April 11, 2022

Dear Drs. Bonino and Singh,

We thank you for having given us the opportunity to revise our manuscript.

We are grateful to the Reviewers for their very thoughtful comments, which we have carefully considered and addressed below. We believe that our manuscript is now much improved because of these comments.

Please find attached two revised manuscripts: one with tracked changes and the same one but without tracked changes, which we resubmit for your consideration.

Thank you for considering our revised manuscript for publication in *Artificial Intelligence in Gastroenterology*.

Sincerely,

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Point-to-point response to reviewers

Name of Journal:
Manuscript NO.: 76203
Column: Minireviews
Title: Artificial Intelligence using Advanced Imaging techniques and Cholangiocarcinoma: Recent advances and future direction
Authors: Aaron R Brenner, Passisd Laoveeravat, Patrick J Carey, Danielle Joiner, Samuel H Mardini, Manol Jovani

Reviewer reports:

Reviewer #1:

In Brenner et al., authors approach some of the most common artificial intelligence (AI)-based techniques used in gastroenterology. In particular, they focus their interest on Cholangiocarcinoma (CCA). In that sense, authors describe how machine/deep learning models help other classical methods to improve the diagnostic and prognostic of CCA patients. In the opinion of this reviewer, the work can be of interest for readers of the journal. Additionally, the manuscript is well written and is also easy to follow. Just a little thing, during introduction authors mentioned deep learning and no description of it is done. Then, this reviewer feel comfortable with the idea of this work being published in Artificial Intelligence in Gastroenterology.

Response: We would like to thank reviewer #1 for the thoughtful comments and positive feedback. We have now added a description of deep learning (Introduction section, paragraph 3).

Reviewer #2:

1. The manuscript is should be organized as per the standard submission requirements. Kindly follow the author guidelines.

Response: We have organized the manuscript per the submission requirements and author guidelines.

2. The abstract section, conclusion section and keywords are missing in the manuscript.

Response: The abstract, conclusion, and keyword section have been added to the formal and final version of the manuscript.

3. The title needs a revision. The present title do not give clarity by mentioning it is there a future?

Response: We thank the reviewer for pointing out this out. We have clarified the title by specifying "Recent advances and future direction."

4. Full form of the abbreviated words should be presented at least once in the manuscript.

Response: We thank the reviewer for bringing this to our attention. All abbreviated words now have been presented at least once prior to the use of their abbreviated form.

5. It would be better if the authors can include a Table on the Summary of recent related studies, methods, study type, outcomes.

Response: A table has now been included with the manuscript that summarizes related studies, type of machine learning used, imaging modality, and outcomes.

6. The authors should include a section on evidence synthesis, search strategy, inclusion and exclusion criteria for shortlisting the relevant studies considered in this review.

Response: We thank the reviewer for this comment. A section on search strategy for relevant studies has been included under the heading "Article Identification Process."

7. Since the authors mentions "In fact, artificial intelligence is utilized in almost every field" Several studies related should be cited in this context to support the sentence and further strengthen the introduction The authors can cite the following article a) Patil V, Vineetha R, Vatsa S, Shetty DK, Raju A, Naik N, Malarout N. Artificial neural network for gender determination using mandibular morphometric parameters: a comparative retrospective study. Cogent Engineering. 2020 Jan 1;7(1):1723783. b) Musunuri B, Shetty S, Shetty DK, Vanahalli MK, Pradhan A, Naik N, Paul R. Acute-on-chronic liver failure mortality prediction using an artificial neural network. Engineered Science. 2021 Aug 24;15:187-96. c) Yang CM, Shu J. Cholangiocarcinoma evaluation via imaging and artificial intelligence. Oncology. 2021;99(2):72-83. d) Haghbin H, Aziz M. Artificial intelligence and cholangiocarcinoma: Updates and prospects. World Journal of Clinical Oncology. 2022 Feb 24;13(2):125-34. e) Shah M, Naik N, Somani BK, Hameed BZ. Artificial intelligence (AI) in urology-Current use and future directions: An iTRUE study. Turkish Journal of Urology. 2020 Nov;46(Suppl 1):S27.

Response: We thank the reviewer for bringing these studies to our attention. The studies have been cited to further strengthen and support the claim.

8) The multivariate analysis section may need to be renamed and provide an appropriate header which includes the relant studies.

Response: The referenced section has been retitled "Use of artificial intelligence in aiding the predictive abilities of multivariable models" to appropriately describe the studies discussed.

9) The authors should consider the techniques including neural networks, machine learning, deep learning which comes under the wing of AI. Studies like below should be included. Zhang Q, Li Q, Yu G, Sun L, Zhou M, Chu J. A multidimensional choledoch database and benchmarks for cholangiocarcinoma diagnosis. IEEE access. 2019 Oct 15;7:149414-21. Negrini D, Zecchin P, Ruzzenente A, Bagante F, De Nitto S, Gelati M, Salvagno GL, Danese E, Lippi G. Machine learning model comparison in the screening of cholangiocarcinoma using plasma bile acids profiles. Diagnostics. 2020 Aug;10(8):551.

Response: We thank the reviewer for bring the above studies to our attention. The above studies are now referenced in the section titled "Artificial Intelligence in Biliary Diseases and Cholangiocarcinoma" as examples of how artificial intelligence has been applied to the diagnosis of cholangiocarcinoma. Because we aim focus on imaging, these articles are not discussed at length in the review.

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Overall the manuscript needs a further organizing of the content for better readability and to be well presented for considering it for publication in the journal

Response: We thank the reviewer for this thoughtful comment. We have made the above changes and are grateful for the opportunity to re-organize the content for better readability and presentation.

Science Editor

The manuscript is not well organized. The abstract section, conclusion section and keywords are missing in the manuscript.

Response: We thank the editor for the opportunity to re-organize our manuscript. The abstract, conclusion, and keywords section are now included in the full manuscript.