• Intelligent Ophthalmology •

Prediction of SMILE surgical cutting formula based on back propagation neural network

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Abstract

● **AIM:** To predict cutting formula of small incision lenticule extraction (SMILE) surgery and assist clinicians in identifying candidates by deep learning of back propagation (BP) neural network.

● **METHODS:** A prediction program was developed by a BP neural network. There were 13 188 pieces of data selected as training validation. Another 840 eye samples from 425 patients were recruited for reverse verification of training results. Precision of prediction by BP neural network and lenticule thickness error between machine learning and the actual lenticule thickness in the patient data were measured.

● **RESULTS:** After training 2313 epochs, the predictive SMILE cutting formula BP neural network models performed best. The values of mean squared error and gradient are 0.248 and 4.23, respectively. The scatterplot with linear regression analysis showed that the regression coefficient in all samples is 0.99994. The final error accuracy of the BP neural network is -0.003791±0.4221102 μm.

● **CONCLUSION:** With the help of the BP neural network, the program can calculate the lenticule thickness and residual stromal thickness of SMILE surgery accurately. Combined with corneal parameters and refraction of patients, the program can intelligently and conveniently integrate medical information to identify candidates for SMILE surgery.

● **KEYWORDS:** small incision lenticule extraction; back propagation neural network; deep learning; cutting formula; prediction

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INTRODUCTION

Small incision lenticule extraction (SMILE) has been widely used in clinic in recent years[1]. This technique offers several advantages over other corneal surgeries, such as femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) and LASIK, as it avoids complications related to corneal flaps and improves postoperative stability, reducing refractive regression and dryness[2-3]. However, the implementation of personalized cutting for SMILE presents a significant challenge that requires improvements in cutting accuracy and control of related factors[4-7]. Accurate prediction of corneal lenticule thickness before and after surgery is also critical to prevent the risk of iatrogenic ectasia, especially in patients with thinner central corneal thickness (CCT) or high myopia[8-9]. Therefore, it is particularly important to study the corneal cutting formula of patients with SMILE.

At present, many studies with the cutting accuracy of SMILE mostly focuses on the nomogram adjustment to avoid over- and under-correction[10-13]. However, for patients with thinner CCT or high myopia, it is very confused to choose the appropriate surgical method, especially in patients with critical value of residual stromal bed thickness. In order to verify whether these critical patients are suitable for surgery, surgeons, especially novice surgeons must rely on VisuMax machines (Carl Zeiss, Germany) to obtain effective lenticule thickness and residual stromal thickness by inputting patient's data, so as to judge the feasibility of surgery[14]. In addition, while VisuMax has provided the reference tables of lenticule thickness for different myopia and astigmatism degrees, the value of lenticule diameter is discontinuous and the corneal curvature is fixed (K=7.7 mm), which shows that a lot of data is lost and could not be queried. A recent systematic review reported a post-refractive ectasia incidence of 0.011%, similar to the estimated incidence of worldwide post-SMILE ectasia (0.020%) in patients without identifiable preoperative risk factors[15]. Therefore, it is very important to find out the cutting formula of SMILE surgery and predict the lenticule thickness conveniently. Fortunately, artificial intelligence (AI) has been widely used to solve medical problems, which given the adequate number of training samples (treatment cases) to design "intelligent" models to create and improve surgical nomograms[16]. At present, deep neural network predictions for medical imaging applications have been widely applied for prediction of diabetic retinopathy, development of glaucoma, and detection of keratoconus[17-19]. In this study, we develop a program to predict the cutting formula and the lenticule thickness by using back propagation (BP) neural network. With this program, we only need to input the patient's data in the software in our own computer and the lenticule thickness would be calculated quickly, which will prompt whether the patient is suitable for surgery conveniently.

SUBJECTS AND METHODS

Ethical Approval The study protocol adhered to the tenets of the Declaration of Helsinki, and was approved by the Ethics Committee of Jiangsu Province Hospital (the First Affiliated Hospital with Nanjing Medical University) (2021-NT-38). All patients signed an informed consent before participation.

