Performance Evaluation of a Simple Strategy to Optimize Formula Constants for Zero Mean or Minimal Standard Deviation or Root-Mean-Squared Prediction Error in Intraocular Lens Power Calculation

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• PURPOSE: To investigate the performance of a simple prediction scheme for the formula constants optimized for a mean (MPE), standard deviation (SDPE) or root-mean-squared refractive prediction error (RMSPE).
• DESIGN: Retrospective cross-sectional study.
• METHODS: Using IOLMaster 700 biometric data from 888 eyes treated with the Hoya Vivinex lens and 821 eyes treated with the Alcon SA60AT lens, plus the power of the implanted lens and postoperative spherical equivalent refraction, optimized constants for SRKT, Hoffer Q, Holladay 1, Haigis, and K6 formulae were calculated using an iterative nonlinear optimization for zero MPE and minimal SDPE and RMSPE. Start values were detuned by ±1.5 from the MPE optimized constants and formula constants generated using the simple prediction scheme were compared to the corresponding directly optimized constants.
• RESULTS: For all 5 formulae under test and with both datasets, constants optimized using the simple scheme showed excellent agreement with those from the iterative method with either MPE or RMSPE used as the optimization metric and good agreement with SDPE as the metric. Constants optimized for zero MPE or minimal RMSPE agreed within 0.05, whereas constants for minimal SDPE could be systematically off by up to 0.6 from the MPE values, making SDPE unsuitable as an optimization metric.
• CONCLUSIONS: This simple formula constant optimization scheme performs excellently for 4 disclosed formulae and one nondisclosed formula in our 2 monocentric datasets with zero MPE or minimal RMSPE as metrics. Multicentric studies with other study populations and biometers are required to further investigate the clinical applicability. (Am J Ophthalmol 2025;269: 282–292. © 2024 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/))

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BACKGROUND

There are currently many options for intraocular lens power (IOLP) calculation and prediction of postoperative refraction.[1-3] In addition to empirical calculation strategies, including regression or artificial intelligence-based and raytracing, most intraocular lenses (IOL) are calculated using classical or modern formulae which are implemented in the optical biometer or provided via dedicated software tools. The classical lens power formulae such as SRK/T,[4,5] Hoffer Q,[6-8] Holladay 1,[9] or Haigis[10] are fully disclosed and can be directly implemented with a little programming in any consumer software. However, most of the more up-to-date lens power calculation concepts have never been disclosed.[3,11] In these cases, we have to use the built-in software tools in the optical biometer or the WEB-based calculations (eg, as provided by the European Society for Cataract and Refractive Surgery [https://iolcalculator.escrs.org]).

The refractive outcome after cataract surgery is mostly determined by the quality of the formula constants,[12-18] which adjust the outcome to achieve the best results in a reference population. For that purpose, constant optimization is mandatory. This optimization aims to minimize one of a number of chosen metrics of the formula prediction error (PE), defined as the deviation of the formula-predicted spherical equivalent refraction from the achieved refraction measured after cataract surgery. Such metrics include zeroing the mean (MPE) or median PE (MEDPE),

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or minimizing the mean (MAPE) or median absolute PE (MEDAPE), the root-mean-squared PE (RMSPE) or the population standard deviation of the PE (SDPE).[12,15,19-23] However, constant optimization is a nonlinear task. This means that there is no unique algebraic concept for optimizing formula constants with respect to any given metric or formula for any study population.[19-23] Nonlinear iterative optimization techniques, as used in many disciplines of engineering or natural sciences, are very powerful but they all require some insight into the lens formula because they typically require the gradient or even the Hessian of the formula-predicted refraction with respect to the formula constant.[19,22,23] In the case of the disclosed classical formulae such as SRK/T, Hoffer Q, Holladay 1, or Haigis, the derivation of the algebraic gradient or Hessian is quite simple.[20] Alternatively, given the ease of implementing these formulae in program code, a numerical approach to calculating the gradients or Hessians would be straightforward.

In contrast, the architecture of modern formulae which also promise a good performance for eyes with less common biometric measures is mostly not disclosed.[1-3,24] This makes it very difficult and time-consuming to calculate the predicted refraction with these formulae for a large dataset. The nondisclosed nature of these formulae precludes deriving the algebraic gradient or Hessian.[19] Consequently, applying nonlinear iterative optimization strategies would involve calculating predicted refractions multiple times for several formula constants to find the best solution for the formula constant. Such a procedure is too complex for clinical routine, and alternative options for formula constant optimization are required.[16,23,25,26]

In 2023, Gatinel et al[15] published a simple straightforward concept for formula constant optimization in terms of zeroing MPE. This concept is a simplified gradient descent method that works quite well for all lens formulae involving a single formula constant directly linked to the mean axial lens position of the simplified thin lens, whether the formula is disclosed[26] or not. This approach could be applied to the classical formulae involving an A constant (SRK/T), pACD constant (Hoffer Q), SF (Holladay 1), the a0 constant of the simplified Haigis formula (with preset values for a1 and a2), or modern undisclosed formulae which use the LF (Barrett Universal II), the ACD constant (Hoffer QST) or A constant (eg, Cooke K6, Yeo EVO formula). This concept uses the MPE for any given start value of the formula constant together with the arithmetic mean of the PIOL and the keratometric power in the dataset, and provides an offset (correction term) for the start value of the mean effective lens position (ELP).[15] Thise correction term $\bar{F}$ then has to be multiplied with the MPE to get the offset of the mean ELP and is defined as: $\bar{F} : \overline{0.0006 \cdot (IOLP^2 + 2 \cdot IOLP \cdot K)}$ where $\overline{()}$ refers to the arithmetic mean.

