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ORIGINAL ARTICLE

Performance of a simplified strategy for formula constant optimisation in intraocular lens power calculation

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Abstract

Purpose: To investigate the performance of a simple prediction scheme for the formula constants optimised for a mean refractive prediction error.

Methods: Analysis based on a dataset of 888 eyes before and after cataract surgery with IOL implantation (Hoya Vivinex). IOLMaster 700 biometric data, power of the implanted lens and postoperative spherical equivalent refraction were used to calculate the optimised constants $(.)_{opt}$ for SRKT, HofferQ, Holladay and Haigis formula with an iterative nonlinear optimisation. For detuning start values by ±1.5 from $(.)_{opt}$, the predicted formula constants $(.)_{pred}$ were calculated and compared with $(.)_{opt}$. Formula performance metrics mean (MPE), median (MEDPE), mean absolute (MAPE), median absolute (MEDAPE), root mean squared (RMSPE) and standard deviation (SDPE) of the formula prediction error were analysed for $(.)_{opt}$ and $(.)_{pred}$.

Results: $(.)_{pred} - (.)_{opt}$ showed a 2nd order parabolic behaviour with maximal deviations up to 0.09 at the tails of detuning and a minimal deviation up to −0.01 for all formulae. The performance curves of different metrics of PE as functions of detuning variations show that the formula constants for zeroing MPE and MEDPE yield almost identical formula constants, optimisation for MAPE, MEDAPE and RMSPE yielded formula constants very close to $(.)_{opt}$, and optimisation for SDPE could result in formula constants up to 0.5 off $(.)_{opt}$ which is unacceptable for clinical use.

Conclusion: This simple prediction scheme for formula constant optimisation for zero mean refraction error performs excellently in our monocentric dataset, even for larger deviations of the start value from $(.)_{opt}$. Further studies with multicentric data and larger sample sizes are required to investigate the performance in a clinical setting further.

KEYWORDS

constant optimisation, formula constant, formula constant prediction, IOL power formula, paraxial calculation

1 | BACKGROUND

The individual refractive power of an intraocular lens implant (IOL) for the replacement of the opaque crystalline lens during cataract surgery is calculated based on the preoperative biometric data and the target refraction (Hoffer & Savini, 2020; Savini et al., 2020). In most cases, paraxial calculation schemes are used in terms of a matrix or vergence calculation. The formulae are designed to fit various lens specifications, including the optical and mechanical material characteristics and the design of the IOL optics and haptics (Aristodemou et al., 2011; Behndig et al., 2014; El-Khayat & Tesha, 2021; Gatinel, Debellemanière, Saad, Wallerstein, et al., 2023). Formula constants are used to customise these calculation schemes to the specifications of individual lens types. These constants are typically optimised post hoc based on the preoperative biometric measures, the power

of the implanted IOL and the postoperative refraction 1 to 3 months after cataract surgery (Aristodemou et al., 2011 Gatinel, Debellemanière, Saad, Wallerstein, et al., 2023; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021; Zhang et al., 2019).

While there are several strategies of formula constant optimisation, there are no common standards or guidelines on how to optimise formula constants in a clinical setup (Aristodemou et al., 2011; Galvis et al., 2013; Gatinel, Debellemanière, Saad, Rampat, et al., 2023; Langenbucher et al., 2022; Langenbucher, Hoffmann, et al., 2023; Langenbucher, Szentmáry, et al., 2023b; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021; Norrby & Koranyi, 1997; Olsen, 2006; Olsen & Hoffmann, 2014; Sardari et al., 2023; Shrivastava et al., 2021; Zhang et al., 2019). In general, as a first step, both the target parameter (e.g. the formula prediction error PE) and the metrics (e.g. zeroing the mean PE or minimising the root-mean squared PE) should be defined. The next step involves finding a proper mathematical strategy for the optimisation process. For instance, solving the IOL calculation formula for the formula constant generates an individual constant for each data point, meaning that any statistical metric, such as the arithmetic mean or the median, could be used to find the best formula constant. However, we have to be aware that this simple procedure cannot be used to optimise constants in formulae with more than one constant or with an arbitrary target parameter or optimisation metric. Iterative nonlinear optimisation strategies are much more powerful, and they work for formulae with one or more constants as well as those with arbitrary target parameters and optimisation metrics. However, their implementation can be somewhat tricky (Langenbucher et al., 2022; Langenbucher, Hoffmann, et al., 2023; Langenbucher, Szentmáry, et al., 2023b; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021). Furthermore, both of these strategies can only be applied if the internal structure of the IOL calculation formula has been disclosed. Fortunately, new optimisation techniques have been developed in the last decade that are fully data-driven and do not require knowledge of the internal architecture of the IOL calculation formula. These newer optimisation techniques, such as Particle Swarm Optimisation (Langenbucher, Szentmáry, et al., 2023a) or Surrogate Model Optimisation, are mostly adapted from machine learning applications. A black box implementation of the formula with preoperative biometric data, formula constant(s) and the IOL power (IOLP) as input parameters and the predicted refraction as output parameter are fully sufficient to drive those algorithms (Langenbucher, Szentmáry, et al., 2023a).

