

Hill-RBF Method: where does it stand?

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ABSTRACT

Introduction: Emmetropia is one of the main goals in cataract surgery. Several intraocular lens power calculation formulas and methods have been developed to achieve successful outcomes. The purpose of this study is to evaluate the accuracy of Hill-RBF method, and compare it with some currently available formulas.

Material and Methods: Retrospective study evaluating eyes with cataract surgery with intraocular (IOL) placement in the bag. Biometric data were obtained using IOLMaster[®]500 (Carl Zeiss Meditec AG). Hill-RBF and traditional formulas (Haigis, Holladay1 and SRK/T) were ranked according to: mean absolute error (MAE) and percentage of final refractions within $\pm 1,00D$ and $\pm 0,50D$ of the predicted value.

Results: Clinical data of 100 eyes were reviewed. MAE values favored Hill-RBF (0.077) over Haigis (MAE 0.660; $p < 0.01$), SRK/T (MAE 0.537; $p < 0.01$) and Holladay1 (MAE 0.663; $p < 0.01$). It was also associated with the highest percentage of eyes within $\pm 1.00D$ and $\pm 0.50D$ of target refraction, 100% of cases. Among other formulas, SRK/T was superior overall. Percentage of final refractions within $\pm 1.00D$ were 78% with Haigis, 86% with SRK/T and 82% with Holladay1, decreasing to 52% vs 60% vs 46%, respectively, if final refractions within $\pm 0.50D$ were considered. Performance of all formulas was remarkably low in small eyes, with maintained accuracy of Hill-BRF.

Conclusions: Hill-RBF method performed significantly better in these subset of patients compared to other 3rd generation formulas and could be less affected by variations in axial length.

Keywords: Hill-RBF; biometry; calculation formula; intraocular lens power; cataract;

RESUMO

Introdução: A emetropia é um dos principais objetivos da cirurgia de catarata. Várias fórmulas e métodos de cálculo da potência da lente intraocular foram desenvolvidos para obtenção de resultados mais precisos. O propósito deste estudo é avaliar a precisão do método Hill-RBF e compará-la com algumas fórmulas disponíveis atualmente.

Material e métodos: Estudo retrospectivo avaliando olhos submetidos a cirurgia de catarata com colocação de lente intraocular no saco capsular. Os dados biométricos foram obtidos

usando IOLMaster® 500 (Carl Zeiss Meditec AG). Hill-RBF e as restantes fórmulas (Haigis, Holladay1 e SRK/T) foram classificadas de acordo com: erro absoluto médio (MAE) e percentagem de refrações finais entre $\pm 1.00D$ e $\pm 0.50D$ do valor previsto.

Resultados: Foram revistos os dados clínicos de 100 olhos. Os valores médios de MAE favoreceram o método Hill-RBF (MAE 0.077) em relação às fórmulas Haigis (MAE 0.660, $p < 0.01$), SRK/T (MAE 0.537, $p < 0.01$) e Holladay1 (MAE 0.663, $p < 0.01$). Além disso, resultou na maior percentagem de olhos com refração alvo entre $\pm 1.00D$ e $\pm 0.50D$: 100% dos casos. Entre as fórmulas tradicionais, a SRK/T foi globalmente superior. A percentagem de refrações finais entre $\pm 1.00D$ foi 78% com Haigis, 86% com SRK/T e 82% com Holladay1, descendo para 52% vs 60% vs 46%, respetivamente, considerando refrações finais $\pm 0.50D$. O desempenho das fórmulas foi notavelmente inferior em olhos pequenos, com precisão mantida do método Hill-RBF.

Conclusões: O desempenho do método Hill-RBF foi significativamente superior neste grupo de pacientes comparativamente com fórmulas de 3ª geração e poderá ser menos influenciado pelas variações do comprimento axial.

Keywords: Hill-RBF; biometria; fórmula de cálculo; potência de lente intraocular; catarata.

INTRODUCTION

Cataract surgery is the most widely performed surgery in ophthalmology.

Targeting emmetropia is one of the main goals and despite novel preoperative measurement devices, surgical technique, related instruments and phacoemulsifiers, as well as improved IOL power calculation formulas and methods, lack of accuracy regarding post-operative refractive status remains.

