Original Article

Intraocular Lens Power Formula Selection Using Support Vector Machines

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Received: 23 November 2014

Accepted: 25 December 2014

Keywords:

Intraocular lens (IOL),

Cataract surgery,

Support vector machine (SVM),

Axial length,

Corneal power.

ABSTRACT

Purpose- In cataract surgery, the defected lens is replaced with an artificial intraocular lens (IOL). The refraction power of this lens is specified by ophthalmologists before the surgery. There are different formulas that propose the IOL power based on corneal power and axial length. Six common formulas is used in this study and the one which minimizes the postoperative error for a specific patient have to be selected.

Methods- Refraction is measured three times at most, during six month after surgery and the best result is considered as postoperative refraction for each patient. A Support Vector Machine (SVM) is used to classify the data to two groups based on axial length and corneal power. Each class needs a formula with a specific tendency toward stronger or weaker IOL lenses according to the feature vector.

Results- Experimental tests lead to a nearly diagonal confusion matrix which supports the performance of the proposed method strongly. Mean Absolute Error (MAE) is 0.47 which shows 6% decrease in postoperative refraction error compared to the best reported result.

Conclusions- In calculating IOL power, we expect stronger IOL powers for eyes having shorter axial length or weaker corneal power. In the contrary, a weaker IOL power is expected for longer axial length and stronger corneal power. But experimental results show that for the first group, formulas proposing weaker powers win the race for decreased postoperative refraction error while for the second group, formulas leading to stronger powers perform better. This shows that these formulas overestimate and underestimate for marginal cases.

1. Introduction

Cataract is a disease in which the lens inside the eye becomes cloudy, so it leads to a decrease in vision. The most important factor that increases the risk of cataract disease is aging. Genetic composition, exposure to ultraviolet light, and diabetes are the second rank factors [1]. In old days, the defected lens was removed and a strong mal-refraction was resulted due to the lack of spectacles. When spectacles came up there were no alternative options for refraction correction until sir ridley developed the intraocular lens implant. Nowadays, an artificial (intraocular) lens is being calculated preoperatively and implanted through a small incision after the cloudy natural lens has been removed using phacoemulsification

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or femtosecond-laser technology [2, 3].

The power of intraocular lens is specified by ophthalmologists according to existing formulas. First, the ophthalmologist defines target refraction for each eye. Then a formula is used to propose the needed IOL power. The resulting postoperative error is calculated by subtracting the target refraction and the actual refraction after surgery. Since there are several formulas recommending different IOL powers, it is difficult to select the right formula for each patient. Normally an ophthalmologist selects one formula according to his/her experience. Whereas postoperative refraction error is directly depended on the selected IOL power and repeated cataract surgery is rarely performed, IOL power selection is critical for the patient to have the minimum refraction error after surgery.

Axial length and corneal power have been the most important factors from early days of IOL power formulation up until now [2]. The distance between anterior surface of cornea and fovea is called axial length. Cornea is the transparent outer layer of the eye which covers up the iris, pupil and anterior chamber. However two-thirds of the refraction power in eye is provided by cornea.

Normally, a-scan ultrasound was utilized to obtain axial length, but this technology has a low resolution for this measurement. Recently optical biometry, also called Partial Coherence Interferometry (PCI), is used to determine the axial length [4, 5]. However in dense cataracts, where optical biometry fails, a-scan ultrasound is still used to calculate axial length. Corneal power is measured by keratometry or corneal topography.

Intraocular lens power formulas are divided to theoretical and regression formulas. Formerly, theoretical formulas were used to calculate the needed IOL power. The following formula was introduced by Fyodorov in 1975.

$$P = \frac{n_2}{(AL - ACD)} - \frac{1}{\left(\frac{1}{K} - \frac{d}{n_1}\right)} \tag{1}$$

Where P is the IOL power for emmetropia, n_1 is the refractive index in the anterior segment, n_2 is the refractive index in the posterior segment, AL is the axial length of the eye in meters, ACD is the effective anterior chamber depth in meters and K is the corneal power [6].

