Deep Learning Model to Predict Postoperative Visual Acuity from Preoperative Multimedia Ophthalmic Data

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Abstract Age-related macular degeneration (AMD) causes visual acuity (VA) loss in people aged ≥ 50 years. Common treatments include intravitreal injection of anti-vascular endothelial growth factor agents such as aflibercept. However, lack of response in some patients makes prediction of posttreatment VA difficult. In this paper, we propose a deep neural network model to predict posttreatment VA using pretreatment medical imaging and patient profile data. The proposed model works with image data (optical coherence tomography and color fundus photograph) and patient profile data including gender, age, affected side and pretreatment decimal visual acuity. The model was tested by comparing mean square errors (MSE) between actual and predicted visual acuity obtained from input of image data alone, input of patient profile data alone, and input of both types of data. When examining the concatenation effectiveness of input of both types of data, the outcomes of concatenation conditions 100:100 and 500:500 were compared. For concatenation condition 100:100, MSE was 0.081 for input of image data alone, 0.052 for input of patient profile data alone, and 0.058 for input of both types of data. For concatenation condition 500:500, the MSE values were 0.081, 0.052, and 0.047, respectively. The model proposed provides highly accurate prediction of posttreatment VA and indication of recovery to physicians and patients. The method can handle incomplete images and patient profile data usually collected from patients before treatment.

Keywords: deep neural network, AMD, visual acuity prediction.

1. Introduction

Age-related macular degeneration (AMD) is a major cause of visual impairment in the aging population. AMD ranges from blurring of central vision to complete blindness. There are two types of AMD, dry and wet. In dry AMD, retinal pigment epithelium (RPE) cells undergo gradual atrophy, leading to damage to the retina and irreversible blindness. In wet AMD, choroidal neovascularization develops beneath the RPE or between the retina and RPE, leading to damage to the retina and loss of vision [1].

For the treatment of wet AMD, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents, such as aflibercept, is commonly used. However, since some patients do not respond to treatment, predicting posttreatment visual acuity (VA) is difficult [2].

Previous studies have reported deep neural network models that use images such as fundus photographs (FP) and optical coherence tomography (OCT) obtained from patients to diagnose ocular diseases [3–5]. Rohm et al. [6] utilized machine learning algorithms including Random Forest and Lasso regression to predict posttreatment VA from clinical data including examination results and treatment history of AMD patients stored in electronic medical records. Shun et al. [7] used convolutional neural network to predict posttreatment VA from pre-treatment OCT images in patients with branch retinal vein occlusion. However, few studies have reported deep learning algorithms to predict posttreatment VA utilizing
both pretreatment images and pretreatment non-image clinical data.

In this paper, we propose a model to predict post-treatment VA, which uses both pretreatment image data and non-image data of AMD patients. We use FP and OCT images as image data, and use patient profile data including gender, age, affected side, and pretreatment decimal visual acuity as non-image data. Multimedia data may include multiple features that differ widely depending on the data type. If a prediction model is created without considering such differences, its accuracy may decrease. To accommodate the different types of input data, the proposed model was designed to (1) receive input that includes a variable number of dimensions; (2) extract features from image data; (3) extract features from patient profile data; (4) equalize the number of dimensions between input types; (5) combine extracted features; and (6) output the predicted VA as a numerical value.

2. Methods

To diagnose AMD, ophthalmologists usually conduct multiple tests. First, they measure VA using a standardized tool such as the Landolt ring or E chart test. Second, they perform a dilated fundus examination using ophthalmoscopy, often recorded as FP. Third, they screen macular exudative change and choroidal neovascularization using OCT images. Finally, to confirm the activity of the lesion, they evaluate the presence of abnormal leakage from the choroidal neovascularization after injecting a contrast agent containing a fluorescent dye into a vein in the arm. Ophthalmologists then comprehensively evaluate the results of all the tests to decide the diagnosis and progression of AMD [1, 8]. However, it is still difficult to accurately predict the extent of VA recovery after treatment.

