Prediction of Effective Lens Position Using Multiobjective Evolutionary Algorithm

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Received: 18 October 2018
Accepted: 5 May 2019
Published: 28 June 2019

Keywords: multiobjective evolutionary algorithm; stepwise multiple regression analysis; effective lens position; cataract; prediction; intraocular lens

Citation: Tamaoki A, Kojima T, Tanaka Y, Hasegawa A, Kaga T, Ichikawa K, Tanaka K. Prediction of effective lens position using multiobjective evolutionary algorithm (MOEA).

Purpose: The purpose of this study was to evaluate the prediction accuracy of effective lens position (ELP) after cataract surgery using a multiobjective evolutionary algorithm (MOEA).

Methods: Ninety-six eyes of 96 consecutive patients (aged 73.9 ± 8.6 years) who underwent cataract surgery were retrospectively studied; the eyes were randomly distributed to a prediction group (55 eyes) and a verification group (41 eyes). The procedure was repeated randomly 30 times to create 30 data sets for both groups. In the prediction group, based on the parameters of preoperative optical coherence tomography (OCT), biometry, and anterior segment (AS)-OCT, the prediction equation of ELP was created using MOEA and stepwise multiple regression analysis (SMR). Subsequently, the prediction accuracy of ELPs was evaluated and compared with conventional formulas, including SRK/T and the Haigis formula.

Results: The rate of mean absolute prediction error of 0.3 mm or higher was significantly lower in MOEA (mean 4.9% ± 3.2%, maximum 9.8%) than SMR (mean 7.3% ± 4.8%, maximum 24.4%) (P = 0.0323). The median of the correlation coefficient ($R^2 = 0.771$) between the MOEA predicted and measured ELP was higher than the SRK/T ($R^2 = 0.412$) and Haigis ($R^2 = 0.438$) formulas.

Conclusions: The study demonstrated that ELP prediction by MOEA was more accurate and was a method of less fluctuation than that of SMR and conventional formulas.

Translational Relevance: MOEA is a promising method for solving clinical problems such as prediction of ocular biometry values by simultaneously optimizing several conditions for subjects affected by various complex factors.

Introduction

In modern cataract surgery, postoperative refractive errors have a significant influence on patient satisfaction, and many studies aim to increase the accuracy of the predicted refraction in the intraocular lens (IOL) power calculation.1–12 Factors that cause postoperative refractive errors in cataract surgery include the lack of measurement accuracy of the ocular biometry and prediction errors in the fixed position of the IOL, that is, effective lens position (ELP). The recent development of optical biometric devices has improved the accuracy of biometric measurements. However, because ELP is affected by many parameters, including the preoperative capsule size, severity of the cataract, and postsurgical capsule contraction, accurate prediction is a challenging issue.12–16

Conventionally, multiple regression analysis based on multiple parameters such as the preoper-
ative axial length (AL), corneal curvature radius, and anterior chamber depth has been used for the prediction of postoperative ELP.\textsuperscript{16,17} In this study, in order to reduce the postoperative refractive error, we introduced a novel approach of an evolutionary algorithm (EA) to minimize the prediction error of ELP.

EA is a new framework of computation that mimics biological heredity and evolution.\textsuperscript{18} Recently, it has been widely applied to processes such as optimization, learning, and adaptation as an important computational methodology that is closely related to artificial intelligence.\textsuperscript{19} The use of EA in optimization involves the representation of a solution (individual) as a sequence of parameters (variables) to be optimized; in addition, for a given problem, the objective function to be minimized (or maximized) can be included. Many individuals are randomly generated in a population and are subsequently evaluated for the purpose of ranking them from top to bottom. Next, two individuals with higher rank are selected as parents, and new offspring are created by recombining the genetic information of the parents. This operation is repeated many times until a satisfactory solution of the objective function is obtained with a high value. In most real-world problems, multiple objective functions are included. In such cases, multiobjective EA (MOEA) can be utilized to simultaneously optimize more than two objective functions.