An evaluation of more than 260 000 optical biometry cases submitted for Haigis formula optimization demonstrated that the vast majority of surgeons achieve a refractive accuracy within $\pm 0.50D$ in no more than 74-78% of cases using 3rd generation formulas.^A In addition, outcomes from real-life practice may be even worse, considering that the most accurate devices for pre-operative evaluation, surgical equipment along with newer generation formulas may not be available. The negative impact of these outcomes is certainly unquestionable in cataract surgery, but may be more significant in situations such as clear lens extraction. For example, patients with small eyes may have cataract surgery earlier due to intraocular pressure issues (possibly related to structural

changes in the anterior segment and in certain circumstances due to the anterior-posterior growth of the lens)¹ or to correct significant degrees of hyperopia.^{2,3} Because lens opacity may be insignificant in the latter, these patients generally have higher visual expectations.

Hill-Radial Basis Function (Hill-RBF) is a recently developed method for IOL power prediction that may improve these outcomes. According to Norrby, the major source of errors in IOL power calculation, accounting for up to 35,5% of cases, is effective lens position (ELP) prediction.⁴ Hill-RBF is a completely new method of IOL power calculation. It was developed by Dr. Hill in partnership with physicians, engineers and mathematicians from Mathworks with support from Haag-Streit. It is based in artificial intelligence, employing a sophisticated software that evaluates data, uses pattern recognition to predict the IOL power. It is entirely data driven and free of calculation bias overcoming the errors introduced by ELP prediction inherent to 3rd generation formulas, and turning this method's predictions less dependent on axial length. Another strength lies in the fact that when there are gaps in the data, it uses a sophisticated form of data interpolation,

filling those gaps and still enabling a result. Finally, it has the advantage of self-improvement as more data are included, one of the reasons why it is known as “Big Data” method, progressing actively towards more accurate results.^{A,C} It uses a validating boundary model, by which it does not provide a refractive prediction if it is likely to be inaccurate, which occurs in approximately 1.4% of cases and an alert “out of bounds” shows up.⁵ Along with these, it has the advantage of being freely available online at <http://rbfcalculator.com>, giving an extra tool to surgeons worldwide.^{A, B}

Unpublished data on this method seems promising, which was corroborated recently in a peer-reviewed paper, showing overall good performance over 3rd generation formulas.⁵

Our purpose is to evaluate the accuracy of this new method and compare it with 3rd generation formulas using a partial coherence interferometry (PCI) device.

MATERIAL AND METHODS

Retrospective case series in which clinical data from patients who underwent cataract surgery from August to December 2016 in the Cornea, Cataract and Refractive Surgery Department of Garcia de Orta Hospital, were reviewed.

Inclusion criteria were uneventful phacoemulsification cataract surgery, with clear cornea incision of 2,75mm, and in-the-bag insertion of a monofocal aspheric biconvex IOL (AcrySoft[®]SN60WF, A-constant 118.7, n=27; Tecnis[®]1 ZCB00, A-constant 119.3, n=30; Akreos[®]MI60L, A-constant 118.4, n=43). In the majority of cases, only one eye per patient was included. Surgeries were performed by all cataract surgeons of the Ophthalmology Department.

Preoperative biometric data was obtained using a PCI device (IOLMaster[®]500, Carl Zeiss Meditec AG). Exclusion criteria included: amblyopia, corneal, optic nerve or retinal disease, and post-radial keratotomy, photorefractive keratectomy or LASIK eyes, that could possibly introduce biases along with patients with ocular measurements “out-of-bounds” on the Hill-RBF calculator.

Manifest refractions were obtained within the first and second month postoperatively on all included eyes.

Refractive results were compared between the original version of Hill-RBF method (results obtained from the website)^B and formulas (Haigis, SRK/T, with no W-K correction for myopic eyes, and Holladay 1) available in IOLMaster[®]500 (Carl Zeiss Meditec AG).

The A-constant for SRK/T, surgeon factor for Holladay 1 formula and a1, a2 and a3 from Haigis formula used for IOL power calculation were those optimized according to ULIB – User Group of Laser Interferometry.

The A-constant suggested by the IOL manufacturer for optical measurement was introduced for different implanted IOLs when Hill-RBF method was used.

The prediction error was calculated as the actual postoperative refraction (converted to spherical equivalent) minus the spherical equivalent predicted by each formula.

Four parameters were evaluated: mean prediction error (ME), mean absolute error (MAE) and percentage of final refractions within $\pm 0.50D$ and $\pm 1.00D$ of the predicted value. Formulas were ranked according to these results.

Overall and subgroup analysis according to axial length (AL) was performed: short eyes (defined by AL <22.5mm) as group 1, medium eyes (AL 22.5 to 26.0mm) in group 2, long eyes (AL >26.0mm) in group 3.