Patient Data Acquisition Patients were recruited from 20 May 2021 to 31 October 2021. The inclusion criteria were: 1) age 18 to 45y; 2) spherical myopia from -0.5 D to -10.00 D, and myopic astigmatism from 0 to -4.00 D; 3) corrected distance visual acuity (CDVA) of 20/40 or better; 4) postoperative residual stromal bed thickness >280 µm. 5) stable refraction for more than 2y. The exclusion criteria were: 1) corneal disease; 2) ocular trauma; 3) suspicion of keratoconus on corneal topography. Patients were required to stop wearing soft contact lenses for at least 2wk and rigid contact lenses for at least 4wk before examination. All patients underwent complete ophthalmologic evaluation preoperatively, including slit-lamp biomicroscopy, Pentacam Scheimpflug imaging (Pentacam HR; Oculus GmbH, Wetzlar, Germany), eye tonometry (Icare, Finland), visual acuity/subjective manifest refraction (RT-2100, NIDEK, Inc., Japan), and corneal sublayer thickness scanning (RTVue 100, OptoVue, Inc., USA). Optical coherence tomography (OCT) imaging was performed first to avoid potential artifacts. Anterior keratometry (Km; mean of Kmin and Kmax), corneal higher-order aberrations and posterior K were obtained using the Pentacam. All patients included in our study underwent SMILE procedures successfully. In this study, there were 13 188 pieces of data selected as training validation. Among them, 5719 pieces of data were recruited from the system (VisuMax 3.0, form of K=7.7 mm), the other 7469 pieces of data were recruited from manual entry and calculated by system that underwent SMILE procedure. Another 840 eye samples from 425 patients of Jiangsu Province Hospital (the First Affiliated Hospital of Nanjing Medical University) were recruited for reverse verification of training results. All 425 patients signed an informed consent before operation.

Machine Learning Model The lenticule thickness was affected by the data of spherical power (SPH), cylindrical power (CYL), corneal curvature radius (mean keratometer, Km) and lenticule diameter, while the residual stromal thickness is affected by corneal thickness, lenticule thickness, basal thickness and cap thickness. An architecture of our proposed machine learning model is shown in Figure 1. The study focuses on BP neural network machine learning methods. It is a multi-layer forward neural network based on error BP, which has good nonlinear function approximation ability and can realize accurate prediction. BP neural network model includes three layers of feedforward neural network structure, which are input layer, hidden layer and output layer respectively. In the study, according to the data from VisuMax system and patients' surgical parameters, we defined the input vectors and the output vectors. Input vector P is composed of SPH, CYL, average corneal curvature Km and lenticule diameter, which are respectively referred to as S, C, K and D, and $P=[S_1,S_2,S_3,\ldots,S_n;\ C_1,C_2,C_3,\ldots,C_n;\ K_1,K_2,K_3,\ldots,K_n;\ D_1,D_2,D_3,\ldots,D_n]$; Output vector T is the composed of lenticule thickness Y, which was taken from the calculated value of VisuMax. $T=[Y_1,Y_2,Y_3,\ldots,Y_n]$, n is the sample number (n=13 188; Figure 2). According to the input vector and the output vector, a BP neural network model conforming to the prediction of SMILE lenticule thickness is constructed, in which the excitation algorithm of the hidden layer and the output layer nodes is Tansig, the network training algorithm is Trainlm, the goodness of fit of the BP neural network model was judged by mean square error, the training times are set to 5000, and the convergence error is set up according to the actual prediction accuracy requirements, that is, the expected error W is set to 10^{-3}. When setting all the properties of BP neural network, the SMILE cutting formula prediction model was performed in Matlab2018b. When the BP neural network sample data is propagated forward, the input samples are introduced from the input layer, and then transmitted to the output layer after being processed by the hidden layer. If the actual output of the output layer is inconsistent with the expected output, the error back propagation updates the network weights. The BP of errors updates the network weights by reversing the output errors layer by layer from the hidden layer to the input layer

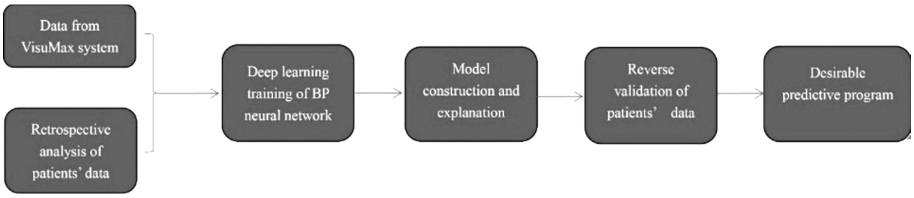

Figure 1 Architecture of the BP neural network machine learning for SMILE surgery BP: Back propagation; SMILE: Small incision lenticule extraction.