In the medical field, EA has recently been applied in various areas such as radiology, neurology, and orthopedics.\textsuperscript{20} However, to the best of our knowledge, research to minimize the prediction error of ELP has not been reported. Reports have indicated that EA is useful in solving optimization problems, including noise.\textsuperscript{21–24} In our study, which includes the measurement data of noise generated from the patient, examiner, measuring instruments, and condition, EA was considered to be a useful approach. Currently, there is no accurate and standard calculation formula to predict the ELP. Therefore, in our study, conventional multiple regression analysis was performed, and the prediction accuracy was compared with that using EA.

## Methods

Ninety-six eyes of 96 consecutive patients who underwent cataract surgery using the same IOL (AN6KA; Kowa Co., Nagoya, Japan) at Japan Community Healthcare Organization (JCHO) Chukyo Hospital were retrospectively reviewed from the patients’ charts and included in the study. The patients’ average age was 73.9 ± 8.6 years (male individuals, 38 eyes; female individuals, 58 eyes). Eyes with ocular diseases other than cataracts and intraoperative or postoperative complications were excluded.

The parameters for ELP prediction were as follows: age, gender, AL, crystalline lens thickness (LT), central corneal thickness (CCT), aqueous depth (AQD, anterior surface of the crystalline lens from the posterior cornea) (Fig. 1A), anterior corneal curvature (ACC), posterior corneal curvature (PCC), angle-to-angle width (ATA-W), and angle-to-angle depth (ATA-D, the distance from the posterior cornea to the ATA line) (Fig. 1B).

ELP was defined as the distance from the cornea to the anterior surface of the IOL at 3 months after surgery plus the distance to the principal point of the IOLs. The prediction equation of ELP was obtained by MOEA and multiple regression analysis, including the above-mentioned parameters, and the difference between the predicted value and measured value (prediction accuracy) was compared between the two methods.

Optical coherence tomography (OCT) (IOLMaster 700; Carl Zeiss Meditec, AG, Jena, Germany) was used to measure the AL, crystalline LT, corneal thickness, and AQD (Fig. 1A). Anterior segment (AS)-OCT (Casia; Tomey, Nagoya, Japan) was used to measure the anterior/posterior corneal curvature (ACC/PCC), horizontal ATA, and angle depth. All cataract surgeries were performed with a 3.2-mm temporal corneal incision, and in all cases, an acrylic biconvex three-piece model IOL (AN6KA, Kowa Co.) was implanted. This retrospective study was approved by the Institutional Review Board at JCHO Chukyo Hospital (approval number: 2018020), and all procedures were performed in accordance with the tenets of the Declaration of Helsinki. As an alternative to written informed consent, the opt-out method approved by our Institutional Review Board was used.

## Multiobjective EA

In this study, to optimize two objective functions that both minimize the average value and standard deviation of the ELP prediction error simultaneously, we employed MOEA for the optimization of the ELP prediction equation.

We used the nondominated sorting genetic algo-
Algorithm (NSGA-II), which is well-known as an MOEA that shows stable performance in various applications. A detailed algorithm of NSGA-II has been reported. Briefly, the feature of this algorithm involves choosing an individual (solution), as shown in Figure 2.

In this study, the prediction equation of ELP was determined as a first-order polynomial as follows:

\[ \text{Predictive ELP} = a_1 x_1 + a_2 x_2 + \ldots + a_n x_n + C \]

Figure 1. Description of anterior segment parameters measured using (A) OCT biometry or (B) anterior segment OCT.

Figure 2. Outline of optimization method of ELP prediction equation using NSGA-II. P(t), parent group; Q(t), child population; R(t), population including P(t) and Q(t).
A flowchart of this procedure is shown in Figure 2. First, 3000 individuals (solutions) were randomly generated, and a parent population \( P(t) \) was created. Next, an offspring population \( Q(t) \) was created by SBX and polynomial mutation from \( P(t) \). NSGA-II ranked the individuals using nondominated sorting and crowding distances for the set \( R(t) = P(t) \cup Q(t) \), which consists of \( P(t) \) and \( Q(t) \). Subsequently, only the upper-half individuals with higher fitness survived as the parent population \( P \) for the next generation, and similar operations were executed for 5000 generations.