Within the last two decades, increasing numbers of new IOL calculation formulae have been released into the clinical community. On the one hand, these newer formulae promise superior performance, but since most are not fully disclosed (Aristodemou et al., 2011; Savini et al., 2020; Zhang et al., 2019), classical constant optimisation strategies cannot be applied. Simple techniques that help the clinician estimate the best formula constant for a specific dataset are highly welcome. Especially in the early stages following the launch of new IOL, the absence of reliable formula constants published, for example on WEB platforms such as IOLCon, means that surgeons have to find simple ways to generate a proper formula constant from their clinical results to operate these formulae. Just as with the classical SRKT, HofferQ, Holladay1 or Haigis formula, most of these formulae modulate the effective lens position (ELP) to shift the overall predicted refraction towards plus (hyperopia) or minus (myopia) (Norrby & Koranyi, 1997; Olsen, 2006; Olsen & Hoffmann, 2014).

Recently, Damien Gatinel and his group published an article in which they outlined a concept to estimate the overall shift in the mean ELP (ELP_{mean}) of a study population necessary to zero the overall refractive error (Gatinel, Debellemanière, Saad, Rampat, et al., 2023). According to this simple rule of thumb, ELP_{mean} has to be modified by the factor $0.006 \cdot (PIOL_{mean}^2 + 2 \cdot K_{mean} \cdot PIOL_{mean})$, where $PIOL_{mean}$ and K_{mean} refer to the arithmetic means of IOLP and K, respectively. If the conversion from a shift in ELP to a shift in the formula constant were known, it would be possible to directly optimise formula constants based on the mean of the postoperative spherical equivalent refraction (SEQ), K_{mean} and $PIOL_{mean}$ (Gatinel, Debellemanière, Saad, Rampat, et al., 2023).

The *purpose of this study* was to evaluate the performance of this simple optimisation tool for four fully disclosed classical IOL power formulae using a large clinical dataset containing preoperative biometric data, the power of the implanted lens and postoperative refractometry data. This performance can be expressed as a function of the disparity between the preset value for the formula constant and the formula constant optimised using a well-established iterative nonlinear optimisation strategy used to zero the mean prediction error.

2 | METHODS

2.1 | Dataset for our study

In this retrospective study, we analysed a dataset containing measurements from 888 eyes from a cataract population from Augen- und Laserklinik Castrop-Rauxel, Castrop-Rauxel, Germany, which were anonymously transferred to us (490 right eyes and 398 left eyes; 495 female and 392 male). The mean age was 71.2 ± 9.1 years (median: 71 years, range: 47 to 91 years). 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 anonymised fashion, which precludes backtracing of the patient.

The anonymised data contained preoperative biometric data derived with the IOLMaster 700 (Carl-Zeiss-Meditec, Jena, Germany), including: axial length AL, anterior chamber depth ACD measured from the corneal front apex to the anterior apex of the crystalline lens and

the corneal front surface radius measured in the flat (R1) and steep (R2) meridians. In all cases, a Vivinex 1-piece hydrophobic aspherical (aberration correcting) monofocal intraocular lens (Hoya Surgical Optics, Singapore) was inserted. In addition to the refractive power of the inserted lens IOLP, the spherical equivalent SEQ of the postoperative refraction 5 to 12 weeks after cataract surgery was documented 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. The descriptive data on biometric data before cataract surgery, IOLP and postoperative SEQ are summarised in Table 1.

2.2 | Preprocessing of the data

The anonymised Excel data (.xlsx-format) was imported into MATLAB (Matlab 2022b, MathWorks, Natick, USA) for further processing with a custom data processing code. The patient's age was derived from the date of cataract surgery and the date of birth. The corneal powers in the flat and steep corneal meridians ($K1=(n_K\text{-}1)/R1$ and $K2=(n_K\text{-}1)/R2$) were calculated from the corneal front surface radii R1 and R2 using a keratometer index n_K as indicated in the formula definition. The mean corneal power K was derived from ½(K1 + K2), and the mean corneal radius of curvature R was calculated as $R=(n_K\text{-}1)/K$. The following lens power calculation formulae were considered in this constant optimisation process:

- SRKT formula published by Sanders, Retzlaff and Kraff (Retzlaff et al., 1990; Sanders et al., 1990),
- HofferQ formula published by Hoffer (Hoffer, 1980, 1981, 1993),
- Holladay 1 formula published by Holladay and Prager (Holladay et al., 1988) and the
- Haigis formula (Haigis et al., 2000).