The Friedman test was used to assess the differences in absolute error between formulas. In the event of a significant result, post hoc analysis was performed using the Conover test with the Bonferroni correction applied to account for multiple comparisons. A p value less than 0.01 was considered statistically significant. Statistical analysis was performed with SPSS (version 21.0).

RESULTS

Complete clinical data of 100 eyes were reviewed. Most patients were female 57% and the mean age was 74.64 years old. Group 1 included 20% of eyes, group 2 with 73% of eyes, and the remainder 7% were in group 3. Table 1 refers to demographics, keratometric and biometric data of all included eyes.

Table 1 - Demographics and biometric data of all eyes (n=100)

Parameters	Value
Female sex (%)	57
Age (mean, range, in years old)	74.64 [59-85]
Laterality (%)	
Right eye	52%
Left eye	48%
Axial Length (mean, range, in mm)	23.15 [20.79 – 27.65]
• <22,5mm	• n = 20
• 22,5-26mm	• n = 73
• >26mm	• n = 7
K1 (mean in D)	43.97 [39.29 – 48.84]
K2 (mean in D)	44.83 [40.47 – 48.95]
Pre operative Anterior Chamber Depth (mean, mm)	2.98 [2.00 – 4.00]
White-to-white, W-t-W (mean, mm)	11.62 [10.6 – 12.7]

OVERALL RESULTS

Regarding the results of all three axial length groups (table 2), Hill-RBF method had the lowest ME and MAE (0,077), being superior to all formulas evaluated, with statistical significance: Haigis (MAE 0.660; p<0.01), SRK/T (MAE 0.537; p<0.01) and Holladay 1 (MAE 0.663; p<0.01). Corroborating these results, this method led to the highest percentage of eyes within $\pm 1.00D$ and $\pm 0.50D$. Comparing Hill-RBF with Haigis, SRK/T and Holladay 1, the results were respectively, 100% vs 78% vs 86% vs 82% of final refractions within $\pm 1.00D$ and 100% vs 52% vs 60% vs 46% of final refractions within $\pm 0.50D$.

Table 2 shows the ME, MAE and the percentage of eyes with a prediction error of $\pm 0.50 D$ and $\pm 1.00 D$, for the entire AL range.

Table 2 - Comparison of Hill-RBF with traditional IOL formulas in all eyes (n=100)

Methods/Formula	ME	MAE	% of eyes within $\pm 1.00D$	% of eyes within $\pm 0.50D$
Hill-RBF	-0.004	0.077	100	100
Haigis	0.029	0.660	78	52
SRK/T	0.049	0.537	86	60
Holladay 1	-0.026	0.663	82	46

(p value<0.01 for ME and MAE)

SUBGROUP ANALYSIS

Subgroup analysis was performed, in greater detail for groups 1 and 2.

In group 1 (AL: <22,5mm) Hill-RBF has shown superior outcomes compared to other formulas. It had the lowest MAE (0,079) compared to Haigis (MAE 1,224), SRK/T (MAE 0,821) and Holladay 1 (MAE 0,807). According to these, the highest percentage of eyes within

$\pm 1.00D$ and $\pm 0.50D$ were in the Hill-RBF method, with 100% in both. Haigis, SRK/T and Holladay 1 results were, respectively: 47% vs 65% vs 62% final refractions within $\pm 1,00D$ and 100% vs 15% vs 60% vs 55% final refractions within $\pm 0,50D$. Although this is a small group, the differences between the percentage of eyes within target refraction using Hill-RBF method and the other formulas was the highest when considering medium eyes subgroup and overall group analysis (table 3).

Table 3 - Comparison of Hill-RBF with traditional IOL formulas in eyes with axial length <22,5mm (n=20)

Methods/Formula	ME	MAE	% of eyes within $\pm 1.00D$	% of eyes within $\pm 0.50D$
Hill-RBF	-0.021	0.079	100	100
Haigis	0.026	1.224	47	15
SRK/T	-0.055	0.821	65	60
Holladay 1	-0.037	0.807	62	55

*(p value<0.01 for ME and MAE)

Regarding group 2 (AL: 22,5-26mm) overall results were superior when compared to results obtained for the entire AL with Hill-RBF showing superior outcomes compared to other formulas. Hill-RBF method had the lowest MAE (MAE 0.078) compared to SRK/T (MAE 0.469), Holladay 1 (MAE 0.562) and Haigis (MAE 0.485).

