Accuracy and Precision of Intraocular Lens Calculations Using the New Hill-RBF Version 2.0 in Eyes With High Axial Myopia

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• **PURPOSE: To compare the accuracy and precision of the new Hill-RBF version 2.0 (Hill-RBF 2) formula with other formulas (Barrett Universal II, Haigis, Hoffer Q, Holladay 1, and SRK/T) in predicting residual refractive error after phacoemulsification in high axial myopic eyes.**

• **DESIGN: Retrospective case series.**

• **METHODS: 127 eyes of 127 patients with axial length (AL) ≥26 mm were included. The refractive prediction error (PE) was calculated as the difference between the postoperative refraction and the refraction predicted by each formula for the intraocular lens (IOL) power actually implanted. Standard deviation (SD) of PE, median absolute PE (MedAE), proportion of eyes within ±0.25, ±0.50, and ±1.00 diopter (D) of PE were compared. A generalized linear model was used to model the mean function and variance function of the PE (indicative of the accuracy and precision) with respect to biometric variables.**

• **RESULTS: The MedAE and SD of Hill-RBF 2 were lower than that of Hoffer Q, Holladay 1, and SRK/T ($P \leq .036$) and were comparable to Barrett Universal II and Haigis ($P \geq .077$). Hill-RBF 2 had more eyes within ±0.25 D of the intended refraction (76 out of 127 eyes [59.84%]) compared to other formulas ($P \leq .034$) except Barrett Universal II ($P = .472$). AL was associated with the mean function or variance function of the PE for all formulas except Hill-RBF 2.**

• **CONCLUSIONS: In this study, the precision of Hill-RBF 2 is comparable to Barret Universal II and Haigis. Unlike the other 5 formulas, its dispersion and the accuracy of the refractive prediction is independent of the AL. (Am J Ophthalmol 2019;205:66–73. © 2019 Elsevier Inc. All rights reserved.)**

THE ADVANCES IN TECHNIQUES IN CATARACT SURgery have led to a paradigm shift from it being a rehabilitation procedure to a refractive procedure, allowing postoperative spectacle independence. A substantial deviation from the intended refractive target leading to refractive surprises is a common reason for litigation.[1] The primary contribution of refractive prediction errors (PEs) include preoperative estimation of postoperative intraocular lens (IOL) position (35%), postoperative refraction determination (27%), and preoperative axial length (AL) measurement (17%).[2] IOL calculation for the average eyes with ALs between 22 and 26 mm have excellent predictability with similar accuracy.[3] In high axial myopia, accurate prediction remains challenging for those requiring low-diopter IOL power or even a negative-diopter lens. Myopia is a global public health problem, with an estimated prevalence of 25%[4] to 46.4%[5] in the United States, with an even higher prevalence in the urban parts of Asia.[6] The incidence of high myopic eyes undergoing cataract surgery is going to increase. Furthermore, high myopia is a risk factor for cataract formation, and these individuals develop cataract at a young age.[7] It is not uncommon to encounter hyperopic surprises in these eyes.[8] To compensate, many surgeons routinely target a postoperative low myopia target (–1 to –2 D) in axial myopia.

The Hill-Radial Basis Function (Hill-RBF) formula is an artificial formula developed to select the power of an IOL independent of a distinct effective lens position calculation. It uses pattern recognition and data interpolation to calculate the IOL power. The RBF algorithm requires AL, central corneal power, and anterior chamber depth (ACD) to predict the desired IOL power. If the parameters required by the prediction algorithm fall outside the validating boundary, the formula can still predict the IOL diopter power, but an out-of-bounds warning will alert the clinician that the respective pattern of biometric measurements is not well studied by the algorithm.[9]

The Hill-RBF version 1 (Hill-RBF 1) was an early iteration of the existing formula compiled with data from 3445 eyes. An updated formula with the inclusion of additional data from 8974 eyes undoubtedly appears to be more advantageous compared with its predecessor. However, in the Holladay 2 formula, Hoffer commented that it improved prediction accuracy in short eyes but at the expense of sacrificing the accuracy in the original Holladay 1 formula

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in eyes with average and medium-long AL.[10] The Hill-RBF version 2.0 (Hill-RBF 2) is a new formula that replaced Hill-RBF 1 in January 2018. At present, no peer-reviewed literature has compared its performance with other validated formulas. It is imperative to analyze the refractive results using updated Hill-RBF and to compare it with the older version. Because no single formula has been consistently demonstrated to be the most accurate one across a spectrum of eye characteristics, some surgeons advocate using different formulas depending on the ocular dimensions.[11] In the present study, we aim to compare the latest Hill-RBF formula with 5 other validated formulas in eyes with axial myopia defined as AL ≥26 mm.