The SRKT, HofferQ and Holladay 1 formulae 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 and without loss of generality, we used the simplified form of the Haigis formula with preset values for a1/a2 = 0.4/0.1, as typically used where only a limited number of clinical results are available for formula constant optimisation.

For all four formulae, we derived the optimised formula constants using the prediction error PE as the target parameter. The mean value was chosen as the metric and zeroed using the iterative nonlinear sequential quadratic programming algorithm (SQP) as described in a previous paper (Langenbucher et al., 2022; Langenbucher, Szentmáry, et al., 2023a, 2023b; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021; Langenbucher, Szentmáry, Cayless, Weisensee, et al., 2021). A step size tolerance of 1e-10 and a function tolerance of 1e-12 were used as the stopping criteria for the algorithm. With these formula constants A_{opt}, $pACD_{opt}$, SF_{opt} and $a0_{opt}$ the performance metrics mean PE (MPE), median PE (MEDPE), mean absolute PE (MAPE), median absolute PE (MEDAPE), root mean squared PE (RMSPE) and the standard deviation of PE (SDPE) were derived.

We then varied the formula constants in a range ± 1.5 from the optimised formula constants $(.)_{opt}$ within 1000 equidistant steps on a linear scale (e.g., A_{opt}-range in steps of 2/999·range to A_{opt} + range) indicated as start values $(.)_{start}$. To obtain some insight into the effect of mistuning the formula constant on the performance metrics, for each formula and each start value of the formula constant, the performance metrics MPE, MEDPE, MAPE, MEDAPE, RMSPE and SDPE were calculated.

In a last step, we predicted the optimised formula constants $(.)_{pred}$ according to the correction factor published by Gatinel, Debellemanière, Saad, Rampat, et al. (2023) using the conversion from ELP to the formula constant (1/0.62467 for the SRKT (Retzlaff et al., 1990; Sanders et al., 1990) and 1.0 for the HofferQ (Hoffer, 1980, 1981, 1993), Holladay (Holladay et al., 1988) and Haigis (Haigis et al., 2000) formulae). The optimised formula constants $(.)_{pred}$ were compared to the formula constants optimised with the iterative nonlinear algorithm for zeroing the mean PE $(.)_{opt}$.

2.3 | Statistical analysis and data presentation

Data are listed descriptively using the arithmetic mean, standard deviation (SD), median and the lower and

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.

N = 888	AL in mm	ACD in mm	R1 in mm	R2 in mm	R	K in dpt	PIOL in dpt	SEQ in dpt
Mean	24.0980	3.1864	7.8598	7.6732	7.7665	43.5180	20.6222	−0.5612
SD	1.4172	0.4081	0.2828	0.2745	0.2682	1.5006	3.7318	0.9239
Median	23.9026	3.1848	7.8473	7.6735	7.7654	43.4763	21.0	−0.2500
Quantile 2.5%	21.6757	2.3720	7.3335	7.1329	7.7654	40.6567	12.0	−2.5
Quantile 97.5%	27.3514	3.9435	8.4284	8.2152	8.3025	46.4324	27.5	0.5

Note: 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), corneal radii of curvature in the flat and steep meridians (R1 and R2, respectively), harmonic average of R1 and R2 (R), 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).

TABLE 2 Formula constants for the SRKT, HofferQ, Holladay and Haigis formulae (preset values a1 = 0.4 and a2 = 0.1) optimised using the iterative nonlinear optimisation technique based on the sequential quadratic programming (SQP) algorithm together with the mean prediction error (MPE), median prediction error (MEDPE), mean absolute prediction error (MAPE), median absolute prediction error (MEDAPE), root mean squared prediction error (RMSPE) and the standard deviation of the prediction error (SDPE) for the dataset with $N = 888$ eyes implanted with the Hoya Vivinex aspheric intraocular lens.