To support prognosis prediction, we propose a VA prediction model that utilizes both medical images and patient profile data. The proposed model receives multimedia data as input and outputs the predicted post-treatment VA. Multimedia inputs consist of medical images and patient profile data from each patient for prediction of posttreatment decimal VA. Figure 1 shows examples of input image data. Fundus photographs are resized into $480 \times 480$ pixels. The central squared regions of fundus OCT images in vertical and horizontal cross-sections (OCT-v and OCT-h) are cropped and resized into $480 \times 480$ pixels (Fig. 1, red square). The patient profile data including gender, age, affected side (right or left), and pretreatment decimal VA [9]. Gender and affected side

![Fig. 1](image)

**Fig. 1** Layers in our proposed model.
are categorized (0 or 1), and age was normalized with min–max normalization as shown in Eq. 1,

$$\text{converted age} = \frac{age - age_{\text{min}}}{age_{\text{max}} - age_{\text{min}}} \tag{1}$$

then normalized age is multiplied by ten to convert to an integer. We convert decimal VA to logarithm of the minimal angle resolution (logMAR) [10] for analysis as a continuous variable. After the logMAR conversion, we convert the floating value of logMAR to integer value with the following processes: (1) multiply decimal VA by ten; (2) add the minimum value of logMAR and then multiplied by ten. Finally, we concatenate all converted vectors as single patient profile data. We also convert posttreatment decimal VA to logMAR, then convert to an integer as for pretreatment logMAR.

To handle multimedia inputs, the model includes three layers that perform different functions. Patient profile feature extraction layers extract features based on gender, age, affected side, pretreatment decimal VA, and pretreatment logMAR; which represents the initial processes of a medical interview and general vision tests (Fig. 1a). Image feature extraction layers extract features from FP and OCT images, which represents the process of fundus examination (Fig. 1b). Feature combination layers concatenate the features from the image feature extraction layers and the patient profile feature extraction layers; which represents the process of assessing the test results and making diagnostic and treatment decisions (Fig. 1c).

### 2.1 Patient profile feature extraction layers

Figure 1a depicts how features are extracted from patient profile data. The process involves an embedding layer and fully connected (FC) layers. We use an embedding layer for vectorizing patient profile data. That is, one item of data is assumed to have latent variables for a given number of classes, and is mapped to a multidimensional vector space. At this stage, since data with similar meanings are brought close to each other in vector space, data continuity is improved compared with the case of using one-hot encoding [11]. To facilitate subsequent concatenation with image data, the patient profile data is converted into particular dimensional features by the embedding layer. The embedding layer turns positive integers (indexes) into dense vectors of fixed size. In this study, we utilize this layer to convert the patient profile data into 20 and 100 dense vectors. Those feature vectors are converted into 100, 500 vectors by the latter FC layer. After conversion, FC layers are applied to each data set of each patient to extract the features. Then extracted features are flattened into one dimensional vector.

### 2.2 Image feature extraction layers

FP, OCT-v, and OCT-h are input into each extraction layer and converted into image features as shown in Fig. 1b. To extract image features, we use DenseNet, which is a deep learning model commonly used to classify and identify images [12]. DenseNet includes a layered structure called a dense block, wherein multiple convolutional layers are combined, which is different from the general convolutional process. DenseNet reduces gradient loss and efficiently transfers image features with the dense block. In our model, each image type is input to a different DenseNet (Fig. 1b-1). The output layer of each DenseNet is deleted, resulting in the Batch Normalization layer [13] (Fig. 1b-2). We connect the DenseNet, which has $7 \times 7 \times 1024$ dimensions, to the Batch Normalization layer, then integrate three outputs from FP, OCT-v, and OCT-h with the concatenation layer. The extracted features are flattened into one dimensional vector (Fig. 1b-3).

### 2.3 Feature combination layers

Features from both image and patient profile data are combined, as shown in Fig. 1c. Each extracted feature may differ greatly in the number of dimensions. Accordingly, the prediction accuracy may be reduced. To adjust for this, the model may equalize the dimensionality of these features in two steps. First, the output from image feature extraction layers is reduced so that its dimensions match those of output from patient profile feature extraction layers. Finally, the model concatenates the image features and the patient profile features together, and the result is connected to regression layers.