According to these, the highest percentage of eyes within $\pm 1.00D$ and $\pm 0.50D$ were in the Hill-RBF method. Comparing Hill-RBF with Haigis, Holladay 1 and SRK/T the results were, respectively: 100% vs 86% vs 90% vs 88% final refractions within $\pm 1.00D$ and 100% vs 64.4% vs 64.4% vs 49.3% final refractions within $\pm 0.50D$ (table 4).

Table 4 - Comparison of Hill-RBF with traditional IOL formulas in eyes with axial length within 22,5 – 26mm (n=73)

Methods/Formula	ME	MAE	% of eyes within $\pm 1,00D$	% of eyes within $\pm 0,50D$
Hill-RBF	-0.001	0.078	100	100
Haigis	0.083	0.485	86	64.4
SRK/T	0.074	0.469	90	64.4
Holladay 1	-0.062	0.562	88	49.3

*(p value<0.01 for ME and MAE)

Figures 1 and 2 illustrate the refractive accuracy of Hill-RBF compared to previous formulas along the entire axial length, with consistently lower MAE for the method. Previous formulas tend to perform better when larger AL are included. (Figure 1).

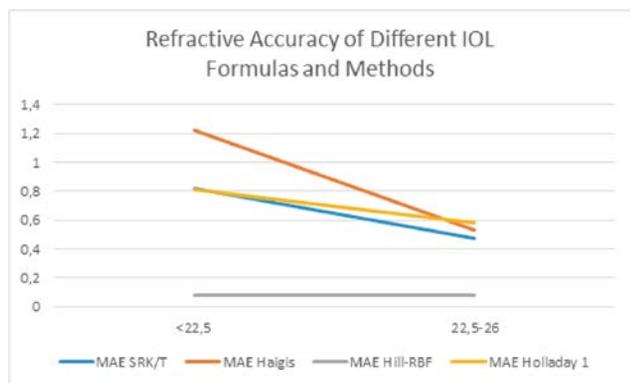


Figure 1 - Performance of Hill-RBF, Haigis, SRK/T and Holladay 1 formulas according to axial length – Mean Absolute Error

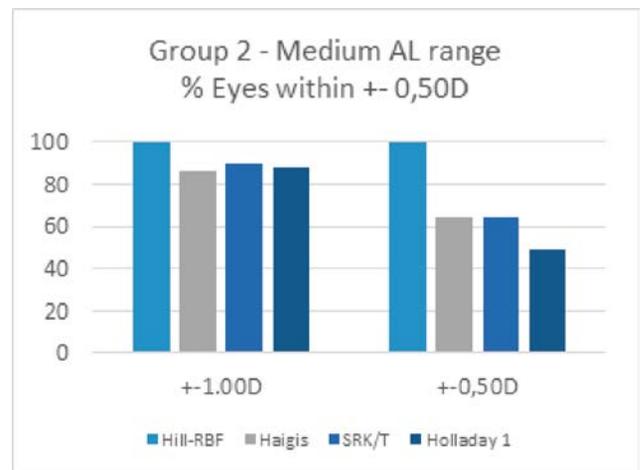
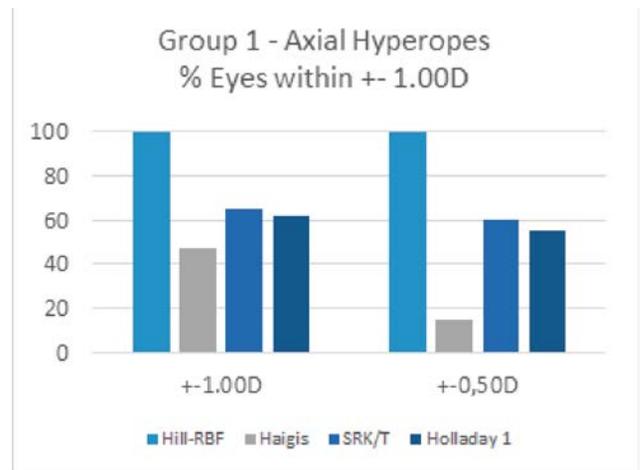


Figure 2 - Performance of Hill-RBF, Haigis, SRK/T and Holladay 1 formulas according to axial length – % of eyes within target refraction.

DISCUSSION

The lack of accuracy in up to 26% of cases with available 3rd generation formulas paved the way for the development of enhanced formulas and methods.^A

Hill-RBF method is a new method of IOL power prediction, developed based on Lenstar LS900 (Haag-Streit AG, Koeniz, Switzerland) biometric data in combination with the Alcon SN60WF IOL (Alcon Labs, Forth Worth, EUA), with which it should perform better. However, according to Warren Hill and co-workers, it may also be used with other optical biometers and biconvex IOL models within the power range of +6.00 to +30.00 diopters, although its accuracy may be impaired.^B It includes a boundary model by which only a specific range data value can be used for calculation and a prediction result can be provided (table 5).