Data in dpt formula	Optimised formula constant	MPE	MEDPE	MAPE	MEDAPE	RMSPE	SDPE
SRKT A_{opt}	119.2697	0.0000	0.0143	0.3408	0.2574	0.4412	0.4414
Hoffer Q $pACD_{opt}$	5.7638	0.0000	−0.0115	0.3346	0.2612	0.4305	0.4307
Holladay SF_{opt}	1.9762	0.0000	−0.0130	0.3277	0.2659	0.4262	0.4265
Haigis $a0_{opt}$	1.5884	0.0000	0.0071	0.3173	0.2618	0.4053	0.4055

upper boundaries of the 95% confidence interval (2.5% and 97.5% quantiles). Values of A_{pred}, $pACD_{pred}$, SF_{pred} and $a0_{pred}$ based on the simplified concept published by Gatinel et al. are displayed as functions of $(.)_{start}$ together with the performance metrics MPE, MEDPE, MAPE, MEDAPE, RMSPE and SDPE for $(.)_{start}$.

3 | RESULTS

Table 2 lists the formula constants for the SRKT formula (A_{opt}), HofferQ formula ($pACD_{opt}$), Holladay formula (SF_{opt}) and Haigis formula ($a0_{opt}$) with preset values a1 = 0.4 and a2 = 0.1 derived using the iterative nonlinear SQP algorithm, together with the performance metrics MPE, MEDPE, MAPE, MEDAPE, RMSPE and SDPE derived with these optimised formula constants.

In Figure 1, the predicted formula constants $(.)_{pred}$ are displayed (solid blue line) together with the formula constants optimised with the iterative nonlinear optimisation ($(.)_{opt}$, dash-dotted blue line, both refer to the left-hand Y axis) for variations of $(.)_{start}$ (X-axis) in a range from −1.5 to 1.5 around $(.)_{opt}$ (A_{opt}, $pACD_{opt}$, SF_{opt} or $a0_{opt}$, respectively) together with the performance metrics MPE, MEDPE, MAPE, MEDAPE, RMSPE and SDPE as functions of $(.)_{start}$ (all refer to the right-hand Y axis).

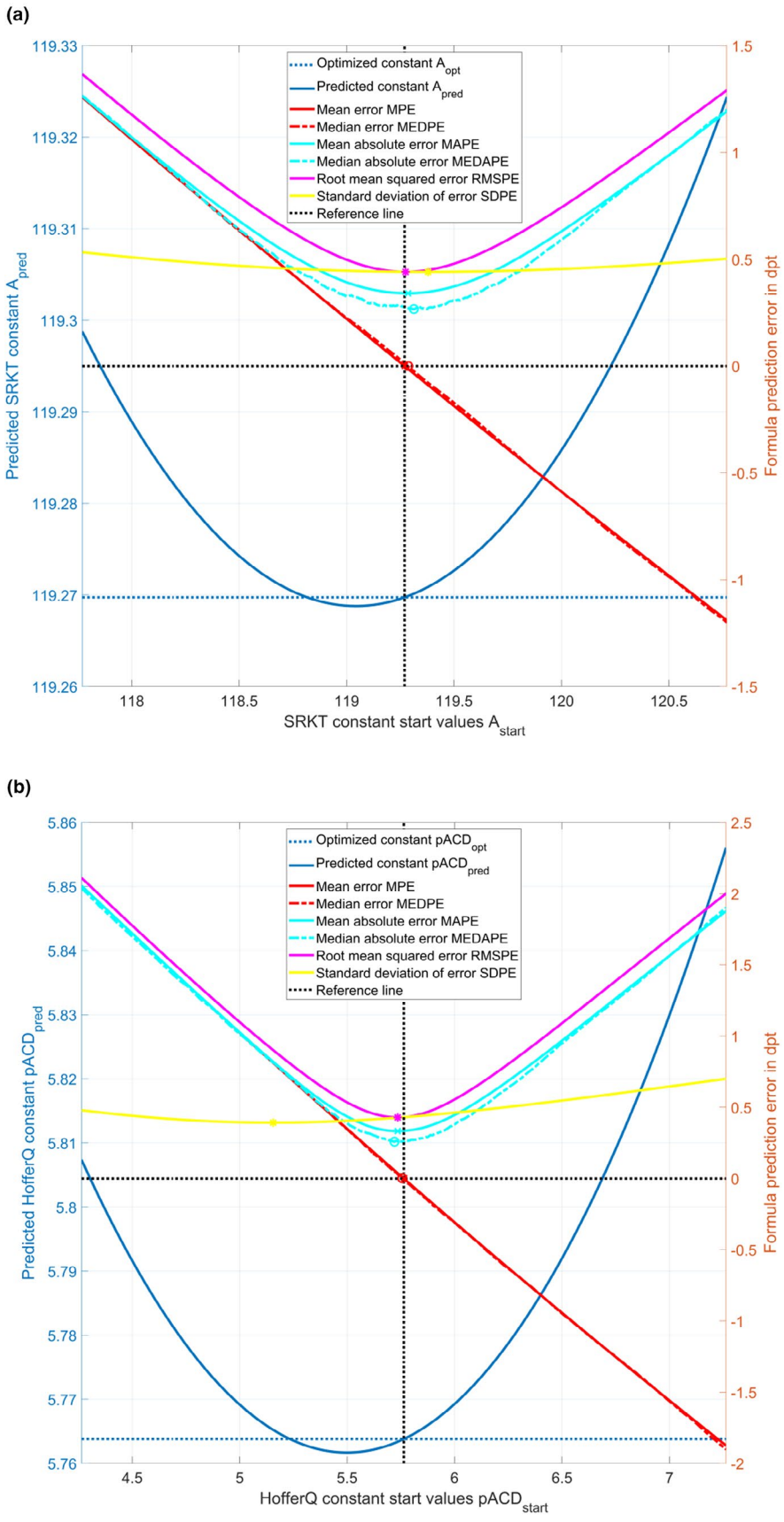
In Figure 1a, the conditions are shown for the SRKT formula. We see that A_{pred} slightly overestimates A_{opt} to both tails of A_{start} (by around 0.03 for A_{opt} – 1.5 and 0.06 for A_{opt} + 1.5). For A_{start}, between 118.8 and Aopt, A_{pred} very slightly underestimates A_{opt}. We also see from the graph that the formula constants for zero MPE (red cross mark) and MEDPE (red circle mark), and minimal MAPE (cyan cross mark) and RMSPE (magenta asterisk mark) are all very close to A_{opt}. In contrast, the formula constant for the minimal MEDAPE (cyan circle mark)/SDPE (yellow asterisk mark) slightly/systematically overestimate A_{opt}, as indicated by the vertical, dashed black reference line.