### Comparison of Prediction Accuracy Between MOEA and Stepwise Multiple Regression (SMR)

The population was randomized, and 30 sets of the prediction group of 55 eyes and the verification group of 41 eyes were created. In each of the 30 populations, the prediction equation was calculated using MOEA and SMR from the prediction group. In the verification group of 41 eyes, the predicted ELP value was calculated using MOEA and SMR, and the difference between the predicted and postoperative measured values between the two groups was compared. The proportion of each prediction error was compared. Moreover, 30 sets of standard deviation values of ELP prediction were collected, and the average value was compared between the MOEA and SMR groups. Furthermore, the proportions in which the mean absolute prediction error was 0.3 mm or higher in each of the 30 sets were compared.

In the validation group, the median coefficient of determination \( (R^2) \) between the predicted and measured ELPs by MOEA was compared with that of the SRK/T and Haigis equations. The IOL constant in the SRK/T and Haigis formulas was optimized using the IOLMaster 500. The optimized A-constant of the SRK/T formula was 119.1, and the \( a_0 \), \( a_1 \), and \( a_2 \) constants of the Haigis formula were \(-0.275\), \(0.243\), and \(0.2\), respectively.

### Statistical Analyses

To evaluate the normality of the populations, a Shapiro-Wilk normality test was performed. A comparison of the absolute prediction errors by the MOEA and SMR methods was carried out using a Wilcoxon matched-pairs signed rank test, and a paired \( t \) test was used to compare the standard deviations of both groups. All statistical analyses were performed using software (SPSS, version 21.0; IBM, Inc. Armonk, NY). A \( P \) value of less than 5% was considered statistically significant.
Results

Table 1 lists the average value of each parameter of the 96 eyes included in this study. Between the prediction group and verification group randomly created 30 times, there were no significant differences in all parameters.

Table 2 shows the mean absolute prediction error (MAPE) calculated by the prediction equation of SMR and MOEA 30 times. In MAPE, 23 out of 30 (76.7%) showed no significant difference between the two groups, but five (16.7%) showed significantly lower values in the MOEA than in the SMR group (P = 0.0001, P = 0.0186, P = 0.0005, P = 0.0161, and P = 0.0111). Two (6.7%) showed significantly lower values in the SMR than in the MOEA group (P = 0.0161 and P = 0.0241).

The maximum value of MAPE was 0.195 mm for the SMR group and 0.140 mm for the MOEA group.

Table 2. Comparison of Mean Absolute ELP Prediction Error Between SMR Analysis and MOEA Methods

<table>
<thead>
<tr>
<th>Validation No.</th>
<th>SMR MAPE</th>
<th>MOEA MAPE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MAPE</td>
<td>SD of MAPE</td>
</tr>
<tr>
<td>Group 1</td>
<td>0.126</td>
<td>0.117</td>
</tr>
<tr>
<td>Group 2</td>
<td>0.129</td>
<td>0.111</td>
</tr>
<tr>
<td>Group 3</td>
<td>0.195</td>
<td>0.116</td>
</tr>
<tr>
<td>Group 4</td>
<td>0.121</td>
<td>0.103</td>
</tr>
<tr>
<td>Group 5</td>
<td>0.109</td>
<td>0.063</td>
</tr>
<tr>
<td>Group 6</td>
<td>0.132</td>
<td>0.063</td>
</tr>
<tr>
<td>Group 7</td>
<td>0.109</td>
<td>0.097</td>
</tr>
<tr>
<td>Group 8</td>
<td>0.123</td>
<td>0.090</td>
</tr>
<tr>
<td>Group 9</td>
<td>0.137</td>
<td>0.111</td>
</tr>
<tr>
<td>Group 10</td>
<td>0.098</td>
<td>0.080</td>
</tr>
<tr>
<td>Group 11</td>
<td>0.103</td>
<td>0.079</td>
</tr>
<tr>
<td>Group 12</td>
<td>0.106</td>
<td>0.104</td>
</tr>
<tr>
<td>Group 13</td>
<td>0.120</td>
<td>0.103</td>
</tr>
<tr>
<td>Group 14</td>
<td>0.133</td>
<td>0.103</td>
</tr>
<tr>
<td>Group 15</td>
<td>0.114</td>
<td>0.094</td>
</tr>
<tr>
<td>Group 16</td>
<td>0.105</td>
<td>0.075</td>
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<tr>
<td>Group 17</td>
<td>0.172</td>
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<tr>
<td>Group 18</td>
<td>0.135</td>
<td>0.118</td>
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<tr>
<td>Group 19</td>
<td>0.100</td>
<td>0.076</td>
</tr>
<tr>
<td>Group 20</td>
<td>0.113</td>
<td>0.108</td>
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<tr>
<td>Group 21</td>
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<td>0.092</td>
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<tr>
<td>Group 22</td>
<td>0.110</td>
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<tr>
<td>Group 23</td>
<td>0.117</td>
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<tr>
<td>Group 24</td>
<td>0.110</td>
<td>0.089</td>
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<tr>
<td>Group 25</td>
<td>0.097</td>
<td>0.091</td>
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<tr>
<td>Group 26</td>
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<td>0.081</td>
</tr>
<tr>
<td>Group 27</td>
<td>0.137</td>
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</tr>
<tr>
<td>Group 28</td>
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<tr>
<td>Group 29</td>
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<td>0.111</td>
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<tr>
<td>Group 30</td>
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<tr>
<td>Average</td>
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</tr>
<tr>
<td>SD</td>
<td>0.021</td>
<td>0.018</td>
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</table>