METHODS

THIS WAS A RETROSPECTIVE STUDY; THE CHARTS OF ALL phacoemulsification performed from May 2016 to July 2017 at the Hong Kong Eye Hospital were retrospectively reviewed. Data on preoperative examinations, operative details, postoperative findings, and refractive error were collected. Inclusion criteria included uneventful sutureless phacoemulsification with in-the-bag monofocal IOL placement, preoperative biometry obtained using partial coherence interferometry (IOLMaster 500, version 7.1.2; Carl Zeiss Meditec, Jena, Germany) with an AL ≥26 mm. If patients had bilateral phacoemulsification, then an eye was randomly selected by a random-number generator for inclusion. Exclusion criteria were dense cataract or poor fixating eyes requiring ultrasound biometry, incomplete data, additional procedures during phacoemulsification (such as astigmatism correction), or postoperative corrected distance visual acuity worse than 6/12. Patients with previous ocular surgery and any other pathologies were excluded. Manifest refraction measurement was obtained at 3 months postoperatively by the optometrists at the same hospital using the same lane length. The study was approved by the Kowloon Central/Kowloon East ethics committee.

Surgeon's optimized lens constant for each IOL in routine cases was used for the evaluation of Haigis, Hoffer Q, Holladay 1, and SRK/T formulas. We also evaluated the Wang-Koch AL adjusted formulas using the modified regression formulas for Holladay 1 and SRK/T[12] (Koch DD, written communication, December 18, 2018) and the 1-center regression formulas for Haigis and Hoffer Q in the original article.[13] These adjusted AL formulas were applied without lens constant optimization.[14,15] The recommended lens constant for the Barrett Universal II (referred hereafter to as "Barrett") formula and Hill-RBF 2 were used because no method exists to optimize them. The Lenstar LS900 (Haag-Strait AG) software (version 9.0.2) was used for the IOL power calculation in Hill-RBF 2, which corresponded to the online calculator available on the Hill-RBF website (http://rbfcalculator.com/, accessed August 10, 2018). Preoperative biometry data were entered into the online Barrett calculator (https://www.apacrs.org/barrett_universal2/, accessed August 10, 2018) to evaluate its prediction performance.

Statistical analysis was performed using R 3.2.5 software (R Foundation, Vienna, Austria). The PE was back-calculated by subtracting the refraction predicted by each formula based on the IOL power actually implanted from the postoperative refractive outcome expressed as spherical equivalent (actual refraction–predicted refraction). A negative PE indicates a higher myopia result than the predicted refraction. The arithmetic mean prediction error (ME) for each formula was calculated; the Wald test (also known as *t* test) was used to evaluate the systematic bias for each formula, which was then zeroed out by adjusting the individual PE up or down by an amount equal to the ME for that formula.[16,17] After adjusting the ME to zero for each formula, the median absolute prediction error (MedAE) were calculated. The standard deviation (SD) of the PE was compared using the empirical F test by bootstrapping with 5000 replicates; the absolute PE between the formulas was compared using the Wilcoxon signed-rank test; these indices measure the dispersion of the PE. The percentages of eyes achieving PEs within the diopter (D) ranges of ±0.25, ±0.50, and ±1.00 D were also determined and compared using McNemar test. A generalized linear model was used to evaluate the factors (mean keratometry, AL, ACD, and model of IOL) contributing to the mean function (i) and the variance function (ii) of the PE in each formula, where the PE, denoted by Y, was modelled as follows:

$$Y = E(Y) + \varepsilon$$

with (i) mean function:

$$E(Y) = \beta_0 + \beta_1 \times AL + \beta_2 \times \text{mean K} + \beta_3 \times ACD + \beta_4 \times \text{IOL model}$$

and (ii) variance function:

$$Var(\varepsilon) = \exp[\delta_0 + 2(\delta_1 \times AL + \delta_2 \times \text{mean K} + \delta_3 \times ACD + \delta_4 \times \text{IOL model})]$$

such that β_i for $i = 1, \ldots, 4$ represents the effect of each factor for the mean PE, when $\beta_i = 0$ for all $i = 1, \ldots, 4$, β_0 represent the mean PE; δ_i for $i = 1, \ldots, 4$ measures the effect of each factor for the variance of PE, $\delta_i = 0$ for all $i = 1, \ldots, 4$, $\exp(\delta_0)$ represents the variance of PE.