Very recently, Gatinel et al[25] published a complementary paper outlining a strategy to optimize formula constants in terms of minimizing the SDPE and RMSPE. This concept is based on the previous publication: to optimize for SDPE, the normalized covariance between the individual correction term and the individual refraction error is considered for the correction term, and to optimize for RMSPE the dot product between the individual correction term and the individual refraction error is used for the correction term for an offset correction to the start value of the ELP.[25]

- **THE PURPOSE OF THIS STUDY WAS:**
  - to evaluate the performance of both variants ([15] and [25]) of this simple optimization tool for four fully disclosed classical IOL power formulae and one nondisclosed modern lens power formula,
  - to compare the results of this simple strategy with the results of a direct iterative nonlinear optimization algorithm with variation of the start value of the formula constant, and
  - to show the clinical applicability using two large clinical datasets containing preoperative biometric data, the power of the implanted lens, and postoperative refractometry data.

METHODS

- **DATASET FOR OUR STUDY:** In this retrospective study, we analyzed two datasets. The first dataset contains measurements from 888 eyes (489 right and 397 left eyes) treated with the 1-piece hydrophobic aspherical (aberration correcting) monofocal intraocular Vivinex lens (Hoya Surgical, Singapore). The second dataset contains measurements from 821 eyes (415 right and 406 left eyes) treated with the 1-piece hydrophobic spherical monofocal intraocular SA60AT lens (Alcon). All eyes were treated with cataract surgery at the Augen- und Laserklinik Castrop-Rauxel, Castrop-Rauxel, Germany. The local Institutional Review Board (Ärztekammer des Saarlandes, registration number 157/21) provided a waiver for this study, and patient informed consent was not required for this study. The data were transferred to us in an anonymized fashion, which precludes back-tracing of the patient.

The anonymized data contained preoperative biometric data from the IOLMaster 700 (Carl-Zeiss-Meditec), including date of surgery and date of birth, axial length AL, anterior chamber depth ACD measured from the corneal epithelium to the anterior apex of the crystalline lens, the central thickness of the crystalline lens LT, the central corneal thickness CCT, the corneal front surface radius measured in the flat and steep meridians, the labeled refractive power of the lens IOLP, and the spherical equivalent of manual refraction as documented 5 to 12 weeks after cataract surgery by an experienced optometrist at a refraction lane distance of 6 m. To ensure the reliability of the postoperative refraction, the dataset included only data with a postoperative

Snellen decimal visual acuity of 0.8 (20/25 Snellen lines) or higher.

• **PREPROCESSING OF THE DATA:** The anonymized Excel data (.xlsx-format) were imported into MATLAB (Matlab 2022b, MathWorks) for further processing with a custom data processing code. The patient's age was derived from the date of cataract surgery and date of birth. The mean corneal radius R was derived as the harmonic mean of the radii of curvature in the flat and steep meridians, and the mean keratometric power K was calculated as the arithmetic mean of the keratometric power transferred from corneal radii in both cardinal meridians using a keratometer index as indicated in the respective lens power formulae.

The following lens power calculation formulae were considered in this constant optimization process:

- SRK/T formula published by Sanders et al,[4,5]
- Hoffer Q formula published by Hoffer,[6-8]
- Holladay 1 formula published by Holladay et al[9]
- Haigis formula in the simplified version,[10] and the
- Cooke K6 formula included as an example of a modern nondisclosed lens power formula, which is known to show excellent performance over the entire parameter range.[3]

The SRKT, Hoffer Q, and Holladay 1 formula consider the AL and R or K data together with one formula constant (A, pACD, and SF, respectively). The Haigis formula considers the AL, ACD, and R together with a formula constant triplet a0/a1/a2. For simplicity, we used the form of the Haigis formula with preset values for a1/a2 = 0.4/0.1, because the strategy of lens constant optimization described by Gatinel et al[15,25] is typically restricted to single constant formulae. For the Cooke K6 formula, we used a WEB API provided to us by the formula authors David and Tim Cooke. This implementation allows for block processing of a large dataset containing biometric data AL, ACD, LT, CCT, WTW, K, IOLP, and a preset A constant (AK6) and yields the respective formula-predicted postoperative refraction.

For all five formulae under test, we first derived the optimized formula constants using the iterative nonlinear sequential quadratic programming algorithm as described in previous papers[19,20,22,23] with the formula prediction error PE (defined as the difference between the formula prediction and the achieved postoperative SEQ) as the target parameter. Constant optimization was performed for zero MPE and minimal SDPE and RMSPE (indicated by $()_{MPE}$, $()_{SDPE}$, and $()_{RMSPE}$). A step size tolerance of 1e-10 and a function tolerance of 1e-12 were used as the stopping criteria for the algorithm. The performance metrics MPE, MEDPE, MAPE, MEDAPE, SDPE and RMSPE were derived for each of these formula constants for the SRK/T formula ($A_{MPE}/A_{SDPE}/A_{RMSPE}$), the Hoffer Q formula ($pACD_{MPE}/pACD_{SDPE}/pACD_{RMSPE}$), the Holladay 1 formula ($SF_{MPE}/SF_{SDPE}/SF_{RMSPE}$), the Haigis formula ($a0_{MPE}/a0_{SDPE}/a0_{RMSPE}$), and the K6 formula ($AK6_{MPE}/AK6_{SDPE}/AK6_{RMSPE}$).