### 3. Experiment

We conducted experiments to test the effectiveness of our proposed method. We prepared five experimental conditions and compared the differences between predicted and outcome data using the mean square error (MSE).

#### 3.1 Experimental conditions

Table 1 shows the five test model conditions. We prepared three models to compare the output accuracy among different input types, including single media and multimedia inputs.

The test model of inputting only image data (OI) or only patient profile data (OP) had FC layers after the component described in 2.1 and 2.2 (Fig. 2; OI, OP100 and OP500). Therefore, OI received FP, OCT-v and OCT-h, and output predicted logMAR; while OP received patient profile data and output predicted logMAR. The model of inputting both image and patient profile data (All-in) had layers 2.1–2.3. Thus, All-in received
FP, OCT-v, OCT-h and patient profile data, and output predicted logMAR. With these models, it was possible to compare accuracy under three conditions: (1) when only image data are input; (2) when only patient profile data are input; (3) when both types of data are input.

We also prepared two conditions in OP and All-in. The two conditions differed in the number of classes of embedding and the number of dimensions when combining features. One condition had 20 embedding classes and 100 dimensions when combining (Fig. 2; OP100 and All-in100), and the other had 100 classes and 500 dimensions when combining (Fig. 2; OP500 and All-in500). These models allowed us to compare the accuracy of predictions due to differences in the number of dimensions combined and the number of dimensional extensions of patient profile data.

### 3.2 Dataset

This study was approved by the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine (R2366) and adhered to The Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan as well as the tenets of the Declaration of Helsinki. Informed consent was obtained using an opt-out method under the permission of the Ethics Committee.

The dataset included 315 data samples from patients who (1) visited the macular clinic at Kyoto University Hospital, (2) were diagnosed with wet AMD, and (3) completed a fixed regimen of intravitreal injection of aflibercept (IVA) for one year. We conducted cross-validation to avoid overfitting since the sample number was relatively small. They were separated into 295 samples for five-fold cross-validation, and 20 for testing. That is, five-fold cross-validation was performed on 295 samples, and we re-validated the trained the model using the test data after the cross-validation.

### 3.3 Results

Table 2 shows the five-measurement averaged MSE between actual and predicted logMAR visual acuity for each model. To highlight the best result, all the results with the smallest MSE are underlined. Regarding differ-

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**Table 1** Conditions of prepared models.

| model name | input data | embedding class | number of dimensions |
|------------|------------|-----------------|----------------------|
| OI         | image      |                 |                      |
| OP100      | profile    | 20              | 100:100              |
| OP500      | profile    | 100             | 500:500              |
| All-in100  | both       | 20              | 100:100              |
| All-in500  | both       | 100             | 500:500              |

**Table 2** MSE of each model.

| model  | training data MSE | validation data MSE | test data MSE |
|--------|-------------------|---------------------|--------------|
| OI     | 0.043             | 0.074               | 0.081        |
| OP100  | 0.060             | 0.079               | 0.058        |
| OP500  | 0.048             | 0.098               | 0.052        |
| All-in100 | 0.097          | 0.103               | 0.082        |
| All-in500 | 0.020          | 0.063               | 0.047        |
ences in input, MSE of All-in500 was the smallest in training data. Among the validation data, MSE of All-in500 was also the smallest. For test data, MSE of OP and All-in500 were smaller than that of OI. In addition, MSE of All-in500 for test data were smaller than that for any other model. Regarding the differences among embedding classes and the number of dimensions when combined, MSE of All-in500 was smaller than that of All-in100 for training, validation or test data. MSE differed little between OP models for training, validation, and test data.

Regardless of the number of dimensions when combined with the embedding class, MSE decreased in the order of OI, OP and All-in with the exception of All-in100, for test data. The All-in500 model resulted in a smaller MSE under all conditions, providing the best prediction accuracy for test data. OI was accurate for training data, but its prediction accuracy for test data was low, indicating low versatility. OP was accurate, but All-in500 was more accurate for training data and slightly more accurate for test data. MSE was well below 0.2 logMAR in both All-in100 and All-in500 for test data. According to previous studies [14, 15], if the MSE of logMAR exceeds 0.2, the clinical intervention can be regarded as significantly effective. Based on the results presented, our proposed model provides sufficient prediction accuracy.

