Few-shot Learning Based on Multi-stage Transfer and Class-Balanced Loss for Diabetic Retinopathy Grading

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Abstract. Diabetic retinopathy (DR) is one of the major blindness-causing diseases currently known. Automatic grading of DR using deep learning methods not only speeds up the diagnosis of the disease but also reduces the rate of misdiagnosis. However, problems such as insufficient samples and imbalanced class distribution in DR datasets have constrained the improvement of grading performance. In this paper, we introduce the idea of multi-stage transfer into the grading task of DR. The new transfer learning technique leverages multiple datasets with different scales to enable the model to learn more feature representation information. Meanwhile, to cope with imbalanced DR datasets, we present a class-balanced loss function that performs well in natural image classification tasks, and adopt a simple and easy-to-implement training method for it. The experimental results show that the application of multi-stage transfer and class-balanced loss function can effectively improve the grading performance metrics such as accuracy and quadratic weighted kappa. In fact, our method has outperformed two state-of-the-art methods and achieved the best result on the DR grading task of IDRiD Sub-Challenge 2.

Keywords: Diabetic Retinopathy, Multi-stage Transfer Learning, Class-balanced Loss, Quadratic Weighted Kappa.

1 Introduction

Diabetic Retinopathy (DR) is one of the main complications of diabetic patients. It can easily lead to blindness, if not discovered and intervened at an early stage. According to current international standards, DR can be graded into five levels or classes: normal, mild, moderate, severe and proliferative DR, corresponding to grades 0 to 4 [1, 2]. Fundus images of different levels of DR from IDRiD training set [16] are shown in Fig. 1.
At present, the main method for diagnosing the severity of diabetic retinopathy relies on fundus images and diagnosis results given by ophthalmologists. However, this process will take a long time for patients to wait for, and diagnosis results are often influenced by the number and experience of ophthalmologists. Moreover, some DR levels are difficult to grade, lead to misdiagnosis and delay in optimal treatment time. Therefore, it is necessary to develop a computer-aided diagnosis system in order to help ophthalmologists make correct decisions and speed up the overall process of DR diagnosis.

In recent years, medical image diagnosis technology based on deep learning has made great progress. Particularly for DR grading, researchers have already proposed many valuable methods [3-8]. Theoretically, a good DR grading model can be trained if there are a large number of high-quality and class-balanced fundus images. However, in fact, problems and challenges still remain in the difficult task of DR grading with deep learning: (1) for few-shot learning, existing transfer learning studies only consider transferring features of one single large dataset to the target small dataset. However, this transfer strategy does not make full use of other related DR datasets; (2) The class distribution is imbalanced almost in all DR datasets. For instance, in Eyepacs [15] training set, DR0 and DR2 account for 73% and 15%, respectively. However, the most serious DR4 only accounts for 2% of the total data volume, which greatly increases the possibility of misclassification of small sample data, and will ultimately weaken generalization ability of the grading model. The aforementioned problems make it difficult to effectively enhance the accuracy of DR grading. Current studies failed to propose simple and effective solutions to these problems.

For the first problem, this paper introduces the idea of multi-stage transfer learning to improve the accuracy of DR grading. Specifically, firstly we carry on transfer learning on a 10,000-level dataset using pretrained weight of ImageNet, then we carry on second-stage transfer learning on a 1,000-level dataset using pretrained weight of first step, and finally we carry on third-stage transfer learning on the target 100-level dataset using pretrained weight of second step. The above method enables the grading model of the final small dataset to fully learn feature representation of the large-scale and medium-scale datasets; for the second problem, based on the concept of “decoupling representation learning and classifier learning” proposed in literature [9][10], our work directly learn with imbalanced data at the stage of feature representation learning. At the stage of classifier learning, based on the best weight of the feature representation
learning, we freeze all layers except for the last fully connected layer. The last layer is reinitialized and trained again. Here we introduce a class-balanced loss [11], initially for natural image classification, into our task as the loss function. We find that training for only a few epochs can be effective for classifier learning. Experimental results show that compared to state-of-the-art methods, the proposed method improves both overall accuracy and quadratic weighted kappa. We achieve an overall accuracy of 79.61% on the DR grading task of IDRiD Sub-Challenge 2, surpassing the first solution by 4.85%.

