OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-21-00752
Title: Artificial Intelligence for Assessment of Stargardt Macular Atrophy
Reviewer's Name: Mital Shah
Reviewer's country: UK

COMMENTS TO AUTHORS

This paper aims to provide a review of AI approaches for the classification of Stargardt disease (STGD) related atrophy on FAF and segmentation of retinal layers on SD-OCT as well as present the authors work on these aspects. Overall the paper did not provide the reader with a coherent and easy to read story with limited information provided about the authors own work on FAF and SD-OCT images in patients with STGD. The subject that this paper addresses is important but the authors have not provided a significant contribution within this manuscript and what information is there can be better organised and written more clearly to help the reader. I have highlighted some comments below that may help the authors to improve the quality of this manuscript should they want to resubmit for consideration of publication.

Major comments:

1) The overall manuscript needs to be edited for spelling, grammar and readability. This will make it easier for any readers to understand the message that the authors are communicating.

2) Why was the literature review only limited to the last 3 years?

3) In the section about screening with FAF images - there is insufficient information regarding the methods and results of the authors study for the reader to assess the validity of their findings. For example, they have not mentioned whether or not the algorithm was tested using data from another centre or a subset of the data used for training purposes. This is important to assess its generalisability. I wonder if a DL methodology is required for this classification purpose and if the authors attempted to use any simpler methodologies to tackle this classification problem? The main difference between early STGD and normal images are within the central macular area and can be readily identified. The images of normals also appear to have a substantially higher contrast than those with STGD, was this investigated? This difference may be related to the disease process in STGD due to accumulation of lipofuscin within the RPE but will depend on the image capture parameters.

4) Section on segmentation of atrophy on FAF - again, as for the section above, there is insufficient information on the methods and results for the reader to assess its validity. For example, the authors describe good results in PDQDAF in Figure 5, however, it is clear from the image that there are small areas of atrophy within the macula that have not been segmented.

5) There are also some clinically inaccurate statements that are made predominantly within the introduction. Please see a few examples below.

Introduction:

Line 35: Early onset STGD is usually more severe and progressive than later onset disease so please either provide a reference for the sentence starting with "Visual acuity may decrease slowly at first…" or remove.

Line 37: What treatment to STGD are the authors referring to? There is currently no treatment available for the underlying disease process.

Line 43: The authors reference a staging system for Early onset STGD by Fujinami et al. but have not referenced it and seem to have missed the point that this is for early STGD.