The first regression formula was presented by sanders-retzlaff-kraff (SRK I, SRK II) in 1981 [7]. SRK I determines IOL power with linear regression using three parameters

$$P = A - 0.9K - 2.5AL \tag{2}$$

where P is the IOL power for emmetropia, K is the corneal power and AL is the axial length [2]. It can be seen that 1 millimeter difference in axial length, yields an error of 2.5 diopters in IOL power, while 1 diopter of error in corneal power measurement introduces 0.9 diopter deviation into the IOL power.

Modern theoretical formulas consider other important factors which affect IOL power. Estimated Lens Place (ELP) is defined as the distance between cornea and IOL and needs to be estimated before implementation. SRK/T, Holladay1, Holladay2, HofferQ and Haigis are the best known modern formulas which use ELP for calculating IOL power.

Based on the literature, difference between selected and desired IOL power in eyes with normal axial length is lower than eyes that have either short or long axial lengths [8]. Figure 1 depicts variation of IOL power between three formulas with constant corneal power [8]. Where axial length is too short or too long, improper selection of IOL power produces high postoperative errors. Besides, none of the formulas can propose IOL power with minimum error, compared to other formulas, in the entire range of axial length. So most previous studies have focused on using different formulas for diverse ranges of axial length.

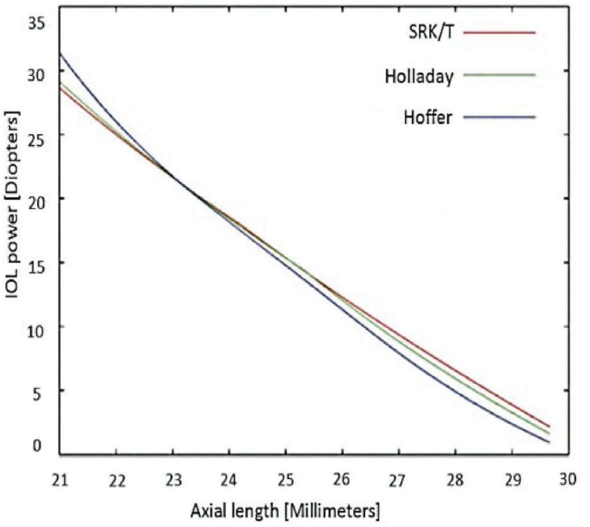


Figure 1. IOL power calculated by three formulas [8].

In 2008, Wang *et al.* calculated IOL power error in eyes with long axial length (>25 mm) and realized that Haigis formula generates minimum error compared to other formulas [9]. Gavin *et al.* in 2007 and Day *et al.* in 2012 concluded that IOL power error for eyes with short axial lengths (<22 mm) is minimized using HofferQ formula [10, 11]. In a study conducted on 8108 eyes in 2011, each formula performed best in one segment of the axial length range. Postoperative error was minimum for axial lengths between 20 mm and 20.99 mm using HofferQ formula, for axial lengths between 21 mm and 21.49 mm with HofferQ and Holladay1, for axial lengths between 23.50 mm and 25.99 mm with Holladay1, and for axial lengths longer than 27 mm with SRK/T [12]. Similarly in 2014 Joshi *et al.* used SRK II, SRK T, Holladay1 and HofferQ formulas and demonstrated that in children which had congenital cataract with axial length less than 20 mm SRK II was the best predicting formula [13].

Although axial length is critical and plays an important role in choosing a formula, it is not the only contributing factor. None of these studies consider corneal power (the second important parameter). This study attempted to decrease IOL selection error by considering both axial length and corneal power in the formula selection task. We utilize a Support Vector Machine (SVM) [14] to predict IOL power according to six formulas (SRK II, SRK/T, Holladay1, HofferQ, Haigis and Binkhorst) used for IOL power calculation in cataract surgery [15].

The next section introduces the data and classification method. Results are presented in section 3 and are discussed in section 4.

2. Materials and Methods

2.1. Data

The data set consists of 781 eyes that have undergone cataract surgery at Basireye center (Tehran, Iran). Axial lengths and corneal refraction powers were measured using Zeiss IOL master (Carl Zeiss Meditec, Jena, Germany) [5]. Table 1 shows the distribution of the data. The ophthalmologist has suggested applied IOLs by selecting formulas for each patient according to his/her experience. Refraction is measured at most three times during six month after surgery and the best result is considered as postoperative refraction.