The main contributions of this paper are as follows:

- As far as we know, this paper introduces the idea of "multi-stage transfer learning" into the DR grading task for the first time, so that grading performance can be further improved on the small dataset based on the "knowledge" of large and medium-scale datasets. This method also provides useful thoughts for other few-shot learning tasks with multi-scale datasets.
- A simple training method for class-balanced loss function is proposed in DR grading task. No need with complicated hyperparameter tuning strategies such as learning rate decay, warmup, etc. [11], grading performance can be further improved by training the network only for a few epochs in the second stage. This method can reduce the difficulty of training class-balanced loss function while mitigating data imbalance of different classes.

## 2 Related Work

Many works have published in the area of automated diagnosis on DR and diabetic macular edema (DME) with deep learning. Li, T. et al.[3] proposed and published a large-scale DR dataset named DDR, which provided useful data for evaluating newly proposed algorithms and exploring clinical applications. For the problem of lacking large balanced training data, Zhou, Y. et al. [4] proposed a so-called DR-GAN to synthesize high-resolution fundus images for effective data augmentation. The same team also proposed a collaborative learning method [5] with attention mechanism and adversarial architecture to jointly improve performance of disease grading and lesion segmentation. Li, X. et al. [6] paid attention to the joint classification problem of DR and DME and proposed a cross-disease attention network. The network included two major modules: disease-specific attention module for learning useful features of each disease and disease-dependent attention module for capturing the internal connection between DR and DME. He, X. et al. [7] proposed auxiliary task learning for DME classification and detection. They first extracted multi-scale features of the lesion and segmented hard exudates and macular masks that played key roles in DME classification, then XGBoost was used as the classifier for DME grading. However, it has not been noticed in above methods that use of different scales of DR datasets may have positive impact on the grading performance of small datasets.

There are relatively few researches focused on class imbalance of DR datasets. He, A. et al. [8] proposed a category attention module (CAB) to alleviate the problem of imbalanced data, which is able to learn the characteristics of specific grade and enlarge the distance of different grades. However, compared to class-balanced loss, CAB failed to solve the imbalance problem of DR grading intuitively and effectively although
performance can be improved by adding CAB into the network. In terms of solving the misclassification caused by DR class correlation, Galdran, A. et al. [12] added a cost-sensitive regularization to three conventional loss functions to improve the DR grading performance. Liu, S. et al. [13] proposed a graph convolutional network with adjacency matrix, which introduced prior knowledge of the class dependency to improve grading performance.

3 Proposed Methods

In this paper, Efficientnet-b5[14] is selected to be the backbone network. Efficientnets are powerful models for classification tasks proposed by Google in 2019. Firstly, neural architecture search was used to design Efficientnet-b0 as the basic model, and then Efficientnet-b0 was rescaled in terms of width, depth and resolution in order to obtain Efficientnet-b1 to b7. Considering the high resolution of fundus images, it may improve grading performance to use larger input resolution. Therefore, we start our experiment from Efficientnet-b0 and finally enlarge the network to Efficientnet-b7. We find that after Efficientnet-b5, larger model and input resolution will not further improve the grading performance.

In “feature representation learning” stage, the idea of multi-stage transfer learning is used to learn continuously from three different datasets. Thus, the final small dataset can learn feature representation from the former large and medium-scale datasets. The overall scheme proposed in this paper can be seen in Fig.2.

![Fig. 2. The proposed scheme.](image)

In “feature representation learning” stage in Fig.2, we carry on the first-stage transfer learning on Eyepacs [15] using ImageNet pretrained weight and save the best weight (with lowest validation loss), then we carry on second-stage transfer learning on DDR [3] using Eyepacs pretrained weight and save the best weight on DDR. The first two stage of transfer learning both use smaller epochs, so that the models can learn representation of different datasets without overfitting on a certain dataset or damaging ability to learn new tasks. The final step is to carry on third-stage transfer learning on IDRiD [16] using DDR pretrained weight and save the best weight on IDRiD as the best weight of the first stage. The above is the first stage of our proposed scheme, namely, the multi-stage transfer and feature representation learning stage.

For the imbalance problem of the target few-shot dataset IDRiD, we adopt re-weighting method to solve it. To be specific, we assign weights to each of the five
classes of DR based on standard cross-entropy loss: large weights for minority classes, and small weights for majority classes. Assuming that the prediction output tensor of the model is \( p = [p_0, p_1, \ldots, p_{C-1}] \), where \( C \) is the number of classes, the corresponding ground truth is \( y \). Thus, the standard cross-entropy loss (CE loss) can be calculated as:

\[
CEloss(p, y) = -\log \left( \frac{\exp(p_y)}{\sum_{j=0}^{C-1} \exp(p_j)} \right)
\]  

(1)