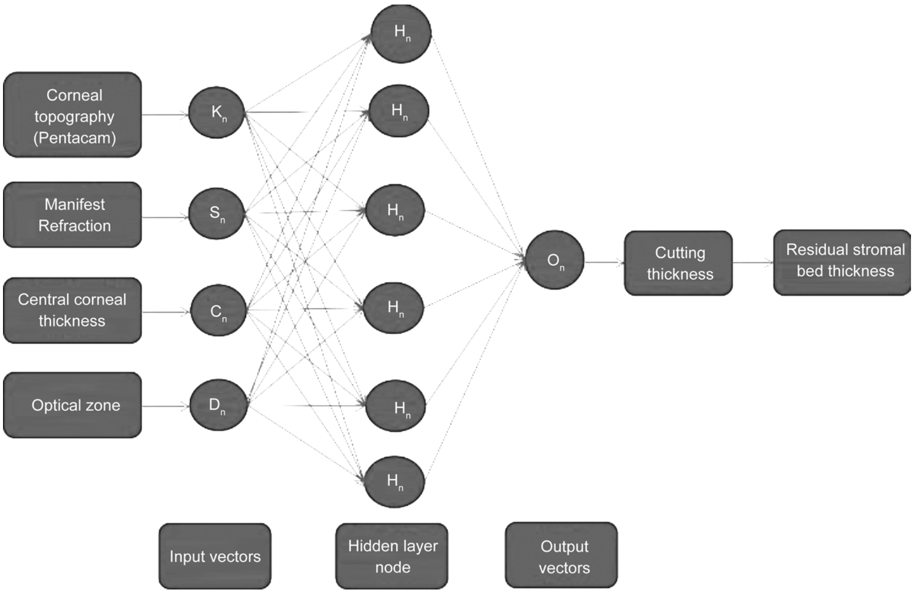

Figure 2 Schematic diagram of BP neural network for predicting the lenticule thickness of SMILE surgery BP: Back propagation; SMILE: Small incision lenticule extraction.

in some form, and distributing the errors to each neuron unit of each layer. This kind of signal forward propagation and error backward propagation, the weight adjustment process of each layer is carried out cyclically, and the weight is adjusted constantly, that is, the learning process of network. This process continues until the error of network output is reduced to an acceptable level, or until the preset learning times. That is, taking the root mean square error between the predicted and expected lenticule thickness values as the input data of BP neural network error BP, the BP neural network model is trained cyclically until the error between the predicted and actual values is less than the set threshold value W, then the model training is completed, and the BP neural network model is saved in the format of *.mat file. In this BP neural network model, the number of input layer nodes is n, the number of output layer nodes is m, and the number of hidden layer nodes was calculated according to the formula $L=\sqrt{(n+m)}+a$[20]. In this study, n was 4, m was 1, and a was taken as 2.764, so the number of neurons in hidden layer L was set to 5.

The BP neural network process is shown in Figure 3. The SPH, CYL, Km and lenticule diameter were input into the input layer, and lenticule thickness was set as the output vector. The data was randomly divided into three groups, as the training set, the validation set and the test set. The training set was used for learning, which is to fit the parameters of the classifier; the validation set was used to tune the parameters of a classifier, for example to choose the number of hidden units in a neural network; the test set was used to only to assess the performance of a fully specified classifier.