Table 1. Distribution of the data for 781 cataract surgeries.

	Axial Length (mm)	Corneal Refraction Power (D)
Mean (± SD)	23.97 (±2.06)	44.43 (±1.76)
Range	19.93-34.18	34.5-51.88

Desired IOL powers are calculated based on the postoperative refraction power. So we have the error for all formulas. The mean absolute of these errors (MAE) are shown in Table 2 for each formula.

Table 2. Mean Absolute Error (MAE) of IOL powers.

Formula	SRK II	SRK/T	Holladay1	HofferQ	Haigis	Binkhorst
MAE	0.64	0.52	0.54	0.62	1.01	0.72

2.2. SVM

SVMs are supervised learning models used for classification and regression analysis. SVM constructs a hyperplane in J dimensional input space to classify data while maintaining maximum classification margin for both classes. Greater margins lead to higher robustness and lower generalization error. A linear hyperplane in the input space is represented as follows.

$$f(\boldsymbol{x}) = \boldsymbol{w}^T\boldsymbol{x} + b = 0 \quad (3)$$

Maximum margin is obtained by minimizing $\|\boldsymbol{w}\|^2/2$ subject to $y_i\left(\boldsymbol{w}^T\boldsymbol{x}_i + b\right) \geq 1$, where $y_i \epsilon \{-1,1\}$ indicates the class of ith input data. Using lagrange multipliers $\boldsymbol{\alpha}$, this constrained optimization problem can be expressed as

$$\max L(\boldsymbol{\alpha}) = \sum_{i=1}^{N} \alpha_i - \frac{1}{2}\sum_{i=1}^{N}\sum_{j=1}^{N} \alpha_i \alpha_j y_i y_j \boldsymbol{x}_i^T \boldsymbol{x}_j$$
$$S.T\ \alpha_i \geq 0 \ and \sum_{i=1}^{N} \alpha_i y_i = 0 \quad (4)$$

where $i \neq j$ and $i=(1,2,\ldots,N)$. Once $L(\boldsymbol{\alpha})$ is minimized, data points corresponding to nonzero α_is are support vectors. $\boldsymbol{w}$ and b are calculated as follows

$$w = \sum_{i=1}^{N} \alpha_i y_i \boldsymbol{x}_i \quad (5)$$

$$b = y_k - \sum_{i=1}^{N} \alpha_i y_i \boldsymbol{x}_i^T \boldsymbol{x}_k \quad (6)$$

where $\boldsymbol{x}_k$ is any of the support vectors, inputs having minimum distance from the hyperplane, and y_k is its associated class.

Sometimes, soft margin classification is employed in SVM learning process. This allows a certain amount of misclassification for data sets that a linear hyperplane cannot separate them to two classes. In this case $\boldsymbol{w}^2/2 + C\sum_i \xi_i$ has to be minimized subject to $y_i\left(\boldsymbol{w}^T\boldsymbol{x}_i + b\right) \geq 1 - \xi_i$, where $1 \leq i \leq N$, $C \geq 0$ is a trade-off coefficient, and $\xi_i \geq 0$ is the slack variable, which is the distance between the ith misclassified input and the classifying hyperplane. By applying lagrange multipliers again, $\boldsymbol{w}$ is calculated as before by equation 5, and b is obtained as follows for any k with $\alpha_k > 0$.

$$b = y_k\left(1 - \xi_k\right) - \sum_{i=1}^{N} \alpha_i y_i \boldsymbol{x}_i^T \boldsymbol{x}_k \quad (7)$$

When facing a nonlinear classification, we can transform data to a higher dimensional space using an appropriate nonlinear function φ, hoping that a linear classification would be possible in the new space. The dual lagrange problem then would be

$$\max L(\boldsymbol{\alpha}) = \sum_{i=1}^{N} \alpha_i - \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} \alpha_i \alpha_j y_i y_j \left(\varphi(\boldsymbol{x}_i)^T \varphi(\boldsymbol{x}_j)\right) \quad (8)$$

