are especially sensitive to position (such as multifocal IOLs) is slightly inferonasal from the optimal location in other eyes, which may also interfere with postoperative visual acuity results (27).

Results

The study included 88 eyes (44 right eyes and 44 left eyes) from 58 patients (38 females and 20 males). Table I displays the descriptive data of all patients. The mean age

Table III. Mean refractive prediction error, MAE and median absolute error of each formula in each group.

Parameter	STK-T	Hoffer Q	Holladay 1	Haigis	Barrett Universal I
Group 1 (AL <22 mm, n=14)I					
Mean RPE (D) ± SD	0.170±0.438	-0.108±0.317	0.120±0.293	-0.184±0.526	-0.077±0.391
Range RPE	1.28	1.04	0.75	1.79	1.28
MAE (D) ± SD	0.332±0.322	0.262±0.198	0.220±0.222	0.370±0.408	0.297±0.254
MedAE	0.240	0.200	0.100	0.280	0.190
Group 2 (AL 22-24.5mm, n=68)					
Mean RPE (D) ± SD	0.110±0.110	0.079±0.405	0.140±0.345	0.056±0.365	0.151±0.315
Range RPE	1.35	1.58	1.22	1.33	1.28
MAE (D) ± SD	0.322±0.189	0.327±0.249	0.302±0.215	0.300 ±0.213	0.292±0.187
MedAE	0.295	0.290	0.265	0.270	0.265
Group 3 (AL >24.5 mm, n=6)					
Mean RPE (D) ± SD	-0.196±0.100	-0.093±0.045	-0.176±0.028	-0.250±0.062	-0.163±0.201
Range RPE	0.22	0.10	0.06	0.13	0.43
MAE (D) ± SD	0.196±0.100	0.093±0.045	0.176±0.028	0.250±0.062	0.223±0.112
MedAE	0.170	0.100	0.190	0.220	0.240

RPE, refractive prediction error; MAE, mean absolute error; MedAE, median absolute prediction error; SD, standard deviation.

Table IV. Number of eyes with refractive prediction errors within ±0.25 D, ±0.50 D, ±1.00 D, and ±2.00 D in group 1 (AL <22 mm).

	Group 1 (n=14) - RPE, no. of eyes				
RPE	SRK-T	Hoffer Q	Holladay 1	Haigis	Barrett Universal II
± 0.25 D	4	4	10	6	4
± 0.50 D	12	12	12	8	12
± 1.00 D	12	14	14	12	14
± 2.00 D	14	14	14	14	14

RPE, refractive prediction error.

was 62.0±10.742 years (from 45 to 77 years). The ACD of the eyes included in the study was 3.236±0.384 mm (from 2.51 to 4 mm) and the AL was 23.207±0.920 mm (from 21.57 to 25.50 mm). The Diopter of the AcrySof IQ PanOptix implants ranged from 17 to 32 D (22.44±3.119 D). Table II presents descriptive data of each group. Table III indicates the mean RPE, MAE, and MedAE (median absolute prediction error) produced by each formula in all three groups. Tables IV-VI indicate the percentage of eyes with RPEs within ±0.25 D, ±0.50 D, ±1.00 D, and ±2.00 D in each AL group. In group 2, the greatest percentage of eyes with RPEs within ±0.25 D was 32.4% for Haigis formula, followed by Barrett Universal II, Hoffer Q and Holladay 1 with 29.4%. However, the percentage of eyes with RPEs within ±0.50 D was 100% only for Barrett Universal II and Holladay 1, 94.1% for SRK/T and 91.2% for Haigis and Hoffer Q. Group 1 and 3 did not include enough eyes to have any statistical significance. However, it is reported that for group 1, Holladay 1 (10 eyes) had the greatest percentage of eyes RPEs within ±0.25 D, followed by Haigis (6 eyes).

Figs. 1-5 show the percentage of eyes with AL between 22 nd 24.5 mm (group 2) with RPEs (postoperative spherical equivalent minus predicted postoperative spherical equivalent) within the aforementioned diopters and the tendency to over- or undercorrect.