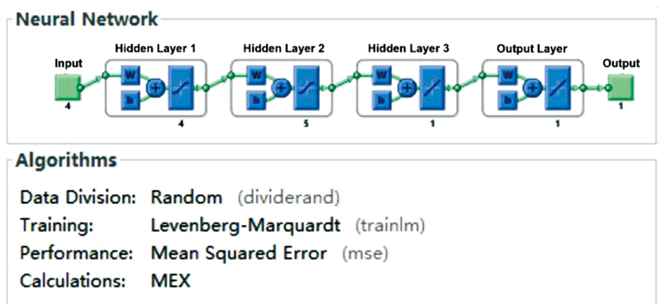

Figure 3 The BP neural network process BP: Back propagation.

Refractive Surgery All patients included in our study underwent SMILE procedures successfully by an experienced surgeon (Yuan DQ). All surgeries were performed using the VisuMax femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) system with 500-kHz repetition rate. A standard eyelid speculum was used to keep the eye open. The eye was positioned under the curved contact glass of the femtosecond laser and fixated on a blinking target. Suction was applied when the center of the pupil was centered to the contact lens.

The posterior of the refractive lenticule was created from the periphery to the center of the cornea, and the anterior surface was created from the center to the periphery. The surgery parameters were set as follows: 1) 7.3 to 7.9 mm cap diameter; 2) 110 or 120 μm cap thickness; 3) 90° side angle; 4) 6.0 to 7.8 mm lenticule diameter (optical zone); 5) 2.0 to 4.0 mm lenticule incision at 120° side angle. The target postoperative refraction was emmetropia for all patients.

Statistical Analysis To compare the difference between patients data and machine learning data, we used SPSS 17.0 (IBM Corp., Armonk, NY, USA), taking independent sample *t*-test and paired samples *t*-test for cutting error and data distribution, respectively. *P* values less than 0.05 were considered to be statistically significant.

RESULTS

Back Propagation Neural Network of Prediction Model of SMILE Lenticule Thickness After training 2313 epochs, the SMILE cutting formula BP neural network models performed best (Figure 4). The values of mean squared error and gradient are 0.248 and 4.23, respectively. The validation check was set to 6.

Predictability Analysis After training, the scatterplot with linear regression analysis of the SMILE cutting formula BP neural network models showed in Figure 5. Figure 5 shows the fitting degree of test set samples, where r refers to regression coefficient, and the closer r is to 1, the better the fitting degree is. Our study showed that the test set regression coefficient is 0.99994.

Efficacy Analysis We put the 13 188 samples into the BP neural network to calculate the error between the predicted lenticule thickness and the lenticule thickness of patients calculated by VisuMax System. As the predicted lenticule thickness in actual use should be an integer, the residual error will be rounded, and the distribution after rounding is shown in Table 1. On the premise that the total data is 13 188, the final error accuracy is -0.00083±0.561255 μm. For addition, we also used another patient's data to verify the efficacy of the BP neural network. In our study, we recruited 840 eye samples and input the data into the BP network. Then we compare the predicted lenticule thickness with the lenticule thickness of the patients. We found that the final error accuracy is -0.003791±0.4221102 μm and the error distribution was shown in Table 2. There was no significant difference in lenticule thickness between patients' data and BP neural network prediction group (*P*=0.942).

DISCUSSION

The use of SMILE for treating myopia and myopic astigmatism is widespread. Several studies have been conducted comparing the surgical results of SMILE with those of FS-LASIK, revealing comparable outcomes in terms of safety, effectiveness, predictability, and stability[21]. However, the safety of the surgery depends on corneal morphology and biomechanical parameters before the operation. The

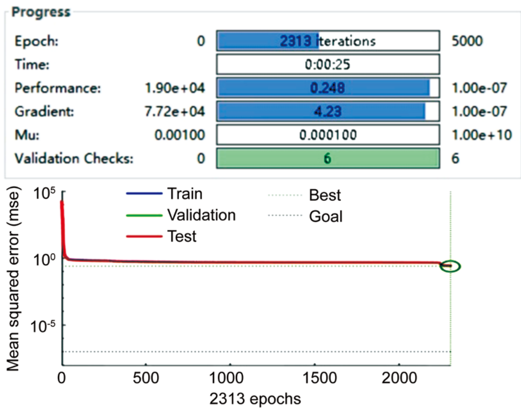

Figure 4 The best SMILE cutting formula validation performance after training 2313 epochs and the mean squared error was 0.248 SMILE: Small incision lenticule extraction.