Values are presented as mean and standard deviation. SD, standard deviation.

a MAPE in MOEA group was significantly smaller than that in SMR group.

b MAPE in SMR group was significantly smaller than that in MOEA group.
and the minimum value was 0.096 mm for the SMR group and 0.086 mm for the MOEA group. There was no significant difference in the MAPE of the ELPs between the two groups (0.122 mm for SMR and 0.116 mm for MOEA) (Fig. 3A, $P = 0.3951$). The standard deviation of MAPE in the MOEA group (0.014 mm) was significantly lower than that in the SMR group (0.021 mm) ($P = 0.0380$) (Fig. 3B). The rate at which MAPE was 0.3 mm or higher was significantly greater in the SMR group (mean 7.31% ± 4.80%) than the MOEA group (mean 4.87% ± 3.15%) (Fig. 3C, $P = 0.0323$). Moreover, the maximum proportion of patients with a MAPE of 0.3 mm or higher in the MOEA and SMR groups was 9.8% and 24.4%, respectively.

The frequency of independent variables selected by the SMR 30 times was 29 for AQD, 28 for LT, 27 for AL, 24 for ATA-D, 11 for ACC, 10 for CCT, 5 for PCC, 4 for age, and 2 for ATA-W. The mean normalized coefficient $\beta$ of the SMR group was 0.815 ± 0.181 for AQD, 0.498 ± 0.113 for LT, 0.301 ± 0.082 for AL, 0.246 ± 0.076 for ATA-D, −0.181 ± 0.063 for ACC, and 0.150 ± 0.003 for CCT (Fig. 4A).

The mean standardized coefficient $\beta$ of the MOEA group was 0.727 ± 0.118 for AQD, 0.4453 ± 0.077 for LT, 0.370 ± 0.125 for AL, 0.213 ± 0.085 for ATA-D, 0.118 ± 0.057 for CCT, 0.086 ± 0.093 for age, −0.077 ± 0.200 for ACC, 0.011 ± 0.044 for gender, −0.010 ± 0.080 for ATA-W, and −0.005 ± 0.085 for PCC (Fig. 4B). The minimum and maximum coefficients of determination ($R^2$) of the predicted ELP by MOEA and the measured ELP in the validation group were 0.632 and 0.873, respectively.

A comparison of the MAPE predicted by SMR and MOEA is shown in Figure 5. The values of the two groups showed a significant but weak correlation ($R^2 = 0.053$). As shown in the figure, five cases showed worse prediction results by SMR versus MOEA (Fig. 5, arrow).

The median of $R^2$ between the predicted and measured ELPs was 0.771 for MOEA, 0.412 for the SRK/T formula, and 0.438 for the Haigis formula (Fig. 6).

**Discussion**

Recently, a report indicated the high measurement reproducibility of OCT biometry and AS-OCT, thus enabling accurate measurement through ocular biometry before cataract surgery and use in IOL calculations.

