Letter of Response

27th March 2021

Manuscript Number: 63075

Title: Deep learning for diagnosis of precancerous lesions in upper gastrointestinal endoscopy: A review

Dear Editor in Chief of World Journal of Gastroenterology,

We are glad to receive the reviewers' and the Editorial Office's comments on our manuscript. The comments are very helpful to our paper. We have revised the manuscript according to the comments, and the revised parts have been highlighted in red in the revised manuscript. Our responses to the comments are shown below:

Response to Editor-In-Chief:

Comment 1: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response 1: Thanks for giving us a conditional acceptance. We have revised the manuscript according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors, and the revised parts have been highlighted in red in the revised manuscript.

Response to Science Editor:

Comment 1: The language classification is Grade B. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

Response 1: Thanks for your comment. We have submitted the manuscript to the recommended editing company, and the manuscript was polished by the recommended editing company. The following is the certificate of language editing.

EDITORIAL CERTIFICATE
(Ref. YTNVME-MS2021032111R)

We herein certify that the following document has been edited for English language by a native English speaking medical editor at MedE Medical Editing Group. The edited paper has reached grade A in language evaluation for SCI journals.

Manuscript title

Deep learning for diagnosis of precancerous lesions in upper gastrointestinal endoscopy: A review

Authors and affiliations

Tao Yan, Hubei University of Arts and Science, Xiangyang 441053, Hubei Province, China

Date issued

March 23, 2021

*We are **NOT** responsible for any errors in the added content to our revised version after this date.

Comment 2: The "Author Contributions" section is missing. Please provide the author contributions.

Response 2: Thanks for your suggestion. We have added the "Author Contributions" section to page 1 and the specific content is as follows:

"**Author contributions**: Pak Kin Wong and Tao Yan contributed to concept design. Tao Yan and Ye Ying Qin collected the data. Tao Yan and Pak Kin Wong drafted the manuscript. All the authors have approved the final version of the manuscript."

Comment 3: The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response 3: Thanks for your suggestion. We have uploaded the approval document copy of the Science and Technology Development Fund, Macau SAR.

Comment 4: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response 4: Thanks for your suggestion. We have provided the original figure document and arranged the figures using PowerPoint.

Comment 5: PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Response 5: Thanks for your suggestion. We re-checked the references and listed all the authors. Besides, we re-searched multiple databases. Some documents only have DOI citation numbers but no PMID numbers, including [14], [24], [36], [57], [58], [63], [64], [65] and [71]. The reference [66] has neither PMID numbers nor DOI citation numbers.

Comment 6: Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

Response 6: Thanks for your suggestion. Due to the copyright issue, we have deleted Figure 3. Now all the rest of the figures are made by our team for this article. Figure 4 and Figure 5 in the original manuscript are now renumbered as Figure 3 and Figure 4 respectively in the revised manuscript.

Responses to Reviewer 1:

Comment 1: This review article describes AI diagnosis of upper gastrointestinal cancers, in particular the ability of deep learning to diagnose precancerous lesions, and describes selection bias in a retrospective study, making it a well-written article. It is a well-written paper. About Figure 5. What does the orange colour mean? Why is the leftmost case, which appears to be a circumferential Barrett's esophagus, only partially orange? Please explain.

Response 1: Thanks for your comment. Due to the copyright issue, we have deleted Figure 3 in the revised manuscript; the number of Figure 5 becomes Figure 4. Therefore, in Figure 4, the orange color (warmer color) means the higher contribution to the decision making, which usually correspond to lesions. The attention maps also have some defects such as inaccurate display of lesions, so the attention maps only cover partially areas (e.g. only partially orange) associated with Barrett's esophagus. This is the inherent shortcomings of attention maps.

On pages 14 of the revised manuscript, we have added the specific content as "The attention maps are displayed as heat maps overlaying upon the original images, where warmer colors mean higher contributions to the decision making, which usually correspond to lesions. However, the attention maps also have some defects such as inaccurate display of lesions as shown in Figure 4, where the attention maps only cover partially areas associated with BE and GIM. This is the inherent shortcoming of attention maps." Besides, in the title of Figure 4, we have added a related sentence: "where warmer colors mean higher contributions to the decision making".

Responses to Reviewer 2:

Comment 1: The study is aimed to review the deep learning for diagnosis of precancerous lesions in upper gastrointestinal endoscopic procedure. The title is "Deep learning for diagnosis of precancerous lesions in upper gastrointestinal endoscopy: A review". 1. This is a review article. 2. Please add more details of the limitations and the disadvantages of the deep learning. 3. What is the new knowledge from this article? 4. Finally, please recommend the readers "How to apply this knowledge for routine clinical practice?".

Response 1: Thanks for your comment. For the second comment, we have explored some of the limitations of deep learning on page 5, and the details are as follows: "However, the DL, especially CNN, has some limitations. Firstly, DL requires a lot of data and easily leads to overfitting. Secondly, the diagnostic accuracy of DL relies on the training data, but the clinical data of different types of diseases are always imbalanced which easily causes diagnosis bias. Besides, a DL model is complex and requires huge calculation, so most researchers can only use the ready-made model.Despite the above limitations, DL-based AI systems are revolutionizing the GI endoscopy."

For the third comment, the new knowledge of this article is that compared with previous reviews, which mainly focus on cancer, this study summarizes the status and shortcomings of deep learning in precancerous lesions of the upper gastrointestinal tract for the first time.

For the fourth comment, this knowledge can provide guidance for intelligent diagnosis of other gastrointestinal tract diseases, so that engineers can develop perfect AI products to

better assist clinical decision-making. In CONCLUSION on page 15, we have added the following description to address the above comments.

"This is the first review on the DL-based diagnosis of precancerous lesions of the upper GI tract. The status, challenges and recommendations summarized in this review can provide guidance for intelligent diagnosis of other GI tract diseases, which can help engineers develop perfect AI products to assist clinical decision making."

After an in-depth amendment to the paper, we would like to request for your further review. We would be very grateful if you could kindly accept this paper for publication in your World Journal of Gastroenterology.

Many thanks with regards,

Pak Kin Wong (Corresponding author)

Professor, Department of Electromechanical Engineering
Faculty of Science and Technology
University of Macau
Macao