

Peer Review File

Article Information: <http://dx.doi.org/10.21037/atm-20-3275>

Comment 1:

There was a similar report (J Digit Imaging. 2018 Dec;31(6):869-878) in the PubMed. What is the novel idea in the paper? Please elaborate in the introduction.

Reply 1:

In the previous report (J Digit Imaging. 2018 Dec;31(6):869-878), the authors developed a deep convolution neural network algorithm based on color fundus images to automatically assess the image quality for diabetic retinopathy screening. In our study, we developed a DLS to assess the quality and gradability of the images which is similar to the article mentioned above. However, the major aim of our research is to further create a DLS for automatic detection of diabetic retinopathy. The combination of the two DLSs can be effectively used for the future DR screening.

In particular, the large volume and high complexity of the raw retinal fundus image data from real-world sources in our study can greatly facilitate developing a novel DLS. We collected a large number of raw retinal fundus images captured by different desktop retinal cameras from 17 hospitals of the Yangtze River Delta Urban Agglomeration. Our DLS achieved high AUC, sensitivity and specificity performance. Besides, we also analyzed the distribution of misclassification for the DLS, including false negatives and false positives, and visualized the output images. These novel data suggested the direction of optimization and updating for the better precision in the future.

The relevant contents were added to elaborate the novel idea in the introduction section (see Page 6, line 11-15). In the discussion section regarding the DLS for assessment of image quality and gradability, we cited the article (J Digit Imaging. 2018 Dec;31(6):869-878) (see Page 13, line 11-12).

Changes in the text: Introduction section- Page 6, line 11-15. Discussion section- Page 13, line 11-12.

Comment 2:

Please supplement the diagnostic progress of DR in the introduction. In the introduction, please enrich the progress of the treatment for DM.

Reply 2:

Agreed. We added relevant content to enhance the introduction regarding the diagnostic progress of DR and the progress of the treatment for DM (see Page 4, line 6-11, 20-21; Page 5, line 1-7).

Changes in the text: Introduction section- Page 4, line 6-11, 20-21; Page 5, line 1-7.

Comment 3:

Are there any associated complications in DM patients?

Reply 3:

Yes. Diabetes is associated with the multiple complications. These complications are grouped under “microvascular disease”, “macrovascular disease”, “diabetic foot ulcers” and “other chronic complications”. Specifically, microvascular disease includes retinopathy, nephropathy, and neuropathy, and macrovascular disease includes atherosclerosis, coronary heart disease and cerebrovascular disease. Other chronic complications of diabetes include depression, dementia, and sexual dysfunction.

Changes in the text: /

Comment 4:

Why to develop the DLS for DR in the paper? What is the meaning of “NPDR” in the abstract?

Reply 4:

Effective diabetic retinopathy screening is essential for early detection and treatment. The traditional screening system always relies on in-person dilated eye examination. There are however a number of problems with this conventional approach, including inadequate funds, access issues, and few trained eye care personnel. The DLS for DR in the paper can automatically detect DR by analyzing fundus images and achieve excellent prediction performance. We hope this cost-effective and time-efficient method can be greatly useful for the DR screening task in the future.

We are sorry for the direct use of abbreviation. The “NPDR” in the abstract means non-proliferative diabetic retinopathy. The full name was added in the abstract (see Page 3, line 6).

Changes in the text: Abstract section- Page 3, line 6.

Comment 5:

Are there any different of fundus images of DR in different region? What are the diagnostic criteria for DR?

Reply 5:

Yes. Contrast between retinal pigmentation background and DR lesions (e.g., hemorrhages) varies considerably across the different regions.

The diagnosis of DR relies on two factors: Diabetic disease history and Ocular examination. Therefore, the diagnostic criteria included: (1) Patients who had a definite history of diabetes mellitus or random blood glucose level of 200 mg/dL or higher. (2) Fundus examination indicated one or more retinal microaneurysms or retinal blot hemorrhages with or without more severe lesions (hard exudates, cotton

wool spots, intraretinal microvascular abnormalities, venous bleeding, new retinal vessels, and fibroproliferations).

In this work, the fundus images of the patients diagnosed as DR were further classified into 5 grades: no DR, mild NPDR, moderate NPDR, severe NPDR, and PDR according to the International Classification of Diabetic Retinopathy (ICDR)

Changes in the text: /

Comment 6:

Has the developed DLS been used in clinical in your hospital?

Reply 6:

It is still not formally used in the clinic in our hospital. The user software based on this DLS is under development. Once software development is complete, we will test the software in our hospital and partner hospitals.

Changes in the text: /

Comment 7:

What are your suggestions for detecting DR using fundus image? Please supplement in the discussion (see Page 15, line 8-13).

Reply 7:

Agreed. We added the relevant suggestions in the discussion section accordingly.

Changes in the text: Discussion section- Page 15, line 8-13