4. Discussion

We discuss the significance, performance, limitations, and applicability of the proposed model based on the experimental results.

4.1 Concatenating feature extractors and predictors into one model

One advantage of a deep neural network is that it can efficiently integrate learning processes using multimedia feature extractors, weighted feature addition, and regression converter. In comparison, a shallow model requires each function to be created separately. Moreover, manual intervention may be required in the latter [16]. Meanwhile, a disadvantage of deep neural network is that we cannot explicitly determine the respective magnitudes of influence of the image and patient profile features, or their extraction algorithms.

Since the relative impact of image and patient profile features is unknown, adopting our novel strategy of using non-image data in combination with image data can take advantage of both methods, suit our purpose. Additionally, this approach allows us to extend the model to include additional patient profile features, increase the amount of information available to make predictions, and potentially improve the accuracy.

4.2 Learning multimedia input

Our proposed model adopts a concatenation layer to utilize image and patient profile features equally. The image and patient profile features are extracted in equal dimensional orders. Especially for patient profile feature extraction, we adopt embedding layers that convert inputs to certain density vectors, to extract scalar and categorical values in the patient profile data (see subsequent discussion for detail).

In order to validate the above concept, we set up two conditions for the concatenation layer in the experiment. One concatenated the features in 100:100 dimensions, and the other in 500:500 dimensions. In the experiments, the 100:100 condition yielded a larger MSE for the test data compared to the 500:500 condition. It is due to the loss of image features with excessive dimensional reduction by the image feature reduction layers. However, MSE of 500:500 condition was smaller than that of other models for training, validation, and test data. Therefore, the experimental results indicate that this concatenation process utilizing multimedia data is useful to predict post-treatment VA.

4.3 Preprocessing for improved accuracy

Preprocessing the patient profile data is essential in our proposed model. As described above, we adopt an embedding layer to convert scalar and categorical values of patient profile data into dense vectors of certain sizes. This conversion contributes to the latter process in concatenating the features equally. Additionally, we adopt logMAR order to represent vision acuity, which is intuitive for measuring differences in vision acuity based on ophthalmologists’ opinions. However, the embedding layer may not always convert data which are related to similar expressions [17]. Reliable conversion of the consultation data is essential to extract valid patient profile data features.

4.4 Limitations

In this study, we utilized fundus camera photographs of patients diagnosed with AMD and treated in Kyoto University Hospital. For an institution to adopt our model, fine-tuning may be required using training data obtained in that facility.

4.5 Applications

Application of our proposed model could inform clinical decisions as a support system for ophthalmologists, such as in deciding medications and treatments. Since the prediction of post-treatment VA alone is insufficient to support ophthalmologists and interpretation of other predicted results is required to inform treatment decisions [18], future research is envisaged to extend this model.
5. Conclusion

In this study, we propose a deep neural network model that predicts posttreatment visual acuity from multimedia input for patients treated with anti-VEGF agents. The proposed model receives FP, OCT-v, OCT-h, and patient profile data collected before treatment as inputs, and outputs predicted posttreatment VA. In the proposed model, features from each input mode are extracted separately and then combined. To ameliorate the effect of any difference in the number of dimensions of input data, the model increases or decreases the numbers of dimensions and features accordingly.

To verify the effectiveness of multimedia input and the number of dimensions when combined together, we compared the MSE of predicted VA using the data of OI, OP100, OP500, All-in100 and All-in500. We found that for test data, MSE was 0.081 for OI, 0.058 for OP100, 0.052 for OP500, 0.082 for All-in100, and 0.047 for All-in500. These experiments reveal that All-in100 and All-in500 give sufficient prediction accuracy because MSE is below 0.2 log MAR, which is a criterion for positive treatment outcome according to previous studies.

The main contributions of our proposed model are as follows. It can predict posttreatment VA with high accuracy from multimedia input, thus supporting doctors and patients as a guide for treatment. It can handle inputs of different sizes. The same image and patient profile data are often utilized in different medical scenarios; thus, this multimedia method may be applied to different predictors and diagnostic models that use similar data.

Conflicts of interest

The authors declare they have no conflict of interest.

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