Variables were selected by backward selection using the Akaike information criterion in the mean function and forward selection using the likelihood ratio test in the variance function. The mean function is indicative of the formula's refractive prediction accuracy whereas the variance function reflects the precision of formula. A *P* value less than .05 was considered statistically significant. False discovery rate (FDR) was evaluated for numerous statistical tests, which measures the percentage of false discovery expected to occur due to random error (ie, among tests that are considered significant, the FDR is the expected proportion of those tests in which the null hypothesis is true).[18] FDR cannot identify which significant result is a false discovery; it only provides an overall summary of all significant results. It is affected by the number of nonsignificant results present in the multiple testing, whereas the presence of both the significant and nonsignificant results affect the familywise error rate (ie, Bonferroni adjustment). The FDR is estimated by[18]

$$\frac{(\text{number of tests})\times(\text{the highest } P \text{ value obtained less than .05})}{(\text{number of significant discoveries})}\times 100\%$$

compared to the other formulas ($P \leq .021$) except for Barrett ($P = .472$). These differences remained significant for the percentages of eyes within ±0.50 D of PE when compared to Hoffer Q and Holladay 1 only ($P \leq .005$); all formulas had comparable percentages of eyes within ±1.00 D of PE compared to Hill-RBF 2 ($P \geq .371$). Supplemental Figures 2 and 3 (Supplemental Material at AJO.com) summarize the refractive outcome and spherical equivalent refraction accuracy across the 6 formulas. After applying the Wang-Koch AL adjustments, only SRK/T had a higher SD compared to Hill-RBF2 ($P = .023$); Hill-RBF 2 and Barrett had a lower MedAE and higher proportion of eyes with PE within ±0.25 and ±0.50 D compared to the 4 Wang-Koch AL adjusted formulas ($P \leq .002$) (Supplemental Table 2, Supplemental Material at AJO.com).

RESULTS

A TOTAL OF 127 EYES OF 127 PATIENTS WITH A MEAN AGE OF 65.8 ± 9.1 years were included in this study (Supplemental Figure 1, Supplemental Material at AJO.com). The mean AL, mean keratometry, and ACD were 27.72 ± 1.59 mm, 43.47 ± 1.41 D, and 3.41 ± 0.30 mm, respectively. Overall, 123 IOLs implanted were plus lens, 3 were plano, and 1 was a negative lens, with dioptric power ranging from –1.00 to +19.00 D. Table 1 shows the clinical characteristics of the study cohort and the IOL models implanted.

Systematic bias in refractive prediction (due to an incorrect formula constant) were found in Barrett, Hill-RBF 2, Hoffer Q, and Holladay 1, where the MEs are –0.10, –0.24, 0.35, and 0.37, respectively ($P \leq .006$), whereas the MEs of Haigis (–0.03) and SRK/T (0.02) were not significantly different from zero ($P \geq .417$) (Supplemental Table 1, Supplemental Material at AJO.com). After adjusting the ME to zero for all the formulas, which would eliminate the systematic error from an incorrect formula constant, Table 2 summarizes the pairwise comparisons among all the refractive prediction outcomes across these 6 formulas; 7.94% of the 35 significant results of the 75 tests are expected to be false discoveries attributable to random error as determined by the FDR. Hill-RBF 2 produced lower MedAE than Hoffer Q, Holladay 1, and SRK/T ($P \leq .027$), but these differences between Hill-RBF 2 and Barrett ($P = .528$) and Hill-RBF 2 and Haigis ($P = .077$) were not significant. A smaller SD was found in Hill-RBF 2 as compared to Hoffer Q, Holladay 1, and SRK/T ($P \leq .036$) but was not significant when compared to Barrett ($P = .632$) and Haigis ($P = .138$). The proportion of eyes with PE within ±0.25 D were between 38.58% and 59.84%; these values increased to 70.87%-86.61% and 94.48%-98.42% for ±0.50 and ±1.00 D of the predicted target, respectively, across the 6 formulas. Hill-RBF 2 had the greatest proportion of eyes with PE within ±0.25 D

The mean function is indicative of the formula's refractive prediction accuracy whereas the variance function reflects the precision of formula in our generalized linear models. The IOL model was not a significant variable of the mean function and variance function of the PE in any formulas. Unlike the other 5 formulas, the mean function and variance function of the PE of Hill-RBF 2 were not associated with the IOL diopter, an IOL <6 D, or a 3-piece IOL (Supplemental Tables 3-5, Supplemental Material at AJO.com). The mean function of the PE identified AL and mean keratometry as significant variables in the Haigis, Hoffer Q, and SRK/T formulas, and AL only for Holladay 1 (Table 3). No variables were significant for the mean function of PE in Hill-RBF 2 and Barrett. The mean keratometry was associated with the variance function of the PE in Haigis, Hill-RBF 2, and Hoffer Q, whereas AL and ACD were associated with the variance function of the PE in Barrett and SRK/T, respectively. The analysis was repeated with the Wang-Koch AL adjusted formulas (Supplemental Table 6, Supplemental Material at AJO.com); AL remains to be associated with the mean function of the PE in Haigis, Holladay 1, and SRK/T, whereas mean keratometry was a significant variable for Hoffer Q.

