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Dear Editor,

Firstly, thank you and the reviewers for the time spent reviewing our manuscript and for your feedback. We have made the changes as suggested and feel that the manuscript has improved as a result. If there are any further changes you require, please do not hesitate to contact us.

Reviewer comments and replies:

Company editor-in-chief: I recommend the manuscript to be published in the Artificial Intelligence in Gastroenterology. Before final acceptance, the author(s) must add a table/figure to the manuscript.

Response: A table comparing Deep Learning and Biophysics Inspired Artificial Intelligence in Healthcare has been added to the manuscript.

1 Scientific quality: The manuscript describes a minireview of the biophysics inspired artificial intelligence for colorectal cancer characterization. The topic is within the scope of the WJG. (1) Classification: Two Grades C; (2) Summary of the Peer-Review Report: This is a narrative report on artificial intelligence based on biophysics for the characterization of colonic polyps and surgical prognostication of anastomotic fields. Biophysics under the utilization of fluorescent substances for pattern recognition is an interesting thought though in an experimental phase.; (3) Format: There are no tables and no figures;

Reply: As above, a table comparing Deep Learning and Biophysics Inspired Artificial Intelligence in Healthcare has been added to the manuscript.

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(4) References: A total of 40 references are cited, including 26 references published in the last 3 years; (5) Self-cited references: There are 5 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

References have been amended so that self-citation no longer constitutes >10% of total references.

Issues raised: (1) The "Author Contributions" section is missing. Please provide the author contributions;

"Author Contributions" have been added to the manuscript.

(2) 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.

DOI and PMIDs have been added to references where applicable.

Please revise throughout; and (3) Please add table/figure to this review.

The table as suggested has been added.

6 Recommendation: Conditional acceptance.

(2) ***Editorial office director:***

(3) ***Company editor-in-chief:*** I recommend the manuscript to be published in the Artificial Intelligence in Gastroenterology. Before final acceptance, the author(s) must add a table/figure to the manuscript.

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PEER-REVIEW REPORT

Name of journal: Artificial Intelligence in Gastroenterology

Manuscript NO: 63530

Title: Biophysics Inspired Artificial Intelligence for Colorectal Cancer Characterisation

Reviewer's code: 04022823

Position: Peer Reviewer

Academic degree: FEBG, MD, MSc

Professional title: Consultant Physician-Scientist, Doctor

Reviewer's Country/Territory: Greece

Author's Country/Territory: Ireland

Manuscript submission date: 2021-01-28

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-04-02 05:09

Reviewer performed review: 2021-04-05 13:03

Review time: 3 Days and 7 Hours

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a narrative report on artificial intelligence based on biophysics for the characterization of colonic polyps and surgical prognostication of anastomotic fields. Biophysics under the utilization of fluorescent substances for pattern recognition is an interesting thought though in an experimental phase. It would be preferable if there was a paragraph underlying the limitations of this method apart from the already presented limitations of the deep learning. Please delineate the term endolaparoscopy between the gastrointestinal and surgical partition. It seems that is given more attention to the surgical exploration and prognostication. Please be more detailed about the application in gastrointestinal endoscopy.

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Response to Reviewer 1:

Firstly, many thanks to the reviewer for their constructive feedback.

Reviewer 1 comment (a): It would be preferable if there was a paragraph underlying the limitations of this method apart from the already presented limitations of the deep learning.

Reply: We agree that the addition of a paragraph on the limitations of a biophysics gives balance to the article and have added the following paragraph to the text in the biophysics section:

"While biophysics inspired approaches such as those mentioned have numerous benefits, it is worth noting however that such methodology can only be employed in cases where an in-depth mechanistic understanding of all involved elements has been achieved. Therefore, utilization is limited to fields with a strong human understanding of relevant biological and physio-chemical components and furthermore efforts may be derailed where incorrect perceptions of what is true exist."

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Reviewer 1 comment (b): Please delineate the term endolaparoscopy between the gastrointestinal and surgical partition.

Reply: We have added a clarifying definition following the introduction of NIR endolaparoscopy:

"In contemporary, gastrointestinal surgical practice, the advent of nearinfrared (NIR) endolaparoscopy (combining endoscopic techniques with minimally invasive laparoscopic approaches)"

Reviewer 1 comment (c): It seems that is given more attention to the surgical exploration and prognostication. Please be more detailed about the application in gastrointestinal endoscopy.

Reply: We agree that the clinical application was not clearly elucidated in the original text and have therefore added the following paragraph outline the clinical utility in GI endoscopy:

"Such systems employed clinically, providing objective feedback to the endoscopic operator, would permit either immediate local resection in the case of early disease or prompt appropriate, expedited referral for definitive surgical management in the case of more advanced disease. "

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PEER-REVIEW REPORT

Name of journal: Artificial Intelligence in Gastroenterology

Manuscript NO: 63530

Title: Biophysics Inspired Artificial Intelligence for Colorectal Cancer Characterisation

Reviewer's code: 04089095

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Ireland

Manuscript submission date: 2021-01-28

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-04-04 00:40

Reviewer performed review: 2021-04-20 03:01

Review time: 16 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish

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Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This manuscript reviews the application of AI in gastrointestinal surgery and gastroenterology in recent years from the aspects of gastrointestinal intervention, biophysics, NIR endolaparoscopy and NIR-ICG Tissue Perfusion. The advantages and development direction of biophysics-inspired AI are discussed at the end of this paper. However, the content of the article does not match the title because of little description of Colorectal Cancer Characterisation.

Reply: Many thanks to the reviewer for their time and review of our paper. We agree that the clinical application was not clarified in the original text and have therefore added the following piece outlining the clinical usefulness in the characterisation of colorectal cancer:

"Such systems employed clinically, providing objective feedback to the endoscopic operator, would permit either immediate local resection in the case of early disease or prompt

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appropriate, expedited referral for definitive surgical management in the case of more advanced disease.

Once again, thank you for your time and constructive criticism. We await the result of your considered reply and are happy to make any other changes should you feel appropriate.

Yours Sincerely,

Niall Hardy