In Figure 1b, the conditions are shown for the HofferQ formula. We see that $pACD_{pred}$ slightly overestimates $pACD_{opt}$ to both tails of $pACD_{start}$ (by around 0.04 for $pACD_{opt}$ – 1.5 and 0.09 for $pACD_{opt}$ + 1.5). For $pACD_{start}$ between 5.23 and $pACD_{opt}$ $pACD_{pred}$ very slightly underestimates $pACD_{opt}$. We also see from the graph that the formula constants for zero MPE (red cross mark) and MEDPE (red circle mark) are very close to $pACD_{opt}$. In contrast, the formula constants for minimal MAPE (cyan cross mark), MEDAPE (cyan circle mark) and RMSPE (magenta asterisk mark) slightly underestimate $pACD_{opt}$ and the formula constant for minimal SDPE (yellow asterisk mark) is around 0.6 lower than $pACD_{opt}$, as indicated by the vertical, dashed black reference line.

In Figure 1c, the conditions are shown for the Holladay formula. We see that SF_{pred} slightly overestimates SF_{opt} to both tails of SF_{start} (by around 0.04 for $pACD_{opt}$ – 1.5 and by around 0.08 for SFD_{opt} + 1.5). For SF_{start} between 1.6 and SF_{opt}, we observe a very slight underestimation of $pACD_{opt}$. We also see from the graph that the formula constants for zero MPE (red cross mark), MEDPE (red circle mark), minimal MAPE (cyan cross mark) and RMSPE (magenta asterisk mark) are very close to SF_{opt}, whereas the formula constant for minimal MEDAPE (cyan circle mark) slightly overestimates SF_{opt} and the formula constant for minimal SDPE (yellow asterisk mark) is around 0.3 lower than SF_{opt}, as indicated by the vertical, dashed black reference line.

In Figure 1d, the conditions are shown for the Haigis formula with preset values a1 / a2 = 0.4/0.1. We see that $a0_{pred}$ slightly overestimates $a0_{opt}$ to both tails

