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# Project hyperopic power prediction: accuracy of 13 different concepts for intraocular lens calculation in short eyes 

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#### Abstract

Purpose To evaluate the accuracy of intraocular lens (IOL) power calculation in a patient cohort with short axial eye length to assess the performance of IOL power calculation schemes in strong hyperopes. Methodology The study was a single centre, single surgeon retrospective consecutive case series at the Augen- und Laserklinik, Castrop-Rauxel, Germany. Inclusion of patients after uneventful cataract surgery implanting either spherical (SA60AT) or aspheric (ZCB00) IOLs. Inclusion criteria were axial eye length $<21.5$ mm and/or emmetropising IOL power $>28.5$ D. Lens constants were optimised on a separate patient cohort considering the full bandwidth of axial eye length. Data of one single eye per patient were randomly included. The outcome measures were: mean absolute prediction error (MAE), median absolute prediction error, mean prediction error with SD and median prediction error and the percentage of eyes with an MAE within $0.25 \mathrm{D}, 0.5$ $\mathrm{D}, 0.75 \mathrm{D}$ and 1.0 D . Results A total of 150 eyes from 150 patients were assessed. Okulix, PEARL-DGS, Kane and Castrop provided a statistically significantly smaller MAE compared with the Hoffer Q and SRK/T formulae. Conclusion In our patient cohort with short axial eye length, the use of PEARL-DGS, Okulix, Kane or Castrop formulae showed the lowest MAE. The Castrop formula has not been published before, but will be disclosed with a ready-to-use Excel sheet as an addendum to this paper.


## INTRODUCTION

Patient demands for spectacle independence following cataract surgery are constantly rising. With growing lifestyle expectations and high mobility in the elderly, spectacle independence has become a new quality standard. The implementation of optical biometry in clinical routine has paved the way for better refractive accuracy. ${ }^{1}$ However, predicting postoperative refraction is still problematic in special cases. ${ }^{2}$ In short eyes especially, the likelihood of a refractive surprise is significantly increased. Smaller compartments and higher intraocular lens (IOL) power typically make short eyes prone to having a higher mean absolute error (MAE) in terms of deviation of received from intended refraction. ${ }^{3}$

IOL power calculation is typically performed either with Gaussian optics or using ray tracing
strategies (eg, Okulix). Newer formulae incorporate artificial intelligence (Hill-RBF, PEARL-DGS) and/or single or multiple regressions (Haigis et al, ${ }^{4}$ Hoffer et al, ${ }^{5}$ Holladay et al, ${ }^{6}$ SRK/T, ${ }^{7}$ and presumably also Barrett, Evo, Holladay II and Kane, although these have been neither published nor disclosed).

Axial length (AL), corneal power, anterior chamber depth (ACD) and more recently lens thickness (LT), white-to-white diameter (WTW) and central corneal thickness (CCT), are typically used to estimate IOL power. Differences between IOL formulae mostly arise from one (ie, Hoffer-Q, Holladay I/II, SRK/T) or more (ie, Haigis) adjustment parameters ('constants') used to customise the IOL formula to a specific lens model. An assumed axial position of the lens implant in the eye called effective lens position (ELP) is tuned with 'fudge factors' to correct for systematic errors within the formula model or for other factors, such as decentration, tilt, spherical aberration, distance to fixation target, and others.
In hyperopic eyes, even slight miscalculations of the postoperative axial IOL position lead to inaccuracies in predicted refraction differing considerably from 'normal' cases.

Considering an example eye with $\mathrm{AL}=21.0 \mathrm{~mm}$, corneal curvature $=7.7 \mathrm{~mm}, E L P=4.27 \mathrm{~mm}$ and IOL power $=35.0 \mathrm{D}$, an underestimation/overestimation of 1 mm in ELP results in a myopisation/ hyperopisation of $2.73 \mathrm{D} / 2.54 \mathrm{D}$ at the spectacle plane. While ray-tracing avoids the general limitations of Gaussian optics, it shares the problem of determining the postoperative axial IOL position. High spherical aberration of the IOL and manufacturing tolerances as described in ISO11979 also contribute to postoperative refraction error. This study presents results obtained using a new IOL power calculation formula, the Castrop formula, developed over several years for internal use; the current version used here is disclosed in the addendum. This study aims to evaluate the performance of different modern IOL calculation methods in terms of MAE in highly hyperopic eyes.

## PATIENTS AND METHODS

## Study design

A total of 269 consecutive eyes of 150 patients who received IOL implantation at the Augen- und

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Laserklinik Castrop-Rauxel between January 2013 and January 2020 were enrolled in this study. In bilateral cases, one eye was randomly selected for inclusion as suggested by Wang et al ${ }^{8}$

Two IOL designs were used; the Alcon SA60AT (Alcon Laboratories, Fort Worth, Texas, USA) (111 eyes) and the Johnson \& Johnson ZCB00 (Johnson \& Johnson Vision, Santa Ana, California, USA) (39 eyes).