The most relevant calculations from the simple constant optimization strategy from Gatinel et al[15,25] are summarized in the following paragraph for an easy step-by-step implementation:

1) We calculate the parameter F from the intraocular lens power IOLP and the keratometric power K for each data point in the dataset using:
   $F = 0.0006 \cdot (IOLP^2 + 2 \cdot K \cdot IOLP)$.
2) We define a start value for the optimization, either for an ACD (or equivalently for pACD, SF, a0) constant or for an A constant, and calculate the formula prediction error PE for each data point in the dataset for that start value ACD_{start} or A_{start}.
3) If we want to optimize an A constant (eg, for the SRK/T formula), A_{start} is converted into ACD_{start} based on the SRK/T formula[5] definition:
   $ACD_{start} = A_{start} \cdot 0.62467 - 68.747$.
4) To optimize the formula constant for a zero mean formula prediction error MPE we use the update function for the start value ACD_{start} to obtain the updated ACD constant $ACD_{updated}$:
   $ACD_{updated} = ACD_{start} - MPE/\overline{F}$, where $\overline{(.)}$ refers to the arithmetic mean of all (.) values in the dataset.
5) To optimize the formula constant for a minimal SD formula prediction error SDPE we use the update function for the start value ACD_{start} to obtain the updated ACD constant $ACD_{updated}$:
   $ACD_{updated} = ACD_{start} - \frac{\sum (F-\bar{F})\cdot(PE-\overline{PE})}{\sum (F-\bar{F})^2}$, where Σ refers to the sum over all data points in the dataset.
6) To optimize the formula constant for a minimal root mean squared formula prediction error RMSPE we use the update function for the start value ACD_{start} to obtain the updated ACD constant $ACD_{updated}$:
   $ACD_{updated} = ACD_{start} - \frac{\sum PE \cdot F}{\sum F^2}$.
7) Finally, (only for optimization of an A constant) we reconvert the updated ACD constant into an updated A constant based on the SRK/T formula[5] definition:
   $A_{updated} = \frac{ACD_{updated}+68.747}{0.62467}$.

In order to obtain some insight into the effect of mistuning the formula constant on the performance metrics, the starting formula constants were then varied in a range ±1.5 from their zero MPE optimized values, within 1000 equidistant steps on a linear scale and used as start values for the optimization strategy described by Gatinel et al[15,25] The metrics MPE, SDPE and RMSPE were calculated[26] for each formula and for each start value of the formula constant.

In the last stage, for each start value, and for each formula we predicted the correction term for the ELP and the respective optimized formula constant according to the papers of Gatinel et al[15] for zeroing the MPE and[25] for minimizing SDPE and RMSPE. These optimized formula con-

TABLE 1. Descriptive Statistics of the Dataset in Terms of Mean, Standard Deviation (SD), Median, and the Lower (quantile 2.5%) and Upper (quantile 97.5%) Boundaries of the 95% Confidence Interval

Explorative Description		AL in mm	ACD in mm	LT mm	CCT in mm	WTW in mm	K in D	PIOL in D	SEQ in D
Dataset 1: Hoya Vivinex ($N = 888$)	Mean	24.0980	3.1864	4.6176	0.5589	12.0334	43.5180	20.6223	–0.5612
	SD	1.4072	0.4081	0.4568	0.0361	0.5786	1.5006	3.7318	0.9239
	Median	23.9026	3.1848	4.5929	0.5588	12.0476	43.4763	21.00	–0.2500
	Quantile 2.5%	21.6757	2.3720	3.7333	0.4890	11.2650	40.6567	12.00	–2.5000
	Quantile 97.5%	27.3514	3.9435	5.5192	0.6258	12.8797	46.4324	27.50	0.5000
Dataset 2: Alcon SA60AT lens ($N = 821$)	Mean	23.1467	3.0434	4.6219	0.5557	12.0123	43,8971	22.7369	–0.4780
	SD	1.5107	0.3986	0.4120	0.0356	0.5713	1.5355	4.5956	0.7152
	Median	23.1800	3.0260	4.6100	0.5550	12.0102	43.6629	22.50	–0.2500
	Quantile 2.5%	20.4510	2.3060	3.8200	0.4850	11.2213	41.2601	13.50	–2.6250
	Quantile 97.5%	26.4297	3.8180	5.4200	0.6250	12.8864	47.5006	33.00	0.5000

Parameters listed are: axial length (AL), external phakic anterior chamber depth measured from the corneal front apex to the front apex of the crystalline lens (ACD), central lens thickness (LT), central corneal thickness (CCT), horizontal corneal diameter (WTW), corneal power converted with the Javal keratometer index $n_K = 1.3375$ (K), refractive power of the intraocular lens implant (PIOL), and the spherical equivalent power achieved 4 to 12 weeks after cataract surgery (SEQ).

stants were compared to the respective formula constants previously generated using the iterative nonlinear algorithm for zeroing the MPE (A_{MPE}, $pACD_{MPE}$, SF_{MPE}, $a0_{MPE}$, $AK6_{MPE}$), SDPE (A_{SDPE}, $pACD_{SDPE}$, SF_{SDPE}, $a0_{SDPE}$, $AK6_{SDPE}$), and RMSPE (A_{RMSPE}, $pACD_{RMSPE}$, SF_{RMSPE}, $a0_{RMSPE}$, $AK6_{RMSPE}$).

• **STATISTICAL ANALYSIS AND DATA PRESENTATION:** Data are listed descriptively in terms of the arithmetic mean, SD, median, and the lower and upper boundaries of the 95% confidence interval (2.5% and 97.5% quantiles). The distributions of the most relevant preoperative biometric data together with IOLP and the SEQ values are shown in raincloud plots (overlay of boxplot and kernel probability density function plot). The values for the formula constants optimized for MPE, SDPE, and RMSPE using the iterative method are listed for all formulae under test, and the performance of the simplified strategy to derive the optimized formula constants for MPE, SDPE, and RMSPE according to Gatinel et al are plotted as a function of the formula constant start values together with the performance metrics MPE, SDPE, and RMSPE.

RESULTS

Table 1 lists the descriptive data for the preoperative biometric measures together with the labeled lens power and the spherical equivalent of postoperative refraction for the two clinical datasets considered in our data analysis. Figure 1 uses raincloud plots to depict the distributions for AL, ACD, LT, CCT, the keratometric power K converted from corneal radius with the Javal keratometer index, IOLP, and SEQ for dataset 1 (Figure 1A), and dataset 2 (Figure 1B). From the 2 peaks configuration of the SEQ distribution, it can be seen that for both datasets some of the originally myopic eyes were planned for a myopic target refraction. The probability density function plots indicate that some of the parameters (especially AL, IOLP, and SEQ) are not normally distributed.