FIGURE 1 Performance of the predicted formula constant $(.)_{pred}$ to zero the mean prediction error (MPE) (according to Gatinel, Debellemanière, Saad, Wallerstein, et al., 2023) for variation of start values of the formula constants ($(.)_{start}$, X axis) together with the listed performance metrics: mean prediction error (MPE), median prediction error (MEDPE), mean absolute prediction error (MAPE), median absolute prediction error (MEDAPE), root mean squared prediction error (RMSPE), and the standard deviation of the prediction error (SDPE) for variation of $(.)_{start}$ in a range ± 1.5 around $(.)_{opt}$ for the SRKT formula (a), the HofferQ formula (b), the Holladay formula (c) and the Haigis formula (d, with preset values a1/a2 = 0.4 / 0.1). The solid blue parabola-shaped line shows the predicted formula constants ($(.)_{pred}$) with variations of the start value ($(.)_{start}$) (scale on the left Y axis). To both tails of $(.)_{start}$ the $(.)_{pred}$ overestimates the 'true value' of the formula constant $(.)_{opt}$. The dashed black lines indicate the situation with the optimised formula constants (A_{opt}, $pACD_{opt}$, SF_{opt} and $a0_{opt}$, respectively) for zeroing the mean prediction error with an iterative nonlinear optimisation strategy (sequential quadratic programming). In addition, the impacts of the variation of $(.)_{start}$ on the performance metrics are plotted against the scale on the right-hand Y axis and indicated as follows: MPE (red solid line), MEDPE (red dash-dotted line), MAPE (cyan solid line), MEDAPE (cyan dash-dotted line), RMSPE (magenta solid line) and SDPE (yellow solid line).



of $a0_{start}$ (by around 0.09 for $a0_{opt} - 1.5$ and by around 0.05 for $a0_{opt} + 1.5$). For $a0_{start}$ between $a0_{opt}$ and 2.1, we observe a very slight underestimation of $a0_{opt}$. We also see from the graph that the formula constants for zero MPE (red cross mark) and MEDPE (red circle mark) are very close to $a0_{opt}$, and the formula constants for minimal MAPE (cyan cross mark), MEDAPE (cyan circle mark) and RMSPE (magenta asterisk mark) are slightly smaller than $a0_{opt}$. The formula constant for minimal SDPE (yellow asterisk mark) is around 0.55 lower than $a0_{opt}$, as indicated by the vertical, dashed black reference line.