Table 5 - Parameters and respective range of accepted values for IOL power prediction in Hill-RBF method – original version

Parameters	Range of Accepted Values
AL (mm)	19 – 30
K1 and K2 (D)	37 – 49
ACD (mm)	1.5 – 4.5
White-to-White (mm)	8 – 14

The original version of Hill-BRF, released in May 2016, was updated to a beta version in October 2017. The expanded version has increased the database from 3,445 to 12,419 eyes, including 1000 cases with a very short axial length and for that reason, the new version is expected to provide more accurate predictions. The range of in-bounds calculations for the high to extreme axial myope and very short axial length has increased and the target spherical equivalent can now be introduced.^C

Only the original version was available at the time this study was performed and, for that reason, it was the consulted version. IOLMASTER[®]500 (Carl Zeiss Meditec AG) was

used for all pre-operative biometric measurements. 3 different IOL models were used in the study: all were biconvex and A-constant for each was considered and introduced in the online Hill-RBF original version for IOL power calculation.

Our results show that Hill-BRF method performed significantly better than previously used formulas, even in non-standardized conditions.

Considering the entire axial length group. It had the lowest MAE of all formulas (MAE Hill-RBF 0,077 vs MAE Haigis 0,660 vs MAE SRK/T 0,537 vs MAE Holladay 1 0,663) with corresponding higher percentage of eyes within the target refraction of $\pm 1.00D$ (100% for Hill-RBF vs 78% for Haigis vs 86% for SRK/T vs 82% for Holladay 1) and final refractions within $\pm 0,50D$ (100% Hill-RBF vs 52% Haigis vs 60% SRK/T vs 46% Holladay 1) (table 4).

Table 6 resumes all studies to date involving evaluation of Hill-RBF performance.

Non-peer reviewed studies advocate excellent accuracy, supporting our results. *Synder M et al*, at ASCRS 2016, presented the results of their prospective study using Lenstar: overall, Hill-RBF showed excellent results with 91% of eyes within $\pm 0.50D$ of target refraction, although less accuracy was noted in axial myopes and hyperopes.^D *Dalton et al*, also reported impressive results, with 95% of eyes within $\pm 0.50D$.^E

Peer reviewed studies have followed. *Feijó and colleagues*, have further supported good results with Hill-BRF, overcoming SRK-T.⁶ Larger studies were published recently^{5,7,8} and although they have shown good refractive outcomes with this newer method, overall results were not as impressive as reports from Synder and Dalton. Despite that, superior outcomes compared to 3rd generation formulas and a trend toward raised accuracy in small eyes compared to newer formulas has been demonstrated.^{5,8,9}

Table 6 - Published data regarding Hill-RBF performance.

Study	Formulas/Methods	Biometer Device	Results
Dalton M ^E n=3212	Hill-RBF	No information	Overall: 95% of eyes within $\pm 0.50D$
Synder M, et al ^D n=497	Hill-RBF	Lenstar LS900 (Haag-Streit AG)	Overall: 91% of eyes within $\pm 0.50D$ <ul style="list-style-type: none"> AL > 26mm 98.4%; AL 22.5-26mm 92.2%; AL < 22.5mm 84.5% (theoretically superior to Barrett II, Olsen, Holladay 2, Hoffer Q)
Feijóo B, et al ⁶ n=188	<ul style="list-style-type: none"> Hill-RBF PhacoOptics, Barret II, SRK/T 	Lenstar LS900 (Haag-Streit AG)	Overall: Hill-RBF with the best results. AL $\leq 22.0mm$: Hill-RBF had the lowest median absolute error.
Kane JX, et al ⁵ n=3122	<ul style="list-style-type: none"> Hill-RBF Ladas Superformula, Fullmonte, Barrett II, Holladay 1 	IOLMaster [®] 700 (Carl Zeiss Meditec AG)	Overall Hill-RBF superior than Fullmonte, inferior than Barrett II, Ladas Superformula, Holladay 1: <ul style="list-style-type: none"> 69,6% of eyes within $\pm 0.50D$. AL $\leq 22.0mm$: Hill-RBF was the best, along with Holladay 1: 66.4% of eyes within $\pm 0.50D$.
Hill DC, et al ⁷ n=51	<ul style="list-style-type: none"> Hill-RBF Intraoperative wavefront aberrometry, Barrett II, Holladay 1 AL-optimized, Holladay 2 	IOLMaster [®] 500, (Carl Zeiss Meditec AG)	AL > 25mm Hill-RBF: <ul style="list-style-type: none"> Similar to 4th generation formulas, inferior to intraoperative wavefront aberrometry and AL-optimized Holladay 1. 76,7% of eyes within $\pm 0.50D$
Gökce, et al ⁸ n=86	<ul style="list-style-type: none"> Hill-RBF Barrett II, Haigis, Hoffer Q, Holladay 1 and 2, Olsen 	Lenstar LS900 (Haag-Streit AG)	AL $\leq 22mm$ Hill-RBF: <ul style="list-style-type: none"> Superior when the mean prediction error was not adjusted to zero; 70,9% of eyes within $\pm 0.50D$
Reitblat, et al ⁹ n=171	<ul style="list-style-type: none"> Hill-RBF Barrett II, Olsen, Holladay 1 and 2, Haigis, Hoffer Q, SRK/T 	Lenstar LS900 (Haag-Streit AG)	K > 46D (average AL 24,10mm): <ul style="list-style-type: none"> Hill-RBF performed better (83% of eyes within $\pm 0.50D$); K < 42D (average AL 25,55mm): Hill-RBF inferior when compared to Barrett II and Olsen formulas.