DISCUSSION

AN UNEXPECTED HYPEROPIC OUTCOME IS NOT UNCOMMON when using standard formulas for eyes with high myopia. The database of the Hill-RBF 2 expanded by 8974 cases; these additional eyes encompasses a broader spectrum of

TABLE 1. Clinical Characteristics of the Study Cohort and Models of Implanted IOL

Eye, n (%)	
Right	76 (59.84)
Left	51 (40.16)
Mean keratometry, D	
Mean ± SD	43.47 ± 1.41
Range	39.70, 47.58
<41.0 D, n (%)	4 (3.15)
41.0-46.0 D, n (%)	117 (92.13)
>46 D, n (%)	6 (4.72)
Axial length, mm	
Mean ± SD	27.72 ± 1.59
Range	26.01, 32.36
Anterior chamber depth	
Mean ± SD	3.41 ± 0.30
Range	2.65, 4.17
IOL power, D	
Mean ± SD	10.31 ± 4.119
Range	−1.00, 19.00
IOL model, n (%)	
Tecnis ZCB00	65 (51.18)
AMO AR40E	5 (3.94)
Alcon SN60WF	6 (4.72)
Alcon SA60WF	31 (24.41)
Alcon SA60AT	11 (8.66)
Alcon MA60MA	7 (5.51)
enVista MX60	2 (1.57)

D = diopter; IOL = intraocular lens; SD = standard deviation.

ALs from 20.43-30.15 mm to 20.25-37.95 mm. As compared to the Hill-RBF 1, which included only 262 eyes with an AL ≥26 mm, this increased to 735 in Hill-RBF 2 (Hill WE, written communication, August 8, 2018). We found that Hill-RBF 2 can achieve a higher level of precision with smaller SD compared to Hoffer Q, Holladay 1, and SRK/T with comparable precision to Barrett and Haigis. All 6 formulas had ≥70.86% of eyes within ±0.50D and ≥94.49% within ±1.00 D of the PE. These predicted outcomes using the 6 different formulas in our study well exceeded the benchmark in the National Health Service, which suggested that 55% and 85% of patients should achieve postoperative spherical equivalent within ±0.50 and ±1.00 D of the intended target.[19] Our findings are comparable to other studies across the spectrum of ALs with phacoemulsification performed by highly experienced surgeons or from an academic teaching institution, where 80% of eyes were within ±0.50 D and 94% of eyes were within ±1.00 D of the predicted outcome.[20,21]

Hoffer Q, Holladay 1, and SRK/T are third-generation formulas that rely on 2 variables (AL and central corneal power) to predict the postoperative IOL position. The ACD is not one of the parameters in the formula. Instead, these formulas assume that shorter eyes will have shallower ACD, and conversely, longer eyes have deeper ACD. This could be one of the reasons why Hoffer Q, Holladay 1, and SRK/T were less precise compared to Hill-RBF 2 and Barrett, which have accounted for the ACD. ACD was associated with the variance function in the generalized linear model only in SRK/T, thus supporting the incorporation of ACD in the newer generation of formulas to improve the precision. Similarly, mean keratometry was associated with the mean function of the PE in Haigis, Hoffer Q, and SRK/T, with a higher K-reading resulting in a more myopic PE on average for SRK/T and the inverse for the former 2 formulas. This is consistent with the findings reported by Melles and associates, who found Haigis and Hoffer Q had a trend toward hyperopic prediction in eyes with steeper mean keratometry and the opposite for SRK/T.[22] Unlike the Haigis, Hoffer Q, Holladay 1, and SRK/T formulas, Hill RBF-2 and Barrett only have a constant bias term in their mean function of the PE (as indicated by the lack of statistically significant variables identified using backward selection in the generalized linear model); these results remain unchanged for the Wang-Kock AL adjusted formulas. This indicates that the refractive predictions of Barrett and Hill-RBF 2 are more robust, and optimization of the IOL constant will eliminate this constant bias. Barrett differs from the other empirical and regression formulas because the location of the IOL's principal planes of refraction is retained as a variable in the formula. It accounts for the different principal planes among the different IOL diopters by considering the effective lens position as a function of ACD and a lens factor related to the physical position and the location of the principal planes of the IOL.[23] The Hill-RBF was modeled using patient data measured on the Lenstar LS900 (Haag-Streit AG, Koeniz, Switzerland) biometer, which uses optical low-coherence reflectometry and the Acrysof (Alcon, Fort Worth, TX, USA) SN60WF IOL. By using multiple IOL models in our current study, we could minimize the bias given to Hill-RBF and Barrett as they have been exclusively formulated based on data using SN60WF only. Furthermore, the IOL model was not significantly associated with the mean function or variance function of the PE across the 6 formulas in our generalized linear equation model. Using optical low-coherence reflectometry and partial coherence interferometry, Cooke and associates noted that different formulas gave different PEs depending on which machine was used to perform the biometric measurements.[24] Thus, if optical low-coherence reflectometry was used to obtain the measurements for the calculation of Hill-RBF, the results could be different.