Table 2 lists the formula constants for the SRKT formula ($A_{MPE}/A_{SDPE}/A_{RMSPE}$), Hoffer Q formula ($pACD_{MPE}/pACD_{SDPE}/pACD_{RMSPE}$), Holladay 1 formula ($SF_{MPE}/SF_{SDPE}/SF_{RMSPE}$), the Haigis formula ($a0_{MPE}/a0_{SDPE}/a0_{RMSPE}$), and the Cooke K6 formula ($AK6_{MPE}/AK6_{SDPE}/AK6_{RMSPE}$) as derived using the iterative nonlinear sequential quadratic programming algorithm, together with the performance metrics MPE, MEDPE, MAPE, MEDAPE, SDPE and RMSPE derived using these optimized formula constants for both datasets.

Figure 2 displays the performance of the formula constant optimization strategy described by Gatinel et al for variation of the start value for the formula constant (shown on the abscissa) for dataset 1 (Figure 2A) and dataset 2 (Figure 2B). The 1st/2nd/3rd/4th/5th plot in both subfigures refers to the results for the SRK/T/Hoffer Q/Holladay 1/Haigis/K6 formulae respectively. The dotted blue/red/green lines refer to the formula constants directly optimized using the nonlinear iterative optimization algorithm for zero MPE/minimal SDPE/minimal RMSPE. The corresponding results from the optimization strategy described by Gatinel et al are displayed with the solid blue/red/green lines. At least when the variations of the constant start value from the directly optimized constant are small, the results of the simple optimization strategy described by Gatinel et al match quite well with the nonlinear iterative optimization algorithm for all 3 performance metrics. In addition, the performance

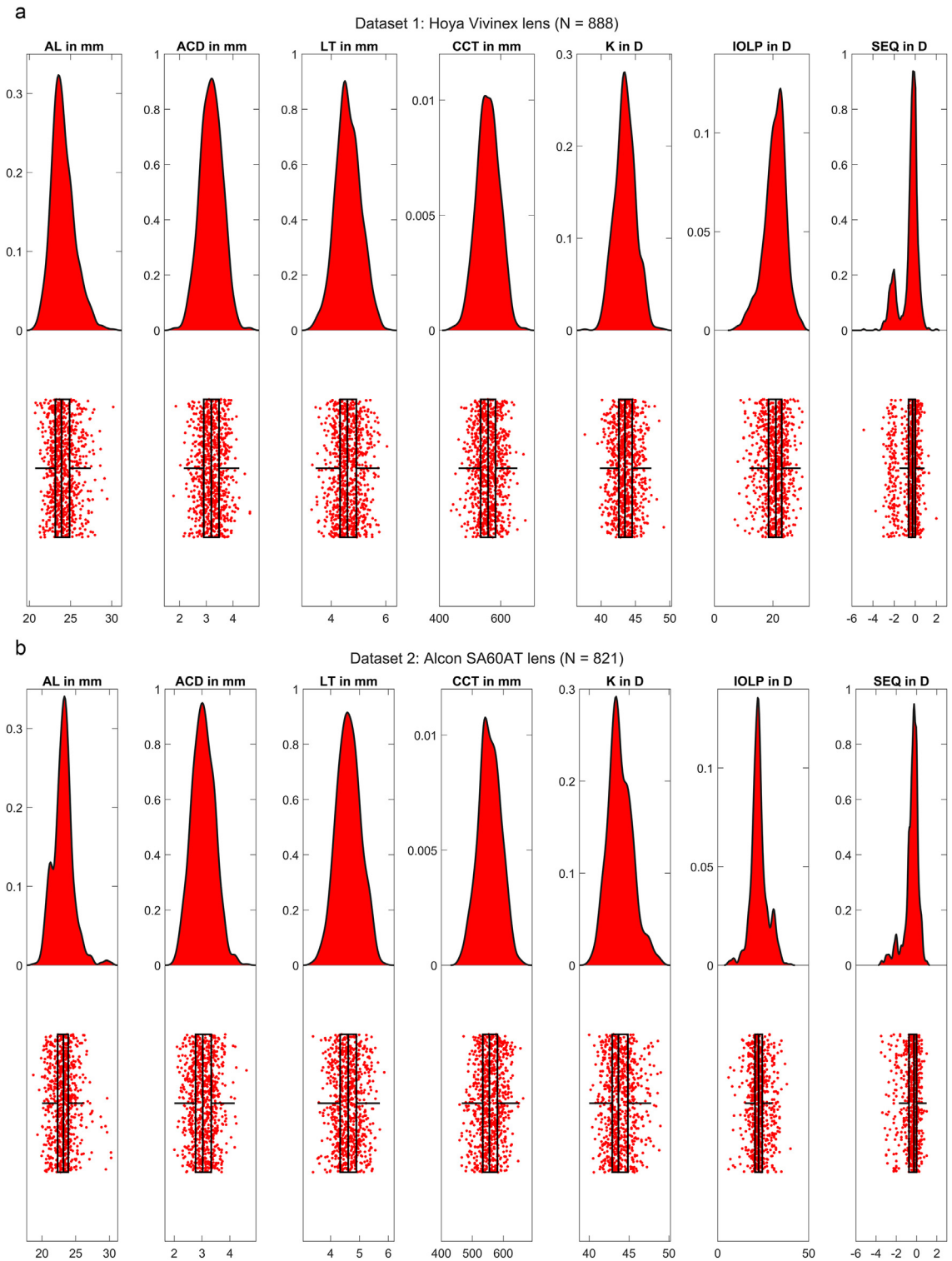

FIGURE 1. Raincloud plots of the most relevant preoperative biometric measures together with the labeled power of the lens implant (IOLP) and the spherical equivalent of the postoperative refraction (SEQ) for dataset 1 (A) and dataset 2 (B). The upper part of the graph shows the distribution of the parameter in terms of a probability density function, and the lower part the data scatter with a boxplot indicating the median and the 25%/75% quantile together with the 95% confidence interval. AL/ACD/LT/CCT/K refer to the axial length/anterior chamber depth/lens thickness/central corneal thickness/mean keratometric power converted from corneal radii using the Javal keratometer index respectively.