Considering our sample, when subgroup analysis was performed, Hill-RBF showed, as expected, good performance over other evaluated formulas, with remarkable differences in group 1 – short axial length. Poor refractive outcomes have been reported in relation to increasing hyperopia. This may be more significant in 3rd generation formulas due to inaccurate calculation of ELP, as the anterior segment in short eyes is not proportional to the axial length and has a high variability. As higher IOL powers are needed for emmetropia as a result of the shorter axial length, any inaccuracy in the ELP has an exaggerated effect. Hill-RBF method, being an artificial intelligence method overcomes this.¹⁰ This explains the huge difference separating performance between Hill-RBF method and other formulas in our group. It had the lowest MAE (MAE 0.079) compared to Haigis (MAE 1.224), SRK/T (MAE 0.821) and Holladay1 (MAE 0.807) and the highest percentage of eyes within $\pm 1.00D$ and $\pm 0.50D$ compared to Haigis, SRK/T and Holladay 1, respectively

100% vs 47% vs 65% vs 62% and 100% vs 15% vs 60% vs 55% final refractions within $\pm 0.50D$) (table 3).

Even considering the small sample of these subgroup, our findings seem promising and should encourage further attention with higher numbers in this subset of patients. The largest case series published in the literature evaluating 3rd generation formulas, showed good performance with Hoffer Q (not evaluated in this study) and Holladay 1 in patients with AL < 21.99mm,¹¹ despite 52-71% of eyes still falling within $\pm 0.50D$. Synder reported outstanding results, with refractive results in hyperopes being significantly better than Barrett II, Olsen, Holladay 2, Hoffer Q.^D Feijóo et al, found similar results,⁶ Kane's group also demonstrated improved accuracy with Hill-RBF over 3rd generation formulas, except Holladay 1⁵ and a possible benefit was demonstrated in the study published by Gökce.⁸

The authors acknowledge major limitations of this study. Firstly, it was retrospective in nature. Adding to this, the multiplicity of surgeons involved and ULIB optimized constants for IOL calculation and not personal optimization (with adjustments made with obtained refractive data from previous surgeries) may imply worse accuracy and reliability on the analysis. This may explain differences between formulas, specially Haigis formula, with which superior results were expected to be achieved. This may point to another strength of Hill-RBF – less dependence on previous time consuming adjustments. Moreover, the number of patients may introduce biases regarding interpretation of results. The lack of some biometric data, such as lens thickness and central corneal thickness, along with the use of IOLS and devices not optimized for this method, could have guided to misleading results, which however did not seem to occur. For this reason, the authors consider that this should be seen as an additional advantage of this method, offering the possibility of good accuracy even using a device different from the one recommended.

CONCLUSIONS

Even though the study was not performed according to standardized recommendations regarding Hill-RBF method performance, refractive outcomes were superior than Haigis, SRK/T and Holladay 1 formulas, and may be less affected by axial length, in this population. Although similar results are reported in non-peer reviewed studies, the results from the case series published in the literature are not so promising. Further studies would be valuable to clarify the clinical value of this new tool.

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