Data were acquired retrospectively. The study was performed in accordance with the ethical standards of the Declaration of Helsinki of 1964 and its current revisions. Written informed consent for data analysis was obtained from all patients. Inclusion criteria were: complete biometric measures and $\mathrm{AL}<21.5$ mm and/or emmetropising IOL power $>28.5$ D. Exclusion criteria were: Ectatic diseases, any history of ophthalmic surgery and intraoperative or postoperative complications, and postoperative visual acuity less than 20/32.

Preoperative optical biometry was performed with the Lenstar LS 900 (Haag-Streit, Koeniz, Switzerland) software V.Eyesuite i9.3.1.0 ( $\mathrm{n}=106$ ), or the IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany) software V.1.80.10.61129.C76806 ( $n=44$ ).

Subjective manifest refraction was performed by an experienced optometrist or clinician 4 weeks after surgery at a distance of 6 m using Landolt C optotypes according to DIN/EN/ISO 8596.

## IOL power calculation

For numerical ray-tracing, datasets were imported into the raytracing package Okulix V9.20 (Panopsis, Mainz, Germany) via an automated interface. The PEARL-DGS formula was calculated via the email-support function (www.IOLsolver.com) without disclosing the postoperative refraction. The Kane formula (www. iolformula.com), the Hill-RBF Beta V.3.0 (www.rbfcalculator. com) and the EVO V.2.0 formula (www.evoiolcalculator.com) were calculated using the respective official websites, and the Castrop formula was calculated via spreadsheet (Excel). Gender, AL, keratometry, ACD, LT, CCT and WTW values acquired with the LenStar, or, if not available, with the IOLMaster, were entered as required by each formula. Each eye was entered independently (JW, TW), and results cross-checked to avoid typing errors.

The Barrett Universal II, Haigis, Hoffer Q, Holladay I, Holladay II (without preoperative refraction), Olsen (2-factor version) and SRK/T formulae were taken from the LenStar or the IOLMaster.

Before analysing the refractive outcome measures of the study population, lens constants were optimised as proposed by Wang et al based on an external dataset of 30 randomly chosen patients from a non-biased cohort (table 1). ${ }^{8}$

## Surgical technique

Surgery was performed under peribulbar anaesthesia by one experienced surgeon (PCH). A self-sealing temporal limbal incision with a 2.2 mm double-bevelled steel blade was performed prior to injection of an ophthalmic viscoelastic device, capsulorhexis, phacoemulsification, irrigation/aspiration of residual cortex and injection of a foldable acrylic IOL into the capsular bag as standard procedure.

## Statistical analysis

We assumed Okulix to be the most suitable IOL power calculation method for dealing with short eyes, ${ }^{9}{ }^{10}$ whereas Hoffer Q was taken as the benchmark formula to test against, since this is specifically recommended for short eyes by the Royal College of

Table 1 Optimised constants used for the dataset

|  | Lens constant | ZCB00 | SA60AT |
| :--- | :--- | :--- | :--- |
| Barrett universal II | Lens factor | 2.16 | 1.69 |
| Castrop | Cas, Raux | $0.41,0.24$ | $0.37,-0.05$ |
| EVO 2.0 | A constant | 119.44 | 118.7 |
| Haigis | a0, a1, a2 | $1.28,0.210,0.251$ | $0.138,0.227,0.182$ |
| Hill-RBF 3.0 | A constant | 119.53 | 118.64 |
| Hoffer Q | pACD | 5.82 | 5.43 |
| Holladay I | Surgeon factor | 2.07 | 1.65 |
| Holladay II | ACD | 5.824 | 5.396 |
| Kane | A constant | 119.36 | 118.7 |
| Olsen 2 | ACD, C constant | $5.12,0.48$ | $4.7,0.39$ |
| PEARL-DGS | A constant | 119.307 | 118.738 |
| SRK/T | A constant | 119.5 | 118.8 |

Constant optimisation was achieved in a trial and error fashion to adjust the constant until a prediction error of 0 was achieved for each eye. We used the mean constant as the optimised one.
ACD, anterior chamber depth.;

Ophthalmologists. Based on the study goal, an assumed effect size of $0.25, \alpha=0.05$ and a power level of 0.9 , a sample size of 145 eyes was calculated.

Outcome measures analysed the prediction error (PE) in terms of the difference between the actual postoperative refraction and the formula-predicted refraction for the implanted IOL, and included mean absolute prediction error (MAE), mean prediction error (ME), SD of ME, median PE (medE), median absolute PE (MedAE), plus the percentage of eyes with absolute PE $\leq 0.25 \mathrm{D}, \leq 0.5 \mathrm{D}, \leq 1.0 \mathrm{D}$ and $>1.0 \mathrm{D}$. A subgroup analysis was performed for the different IOL types.