There are controversies among the literature regarding which formula is the most accurate or the most precise for high axial myopia. Based on the mean function of the PE in our generalized linear model, longer AL would, on average, result in a more hyperopic refraction using Haigis, Hoffer Q, Holladay, and SRK/T, whereas AL was not associated with the prediction accuracy in Hill-RBF 2 or Barrett.

TABLE 2. Prediction Outcomes in Barrett, Haigis, Hill RBF-2, Holladay 1, Hoffer Q, and SRK/T

							P Value*														
							Hill-RBF2 vs					Barrett vs				SRK/T vs			Holladay 1 vs		Hoffer vs
	Hill-RBF 2	Barrett	SRK/T	Holladay 1	Hoffer Q	Haigis	Barrett	SRK/T	Holladay 1	Hoffer Q	Haigis	SRK/T	Holladay 1	Hoffer Q	Haigis	Holladay 1	Hoffer Q	Haigis	Hoffer Q	Haigis	Haigis
SD of PE	0.40	0.39	0.49	0.50	0.54	0.44	.632	.036	.004	.003	.138	.007	<.001	.001	.032	.576	.169	.154	.104	.021	<.001
Median absolute PE, D	0.20	0.21	0.27	0.30	0.33	0.28	.528	.027	<.001	<.001	.077	.019	<.001	<.001	.022	.017	.003	.494	.063	.004	<.001
% of eyes within ±0.25 D of PE	59.84	55.91	47.24	41.73	38.58	47.24	.472	.021	.004	.001	.034	.082	.012	.001	.109	.248	.109	>.999	.571	.310	.037
% of eyes within ±0.50 D of PE	86.61	86.61	82.68	70.87	73.23	83.46	>.999	.404	.002	.005	.480	.359	.001	.004	.480	<.001	.019	>.999	.579	.002	.006
% of eyes within ±1.00 D of PE	96.85	98.42	95.28	94.49	94.49	97.64	.480	.617	.371	.450	>.999	.134	.074	.074	>.999	>.999	>.999	.248	>.999	.134	.134

The arithmetic mean error was zeroed out by adjusting the refractive prediction error for each eye up or down by an amount equal to the arithmetic mean error in that formula. Elimination of the systematic error was performed before the evaluation of the above parameters.

D = diopter; PE = refractive prediction error; SD = standard deviation.

*7.94% of the 35 significant results of the 75 tests are expected to be false discoveries attributable to random error as determined by the false discovery rate.

Recent case series based on 13 301 eyes implanted with the SN60WF and 5200 eyes with the SA60AT found that Barrett has the lowest PE compared to 6 other formulas across all AL ranges (including 1548 eyes with AL >25.5 mm). However, the authors did not include Hill-RBF 1 in their analysis as this version was intended only for a plano target.[22] Conclusions drawn from studies evaluating the choice of IOL formula in axial myope depends on its definition. Wang and associates reported that in eyes with AL >28 mm (n = 34), Haigis outperformed SRK/T; in the same study, in eyes with AL between 25 and 28 mm, these 2 formulas were comparable, and they were both more precise than Holladay 1 and Hoffer Q.[25] Whereas in the study by Voytsekhivskyy, SRK/T was comparable to the T2 formula, the former had significantly lower MedAE than Haigis, Hoffer Q, Holladay 1, and Holladay 2 in eyes with AL >26 mm (n = 51).[26] Similarly, in eyes with an AL >27 mm (n = 117), Aristodemou and associates demonstrated the SRK/T formula gave better results than the Hoffer Q and Holladay 1 formulas.[3] The prediction accuracy of Barrett was followed by SRK/T in eyes with AL ≥26 mm (n = 77) across 7 formulas in the study by Kane and associates.[27] A recent meta-analysis including 4047 eyes from 11 observational studies found that Barrett had a lower mean absolute error and higher proportion of eyes within ±0.50 D of the PE in eyes with AL >24.5 mm compared to SRK/T, Hoffer Q, and Holladay 1 and 2. However, no statistical significance was detected when only eyes with AL >26 mm were included, and a comparison with the Hill-RBF was not performed in this review.[28]