Where $\varphi(\boldsymbol{x}_i)^T \varphi(\boldsymbol{x}_j)$ can be rewritten as $K(\boldsymbol{x}_i, \boldsymbol{x}_j)$ which is called a kernel function. In the present study, we use radial basis kernel function given by

$$K(\boldsymbol{x}_i, \boldsymbol{x}_j) = \exp\left(-\frac{\|\boldsymbol{x}_i - \boldsymbol{x}_j\|^2}{2\sigma^2}\right) \quad (9)$$

Where σ is the standard deviation of the Gaussian function.

2.3. Data Classification

Assume the two dimensional feature vector consists of axial length and corneal power. If we assign the best formula to each eye based on postoperative error, a complicated partition of the input space to six classes is obtained. Even if the data is divided to two categories (e.g. based on conformity with SRK/T which has the minimum MAE according to Table 2) as shown in Figure 2, we could not arrive at a reasonable classification task. In this case, 531 out of 781 eyes have nonzero postoperative error and are distributed all around the input space. The same scenario goes for nearly all other formulas. It is obvious that this approach for classification is impractical here.

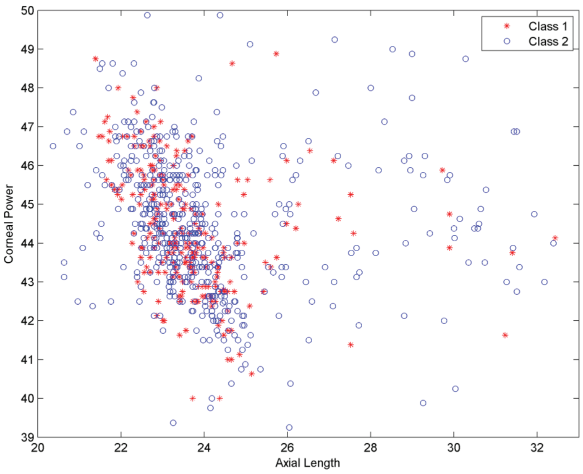


Figure 2. Division of the data to two classes according to SRK/T formula. Class 1: zero postoperative error (250 cases). Class 2: nonzero postoperative error (531 cases).

Let us assume $\boldsymbol{P}_f$ being a vector containing the IOL powers for a patient suggested by SRK II, SRK/T, Holladay1, HofferQ, Haigis and Binkhorst formulas respectively. Further, let P_{fl} and P_{fu} represent the minimum and maximum within $\boldsymbol{P}_f$ elements. For 228 eyes, none of the formulas led to zero postoperative error, of which 110 eyes need IOL powers out of $[p_{fl}, p_{fu}]$ closed interval. We call these, *out of range* data. If either p_{fl} or p_{fu} would produce zero postoperative error, we call that case a *marginal* data. These two groups (out of range and marginal data) are called *distant* data together. Other cases, which we call *regular*, must have IOL powers within $[p_{fl}, p_{fu}]$ open interval.

To train the nonlinear soft margin SVM, we just use the distant data which we will divide to two classes. If the desired IOL power for an eye is equal to or more than P_{fu} (equal to or less than P_{fl}), we put it in the C_1 class (C_2 Class). A two dimensional plot shows the separability of the *distant* data to these two classes (Figure 3). Based on this strategy, C_1 and C_2 would contain 130 and 241 members respectively.

It is obvious, and Equation 2 corroborates it as well, that for an eye having stronger corneal power or longer axial length, the needed IOL power would be weaker. Comparison of the desired IOL powers of C_1 class (which have bigger and stronger axial length and corneal powers) with that of C_2, shows that in general C_1's desired IOL powers are lower than the other class as we expected. Notice the superficial conflict: C_1 cases need lower IOL powers compared to C_2 cases while they require powers greater than P_{fu} at the same time and vice versa for C_2 cases. In fact, we can conclude that these six formulas underestimate the needed power for C_1 cases and overestimate for C_2 class members.