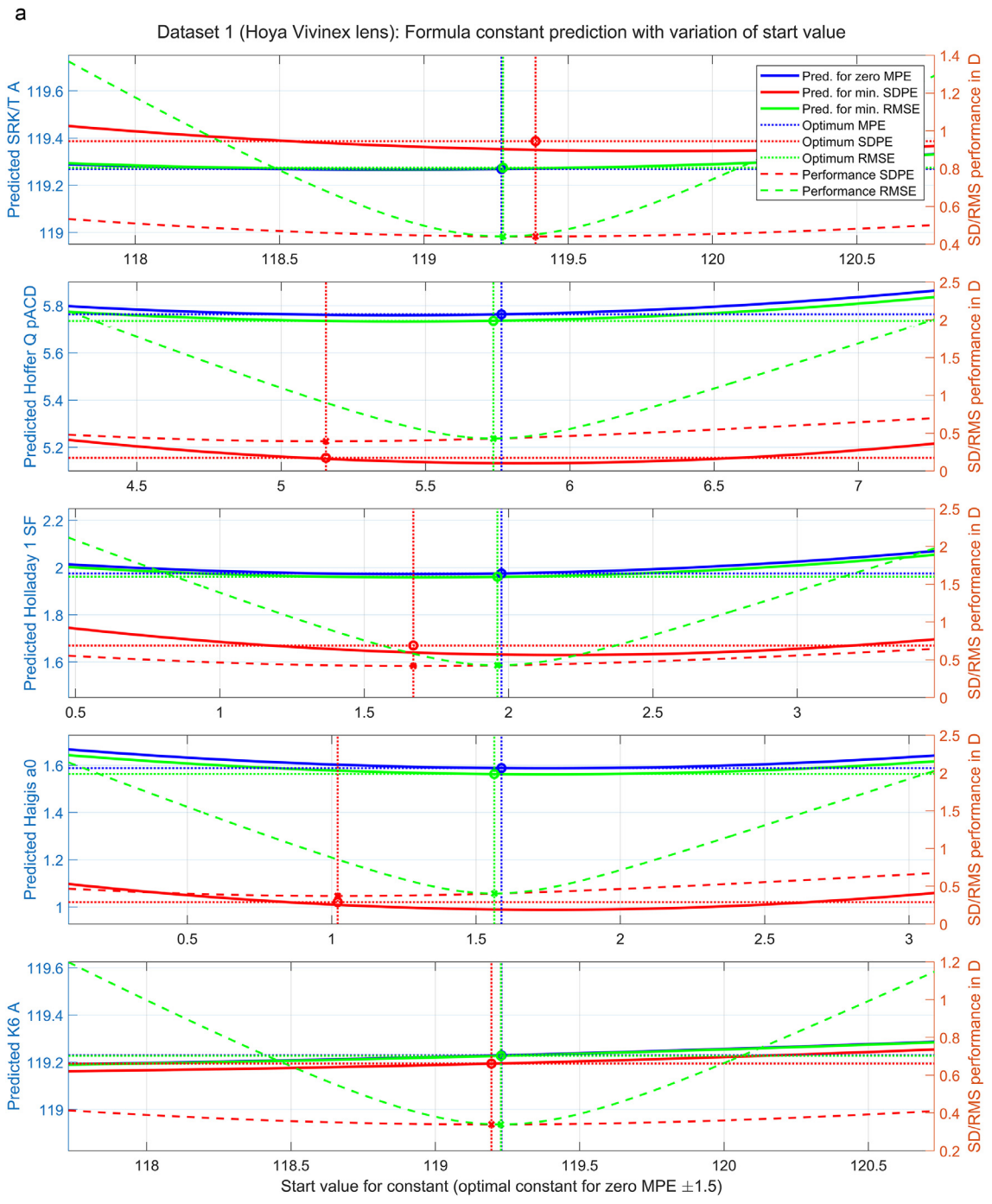

FIGURE 2. Performance of the formula constant optimization strategy described by Gatinel et al for variation of the start value for the formula constant (shown on the abscissa) for dataset 1 (A) and dataset 2 (B). The 1st/2nd/3rd/4th/5th plot in both subfigures refers to the results of the SRK/T/Hoffer Q/Holladay 1/Haigis/K6 formula. The dotted (vertical and horizontal) blue/red/green lines refer to the formula constant directly optimized using the nonlinear iterative optimization algorithm for zero MPE/minimal SDPE/minimal RMSPE. The corresponding result of the optimization strategy described by Gatinel et al is displayed with the solid blue/red/green lines. At least when the variations of the constant start value from the directly optimized constant are small, the results of the simple optimization strategy show a good match with the formula constant directly optimized with the nonlinear iterative optimization algorithm for all 3 performances metrics. In addition, the performance curves showing the SDPE and RMSPE values in diopters as functions of the formula constant have been added (red and green dashed lines, with scale on the right side). It can be seen directly from the performance curves that the RMSPE has a well-defined minimum, making it an appropriate metric for formula constant optimization, whereas the extremely flat SDPE curve would be unsuitable as a constant optimization metric, having a minimum that could be located far away from the formula constants optimized for MPE or RMSPE.