Statistical analysis was performed using the SPSS software V.24.0 (IBM) and Prism V.5.00f, GraphPad Software, San Diego, California, USA. For both subgroups, postoperative refraction was predicted using the respective optimised constants. Analysis of MAE was performed using Friedman test and Dunn's multiple comparison post-test. Normal distribution in ME was analysed via Shapiro-Wilk test. $\mathrm{P}<0.05$ was considered statistically significant.

## RESULTS

## Demographic data

The study included 150 eyes ( 87 eight eyes, 63 left eyes) from 150 patients ( 111 female, 39 male) (online supplemental material 1: statistics). A total of 111 eyes were treated with spherical IOLs (Alcon SA60AT) and 39 eyes with aspheric aberrationcorrecting IOLs (Johnson \& Johnson Tecnis ZCB00). Table 2 displays the demographic data. The LenStar biometer was used in $71 \%$ of patients and IOLMaster in $29 \%$.

## Accuracy

Table 3 summarises the calculation concepts under test.
Okulix provided a statistically significant lower MAE than the benchmark formula (Hoffer Q) (Friedman, p=0.038). The lowest MAE was provided by the PEARL-DGS (Friedman, $\mathrm{p}=0.002$ ), Castrop formula (Friedman, $\mathrm{p}=0.003$ ), Okulix(Friedman, $\mathrm{p}=0.038$ ) and Kane formula (Friedman, $\mathrm{p}=0.045$ ), while the highest MAE was provided by the Hoffer Q (Friedman, $\mathrm{p}=0.038$ ) and SRK/T (Friedman, $\mathrm{p}=0.002$ ) formula. This is also reflected in the mean ranks (figure 1A).

Splitting methods into groups, modern concepts showed significantly better results than fourth generation formulae and third generation formulae (figure 1C).

In one eye, the Hill Beta V.3.0 calculator yielded no result at all, while it showed an out-of-bounds warning ('accuracy is not

Table 2 Demographic data

| n=150 | Mean | SD | Median | IQR | Min | Max |  | $95 \% \mathrm{Cl}$ <br> of mean <br> lower <br> bound |
| :--- | ---: | ---: | ---: | ---: | ---: | ---: | ---: | ---: |
| AL | 20.98 | 0.54 | 21.05 | 0.69 | 18.71 | 22.53 | $95 \% \mathrm{Cl}$ <br> of mean <br> higher <br> bound |  |
| ACD | 2.69 | 0.34 | 2.65 | 0.51 | 2.01 | 3.67 | 21.63 | 2.74 |
| LT | 4.75 | 0.43 | 4.70 | 0.54 | 18.71 | 22.53 | 4.69 | 4.82 |
| CCT | 565.18 | 37.44 | 562.50 | 52.0 | 476 | 664 | 559.14 | 571.22 |
| WTW | 11.81 | 0.49 | 11.82 | 0.57 | 10.41 | 13.79 | 11.73 | 11.89 |
| Ksteep | 44.98 | 1.84 | 44.80 | 2.37 | 40.95 | 49.85 | 44.69 | 45.28 |
| Kflat | 43.71 | 1.83 | 43.55 | 2.35 | 38.71 | 47.74 | 43.42 | 44.01 |
| IOL power | 30.23 | 2.75 | 30.75 | 3.50 | 24.0 | 40.0 | 29.79 | 30.67 |
| SEQ | -0.49 | 0.61 | -0.38 | 0.78 | -2.75 | 1.0 | -0.58 | -0.39 |

ACD, anterior chamber depth; AL, axial eye length; CCT, central corneal thickness; IOL, intraocular lens; K,
keratometry; LT, lens thickness; SEQ, spherical equivalent; WTW, white to white.
guaranteed') in 22 out of 150 cases (14.67\%). It was, therefore, not included in the final statistical analysis, although showing promising results. The MAE was 0.36 D for in-bound and 0.53

D for out-of-bound calculations (Mann-Whitney $\mathrm{p}=0.01$ ), while Okulix yielded 0.34 and 0.36 in the same patients.

The lowest SD and medAE was found with PEARL-DGS, Castrop, Okulix and Kane (table 3, figure 2A,B). Regarding ME, we observed a myopic offset in Barrett, Hoffer Q, and Holladay 2 and a hyperopic offset for SRK/T and EVO 2. Shapiro-Wilk tests showed normally distributed ME for all methods except Barrett $(\mathrm{p}=0.04)$ and PEARL-DGS $(\mathrm{p}<0.01)$. Figure 3 shows the ME as a function of AL, IOL power, corneal curvature and ACD. The percentage of eyes with absolute PE of below $0.25,0.5$, $0.75,1.0$ and more than 1.0 D is shown in figure 2 C , the $95^{\text {th }}$ percentile below a certain absolute PE in figure 2D.