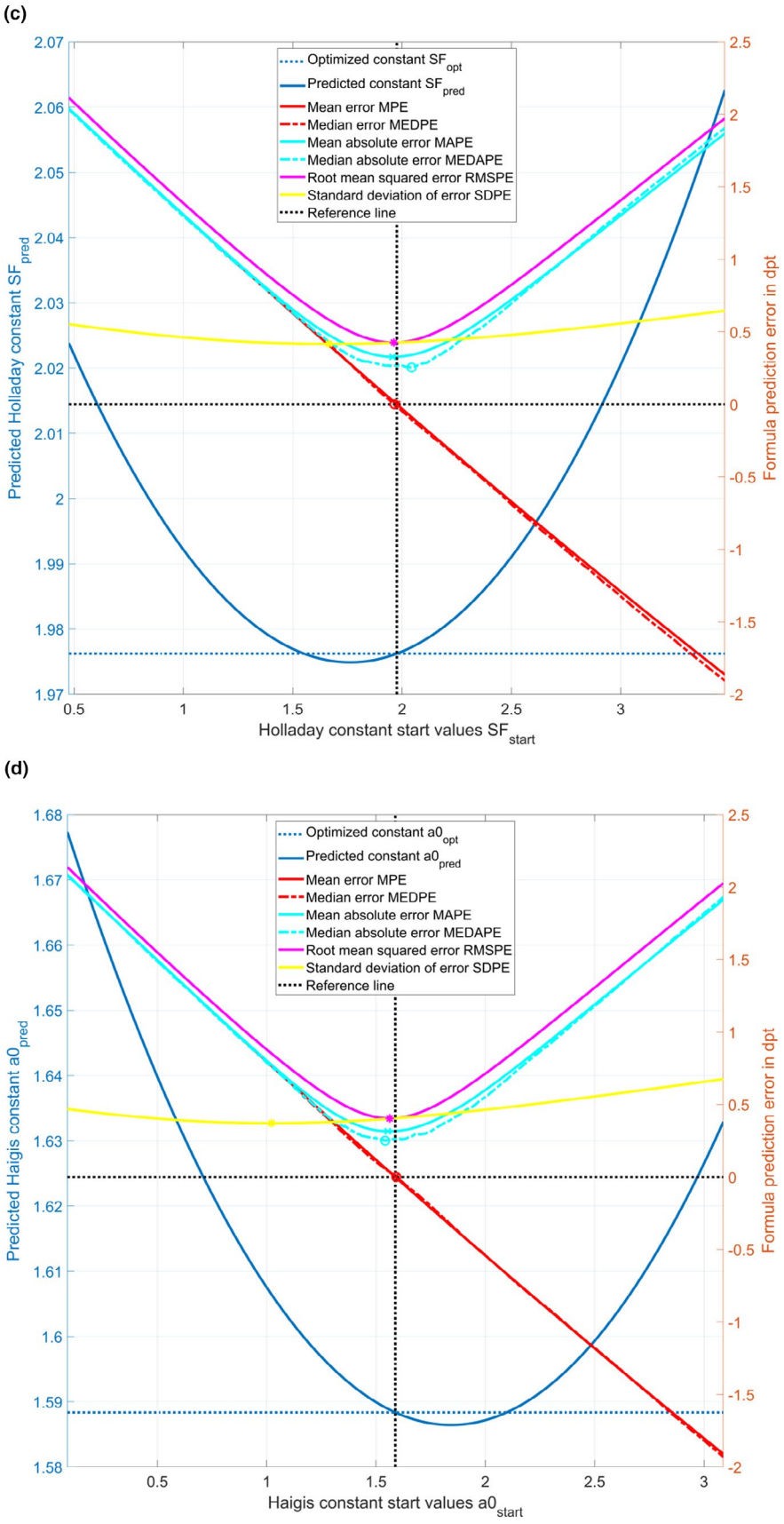


FIGURE 1 (Continued)

4 | DISCUSSION

The performance of lens power calculation schemes depends primarily on the quality of the formula constants (Aristodemou et al., 2011; Behndig et al., 2014; Galvis et al., 2013; Langenbucher et al., 2022; Langenbucher, Szentmáry, et al., 2023b; Langenbucher, Szentmáry, Cayless, Müller, et al., 2021; Sardari et al., 2023; Zhang

et al., 2019). These constants are optimised based on clinical data considering 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, defined as a fictitious parameter describing the axial position of a thin lens implant that does not necessarily correspond to the real geometrical axial position of the lens (Langenbucher, Szentmáry, Cayless, Weisensee, et al., 2021; Norrby & Koranyi, 1997; Olsen, 2006). We know that a systematic shift in ELP (e.g. by tuning the formula constant) shows 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). Therefore, systematically shifting the ELP with optimisation 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 should remain unchanged). Therefore, some modern IOLP calculation concepts (e.g. the Olsen [Olsen, 2006; Olsen & Hoffmann, 2014] or Castrop formula [Langenbucher, Szentmáry, Cayless, Weisensee, et al., 2021]), try to overcome this issue by using formula constants that do not directly interact with the ELP by a fixed factor.

In the early stage of new lens models on the market, all users try to estimate the appropriate formula constant while reliable constants are still unavailable. Since there is no accepted standard for optimising formula constants, many competing optimisation concepts have been proposed, and the results are not really comparable. Therefore, the paper published by Gatinel et al. in 2023 was a milestone because it presents a very simple concept of how to tune the mean ELP of a study population to shift the mean postoperative spherical equivalent of refraction to zero (Gatinel, Debellemanière, Saad, Rampat, et al., 2023). This concept requires only the mean keratometric power K_{mean} and the mean power of the implanted lens ($IOLP_{mean}$) to derive the shift in mean ELP. In the Supplementary Data, we provide a simple and self-explanatory Excel spreadsheet programmed with this concept. To use this spreadsheet, the user enters the start value for the formula constant and the type of constant, together with the mean values of keratometric power, IOLP and MPE. The sheet then calculates the 'formula constant' optimised for zero MPE according to Gatinel (Gatinel, Debellemanière, Saad, Rampat, et al., 2023). To optimise the formula constant for zero MPE, we have only to analyse the 'conversion' from a shift in ELP to a shift in the formula constant. This can be derived directly from the formula definition, where the IOLP calculation concept is fully disclosed.

However, even though this concept is impressively simple, this prediction for the optimised formula constant may have some limitations. Firstly, it considers the K_{mean} and $IOLP_{mean}$, which might not be representative if these measures are not normally distributed. Further, all the IOLP calculation concepts are nonlinear transforms of the biometric measures and the IOLP into predicted refraction (Hoffer & Savini, 2020; Savini et al., 2020), which might cause additional inaccuracies. Therefore, this prediction must be validated in a clinical environment to get an idea of how precise the predicted formula constants are.

As a reference, we used a large and clean dataset from one clinical centre and optimised the formula constants for four classical formulae (SRKT, HofferQ, Holladay and Haigis formula) based on a well-described iterative nonlinear optimisation strategy (Langenbucher, Szentmáry, Cayless, Müller, et al., 2021; Langenbucher et al., 2022; Langenbucher, Szentmáry, et al., 2023a). Then, starting from the optimised formula constant (used as the gold standard), we detuned the formula constant systematically by up to ±1.5 as start values for the constant prediction concept, and we analysed the results of the predicted formula constant $(.)_{pred}$ as a function of the start values (detuned $(.)_{opt}$). To get some insight into the effect of detuning the formula constant, we derived the performance metrics for the optimised formula constants $(.)_{opt}$ as well as for all variations (start values $(.)_{start}$). Overall, we feel that the prediction concept performs surprisingly well. We see from Figure 1 that for the entire range of detuning of the formula constants (±1.5), the predicted formula constant $(.)_{pred}$ for all formulae was within a range of about −0.01 to +0.09, which is fully acceptable in a clinical environment. We observed some asymmetry between detuning in the negative and positive directions, and as the prediction error $(.)_{pred} - (.)_{opt}$ shows a 2nd-order parabolic shape, the error increases towards both tails of detuning.