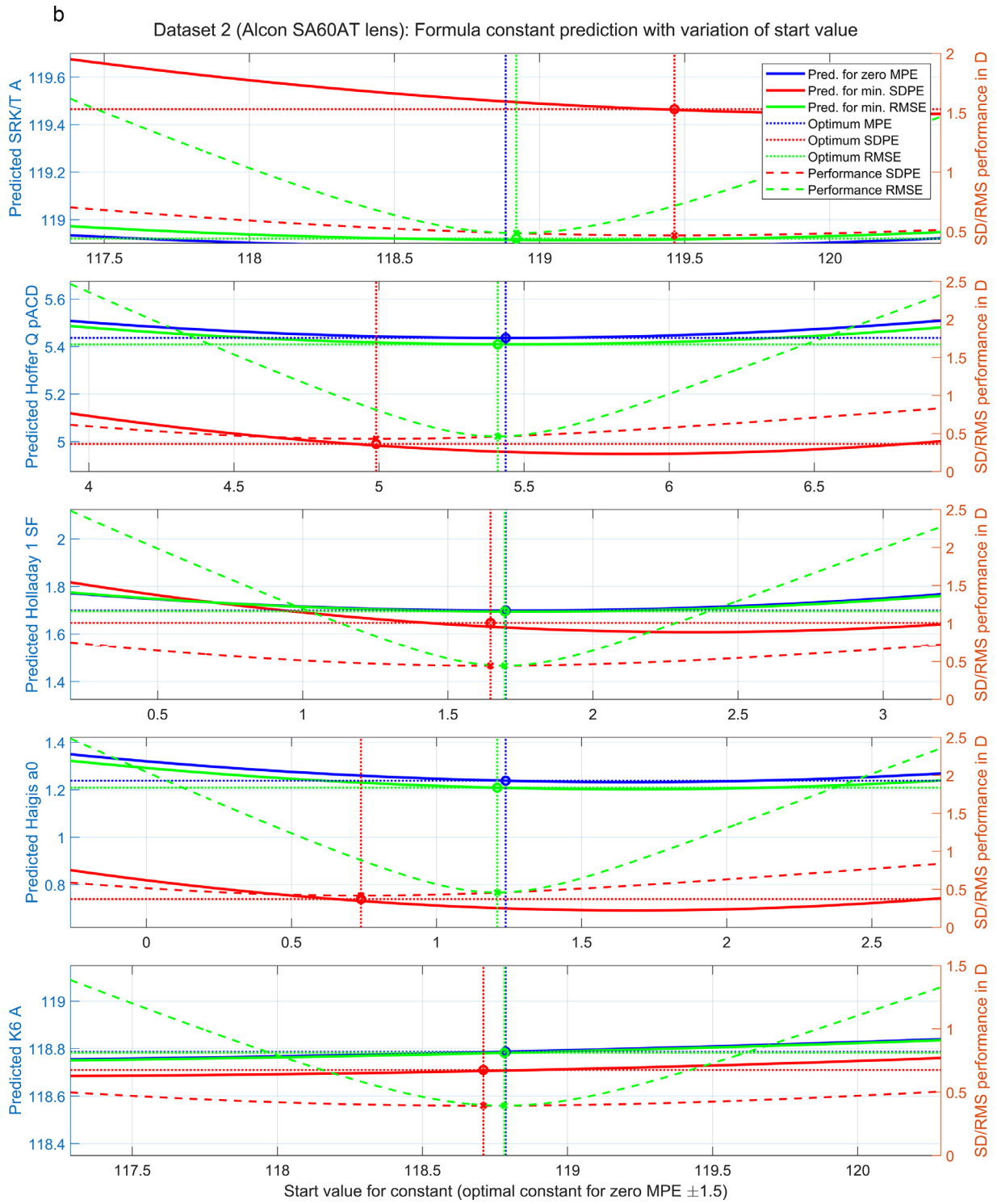

FIGURE 2. Continued

curves showing the SDPE and RMSPE values in diopters as functions of the formula constant have been added (red and green dashed lines, with scale on the right side). It can be seen directly from the performance curves that the RMSPE has a well-defined minimum, making it an appropriate metric for formula constant optimization, whereas the extremely flat SDPE curve would be unsuitable as constant optimization metric, having a minimum that could be located far away from the formula constants optimized for MPE or RMSPE. This is also well reflected in the lo-

TABLE 2. Formula Constants for the SRK/T, Hoffer Q, Holladay 1, Haigis (Preset Values a1 = 0.4 and a2 = 0.1) and K6 Formula Optimized for Zero Mean Prediction Error ($()_{MPE}$), Minimal Standard Deviation of Prediction Error ($()_{SDPE}$) and Minimal Root-Mean-Squared Prediction Error ($()_{RMSPE}$) Using The Iterative Nonlinear Optimization Technique Based on the Sequential Quadratic Programming (SQP) Algorithm Together With The Resulting Mean Prediction Error (MPE), Median Prediction Error (MEDPE), Mean Absolute Prediction Error (MAPE), Median Absolute Prediction Error (MEDAPE), Standard Deviation of the Prediction Error (SDPE), and Root Mean Squared Prediction Error (RMSPE) for Both Clinical Datasets