## DISCUSSION

Accuracy is the main requirement for any study on IOL PE. ${ }^{11} 12$ Our main objective was the prediction accuracy of modern IOL power calculation strategies in short eyes with high lens power based on the absolute PEs recommended by Wang et al and Kane et $a l^{8}{ }^{13}$

Table 3 Accuracy and prediction error for the total population and subgroups

| Method | Subgroup | MAE | MedAE | ME | SD | MedE | $\begin{aligned} & \% \text { PE } \\ & \leq 0.25 \mathrm{D} \end{aligned}$ | \% PE $\leq 0.5 \mathrm{D}$ | \% PE $\leq 0.75 \mathrm{D}$ | \% PE $\leq 1.0 \mathrm{D}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Barrett | SA60AT | 0.49 | 0.32 | -0.16 | 0.65 | -0.05 | 40.5 | 63.1 | 78.4 | 82.9 |
|  | ZCB00 | 0.50 | 0.34 | -0.34 | 0.61 | -0.20 | 41 | 61.5 | 71.8 | 89.7 |
|  | All | 0.49 | 0.33 | -0.20 | 0.64 | -0.09 | 40.7 | 62.7 | 76.6 | 84.7 |
| Castrop | SA60AT | 0.33 | 0.28 | -0.03 | 0.43 | 0.02 | 43.2 | 73.9 | 92.8 | 97.3 |
|  | ZCB00 | 0.32 | 0.27 | -0.07 | 0.40 | -0.02 | 48.7 | 76.9 | 94.9 | 100 |
|  | All | 0.33 | 0.27 | -0.04 | 0.42 | -0.01 | 44.7 | 74.7 | 93.3 | 99.3 |
| EVO 2.0 | SA60AT | 0.38 | 0.34 | 0.21 | 0.45 | 0.20 | 39.6 | 71.2 | 90.1 | 95.5 |
|  | ZCB00 | 0.41 | 0.26 | 0.24 | 0.42 | 0.31 | 28.2 | 66.7 | 89.7 | 100.0 |
|  | All | 0.39 | 0.30 | 0.22 | 0.44 | 0.22 | 36.7 | 70 | 90 | 96.7 |
| Haigis | SA60AT | 0.39 | 0.31 | -0.07 | 0.49 | -0.05 | 42.3 | 70.3 | 85.6 | 93.7 |
|  | ZCB00 | 0.41 | 0.41 | -0.02 | 0.49 | 0.02 | 33.3 | 61.5 | 84.6 | 100 |
|  | All | 0.39 | 0.32 | -0.06 | 0.49 | -0.01 | 40.0 | 68.0 | 85.3 | 95.3 |
| Hill-RBF | SA60AT | 0.39 | 0.32 | -0.10 | 0.50 | -0.08 | 42.3 | 73.0 | 83.8 | 94.6 |
|  | ZCB00 | 0.37 | 0.35 | -0.11 | 0.46 | -0.06 | 43.6 | 74.4 | 87.2 | 97.4 |
|  | All | 0.38 | 0.32 | -0.10 | 0.49 | -0.06 | 42.7 | 73.3 | 84.7 | 95.3 |
| HofferQ | SA60AT | 0.46 | 0.38 | -0.28 | 0.53 | -0.24 | 40.5 | 62.2 | 82.9 | 90.1 |
|  | ZCB00 | 0.50 | 0.34 | -0.45 | 0.48 | -0.34 | 38.5 | 56.4 | 71.8 | 84.6 |
|  | All | 0.47 | 0.38 | -0.32 | 0.52 | -0.26 | 40.0 | 60.7 | 80 | 88.7 |
| Holladay | SA60AT | 0.42 | 0.36 | 0.11 | 0.53 | 0.12 | 40.5 | 64.0 | 84.7 | 93.7 |
|  | ZCB00 | 0.37 | 0.25 | -0.18 | 0.45 | -0.17 | 51.3 | 74.4 | 87.2 | 94.9 |
|  | All | 0.41 | 0.34 | 0.03 | 0.53 | 0.06 | 43.3 | 66.7 | 85.3 | 94.0 |
| Holladay 2 | SA60AT | 0.43 | 0.38 | -0.22 | 0.50 | -0.23 | 39.6 | 64.9 | 82.0 | 92.8 |
|  | ZCB00 | 0.42 | 0.41 | -0.35 | 0.46 | -0.29 | 41.0 | 69.2 | 76.9 | 89.7 |
|  | All | 0.43 | 0.38 | -0.26 | 0.49 | -0.24 | 40.0 | 66.0 | 80.7 | 92.0 |
| Kane | SA60AT | 0.34 | 0.30 | 0.06 | 0.43 | 0.05 | 40.5 | 79.3 | 92.8 | 95.5 |
|  | ZCB00 | 0.38 | 0.35 | -0.21 | 0.44 | -0.24 | 38.5 | 76.9 | 89.7 | 97.4 |
|  | All | 0.35 | 0.30 | -0.01 | 0.45 | 0.02 | 40.0 | 78.7 | 92.0 | 96.0 |
| Okulix | SA60AT | 0.34 | 0.30 | -0.08 | 0.43 | -0.07 | 44.1 | 80.2 | 90.1 | 98.2 |
|  | ZCB00 | 0.33 | 0.28 | 0.07 | 0.39 | 0.10 | 48.7 | 76.9 | 94.9 | 100 |
|  | All | 0.34 | 0.30 | -0.04 | 0.42 | -0.05 | 45.3 | 79.3 | 91.3 | 98.7 |
| Olsen | SA60AT | 0.40 | 0.33 | 0.12 | 0.47 | 0.18 | 35.1 | 68.5 | 88.3 | 98.2 |
|  | ZCB00 | 0.41 | 0.32 | -0.23 | 0.48 | -0.21 | 46.2 | 74.4 | 87.2 | 92.3 |
|  | All | 0.40 | 0.33 | 0.03 | 0.50 | 0.08 | 38.0 | 70.0 | 88.0 | 96.7 |
| Pearl-DGS | SA60AT | 0.34 | 0.27 | 0.10 | 0.43 | 0.10 | 48.6 | 77.5 | 93.7 | 96.4 |
|  | ZCB00 | 0.29 | 0.26 | -0.10 | 0.36 | -0.07 | 48.7 | 87.2 | 94.9 | 97.4 |
|  | All | 0.33 | 0.26 | 0.03 | 0.42 | 0.03 | 48.7 | 80 | 94.0 | 96.7 |
| SRK/T | SA60AT | 0.54 | 0.45 | 0.35 | 0.61 | 0.35 | 31.5 | 53.2 | 73.9 | 88.3 |
|  | ZCB00 | 0.40 | 0.36 | -0.05 | 0.48 | 0.08 | 30.7 | 59.3 | 77.3 | 90.0 |
|  | All | 0.50 | 0.42 | 0.25 | 0.60 | 0.22 | 28.2 | 76.9 | 87.2 | 94.9 |