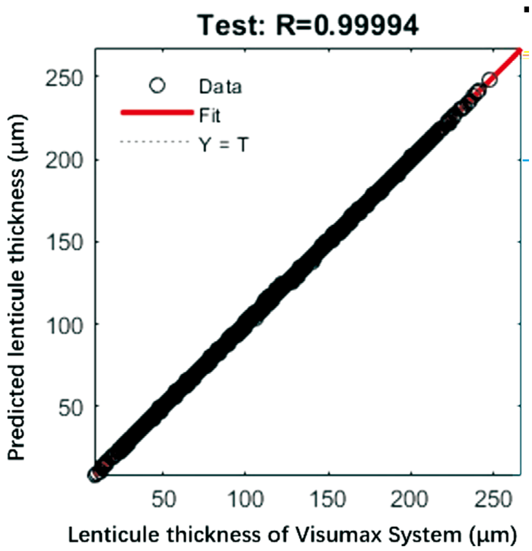

Figure 5 The scatterplot with linear regression analysis of the SMILE cutting formula BP neural network program. Horizontal coordinate the fitting degree of test set is 0.99994. BP: Back propagation; SMILE: Small incision lenticule extraction.

Table 1 The lenticule thickness error between predicted lenticule thickness and lenticule thickness calculated by VisuMax system in all 13 188 samples

Parameters	Lenticule thickness error				
	-2 μm	-1 μm	0	1 μm	2 μm
Distribution (*n*)	32	281	12583	254	39
Proportion (%)	0.24	2.13	95.41	1.92	0.29

Table 2 The lenticule thickness error between predicted lenticule thickness and lenticule thickness in 840 eyes of patients calculated by VisuMax system

Parameters	Lenticule thickness error				
	-2 μm	-1 μm	0	1 μm	2 μm
Distribution (*n*)	0	9	821	10	0
Proportion (%)	0	1.07	97.74	1.19	0

appropriate corneal thickness and lenticule thickness are also critical factors. The risk of complications, such as iatrogenic ectasia, increases with a thicker lenticule thickness and a thinner remaining stromal thickness[22]. To predict the corneal lenticule thickness before the operation, a BP neural network was employed in our research. It enabled the prediction of the cutting formula of SMILE, which helped in selecting appropriate surgical techniques. Our study discovered that our BP neural network program provides a deep learning framework for the selection of SMILE surgery. Our program required only the input of the refractive power and corneal parameters into the network. Then, the lenticule thickness and residual stromal thickness were calculated, which integrated medical information. It assisted in identifying SMILE surgery candidates and helped in making clinical decisions that are user-friendly and less risky.