In the current study, to strictly compare the two prediction methods, we created 30 populations and examined the results. As a result, there was no difference in MAPE between the two methods. MOEA showed a statistically significant reduction in the standard deviation compared with SMR. Although this difference between SMR (0.021 mm) and MOEA (0.014 mm) was considered to be clinically small, an indicated trend of superior performance of MOEA versus SMR occurred 5 out of 30 times. By contrast, none of the groups in SMR showed superior evaluation of MAPE by the SMR method compared with the MOEA method. We examined why the prediction accuracy of SMR fell for these five groups, but no clear answer was found. We examined whether there were differences in the independent variables between the prediction group...
and the verification group, but there were no differences between the two groups, including these five.

In a future study, there is a possibility that MOEA’s accuracy can be further improved by

Figure 4. Standardized regression coefficient $\beta$ of prediction equation by (A) SMR and (B) MOEA. Values are similar between the two groups.

Figure 5. Correlation between MAPE by SMR analysis and MOEA. MAPE values of MOEA and SMR were compared 30 times, with majority values equivalent between the two groups; however, in five groups SMR showed significantly higher MAPE than those in MOEA (arrow). By contrast, MOEA showed significantly higher MAPE in two groups than those in SMR (arrowhead).

Figure 6. Comparison of prediction accuracy of ELP between conventional methods and MOEA. Predicted value of ELP was calculated using SRK/T and Haigis formulas, and prediction accuracy was compared between the three groups. MOEA in current study showed ability to predict more accurately than conventional formulas.
examining in more detail the cases for which MOEA is superior to SMR. Furthermore, in the MOEA group, the proportion of MAPE of 0.3 mm or higher was significantly lower than that of SMR. When the prediction error of ELP was 0.3 mm, the refractive error was estimated to be 0.2 diopters (D) (under the following conditions: AL, 24 mm; cornea thickness, 0.5 mm; average corneal radius of curvature, 7.7 mm; IOL power of AN6KA, 20 D; and IOL position, 4.1 mm). If the high-power IOL was implanted in the eye at a short AL, the refractive error would be greater than 0.5 D, which is clinically significant. In this study, in the SMR and MOEA groups, the maximum proportion of MAPE of 0.3 mm or higher was 24.4% and 9.8%, respectively. Although there was no difference in the mean value of the MAPE, MOEA was considered to be a promising method that can offer more stable results than SMR in different samples.

Several studies reporting the predicted ELP value are summarized in Table 3. Three studies predicted ELP using SMR, and another study used a neural network--type multilayer perceptron, which is an artificial intelligence modality. Independent variables for ELP prediction as determined by SMR showed differences in each study, including the current study. It is likely that this is largely related to the differences in the IOL type and measuring instruments. The average of MAPE performed 30 times using MOEA in this study was 0.116 ± 0.014 mm. Goto et al. conducted research that created a prediction group and a verification group in the same way as for the current research. In their report, they did not create the prediction and verification groups 30 times, as we did, but rather only once. They reported that the MAPE was 0.11 ± 0.08 D, which was equivalent to the average value of our outcomes by MOEA. As for comparisons with other reports, a direct comparison cannot be made because the methodology of study is different.

Comparable variables were selected in both prediction methods; however, differences in the standardization coefficients were observed. In MOEA, the standardized coefficient value of AL was higher than that in SMR, whereas the standardized coefficient value of AQD and LT in SMR was higher than that in MOEA. These differences may be due to differences in the prediction algorithms, especially because MOEA is designed to minimize the average MAPE as well as the standard deviation. Research to determine the influence on the results of the differences in standardized coefficients is required.

Generally, in optimization using MOEA, the average value and standard deviation of the difference between the predicted and actual measurement values show a reciprocal relationship. However, because we considered that suppressing variation among cases is clinically important, we adopted a solution that minimizes the two objectives of mean value and standard deviation. It is likely that the result may differ depending on the method used to set the objective variable, and further investigation is required to clarify this aspect.

In this study, the average value of MAPE by MOEA was 0.116 mm. The refractive error caused by a 0.1-mm movement of the IOL in the standard eye is considered to be 0.07 D under the same conditions as above. Considering this value, the prediction error of the ELP in our study is considered clinically small, and our prediction equation is considered sufficient for clinical application.