Figure 1 (A) Applying Friedman test and post hoc Dunn's multiple comparison test on absolute prediction error. Mean ranks are provided in the 12 ring segments. Significant differences in rang sums between methods are shown with black lines. It has to be noted that $\mathrm{p}<0.05$ does not mean that methods are equal, but that the null hypothesis could not be rejected. Non-significant results may defer in direct comparison of two specific methods when a more sensitive test can be applied. (B) Explorative Wilcoxon-signed rank test. Mean absolute prediction errors are provided in the 12 ring segments. Significant differences in absolute prediction error are shown with black lines. All tests are only of explorative nature and performed as single formula versus single formula. Therefore, $\alpha$ was set to 0.05 and no post hoc correction for multiple comparisons applied. (C) Paired Friedman ANOVA test for three groups sorted by Modern: Pearl, Castrop, Okulix, Kane, EVO; Intermediate: Holladay II, Barrett II, Olsen, Haigis; Classic: Hoffer Q, Holladay, SRK/T. Yellow lines show significant differences, black lines show nonsignificant differences. (D) Paired Friedman ANOVA test for three groups sorted by mean rank: Top 4: Pearl, Castrop, Okulix, Kane; Middle 4: Haigis, Holladay, Olsen, EVO; Bottom 4: Holladay II, Barrett II, Hoffer Q, SRK/T. Yellow lines show significant differences, black lines show nonsignificant differences. ANOVA, analysis of variance.


Figure 2 (A) The bars display the median absolute prediction error of each formula, the whisker refers to the IQR. (B) Box and Whiskers plot: the box displays 25 and $75 \%$ quantiles, while the line marks the median. The whiskers refer to the 2.5 and $97.5 \%$ quantile and the dots to outliers. (C) Percentage of eyes in the entire population within a limit of $0.25,0.5,0.75,1.0 \mathrm{D}$. (D) $95 \%$ of absolute errors are smaller than the value indicated by the bar.

Splitting groups by mean rank, the top four methods (PEARL-DGS, Castrop, Okulix and Kane) showed significantly better results than the middle four methods and the bottom four methods (figure 1D). These four methods yield very similar results, but their equality cannot be proven as $\mathrm{n}>1600$ would be required (post hoc analysis of achieved power). This agrees with a recent study by Kane and Melles. ${ }^{14}$ In patients treated with the SA60AT with a IOL-power $\geq 30 \mathrm{D}$, the Kane formula provided the lowest MAE. ${ }^{14}$ Hill-RBF V.2.0 proved to be among the methods with the highest MAE along with Barrett and Hoffer Q. ${ }^{14}$ This is interesting for two reasons: The Hoffer Q Formula is recommended by the Royal School of Ophthalmologists for short eyes with $\mathrm{AL} \leq 22 \mathrm{~mm}$ (National Institute for Health and Care Excellence Guidelines on the management of cataracts in adults, 26 October 2017 point 1.3.5), while recent papers recommend the Barrett Universal II formula, a mix of thick and thin lens linear Gaussian optics, as the standard formula throughout all AL eyes. ${ }^{3}{ }^{15}$ Our results are similar to the outcome of Kane and Melles, where the SRK/T, Hoffer Q and Barrett yielded the highest MAEs. ${ }^{14}$ In our patient cohort, Barrett and SRK/T seemed to have systematic deviations in IOL power (figure 3B), whereas Hoffer Q and SRK/T seemed to have systematic deviations in AL (figure 3A). This might be the reason that in literature SRK/T is often recommended for long eyes and