We repeated our analysis using the Wang-Koch AL adjusted Haigis, Hoffer Q, Holladay 1, and SRK/T formulas. When these AL adjusted formulas were compared to Hill-RBF 2 and Barrett (Supplemental Table 2, Supplemental Material at AJO.com), their accuracies and precisions were no better than their unadjusted AL formulas' comparisons with Hill-RBF and Barrett (Table 2). Melles and associates found that the Wang-Koch adjustment caused an overcorrection of hyperopic outcomes in long eyes to result in myopic errors, with no improvements for the Holladay 1 and Hoffer Q formulas and worse outcomes for the Haigis and SRK/T formulas in eyes with the SA60AT IOL.[22] A previous study also found that in eyes with AL >26 mm implanted with IOL >6 D, applying the AL-adjusted method resulted in a modest overcorrection, suggesting that the adjusted AL equations for an IOL >6.0 D may be too aggressive.[14]

Studies reporting the outcomes on Hill-RBF 1 demonstrated that it is at least comparable to the standard formulas.[15,29] Myopic PE was found in eyes with keratometry reading more than 46 D in Hill-RBF 1[30]; this finding agrees with the variance function of the PE in our generalized linear models, which showed a negative association with the mean keratometry in Hill-RBF 2. Unlike Barrett, AL was not associated with the variance function in Hill-RBF 2; thus, the latter formula is more robust in

TABLE 3. Generalized Linear Model of the Mean Function and Variance Function of Refractive Prediction Error

Variable	Coefficient	Standard Error	*P* Value
Barrett			
Mean function			
Intercept	−0.08	0.03	.017
Variance function			
Intercept	1.68	1.17	N/A
AL	−0.10	0.04	.032
Haigis			
Mean function			
Intercept	−6.92	1.30	<.001
AL	0.10	0.02	<.001
Mean K	0.10	0.02	<.001
Variance function			
Intercept	3.14	1.81	N/A
Mean K	−0.10	0.04	.030
Hill-RBF 2			
Mean function			
Intercept	−0.25	0.03	<.001
Variance function			
Intercept	2.89	1.71	N/A
Mean K	−0.09	0.04	.031
Hoffer Q			
Mean function			
Intercept	−10.04	1.46	<.001
AL	0.17	0.02	<.001
Mean K	0.13	0.03	<.001
Variance function			
Intercept	3.38	1.84	N/A
Mean K	−0.10	0.04	.030
Holladay 1			
Mean function			
Intercept	−3.82	0.69	<.001
AL	0.15	0.02	<.001
Variance function			
Intercept	−1.63	N/A	N/A
SRK/T			
Mean function			
Intercept	−0.77	1.38	.575
AL	0.11	0.02	<.001
Mean K	−0.05	0.03	.049
Variance function			
Intercept	1.50	1.02	N/A
ACD	−0.69	0.30	.023

The intraocular lens model was not a significant variable of the mean function and variance function in any formulas.

ACD = axial length; AL = axial length; mean K = mean keratometry; N/A = not applicable.

its average refractive prediction precision than Barrett across the spectrum of ALs in high myopia. A prospective study showed that the mean absolute error of Hill-RBF 1 and Barrett increased significantly from 1 week to 1 month and from 1 month to 3 months postoperatively[31]; thus, standardizing the postoperative timing of refraction measurement is essential. Unlike the previous retrospective studies that measured the refraction as early as 1 month,[15,16,29] we measured the postoperative manifest refraction in between 3 and 4 months postoperatively in this study to ensure that the refraction is stable.[32]

To eliminate the systematic error from an incorrect formula constant, Hoffer and associates proposed an iterative method to recalculate and nullify the mean PE.[32] After optimizing the formula-specific lens constants such that the ME is zero, a comparison of the means is no longer statistically possible. As it is difficult to obtain optimized lens constants in these newly released formulas, we adjusted the individual PE by the amount equal to the ME for that formula in order to produce an ME of zero.[16,17] The outcomes prior to the adjustment (subjected to systematic errors) are shown in Supplemental Table 1 (Supplementary Material at AJO.com). Once the ME is nullified, the SD of PE measures the dispersion as to how the data scatter around the mean of zero, rather than around the mean (systematic error). The disadvantages of using the SD as compared to the MedAE is that it is affected by outliers, as the SD is related to the square value of the difference of each value from the mean. However, outliers are also of interest because these are outcomes we want to avoid in IOL power calculation.