In addition, our results indicate that optimisation for zero MPE or MEDPE results in more or less identical results for the formula constants for all formulae under test (red solid and red dashed-dotted lines). In contrast, the formula constant for the smallest RMSPE, MAPE and MEDAPE shows a very slight but clinically irrelevant deviation from $(.)_{opt}$ for zero MPE. However, the graphs clearly show that any optimisation for SDPE does not make any sense, as for all formulae under test, the minimum of the SDPE performance curve (yellow line) is typically far off the zero MPE/MEDPE as well as far off the minimum of the MAPE/MEDAPE and RMSPE performance curves. Therefore, optimising formula constants for SDPE is not recommended!

In related recent research by Gatinel and his group, the effect of adjusting the effective lens position value to zero the mean error on the precision of intraocular lens (IOL) power calculation formulae has also been explored, focusing on how this adjustment affects the standard deviation of their prediction error (Gatinel, Debellemanière, Saad, Wallerstein, et al., 2023). This study also assessed how the effects of these adjustments might depend on the source of the prediction error. All other variables were kept constant, and only specific parameters such as the radius of corneal curvature and axial length were varied one at a time. Using zeroing to correct mistakes in estimating corneal power results in a significant and exponential growth in the standard deviation, which adversely affects the precision of the formula. Conversely, zeroing for errors in axial length measurements or predicted implant position had a minimal or even positive effect on precision.

The finding that the minimum SD value is reached for a value different from the emmetropisation constant in

our present results stems from the fact that the sources of error in the formulae examined are related to systematic or variable factors concerning the measurement of corneal power.

However, the selection of proper metrics for the target parameter (mostly PE) depends on the preference of the surgeon: for example, optimising for zero MPE might be a good choice if the PE is normally distributed, but this optimisation might not be robust if extreme values and outliers of PE are not filtered out properly (Langenbucher, Szentmáry, et al., 2023b). Optimising for RMSPE as an allrounder (Langenbucher, Szentmáry, Cayless, Müller, et al., 2021) is very popular in all disciplines of engineering and mathematics and is known to be very robust for an outlier. This approach is used, for example as a standard for optimising formula constants on the IOLCon WEB platform (https://IOLCon.org). However, especially in skewed distributions of PE, an optimisation for MEDPE or MEDAPE might be a good alternative to achieve robust results (Langenbucher, Szentmáry, Cayless, Müller, et al., 2021). Beyond these considerations, the robustness of formula constant optimisation is outside the scope of the present study.

Our current study is, however, also subject to some limitations. Firstly, we restricted the analysis of this simple concept for predicting the formula constant for zero MPE to 4 classical fully disclosed formulae. Since the internal architecture of most modern formulae is undisclosed, we cannot read out the conversion of an ELP offset to an offset in the formula constant for such formulae. Secondly, we restricted the analysis to a detuning of the start values $(.)_{start}$ from the $(.)_{opt}$ up to ±1.5. We feel that formula constants could be estimated from the material and design within the limits of this tolerance of ±1.5. However, our results do not show how this simple prediction performs for larger values of detuning. Further, in a post-hoc optimisation context carried out to compare the accuracy of different implant calculation formulae after zeroing, it should be possible to iterate the procedure until a constant value is reached, allowing an MPE to be obtained as close to zero as desired. And finally, we applied all the calculations to a dataset from one single surgical centre (all biometric measurements with the same biometer and postoperative refractions made by an experienced optometrist). In the general case of multicentric data with several surgeons and variations of measurement techniques, the prediction performance of this simple prediction concept and the performance curves for the error metrics might be slightly worse.

In *conclusion*, this paper shows that even using a very simple prediction scheme based on the mean ELP, mean keratometric power and mean refractive power of the intraocular lens, the best formula constant for zero mean prediction error could be estimated with high precision. Especially in a clinical setting where more advanced formula constant optimisation strategies are unavailable, this concept, which could be easily implemented in EXCEL, could help to optimise postoperative refractive outcomes after cataract surgery.

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