Dataset	Formula	Constant	Optimized Constant	MPE	MEDPE	MAPE	MEDAPE	SDPE	RMSPE
Dataset 1: Hoya Vivinex ($N = 888$)	SRK/T	A_{MPE}	119.2688	0.0000	–0.0143	0.3409	0.2760	0.4414	0.4414
		A_{SDPE}	119.3868	0.0962	0.0850	0.3485	0.2748	0.4409	0.4512
		A_{RMSPE}	119.2742	0.0044	–0.0097	0.3407	0.2729	0.4413	0.4413
	Hoffer Q	$pACD_{MPE}$	5.7631	0.0000	0.0117	0.3344	0.2599	0.4305	0.4305
		$pACD_{SDPE}$	5.1551	–0.8126	–0.8144	0.8206	0.8144	0.3924	0.9024
		$pACD_{RMSPE}$	5.7352	–0.0367	–0.0292	0.3326	0.2618	0.4273	0.4288
	Holladay 1	SF_{MPE}	1.9754	0.0000	0.0127	0.3273	0.2655	0.4260	0.4260
		SF_{SDPE}	1.6701	–0.4016	–0.4113	0.4739	0.4254	0.4168	0.5788
		SF_{RMSPE}	1.9613	–0.0183	–0.0043	0.3265	0.2669	0.4252	0.4256
	Haigis	$a0_{MPE}$	1.5880	0.0000	–0.0062	0.3175	0.2613	0.4056	0.4056
		$a0_{SDPE}$	1.0206	–0.7694	–0.7637	0.7761	0.7637	0.3709	0.8541
		$a0_{RMSPE}$	1.5631	–0.0333	–0.0336	0.3159	0.2535	0.4028	0.4041
	Cooke K6	$AK6_{MPE}$	119.2290	0.0000	0.0059	0.2618	0.2104	0.3395	0.3395
		$AK6_{SDPE}$	119.1943	–0.0255	–0.0202	0.2622	0.2134	0.3394	0.3404
		$AK6_{RMSPE}$	119.2271	–0.0014	0.0044	0.2618	0.2098	0.3395	0.3395
Dataset 2: Alcon SA60AT lens ($N = 821$)	SRK/T	A_{MPE}	118.8833	0.0000	0.0181	0.3718	0.2983	0.4881	0.4635
		A_{SDPE}	119.4649	0.5425	0.5564	0.5991	0.5670	0.4293	0.8108
		A_{RMSPE}	118.9199	0.345	0.0547	0.3721	0.2980	0.4597	0.4615
	Hoffer Q	$pACD_{MPE}$	5.4364	0.0000	0.0074	0.3612	0.3080	0.4635	0.4635
		$pACD_{SDPE}$	4.9902	–0.6879	–0.6822	0.7087	0.6822	0.4293	0.8108
		$pACD_{RMSPE}$	5.4091	–0.0416	–0.0324	0.3593	0.3015	0.4597	0.4615
	Holladay 1	SF_{MPE}	1.6993	0.0000	0.0018	0.3437	0.2808	0.4440	0.4440
		SF_{SDPE}	1.6471	–0.0788	–0.0756	0.3482	0.2884	0.4435	0.4505
		SF_{RMSPE}	1.6960	–0.0049	–0.0023	0.3337	0.2796	0.4439	0.4440
	Haigis	$a0_{MPE}$	1.2382	0.0000	–0.0006	0.3661	0.3015	0.4610	0.4610
		$a0_{SDPE}$	0.0795	–0.7795	–0.7726	0.7874	0.7726	0.4184	0.8847
		$a0_{RMSPE}$	1.2090	–0.0450	–0.0441	0.3644	0.3060	0.4564	0.4587
	Cooke K6	$AK6_{MPE}$	118.7869	0.0000	0.0065	0.3098	0.2693	0.3934	0.3934
		$AK6_{SDPE}$	118.7101	–0.0647	–0.0555	0.3129	0.2595	0.3930	0.3983
		$AK6_{RMSPE}$	118.7825	–0.0037	0.0030	0.2597	0.2597	0.3934	0.3934

cations of the blue/red/green vertical or horizontal dotted lines which mark the formula constant directly optimized with the nonlinear iterative optimization algorithm for zero MPE/minimal SDPE/minimal RMSPE: the best formula constant for zero MPE closely matches the best constant for minimal RMSPE for all formulae under test (deviation less than 0.05), whereas the best formula constant for minimal SDPE could deviate by up to 0.6.

DISCUSSION

Correct and accurate formula constants are crucial for the performance of lens power calculation in cataract surgery.[12-14,16-18,24] In the best case, the formula constants should be optimized on a dataset of representative patients having similar ethnic characteristics, the same (optical) biometer, comparable surgical technique and the same type of postoperative refractometry (eg, lane distance) in order to provide the best predictability of the lens power calculation result.[19,20,22,23] These constants are optimized considering the preoperative biometry, the power of the implanted lens, and postoperative refraction data. In most disclosed lens power formulae, the constant interacts directly with the ELP. This is a theoretical parameter describing the axial position of a thin lens implant with respect to the corneal front apex and does not necessarily correspond to the real geometrical axial position of the lens.[27-29] With an increase of the formula constant, the average lens power increases

and this could compensate for a hyperopic outcome after surgery, whereas with a decrease of the constant the average lens power will decrease and this could compensate a myopic outcome after cataract surgery. We know that a systematic shift in ELP (eg, by tuning the formula constant) has a larger effect on the refraction in short eyes (where high-powered IOLs are implanted) as compared to longer eyes (where low-powered IOLs are implanted).[19] Therefore, systematically shifting the ELP through optimization of the formula constant might, in general, not be the best option to shift the resulting refraction after cataract surgery (if the characteristics of the distribution of SEQ are required to remain unchanged).[19,20] Therefore, some modern IOLP calculation concepts (eg, the Olsen[27-29] or Castrop[21] formulae) try to overcome this issue by using formula constants which do not directly interact with the ELP by a fixed offset.

However, most of the single constant formulae in clinical use, such as the SRK/T,[4,5] Hoffer Q,[6-8] Hoffer QST,[2] Holladay 1,[9] Barrett Universal II, Cooke K6,[3] EVO,[3] and many others use formula constants such as A, pACD, ACD, SF, LF which are directly linked to the axial lens position. And even in those formulae that use more than one constant, one of the formula constants can be directly related to an axial shift in the lens position, for example, the a0 in the Haigis[10] or the H in the Castrop formula.[21] This means that with appropriate preset values of the other formula constants (a1 and a2 for Haigis or C and R for Castrop), the simplified strategy described by Gatinel et al[15,25] could be used to predict the formula constant optimized for zero MPE or minimal SDPE or RMSPE.