Our study is one of the largest reported case series with eyes having an AL ≥26 mm and the first study to report the outcomes of Hill-RBF 2. Of the 127 eyes in this study, only 7 eyes had MA60MA and 5 eyes had AR40E. Future studies are needed to evaluate the performance of these new formulas in extreme high myopic eyes implanted with IOL <6 D. Controversy remains as to the most appropriate approach to evaluate the outcomes of IOL formulas in clinical practice. One theory is that because the formula will be widely used by different surgeons using various IOLs, the study should consist of data from multiple surgeons using multiple IOLs. On the other hand, if the study is carried out by a single surgeon using one model of IOL, then the formula will be the only variable. Our study adopted the former approach, which is representative of the actual assortment of cases encountered in a tertiary referral center. The IOL dioptric power, an IOL <6 D, or a 3-piece IOL were not associated with the mean function or variance function of the PE in Hill-RBF 2 but were associated with the other 5 formulas. The inclusion of cases performed by multiple surgeons and refracted by different optometrists at a single center could introduce bias. However, the refractive outcome from intersurgeon differences in phacoemulsification are clinically insignificant,[33] and differences in manifest refraction arising from different optometrists' practices from a single center are minimal.[34] Future studies comparing Hill-RBF with other new-generation formulas would be important.

Hill-RBF is not a static formula; it continues to evolve and is expected to improve over time. In our study, the proportion of eyes with an absolute error within ±0.50 and ±1.00 D for all 6 formulas were well above the standards. Both Hill-RBF 2 and Barrett were more precise than

Haigis, Hoffer, Holladay 1, and SRK/T in high axial myopia, where only for the Hill-RBF 2 formula were the accuracy and dispersion of the PE independent of the AL. Accumulating additional cases at the extreme boundaries in the Hill RBF registry is likely to refine in accuracy and expand the range of eyes it can predict.