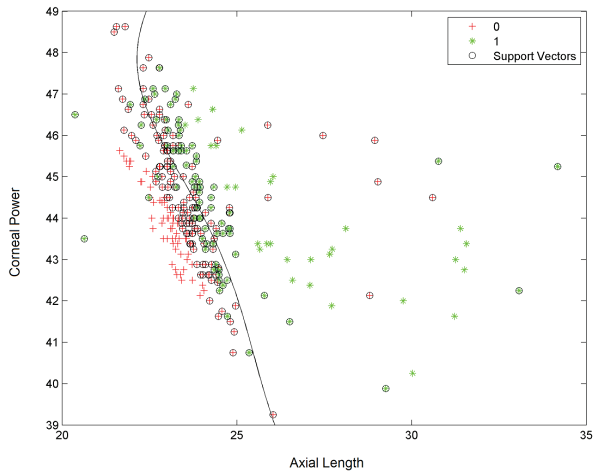


Figure 3. Classification of the *distant* training data for one fold using a soft margin nonlinear SVM.

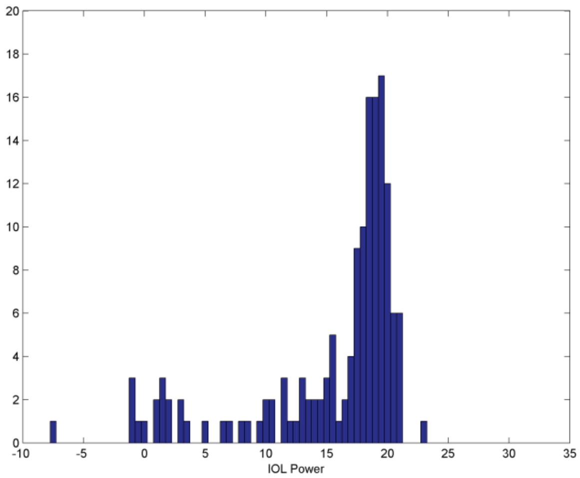
One formula has to be selected for every eye. We can infer overestimation or underestimation tendency of formulas for each case by classifying it using the trained SVM. For each case, we sort $\boldsymbol{P_f}$ in ascending order and call the resulted permuted power vector $\boldsymbol{P_{fp}}$. Then we classify all of the *training* data by SVM and calculate power estimation MAE for every member index in $\boldsymbol{P_{fp}}$ within each class. Based on the results for training data (or by running a simple optimization technique e.g. Least Absolute Errors, LAE), we choose one member index of $\boldsymbol{P_{fp}}$ having minimum postoperative refraction error for that class.

2.4. Validation

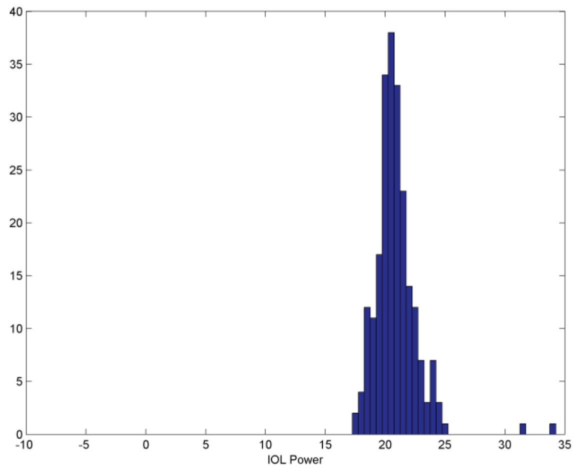
Five-fold cross validation is applied for SVM learning and evaluation. First, the data is divided to five equally sized subsets. Then in each fold, four subsets are used for training and the remaining subset is used for test. The process is repeated five times, so that each data has a chance of being tested against.

3. Results

The suggested algorithm was used to divide the training data to two classes. Figure 4 depicts the histograms of desired IOL powers which eliminate MAE for these two classes. As we expected, it is clear that C_1 cases need weaker IOL powers. In the previous section we mentioned that using P_{fu} and P_{fl}, within elements of $\boldsymbol{P_f}$ for each eye in *distant cases*, minimize the MAE in C_1 and C_2 classes respectively. But we should remind that for a newly introduced case, we do not have any evidences about the data being *distant* or *regular*. Considering regular cases as well, we probably need to select powers other than these two extreme values.