In order to analyze the differences between the RPEs of each formula in group 2, which are variables with Gaussian distribution, the parametric test ANOVA was applied. It showed no statistical difference (P=0.166) between the RPEs measured for each formula in this AL group.

Table V. Number and percentage of eyes with refractive prediction errors within ±0.25 D, ±0.50 D, ±1.00 D, and ±2.00 D in group 2 (AL 22-24.5 mm).

	Group 2 (n=68) - RPE, nr. eyes,%				
RPE	SRK-T	Hoffer Q	Holladay 1	Haigis	Barrett Universal II
± 0.25 D	12 (17.6)	20 (29.4)	20 (29.4)	22 (32.4)	20 (29.4)
± 0.50 D	64 (94.1)	62 (91.2)	68 (100)	62 (91.2)	68 (100)
± 1.00 D	68 (100)	68 (100)	68 (100)	68 (100)	68 (100)
± 2.00 D	68 (100)	68 (100)	68 (100)	68 (100)	68 (100)

RPE, refractive prediction error; AL, axial length.

Table VI. Number of eyes with refractive prediction errors within ±0.25 D, ±0.50 D, ±1.00 D, and ±2.00 D in group 3 (AL >24.5 mm).

	Group 3 (n=6)- RPE, nr. eyes				
RPE	SRK-T	Hoffer Q	Holladay 1	Haigis	Barrett Universal II
± 0.25 D	0	0	0	0	0
± 0.50 D	6	6	6	6	6
± 1.00 D	6	6	6	6	6
± 2.00 D	6	6	6	6	6

RPE, refractive prediction error; AL, axial length.

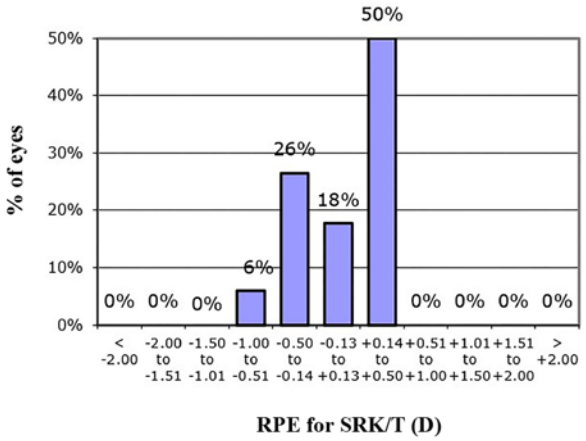

Figure 1. RPE for SRK/T in group 2 (AL=22-24.5 mm). RPE, refractive prediction error.

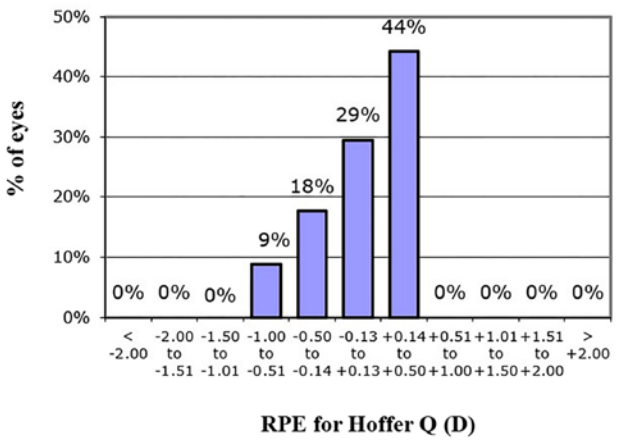

Figure 2. RPE for Hoffer Q in group 2 (AL=22-24.5 mm). RPE, refractive prediction error.

Discussion

With the progress of technology, multifocal IOL implants have become increasingly popular. Patients' expectations for a better refractive outcome and independency of spectacles have grown. In order to meet these expectations, it is important to choose the right lens diopter based on biometric formulas. Alcon Acrysof IQ PanOptix lenses have been on the European market since 2015 (26) and have recently been approved by the FDA as the first trifocal lens for USA patients undergoing cataract surgery (2019) (27). The accuracy of each biometric formula for this type of lens should be assessed in more studies in order to avoid refractive surprises, given the fact that both patients' expectations and lens fabrication prices are higher.