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REFERENCES

1. Brick DC. Risk management lessons from a review of 168 cataract surgery claims. *Surv Ophthalmol* 1999;43(4):356–360.
2. Norrby S. Sources of error in intraocular lens power calculation. *J Cataract Refract Surg* 2008;34(3):368–376.
3. Aristodemou P, Knox Cartwright NE, Sparrow JM, Johnston RL. Formula choice: Hoffer Q, Holladay 1, or SRK/T and refractive outcomes in 8108 eyes after cataract surgery with biometry by partial coherence interferometry. *J Cataract Refract Surg* 2011;37(1):63–71.
4. Sperduto RD, Seigel D, Roberts J, Rowland M. Prevalence of myopia in the United States. *Arch Ophthalmol* 1983;101(3):405–407.
5. McCarty CA, Livingston PM, Taylor HR. Prevalence of myopia in adults: implications for refractive surgeons. *J Refract Surg* 1997;13(3):229–234.
6. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. *Lancet* 2012;379(9827):1739–1748.
7. Hoffer KJ. Biometry of 7,500 cataractous eyes. *Am J Ophthalmol* 1980;90(3):360–368.
8. Tsang CS, Chong GS, Yiu EP, Ho CK. Intraocular lens power calculation formulas in Chinese eyes with high axial myopia. *J Cataract Refract Surg* 2003;29(7):1358–1364.
9. Haag-Streit White Paper. Hill-RBF Method. https://www.haag-streit.com/fileadmin/Haag-Streit_Diagnostics/biometry/EyeSuite_IOL/Brochures_Flyers/White_Paper_Hill-RBF_Method_20160819_2_0.pdf. Accessed March 26, 2019.
10. Hoffer KJ. Clinical results using the Holladay 2 intraocular lens power formula. *J Cataract Refract Surg* 2000;26(8):1233–1237.
11. Hoffer KJ. The Hoffer Q formula: a comparison of theoretic and regression formulas. *J Cataract Refract Surg* 1993;19(6):700–712 [errata: 1994;1920:1677 and 2007;1933(1991):1992-1993].
12. Wang L, Koch DD. Modified axial length adjustment formulas in long eyes. *J Cataract Refract Surg* 2018;44(11):1396–1397.
13. Wang L, Shirayama M, Ma XJ, Kohnen T, Koch DD. Optimizing intraocular lens power calculations in eyes with axial lengths above 25.0 mm. *J Cataract Refract Surg* 2011;37(11):2018–2027.
14. Abulafia A, Barrett GD, Rotenberg M, et al. Intraocular lens power calculation for eyes with an axial length greater than 26.0 mm: comparison of formulas and methods. *J Cataract Refract Surg* 2015;41(3):548–556.
15. Hill DC, Sudhakar S, Hill CS, et al. Intraoperative aberrometry versus preoperative biometry for intraocular lens power selection in axial myopia. *J Cataract Refract Surg* 2017;43(4):505–510.
16. Gokce SE, Zeiter JH, Weikert MP, et al. Intraocular lens power calculations in short eyes using 7 formulas. *J Cataract Refract Surg* 2017;43(7):892–897.
17. Wang L, Koch DD, Hill W, Abulafia A. Pursuing perfection in intraocular lens calculations: III. Criteria for analyzing outcomes. *J Cataract Refract Surg* 2017;43(8):999–1002.
18. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J Royal Stat Soc B* 1995;57(1):289–300.
19. Gale RP, Saldana M, Johnston RL, Zuberbuhler B, McKibbin M. Benchmark standards for refractive outcomes after NHS cataract surgery. *Eye (Lond)* 2009;23(1):149–152.
20. Hahn U, Krummenauer F, Kolbl B, et al. Determination of valid benchmarks for outcome indicators in cataract surgery: a multicenter, prospective cohort trial. *Ophthalmology* 2011;118(11):2105–2112.
21. Simon SS, Chee YE, Haddadin RI, et al. Achieving target refraction after cataract surgery. *Ophthalmology* 2014;121(2):440–444.
22. Melles RB, Holladay JT, Chang WJ. Accuracy of intraocular lens calculation formulas. *Ophthalmology* 2018;125(2):169–178.
23. Barrett GD. An improved universal theoretical formula for intraocular lens power prediction. *J Cataract Refract Surg* 1993;19(6):713–720.
24. Cooke DL, Cooke TL. Comparison of 9 intraocular lens power calculation formulas. *J Cataract Refract Surg* 2016;42(8):1157–1164.
25. Wang JK, Hu CY, Chang SW. Intraocular lens power calculation using the IOLMaster and various formulas in eyes with long axial length. *J Cataract Refract Surg* 2008;34(2):262–267.
26. Voytsekhivskyy OV. Development and clinical accuracy of a new intraocular lens power formula (VRF) compared to other formulas. *Am J Ophthalmol* 2018;185:56–67.
27. Kane JX, Van Heerden A, Atik A, Petsoglou C. Intraocular lens power formula accuracy: comparison of 7 formulas. *J Cataract Refract Surg* 2016;42(10):1490–1500.
28. Wang Q, Jiang W, Lin T, et al. Accuracy of intraocular lens power calculation formulas in long eyes: a systematic review and meta-analysis. *Clin Exp Ophthalmol* 2018;46(7):738–749.
29. Kane JX, Van Heerden A, Atik A, Petsoglou C. Accuracy of 3 new methods for intraocular lens power selection. *J Cataract Refract Surg* 2017;43(3):333–339.
30. Reitblat O, Levy A, Kleinmann G, Lerman TT, Assia EI. Intraocular lens power calculation for eyes with high and low average keratometry readings: Comparison between

various formulas. *J Cataract Refract Surg* 2017;43(9): 1149–1156.

31. Wallace HB, Misra SL, Li SS, McKelvie J. Predicting pseudophakic refractive error: Interplay of biometry prediction error, anterior chamber depth, and changes in corneal curvature. *J Cataract Refract Surg* 2018;44(9):1123–1129.
32. Hoffer KJ, Aramberri J, Haigis W, et al. Protocols for studies of intraocular lens formula accuracy. *Am J Ophthalmol* 2015; 160(3):403–405.e1.
33. Aristodemou P, Knox Cartwright NE, Sparrow JM, Johnston RL. Intraocular lens formula constant optimization and partial coherence interferometry biometry: Refractive outcomes in 8108 eyes after cataract surgery. *J Cataract Refract Surg* 2011;37(1):50–62.
34. Reinstein DZ, Yap TE, Carp GI, Archer TJ, Gobbe M. Reproducibility of manifest refraction between surgeons and optometrists in a clinical refractive surgery practice. *J Cataract Refract Surg* 2014;40(3):450–459.