Figure 3 (A) Trend analysis of PE over axial length. (B) Trend analysis of PE over IOL power. (C) Trend analysis of PE over corneal power ( $\mathrm{K}_{\text {mean }}$; $n_{c}=1.3775$ ). (D) Trend analysis of PE over anterior chamber depth. ACD, anterior chamber depth; IOL, intraocular lens; PE, prediction error.

Hoffer-Q for short eyes. Ideally, the slope of a formula's regression line should be as flat as possible, otherwise it is less applicable universally. Haigis and Olsen ${ }_{4}$ (4-factor version) were good performers for Kane and Melles. ${ }^{14}$ Haigis and Olsen 2 performed well in our study, as well as the Hill-RBF V.3.0. Unfortunately, at this time, the benefit of the Hill-RBF V.3.0 for short eyes proved to be limited as $14.7 \%$ of all calculations were out-of-bounds. These out-of-bounds might result from relatively sparse data for training the algorithm in these complicated eyes.

In one of the largest studies on IOL formula performance, Melles et al looked at results of the SN60WF and SA60AT IOL models. Unfortunately, the maximum power of the SN60WF is 30 D , meaning that the most difficult eyes were excluded. They found that the Kane, $\mathrm{Olsen}_{4}$, Barrett and EVO formulae are the most accurate for eyes of all AL. The EVO formula might be the exception as it showed worse results in short eyes. ${ }^{15}{ }^{16}$ Kane and Melles reported good results regarding the EVO formula. ${ }^{14}$ In another recent study on the SN60WF, Connell and Kane proved the Kane formula to have the lowest MAE, followed by Olsen $_{4}$, Hill V.2.0 and Barrett. There were no significant differences between formulae in short eyes. ${ }^{3}$ Likewise, Gökce et al ${ }^{17}$ observed no significant differences between any of the formulae for IOLs based on the Alcon and Tecnis platforms.

Among third and fourth generation formulae, a recent metaanalysis reported that Haigis, Holladay I and Holladay II showed superior results in short eyes. ${ }^{18}$ This is consistent with our results: the Haigis formula does not differ significantly from Holladay I or Holladay II (figure 1A,B). The Holladay II formula was used without preoperative refraction as previous studies report better outcome without this value. ${ }^{19}$

Existing formulae achieve excellent results in normal eyes, whereas eyes outside the normal range require more attention in IOL power calculation and PEs may increase considerably. ${ }^{15}{ }^{17}$ The influence of ELP and its components ACD, AL and corneal curvature is hardly separable. Nevertheless, for an average eye, Norrby attributes $35.5 \%$ of non-systematic errors to the ELP, whereas $6.2 \%$ are attributed to the eccentricity
and measurement of radii of the cornea, ${ }^{11}$ as the knowledge of corneal asphericity and the posterior corneal curvature allow for more accurate results. ${ }^{20}$ Inspired by Norrby, ${ }^{11}$ error propagation analysis of the average hyperopic eye in our study attributes 67\% of non-systematic errors to the ELP, $17 \%$ to AL and around $10 \%$ to corneal measurement. Subsequently, formulae where ELP is heavily dependent on corneal radii such as the SRK/T will perform particularly badly in eyes with high refractive power. Okulix uses a mixture of AL based and anatomically based IOL position prediction. ${ }^{2021} \mathrm{AL}$ measurement, IOL power itself and the tolerance limits of ISO11979 may interfere with prediction accuracy in high powered IOLs, as tolerances have been shown to be a possible source of higher PE. ${ }^{2223}$ Corneal asphericity can also interfere with corneal power calculation, ${ }^{24}$ but asphericity Q is not readily available in standard biometry.

Aristodemou et al showed the importance of IOL constant optimisation, reporting differences in A-constants for 27 surgeons. ${ }^{25}$ They found 26 of 27 surgeons within limits of $\pm 0.15$ of their collectively optimised constant that differed from manufacturer's and ULIB optimised constants. ${ }^{25}$ This raises the question whether constants should be optimised overall for a pool of data from all sources or customised to surgeons, surgical techniques, biometers or patient ethnicities. Unfortunately, the newest generation of IOL formulae providing the most accurate results according to modern literature are unpublished, ${ }^{316}$ nor do these unpublished formulae provide ready-to-use spreadsheets that would enable clinicians to optimise constants and facilitate scientific repeatability without considerable effort. We, therefore, provide a description of the Castrop formula and an Excel spreadsheet for clinical and scientific use as online supplementary material.