There are many ways to design weights, such as directly take inverse class frequency [17]. In this paper, we adopt a class-balanced cross-entropy loss (CBCE loss) proposed in [11], namely:

\[
CBCEloss(p, y) = \text{weight}[y] \cdot CEloss(p, y) = -\frac{1-\beta}{1-\beta^y} \log \left( \frac{\exp(p_y)}{\sum_{j=0}^{C-1} \exp(p_j)} \right)
\]

(2)

The hyperparameter \( \beta \) ranges in \([0, 1)\) in class-balanced loss so that the weight is between no re-weighting and re-weighting by inverse class frequency. Because the number of classes of DR is close to that of CIFAR-10, here we set \( \beta \) to be 0.9999. \( n_y \) is the number of corresponding class in the IDRiD training set, and the weight tensor can be calculated according to the above values. However, it often requires lots of tuning skills to directly train with this class-balanced loss on original DR data end to end. According to our multiple experiment results, we find that directly applying the implementation strategy in literature [11] will hurt the performance rather than improve it.

In order to avoid the uncertainty caused by overuse of hyperparameter tuning skills, inspired by literature [9] [10], we decouple feature representation learning and classifier learning, as shown in Fig.2. The first stage adopts standard (unweighted) cross-entropy loss to learn from original data distribution of three datasets. No re-balancing strategies are added except for data augmentation to fully learn the feature representation information of the original data. The second stage in Fig.2 refers to classifier learning with weighted or class-balanced cross-entropy loss. Based on the best weight of first stage on IDRiD, we freeze all layers except for the last fully connected layer and reinitialized this layer randomly. We use larger learning rate to train this layer. After a few epochs, a significantly higher performance can be achieved without inefficiently searching for hyperparameter tuning strategies.

4 Experiments

4.1 Datasets

Eyepacs: The 2015 Kaggle official competition dataset, a total of 88702 fundus images, including 35,126 training set, 53,576 testing set. DR is graded into five classes consistent with international protocols. Though Eyepacs has large amount of data, there exists much noise in both training set and testing set. Researchers claimed that many ungradable images are classified as DR0 and there are some poor-quality images in it.

DDR: A fundus dataset published by Nankai University in 2019, which are collected from Chinese patients. The DR grading subset consists of 13,673 fundus images with
pixel-level annotations, including 6835 training images, 4105 testing images and 2733 valid images. These images are with six classes, classifying low-quality or ungradable images as DR5 except for the first five standard classes. In our experiments, in order to be consistent with the current international protocols and other datasets, the sixth-class images are removed.

**IDRiD**: The 2018 ISBI diabetic retinopathy challenge dataset, collected from Indian patients. There are a total of 516 pictures used for disease grading, including 413 in the training set and 103 in the testing set. This dataset is characterized with small data, but high quality and accurate labeling. This dataset is used as the few-shot dataset to evaluate grading performance of different methods.

### 4.2 Evaluation Metrics

To quantitively evaluate the effectiveness of methods proposed in this paper, we introduce overall accuracy (abbreviated as Acc below) and quadratic weighted kappa (abbreviated as Kappa below), which are widely used in papers and competitions. Acc reflects the overall prediction accuracy, namely the ratio of number of images that are correctly predicted to total number of images in the whole test set. For measuring the agreement between ground truths and predicts, Kappa is also introduced in order to compare with results of other methods.

### 4.3 Implementation Details

Our backbone network uses Efficientnet-b5 with an input resolution of 456*456. In order to increase the data diversity, we use random horizontal flip, random vertical flip, random rotation and color jitter as data augmentation. For IDRiD, we use stratified sampling and select 10% of the data in the training set as the validation set. For the first stage training of DDR and IDRiD, batchsize is set to 8, learning rate is set to 0.001, the loss function is standard cross-entropy loss, the optimizer is SGD, and the momentum is set to 0.9. For the value of epoch, Eyepacs is set to 30, DDR is set to 18, and IDRiD is set to 150. For IDRiD second stage training, learning rate is set to be 0.01, the loss function adopts the weighted cross-entropy loss, and epoch is set to 5. We find that increasing epoch will not further improve the grading performance in second stage after a lot of experiments.

For each output in Fig.2, we select the best weight (with lowest validation loss) as the next pretrained weight. We use Pytorch as experiment framework. We also use P100 provided by Google Colab and 2*2080Ti for training and testing.