This study shows no statistical difference between formulas for this multifocal lens implant in the AL group between 22 and 24.5 mm. There is, however, a tendency for the RPE to be within ±0.25 D for most of the eyes with the Haigis formula, and within ±0.50 D for all the eyes with the Barrett Universal II and Holladay 1 formula in this group. For

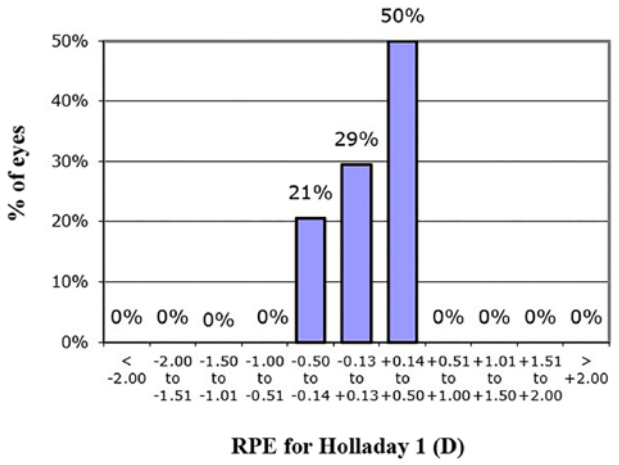

Figure 3. RPE for Holladay 1 in group 2 (AL=22-24.5 mm). RPE, refractive prediction error.

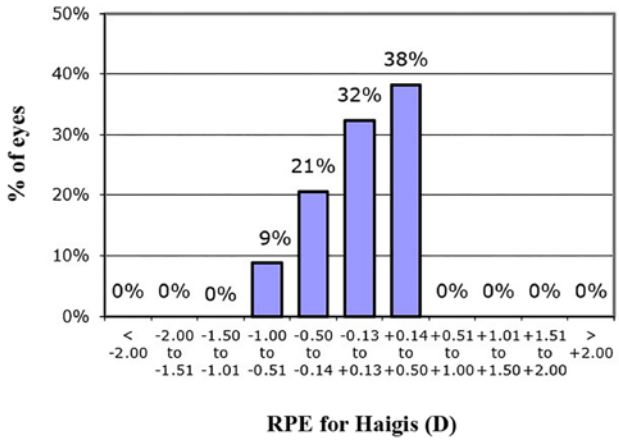

Figure 4. RPE for Haigis in group 2 (AL=22-24.5 mm). RPE, refractive prediction error.

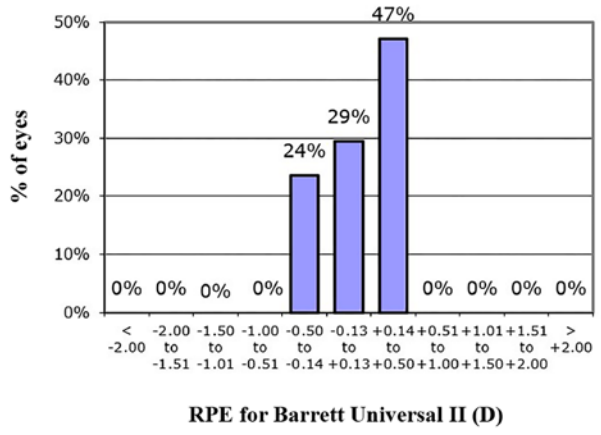

Figure 5. RPE for Barrett Universal II in group 2 (AL=22-24.5 mm). RPE, refractive prediction error.

long and short eyes, data on more surgeries should be collected in order to obtain statistically significant results.

For myopic eyes, Zhu *et al* (28) showed greater inferior decentration of multifocal IOLs (Tecnis ZMB00), indicating that the increasing incompatibility between IOL and capsular bag size with AL elongation should not be underestimated. For hyperopic eyes, the ideal centration axis in devices that are especially sensitive to position (such as multifocal IOLs) is slightly inferonasal compared with the optimal location in other eyes (15,29). However, multifocal lenses should be centered as closely as possible on the entrance pupil because they need balanced light input to create two focal points via constructive interference of the diffracted light (29).