Even with optimised constants, varying shape factors of different IOL designs might lead to differences in formula performance. ${ }^{21} 25$

Aspheric IOLs improve image performance by reducing higher order aberrations. Specifically, the ZCB00 design provides a spherical aberration correction of $-0.27 \mu \mathrm{~m}$, but is

## Clinical science

Table 4 Comparison with literature (studies on short eyes)

| Study | Connell**, ${ }^{3}$ | This study |  |  |  | Kane ${ }^{14}$ |  | Gökcett, ${ }^{17}$ |  | Kane $\ddagger \ddagger$, ${ }^{13}$ |  | Kane $\ddagger \ddagger$, ${ }^{28}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| IOL | SN60WF | SA60AT |  | ZCB00 |  | SA60AT |  | SN60WF <br> SA60AT/SN60AT <br> ZCB00/ZCTOO |  | SN60WF |  | SN60WF |  |
| N | 46 | 111 |  | 39 |  | 182 |  | 86 |  | 156 |  | 137 |  |
| Criteria | $\mathrm{AL} \leq 22.0 \mathrm{~mm}$ | AL $\leq 21.5 \mathrm{~mm}$ and/or IOL Power $\geq 28 \mathrm{D}$ |  |  |  | IOL Power $\geq 30 \mathrm{D}$ |  | $\mathrm{AL} \leq 22.0 \mathrm{~mm}$ |  | $\mathrm{AL} \leq 22.0 \mathrm{~mm}$ |  | $\mathrm{AL} \leq 22.0 \mathrm{~mm}$ |  |
| Factor | MAE | MAE | ME (SD) | MAE | ME (SD) | MAE | ME <br> (SD) | MAE | ME <br> (SD) | MAE | ME <br> (SD) | MAE | ME (SD) |
| Barrett | 0.48 | 0.48 | -0.16 (0.65) | 0.50 | -0.34 (0.61) | 0.82 | -0.62 (0.87) | 0.39 | -0.04 (0.49) | 0.47 | -0.26 | 0.45 | -0.28 |
| Castrop | - | 0.33 | -0.03 (0.43) | 0.32 | -0.07 (0.40) | - | - | - | - | - | - | - | - |
| EVO 2.0 | - | 0.38 | 0.21 (0.45) | 0.51 | 0.24 (0.42) | 0.56 | -0.06 (0.74) | - | - | - | - | - | - |
| Haigis | 0.47 | 0.39 | -0.07 (0.49) | 0.41 | -0.02 (0.49) | 0.60 | -0.18 (0.78) | 0.42 | -0.09 (0.54) | 0.47 | -0.09 | - | - |
| Hill 1.0 | - | - | - | - | - | - | - | 0.36 | -0.80 (1.41) | - | - | 0.42 | -0.15 |
| Hill 2.0 | 0.44 | - | - | - | - | 0.71 | 0.30 (0.82) | - | - | - | - | - | - |
| Hill 3.0 | - | 0.39 | -0.10 (0.5) | 0.37 | -0.11 (0.46) | - | - | - | - | - | - | - | - |
| Hoffer Q | 0.48 | 0.46 | -0.28 (0.53) | 0.50 | -0.45 (0.48) | 0.84 | -0.71 (0.81) | 0.44 | -0.22 (0.49) | 0.50 | -0.22 | - | - |
| Holladay1 | 0.44 | 0.42 | 0.11 (0.53) | 0.37 | -0.18 (0.45) | 0.63 | -0.18 (0.80) | 0.39 | -1.0 (1.64) | 0.45 | -0.07 | 0.42 | -0.09 |
| Holladay2 | 0.48 | 0.43 | -0.22 (0.50) | 0.42 | -0.35 (0.46) | 0.62 | -0.32 (0.77) | 0.40 | -0.25 (0.46) | 0.47 | -0.07 | - | - |
| Kane | 0.44 | 0.34 | 0.06 (0.43) | 0.38 | -0.21 (0.44) | 0.53 | -0.07 (0.71) | - | - | - | - | - | - |
| Okulix | - | 0.34 | -0.08 (0.43) | 0.33 | 0.07 (0.39) | - | - | - | - | - | - | - | - |
| $\mathrm{Olsen}_{2}$ | - | 0.40 | 0.12 (0.47) | 0.33 | -0.23 (0.48) | - | - | 0.46 | 0.27 (0.51) | - | - | - | - |
| Olsen $_{4}$ | 0.44 | - | - | - | - | 0.61 | -0.34 (0.75) | - | - | - | - | - | - |
| PEARL-DGS | - | 0.34 | 0.10 (0.43) | 0.29 | -0.10 (0.36) | - | - | - | - | - | - | - | - |
| SRK/T | 0.48 | 0.54 | 0.35 (0.61) | 0.40 | -0.05 (0.48) | 0.70 | 0.30 (0.82) | - | - | 0.46 | -0.04 | - | - |
| *ME/SD not known, the whole dataset (including normal and long eyes) was optimised for $M E=0$. †Values only known as IOL-collective. <br> $\ddagger$ ED not known. <br> AL, axial eye length; IOL, intraocular lens; MAE, mean absolute error; ME, mean error. |  |  |  |  |  |  |  |  |  |  |  |  |  |