(a)



(b)

Figure 4. Histograms of desired IOL powers that eliminate MAE for training data classified by the SVM as (a) C_1 and (b) C_2.

Tables 3 and 4 show MAE of *all* training data for $\boldsymbol{P}_f$ and $\boldsymbol{P}_{fp}$ elements in each class. we can see that for the data in C_1 (C_2) class, The 5th (4th) element of $\boldsymbol{P}_{fp}$ generates minimum error.

The proposed method is applied to three out of six formulas in order to compare the results with the previous method [8]. The confusion matrices are depicted in Tables 5 and 6 for previous and proposed methods respectively. In these matrices, numbers in each row sum up to 100 and show the percentages of different formulas proposed by the method for each case instead of the actual best formula for that case.

Comparison results are also shown in Tables 7 and 8 for previous and proposed methods respectively using six formulas.

Overall selection rate of each formula for these two strategies is depicted in Table 9.

Table 3. Mean Absolute Error (MAE) of IOL powers for $\boldsymbol{P}_f$ elements.

Formula	SRK II	SRK/T	Holladay1	HofferQ	Haigis	Binkhorst
MAE For C_1	0.78	0.64	0.69	0.90	0.63	1.01
MAE For C_2	0.57	0.469	0.464	0.466	1.23	0.58

Table 4. Mean Absolute Error (MAE) of IOL powers for $\boldsymbol{P}_{fp}$ elements.

Formula	1	2	3	4	5	6
MAE for C_1	1.12	0.87	0.68	0.60	0.55	0.82
MAE for C_2	0.60	0.50	0.47	0.44	0.54	1.23

Table 5. Confusion matrix for the method presented in [8] using three formulas.

		Suggested Formula (%)		
		SRK/T	Holladay1	HofferQ
Best Formula	SRK/T	77.2	8.5	14.3
	Holladay1	10.9	80	9.1
	HofferQ	13.7	6.8	79.5

Table 6. Confusion matrix for the proposed method using three formulas.

		Suggested Formula (%)		
		SRK/T	Holladay1	HofferQ
Best Formula	SRK/T	90.4	3.9	5.7
	Holladay1	8.5	87.1	4.4
	HofferQ	14.2	5.1	80.7

Table 7. Confusion matrix for the method presented in [8] using six formulas.

		Suggested Formula (%)					
		SRK II	SRK/T	Holladay1	HofferQ	Haigis	Binkhorst
Best Formula	SRK II	59.7	5.6	6.5	7.6	10.1	10.5
	SRK/T	7.6	69.4	3.9	5.5	6.2	7.4
	Holladay1	5.3	5.1	75.4	2.9	7.2	4.1
	HofferQ	0	5.9	6.3	79.8	3.4	4.6
	Haigis	0	10.5	5.5	8.6	66.2	9.2
	Binkhorst	0	0	0	16.6	16.6	66.8

Table 8. Confusion matrix for the proposed method using six formulas.

		Suggested Formula (%)					
		SRK II	SRK/T	Holladay1	HofferQ	Haigis	Binkhorst
Best Formula	SRK II	68.6	8.7	7.9	7.6	2.7	4.5
	SRK/T	3.4	83.1	4	5.8	1	2.7
	Holladay1	4.6	6.8	77.9	4.4	2.7	3.6
	HofferQ	6.8	10.7	4.2	73.1	1.9	3.3
	Haigis	9.4	13.6	9	7.3	57.8	2.9
	Binkhorst	8.6	13.2	9.9	7.8	3.2	57.3

Table 9. Selection rate for each formula (%).

	SRK II	SRK/T	Holladay1	HofferQ	Haigis	Binkhorst
Previous Method [8]	30.5	23.8	15.5	8.3	18.5	3.4
Proposed Method	18.6	20.2	18.2	16.9	11.1	15

While the Self-Organizing Map (SOM) neural network, as presented in [8], have a Mean Absolute Error (MAE) of 0.50 at best, the proposed technique ends up with an MAE of 0.47. This improvement means 23.43 diopters decrease in errors for all patients. Histogram of errors is depicted in Figure 5.