Previous research has shown that the thickness of the lenticule in SMILE surgery is mainly determined by the patient's refractive power, and patients with high myopia and thinner central corneal thickness may not be suitable candidates for this procedure[23-24]. Corneal curvature and optical diameter can also affect the thickness of the lenticule, with flatter corneal curvature leading to a smaller lenticule thickness and larger optical diameters leading to greater thickness[25-26]. To ensure that enough stromal thickness is preserved in patients with relatively thin central corneal thickness, we may reduce the size of the optical zone. Collagen fibers in corneal stromal are arranged anisotropically, which is more and more obvious from the center to the periphery[27]. The arrangement of collagen fibers in the corneal stroma is anisotropic and more pronounced towards the periphery. The fibers in the peripheral area are arranged tangentially, which helps to maintain corneal limbal tension. Research has found that a smaller optical zone has relatively little impact on corneal biomechanical properties[28]. Considering that the corneal tissue may be cut less during operation than those with smaller optical zone, more stromal tissue around the cornea is retained, which can maintain the integrity of corneal morphology, structure, and function to a greater extent. However, too small optical zone will reduce the visual quality of patients. Therefore, the visual quality and surgical safety should be considered comprehensively when setting the size of the surgical optical zone, and the optical zone should not be blindly reduced or expanded. In our study, the BP neural network program input layer recruited all the influencing factors and calculated the lenticule thickness and the residual stromal thickness conveniently. If the remaining stromal bed thickness ≥280 μm, it indicates that the risk of surgery is small, and SMILE surgery should be considered. If the thickness of the remaining stromal thickness was less than 250 μm, it indicated that the operation was risky and it was recommended not to be operated on. If the remaining matrix thickness is between 250 and 280 μm, the surgery can be performed under certain conditions. At this time, the remaining corneal stromal thickness can be increased to the operable range by appropriately adjusting the preset lenticule diameter, substrate thickness, cap diameter, and cap thickness. However, if the preset parameters are adjusted within a certain interval range, for example, while the diameter is too small, it should be considered that the introduced higher-order aberration may be too large, thus affecting the visual quality. Therefore, it is necessary to reasonably select the preset parameters of patients in order to select a safer, more effective and reasonable surgery. The act of cutting tissue can sever the collagen fibers in the corneal stromal, leading to a reduction in the number of collagen lamellae at the center of the cornea, ultimately resulting in a decline in corneal biomechanical abilities. Hence, the extent of tissue cutting plays a critical role in determining corneal biomechanics. According to Huang *et al*[29], a smaller central corneal thickness results in greater tissue lenticule thickness, which exacerbates the decline in postoperative corneal biomechanics. It is considered safe when the tissue lenticule thickness is less than 140 μm and the tissue lenticule thickness percentage is less than or equal to 25%. Liu *et al*[30] discovered that the ratio of residual stromal bed thickness to preoperative CCT is inversely proportional to the change in corneal biomechanics resulting from SMILE surgery. Although CCT can only measure changes in the central cornea, it cannot fully evaluate the impact of corneal structural characteristics on biomechanical properties during corneal tissue ablation. Wei *et al*[31] observed that corneal volume decreased significantly after SMILE surgery and that the volume changes within a 3 mm radius of the central cornea were positively linked to corneal biomechanical changes.

The use of big data training in the BP neural network allows for the accurate prediction of output data of a system at a given input, without requiring prior knowledge of the mapping relationship[32]. This mathematical model is commonly utilized for function approximations, as well as pattern recognition and classification tasks in various fields[33-34]. In our study, we used the BP neural network to predict the cutting formula of SMLILE surgery and the relationship of lenticule thickness and corneal parameters and refractive power. To the best of our knowledge, no such work on prediction of cutting formula on SMILE surgery has been reported yet. The BP neural network is composed of an input layer, a hidden layer, and an output layer, and each layer contains several neurons. The neurons in the input layer are only responsible for receiving the normalized input data and passing the data to the neurons in the next layer. In our study, the number of input layer neurons is the dimension of the input vector (without considering the bias). The output layer is the last layer of the entire network and has the same function as the hidden layer, and the number of neurons in output layer is the same as the dimension of the output vector. The neurons in the hidden layer multiply or accumulate the data from the previous layer by weights and map the data to the input of the next layer using the activation function after adding the bias of the neuron. The number of neurons in the hidden layer (NH) is usually determined by experience[35]. In this study, we set the NH as 5 and could achieve high predictive accuracy.

Compared with the previous studies, this study proposes the following contributions. First, it is a novel approach to apply BP network to calculate the lenticule thickness for suspicious subjects to SMILE. There has been no particular approach to determine whether surgery is possible unless to input the data to the VisuMax machine. Second, our program supplied the new method to predict the lenticule thickness conveniently and which was not need to enter the operating room and occupy the operation time. Third, it could be used as a batch screening tool for patients with myopia to SMILE. However, there were also some limitations of this retrospective study. The number of the clinical validation data was limited and which need to be larger to verify the predictability for the postoperative surgical outcomes of SMILE. Otherwise, there were many factors affect the postoperative visual acuity and the safety of SMILE. Although it is predicted to be safe enough for the surgery, but the occurrence of postoperative keratectasia cannot be completely ruled out and individual heterogeneity might be the reason.

In conclusion, with the help of the BP neural network, our program can calculate the lenticule thickness and residual stromal thickness of SMILE surgery accurately and have extensive application prospects. Combined with corneal parameters and refraction of patients, the program can intelligently and conveniently integrate medical information to identify candidates for SMILE surgery.

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