Our study has several limitations. First, the eyes implanted with only one type of IOL were included. Because the IOL is a three-piece type, it is necessary to consider whether the prediction equation calculated in this study can be applied to a one-piece--type IOL. Next, patient data were collected from a single hospital. It is possible that the methods of examination and cataract surgery affected the results. Research to determine the accuracy of the prediction equation including the multicenter data is required in the future. We used the AS-OCT Casia to measure the anterior parameters of the eyes. However, whether other AS-OCT apparatus values can be used remains unclear. Moreover, among the patients included in this study, there were few cases with long and short AL. Further study including a large number of cases with eyes having long and short AL is required in the future.

Although MOEA showed usefulness in predicting ELP in our study, it may be useful in predicting other ocular biometry measurements as well. For example, because the ciliary sulcus-to-sulcus distance cannot be measured with AS-OCT, but rather only with ultrasound biomicroscopy (UBM), it may be possible to accurately predict its value by MOEA based on AS-OCT parameters. With regard to the position of the equatorial part of the crystalline lens, UBM is currently the only feasible measurement tool, but the versatility of UBM is not high.

In this study, the ELP prediction equation was created by means of MOEA with sufficient accuracy.
for the purpose of clinical applicability. The current ELP is based on the measurement values of AS-OCT and the optical coherence biometer IOLMaster700. The AS-OCT measures the distance using the group refractive index of the tissue at a 1310-nm wavelength. In calculations using the thick lens system, such as ray tracing, accurate biometric measurements with the refractive index corrected for each tissue are required. With regard to measurement of the AL, correction is required when using measurement devices with an equivalent refractive index such as the IOLMaster or Lenstar LS 900 (Haag Streit AG, Koeniz, Switzerland).

In conclusion, MOEA showed potential as a useful and feasible method for ELP prediction for both minimizing the average error and its standard deviation simultaneously. MOEA is a promising method for complex processing involving various factors and generating high-accuracy prediction equations. As described above, MOEA has a characteristic advantage in that the result is stable even when it is performed multiple times. Taking advantage of this feature, it may be possible to use MOEA for the verification and improvement of other prediction equations in the future.

**Table 3.** Extended

<table>
<thead>
<tr>
<th>Authors</th>
<th>Prediction Method</th>
<th>Regression Coefficient</th>
<th>Prediction Error</th>
<th>Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olsen et al.⁴</td>
<td>Regression formula</td>
<td>$R = 0.75$</td>
<td>$-0.11 \pm 0.34 \text{ mm}$</td>
<td>Ultrasound biometry</td>
</tr>
<tr>
<td>Olsen &amp; Hoffmann²⁶</td>
<td>Regression formula</td>
<td>$R = 0.86$</td>
<td>$0.00 \pm 0.17 \text{ mm}$</td>
<td>Optical low-coherence reflectometry</td>
</tr>
<tr>
<td>Findl et al.²⁷</td>
<td>Neural network–type multilayer perceptron</td>
<td>$R = 0.68$</td>
<td>$0.0152 \pm 0.0197 \text{ mm}$</td>
<td>Manual keratometer, slit lamp, partial coherence interferometry</td>
</tr>
<tr>
<td>Shammas &amp; Shammas¹²</td>
<td>Multiple linear regression</td>
<td>$R = 0.85$</td>
<td>$0.002 \pm 0.16 \text{ mm}$ (maximum: 0.34 mm)</td>
<td>Optical low-coherence reflectometry</td>
</tr>
<tr>
<td>Goto et al.¹⁷</td>
<td>Single and stepwise multiple linear regression</td>
<td>$R^2 = 0.71$</td>
<td>MAPE: $0.11 \pm 0.08 \text{ mm}$</td>
<td>Partial coherence interferometry, AS-OCT</td>
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</tbody>
</table>

ACD, anterior chamber depth; K, keratometric value; WTW, white to white.
Acknowledgments

Disclosure: A. Tamaoki, None; T. Kojima, None; Y. Tanaka, None; A. Hasegawa, None; T. Kaga, None; K. Ichikawa, None; K. Tanaka, None

References