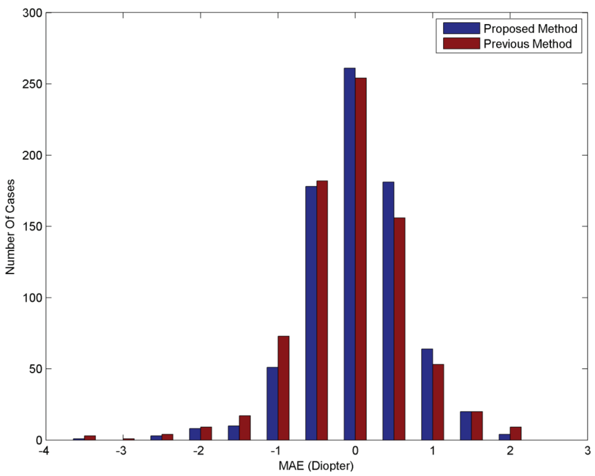


Figure 5. Histogram of error for proposed method and SOM method [8].

4. Discussion

As mentioned previously, the classification task in this study is difficult since no formula is suitable for all cases. Besides, the data is highly nonlinear and lacks many variables that have little effect on the results individually while introduce considerable deviation together. Ophthalmologists usually select the appropriate model based on axial length, but Figure 3 shows that corneal power is also an important factor in selecting the formula for IOL power calculation. So we used this influencing parameter as well.

Although the bigger the axial length or the stronger the corneal power is, the weaker the IOL lens should be (and vice versa), Figure 4 shows that best IOL powers for class C_1 eyes are lower than powers for class C_2 eyes. So we can infer that known formulas show too much propensity to this fact. It means that they underestimate for C_1 cases and overestimate for C_2 cases. Putting it another way, the formulas have a tendency toward the normal cases even for the extreme cases. The classification task is accomplished by dividing the input space to two subspaces, namely C_1 and C_2, based on the *distant* (extreme) data.

Although for distant data always maximum or minimum is the best power within $\boldsymbol{P}_f$ members, but this is not the case for all data. Members of $\boldsymbol{P}_f$ have been sorted into ascending order. Then the MAE is calculated for each permuted member. The results (Table 4) show that the fifth and forth formula have the minimum postoperative error for C_1 and C_2 classes respectively. In C_1 class, the desired IOL powers are weaker compared to class two. But we should select a strong IOL power within six available suggestions (the fifth element in this case) to overcome the underestimate caused by the previously mentioned tendency toward the normal cases. For class C_2 the normal tendency is toward stronger powers while we should select a somewhat weaker power (the forth element in this case) to overcome the mentioned overestimate embedded in formulas.

Tables 5 and 6 show the confusion matrices and could be used to compare the proposed method and previous method for SRK/T, Holladay1 and HofferQ formulas. Larger diagonal elements and smaller off-diagonal elements in Table 6 compared to Table 5 show superiority of suggested strategy for all formulas. Table 9 shows that the previous method uses Haigis formula more frequently compared to the proposed algorithm. Combined with Tables 7 and 8, it means that this method uses Haigis formula for 18.5% of inputs with 66.2% successful formula suggestion rate among them, whereas the proposed method uses this formula 11.1% of times, where 57.8% of them lead to optimal power calculation. But conducting the same comparison for other formulas, reveals superiority of the proposed method.

Table 9 shows the selection rate of each formula in the proposed method. SRK/T formula is selected more than other formulas which are in accordance with the errors reported in Table 2.

Figure 5 depicts the histogram of MAE for previous and proposed methods. It is obvious that the number of patients with zero postoperative error is increased in the proposed method. Zero postoperative error means that refraction after surgery meets target refraction. Therefore, power of needed spectacles for these cases will be reduced.

Postoperative refraction error for the proposed method is 0.47 which is 6% better than previous methods for our data. Number of cases with zero postoperative error is also increased by 2.7%. These results are promising and encourage clinicians to consider using this method for lens power selection instead of just relying on experience of ophthalmologists.

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