There are some studies reporting good visual outcomes in patients with Acrysof IQ PanOptix trifocal implants. Belikova and Borzykh published a study evaluating patient spectacle independence and high-quality of vision in mesopic conditions after bilateral implantation of AcrySof IQ PanOptix in 16 patients, indicating good results (30). Sezgin Asena compared the clinical performance of a hydrophobic (AcrySof PanOptix) and a hydrophilic (AT LISA tri 839MP) diffractive trifocal IOL using the SRK/T (AL >22.0 mm) or Hoffer Q formula (AL<22.0 mm), concluding that hydrophobic diffractive IOL might be more suitable for patients who require good closer intermediate viewing (31). Alió *et al* also reported that the AcrySof IQ Panoptix IOL is able to restore visual function with an acceptable intermediate and near vision after cataract surgery with good contrast sensitivity and an improvement in the near activity visual questionnaire (32).

Regarding target refraction in eyes with this type of lenses, Hayashi *et al* published a study suggesting that slight myopia is a better target refraction than slight hyperopia, although emmetropia is the optimum target (33). In this study, the minus diopter closest to zero was also targeted, and the postoperative spherical equivalent to it was compared, in order to obtain the RPE for each formula.

Cochener *et al* compared the performance of two diffractive trifocal (one of which was PanOptix) and one extended depth of focus hydrophobic (EDOF) IOLs using Haigis formula. The study concluded that near vision was statistically better for both trifocal IOLs compared with the EDOF IOL (34).

However, none of these studies focused on which formula is best when choosing the right diopter for the trifocal lens. Comparing the accuracy of the Barrett Universal II formula, several studies concluded that this formula is well suited in calculating IOL power for all types of eyes (1-3), including those with high myopia (35,36) rendering the lowest predictive error compared with SRK/T, Haigis, Holladay 1, and Hoffer Q formulas. The performances of the Barrett Universal II and Hill-RBF formulas were proven comparable in long eyes in two studies evaluating the accuracy of new generation vergence formulas and formulas based on artificial intelligence (37,38).

Regarding short eyes, studies have shown Haigis' formula superiority over second generation Hoffer Q, considering that Haigis takes ACD into account when calculating the IOL power (39,40). The differences between the predicted refractive errors of the Hoffer Q and Haigis formula increased as ACD decreased in hyperopic eyes (39).

The fact that Haigis showed the smallest RPE in our study might be explained by the fact that the formula constants were optimized regularly in collaboration with the lens manufacturers, which obtained data from databases containing all the recent cases. The Barrett Universal II formula, which showed the greatest results in the most recent studies (1,3,35,36) is newer, and not yet widely used, which may affect the

optimization process. Nevertheless, it did come in second place for this group. The ANOVA test, however, showed no statistical difference between all the evaluated formulas, which means that for this cohort there was no inferiority between formulas.

This study represents only a first stage in a wider evaluation of biometric formulas and refractive postoperative results. It will be expanded by collecting many more cases of trifocal IOL implants from all three AL categories and it will statistically revaluate groups 1 and 3, after they will exceed 30 cases.

It is important to assess the efficacy of the biometric formulas for each type of lens, especially for multifocal lenses, considering the rise in patients' expectations and demand for this type of implants. To our knowledge, there is no other study comparing the efficacy of formulas for a trifocal lens.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

MM and HTS contributed to the conception and design of the study, and the acquisition, analysis and interpretation of the data. MM and HTS also contributed to the drafting of the manuscript and its critical revision for important intellectual content. SS contributed to the design of the study, the drafting of the manuscript and its critical revision for important intellectual content. BT contributed to the acquisition, analysis and interpretation of the data, the drafting of the manuscript and its critical revision for important intellectual content. AS contributed to the analysis and interpretation of the data, the drafting of the manuscript and its critical revision for important intellectual content. CD contributed to the conception and design of the study and the critical revision of the manuscript for important intellectual content. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the study in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of 'Prof. Dr. Agrippa Ionescu' Emergency Clinical Hospital in Bucharest, Romania. All patients provided a signed informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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