also optimised to perform in a state of $5^{\circ}$ tilt. ${ }^{26}$ Hyperopic eyes typically have higher angle alphas that induce aberrations and make subjective refraction more difficult. Therefore, these IOLs improve optical quality and allow for better determination of refraction.

A noteworthy observation should be reported for the EVO V.2.0 online calculator. For IOL calculations, the IOL model must be specified. Options are 'standard'" or 'tecnis', the latter being the obvious choice and therefore used for all ZCB00 IOLs. Setting the IOL model to 'standard' would have led to considerably better results for this IOL (MAE 0.32 instead of 0.41 ). The reason remains unclear as the function of the 'tecnis' option has not been disclosed.

In our study, the EVO V. 2.0 shows a hyperopic offset, leading to a higher MAE, while the SD was quite low. Figure 3B shows systematic deviations with IOL power, noticeable dependencies were observed for Barrett, Olsen 2 , Haigis and Evo. Reitblat et al compared the accuracy of IOL formulae for steep and flat corneas. ${ }^{27}$ In flat corneas, all formulae yielded $>70 \%$ of eyes within $\pm 0.5 \mathrm{D}$, whereas in steep corneas this was achieved by Barrett, Haigis, Holladay 2 and Olsen, but not by third generation formulae. ${ }^{27}$ This might be interesting to clinicians because it is ongoing practice to either choose a formula universally (ie, Barrett or Kane Formula) or to use formulae according to case stratifications (ie, long eye SRK/T; short eye Hoffer Q). Figure 3C shows that systematic deviation with corneal curvature was observed for Barrett, Evo, Haigis and Olsen. Figure 3D shows that systematic deviations with ACD are relatively low for Castrop, Haigis, Kane, Okulix and PEARL-DGS.

The strength of this study is that our patient cohort of short and unusual eyes is large enough to provide sufficient statistical power. Table 4 reports the number of short eyes in recent studies. ${ }^{313141728}$

Many studies analyse a limited number of eyes treated with many IOL models, or include both eyes of a patient. ${ }^{17}$ In
contrast, we included a larger series of eyes (only one eye per patient) treated with two different lens models, and all interventions were performed by the same surgeon under identical conditions. Hence, the environment remained the same for the entire study population and all IOL constants were optimised for this very same setting.

To keep the cohort size sufficient, measurements from two biometers were included. Previous studies showed excellent coherence between results of both machines in small and normal eyes with an AL below 25.5 mm . ${ }^{29}{ }^{30}$ By including only two IOL designs, we were able to optimise lens constants as proposed previously. ${ }^{831}$ In keeping with similar studies, ${ }^{14}$ we chose to optimise constants for each formula with a set of random patients of all axial eye lengths instead of optimising constants for short eyes as this is the more likely scenario in a practice, and then applied the optimised formula to the dataset. The optimised constants were very close to those used in daily routine. Evaluations showed a stabilisation of single-constant values after 30 eyes, without further significant changes (figure 4). Finally, the Castrop formula provided the best results among methods with a fully published formula/equation, allowing a fair comparison with complementary calculation schemes. This is based on the basic IOL power formula (see online supplemental material 2 and 3), uses a thick lens model for the cornea, Cooke's sum-of-segments AL algorithm, ${ }^{32}$ and a regressive IOL position algorithm derived from 450 anatomical IOL positions. Adjustments can be performed dependent or independent of ELP by two variables C and R. For this study, both variables were used. A possible bias in prediction accuracy studies arises when power selection is based mostly on one formula/method. Slight residual ametropia of 0.25 D or less might be set to 0 in subjective refraction, which may negatively affect the results of all other formulae/methods. As primary IOL calculation was carried out using the Okulix software that does not include constants or any means of adjustment, it is unlikely that other retrospectively applied formulae will be negatively affected.


Figure 4 Prior internal optimisation processes showed a stabilisation of A-constant values after 30 eyes. Changes after 30 patients were minor with fluctuations within 1 decimal place.

Overall, Okulix, PEARL-DGS, Kane and Castrop proved to be excellent alternatives in hyperopic eyes. Results in terms of a lower MAE are significantly better than the benchmark formula Hoffer Q and other formulae tested. To ensure good results, segments of the optical path, especially aqueous depth and LT are mandatory.

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