### 4.4 Ablation Studies

Table 1 shows the results of ablation experiments. On the IDRiD testing set, compared with baseline scheme that directly use pretrained weight on Eyepacs, the scheme adding class-balanced cross-entropy loss can increase Kappa by 3.66% and the scheme adding multi-stage transfer learning (MSTL) can increase Acc by 0.97% and Kappa by 0.12%. After using class-balanced loss at the second stage training, Acc and Kappa further
increase 3.88% and 4.47%, respectively. The experiment results show that introducing multi-stage transfer learning and class-balanced loss to the task of DR grading is effective.

| Backbone  | Methods                      | Acc   | Kappa |
|-----------|------------------------------|-------|-------|
| Efficientnet-b5 | Baseline                   | 0.7476| 0.8304|
|           | Baseline + CBCE loss         | 0.7476| 0.8670|
|           | Baseline + MSTL              | 0.7573| 0.8316|
|           | Baseline + MSTL + CBCE loss  | 0.7961| 0.8763|

### 4.5 Comparisons with State-of-the-art Methods

Table 2 shows the comparison between our method and the top three places on the DR grading task of IDRiD Sub-Challenge 2. Seen from this table, Acc obtained by our method exceeds the first place of LzyUNCC by 4.85%. It is worth noting that the input resolution of our proposed scheme is much lower than that of LzyUNCC (456*456 vs. 896*896). Meanwhile, in order to verify the effectiveness of our method further, we compare it with two state-of-the-art DR grading methods. CF-DRNet [18] firstly divides the input images into two categories through the coarse-grained network: with DR and without DR, and further divides the images with DR into grade 1 to 4 through a fine-grained network. DR|GRADUATE [19] improves the results of DR grading by outputting a grade uncertainty. Compared with CF-DRNet, the Acc of our method exceeds 19.41%. Compared with DR|GRADUATE, the Kappa of our method exceeds 3.63%. In summary, the grading performance of our proposed scheme is obviously competitive.

| Methods              | Acc   | Kappa |
|----------------------|-------|-------|
| LzyUNCC [16] (rank 1)| 0.7476| -     |
| VRT [16] (rank 2)    | 0.5922| -     |
| Mammoth [16] (rank 3)| 0.5437| -     |
| CF-DRNet [18]        | 0.6020| -     |
| DR|GRADUATE [19]        | -     | 0.84  |
| Ours                 | 0.7961| 0.8763|
5 Discussion

Fig. 3. Confusion matrix of different methods: (a) Baseline; (b) Baseline+MSTL; (c) Baseline+MSTL+CBCE loss.
Fig. 3 shows the confusion matrix corresponding to different methods. The value of Acc can be calculated as sum of the main diagonal elements of the confusion matrix divided by sum of all the elements of the matrix. After introducing MSTL and CBCE loss, Acc is steadily improving from Fig. 3(a) to Fig. 3(c). However, relying only on Acc is difficult to fully reflect the consistency between the prediction results and the true labels. In order to better show the difference between the predicted distribution and the true distribution, we need to analyze Kappa further. If the predicted labels are completely consistent with the true labels, all elements in the matrix should be distributed on the main diagonal, when Kappa has to be 1. Therefore, it gives a better predicted result that the data distribution of confusion matrix gets closer to the main diagonal (Kappa gets closer to 1). The Kappa value of Figure 3(a)-(c) has been increasing steadily and the method of adding both MSTL and CBCE loss has the closest consistency to the true distribution. Because distance weight is set in Kappa, for the false prediction, the farther the distance from the true label, the greater penalty will be given. In other words, for each grade, the more the predicted label concentrated on the main diagonal value of certain row, the more helpful it is for the improvement of Kappa.

Comparing Fig. 3(b) and Fig. 3(c), grading performance of the small sample grades is significantly improved. For grade 3, the number of correct predicted images increased from 12 to 14 after adding CBCE loss; For grade 4, not only the number of correct predicted images increased by 30%, but also the data distribution is more concentrated to the main diagonal position. In general, the introduction of MSTL and CBCE loss has contributed to the improvement of Acc and Kappa, respectively.

6 Conclusion

In this paper, we introduce multi-stage transfer learning and class-balanced loss to improve grading performance of small DR dataset. We decouple feature representation learning and classifier learning and design a two-stage training scheme. The first stage trains continuously on Eyepacs, DDR and IDRiD datasets to make the model learn much representation features sufficiently. The second stage only trains the classifier with class-balanced loss. The proposed scheme does not need to search for a complicated and time-consuming hyperparameter-tuning strategy. It will alleviate the problem of class imbalance using the aforementioned simple ways. The ablation studies on IDRiD dataset demonstrate effectiveness of the proposed method. Meanwhile, the proposed methods show obvious competitiveness in both Acc and Kappa. We also achieve the best result on the DR grading task of IDRiD Sub-Challenge 2.

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