In this paper, we used the simplified method described by Gatinel et al[15] to estimate the offset required to correct the mean effective axial lens position from a start value to update the constant for a zero MPE, or a minimal SDPE or RMSPE.[25] The concept of zeroing the MPE uses the arithmetic mean of the IOLP and K in our dataset together with the MPE to define this offset. In the case of formulae using constants such as pACD, ACD, SF of LF this offset could be directly added to obtain the optimized constant, whereas for formulae using an A constant a conversion from the offset to a change in the A constant is required.[15,25] Calculating the proper value for mean K in the dataset could be challenging.[26] In fully disclosed formulae, the keratometer index is well known, but in undisclosed formulae the conversion from corneal radius to corneal power is not known, and the conversion might not be fully described by a simple keratometer index. The strategy of optimization for minimal SDPE or RMSPE described by Gatinel et al[25] is slightly different: instead of the MPE and an overall correction term, we use the normalized covariance term of the individual correction term and the PE (for SDPE optimization) or the normalized dot product of the individual correction term and the PE (for RMSPE optimization). Optimizations for SDPE and RMSPE could be performed directly on the basis of the start value of the formula constant, or alternatively using the constant derived from an optimization for zero MPE as performed in the paper of Gatinel et al[25] When using the latter strategy, a new calculation of the PE and the correction terms for SDPE and RMSPE for the result of the constant optimization for zero MPE is required, and this could be time-consuming especially with undisclosed formulae where only WEB calculators which do not allow block processing may be available.

Our results, based on two large clinical dataset with preoperative biometric data, labeled lens power data, and postoperative manual refraction data after cataract surgery with implantation of commonly used monofocal 1-piece hydrophobic lenses, show that the optimization works surprisingly well for all 3 metrics. From Figure 2, we see that the estimation of the optimized constant is very close to the best constant derived from a direct formula constant optimization using a nonlinear iterative optimization method, as used as the gold standard with a proof of concept with many datasets in the past.[19-23,26] This means that if an iterative optimization strategy is not available or if we would like to implement a constant optimization in any consumer software such as Excel, this method of optimizing constants for zero MPE or minimal SDPE or RMSPE provides excellent results even when the start value is somewhat offset from the best constant. However, this graph also shows that if we use the formula constant which is for example, optimized with a nonlinear iterative method for minimal SDPE as start value (crossing of the red dotted lines), the simplified method described by Gatinel et al[25] gives for both datasets with some formulae a small nonzero correction term (distance between the crossing of both red dotted lines from the solid red line). In contrast, for the optimization of zero MPE or minimal RMSPE, the correction term equals zero for both datasets and all formulae under test if we use the respective formula constants derived from nonlinear iterative optimization as a starting value (crossing of the blue or green dotted lines matches to the blue or green solid lines). This means that applying the simplified method described by Gatinel et al[15,25] iteratively will result in the exact value for the formula constants optimized with the gold standard for zero MPE or minimal RMSPE, but not with the gold standard for minimal SDPE.

However, as already discussed in our previous papers[19,20,22,23] and confirmed by the recent paper of Gatinel et al,[25] optimization of the formula constant for minimal SDPE cannot be recommended at all for clinical purposes! Figure 2 clearly shows that the optimized formula constants for zero MPE and minimal RMSPE are quite close together for all formulae in both datasets under test (dotted blue and green lines). By contrast, the optimized constant for minimal SDPE could be completely off for some formulae with both datasets: for example, with the Vivinex lens in dataset 1, the pACD, SF, and a0 constant are systematically lower and the A constant is systematically higher than the constants derived using zero MPE or minimal RMSPE, whereas in the K6 formula all constants match. In contrast, with the

SA60AT lens in dataset 2, the pACD and a0 constant are systematically lower, the SF and AK6 constant are slightly lower, and the A constant is systematically higher than the respective constants for zero MPE or minimal RMSPE. Using the optimization for minimal SDPE could therefore cause a large offset in the refractive outcome toward myopia (when the constants for minimal SDPE are higher) or toward hyperopia (when the constants for minimal SDPE are lower).

However, our study has some limitations: Firstly, we restricted the study to presenting the results based on two clinical datasets with commonly used modern intraocular lens models. In both datasets, the optimization strategy of Gatinel et al[15,25] shows excellent performance, but we cannot generalize this to other lens models or other datasets (eg, where other biometers are used). Secondly, we restricted the study to a variation of the start value of the formula constant of up to ±1.5 from the constant optimized for zero MPE. In future studies, we would aim to validate the simplified optimization with start values having larger offsets from the optimized formula constant. Thirdly, this simplified optimization strategy requires keratometric power data as used in the lens power formula, but for undisclosed lens formulae, the conversion from corneal radii to keratometric power is not known and might not be described by a simple keratometer index. Fourthly, for both datasets (from the same clinic) the IOLMaster 700 was used as biometer. Therefore, further studies are needed to assess the performance of the simplified optimization with other biometers or other study populations.

In conclusion, this paper shows that for most of the single constant formulae involving formula constants linked to the ELP there is a simple technique of estimating the optimized formula constant. This technique can use zero mean PE, minimal SD, or root-mean-square of the PE as a metric and is based on the labeled lens power, keratometric corneal power, and a start value for the formula constant with the respective formula PE. Of these, zero mean PE and minimal root-mean-squared error showed excellent performance and would be recommended in preference to minimal SD error. This simple technique can be applied to disclosed and nondisclosed formulae and can be easily implemented in any consumer software in situations where a direct iterative nonlinear optimization strategy is unavailable.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Achim Langenbucher: Writing – original draft, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Nóra Szentmáry:** Visualization, Validation, Methodology, Conceptualization. **Jascha Wendelstein:** Validation, Supervision, Methodology, Investigation, Conceptualization. **Alan Cayless:** Writing – original draft, Supervision, Project administration, Investigation. **Peter Hoffmann:** Validation, Supervision, Methodology, Formal analysis. **Damien Gatinel:** Visualization, Validation, Methodology, Investigation, Formal analysis.

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