

Brussels, 18th November 2020

To the Editor-in-Chief of *World Journal of Gastroenterology*

Dear Editor,

Thank you for giving us the opportunity to revise our manuscript entitled “Artificial intelligence-aided colonoscopy: recent developments and future perspectives”. We submit the revised manuscript version, having answered all comments raised by the editors and the reviewers. Detailed point-to-point responses are listed below, and edits are in track-changes throughout the document to assist the reviewers. We hope that our amended paper fulfils the requirements for publication in your prestigious journal.

Sincerely,

Paraskevas Gkolfakis, MD

Gastroenterologist

Science editor's comments: 1 Scientific quality: The manuscript describes an opinion review of the artificial intelligence-aided colonoscopy. The topic is within the scope of the WJG. (1) Classification: Grade B and Grade A; (2) Summary of the Peer-Review Report: This is a review on the role of artificial intelligence in the field of colonoscopy and polyp recognition and analysis. The paper is very well written and addresses nearly all the relevant aspects of this new and exciting technology. However, the questions raised by the reviewers should be answered; and (3) Format: There are no tables and figures. A total of 32 references are cited, including 20 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A and Grade B. 3 Academic norms and rules: The authors should provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJG. 5 Issues raised: (1) The authors should add some figures or tables; and (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. Please revise throughout. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

Authors' reply: *Following your recommendation we added one table in our revised manuscript as well as all PMID and DOI citation numbers previously missing.*

Reviewer #1:

Specific Comments to Authors: This is a well done review on CNN-AI colonoscopy. Authors should consider elaborating on some aspects:

1. Consider adding a table enlisting the key AI algorithms in use - either by academic facilities or by industry. While there are several studies on AI-colonoscopy (comparing control to CNN-AI guided colonoscopy), what is at the core of the issue is the source algorithm in use for the CNN-AI. Who developed it and how was it developed. Some of these studies may be using the same algorithm. Algorithms need to be refined for use over time and also updated with more data. There are very few very good AI algorithms and most of these have been developed in Asian countries (China, Japan, others?).

Authors' reply: We thank the reviewer for this comment that is helpful to deepen the concept of AI training and testing. The actual algorithms in use by the systems are different by definition, since deep learning systems build their own algorithms based on the information (data, images) that is provided to them in the learning phase. AI systems that have been tested in endoscopy have a backbone that is nearly always a Convolutional Neural Network that "learns" (i.e. builds its algorithms) autonomously, and indeed most of them have been developed, trained and tested in Asian countries. A couple of the reported studies indeed use the same CNN system, since they are subsequent reports from the same research group. Among regulator approved systems, GI-Genius (Medtronic) is the only exception to date. Furthermore, we fully agree that the algorithms may improve over time and we imagine that software updates will certainly be part of the lease/acquisition plans offered by industry.

As suggested by the reviewer, we have added a table (**Table 1**) resuming currently regulator-approved AI systems on the market.

2. The authors need to mention about any ongoing studies which are working on a cloud based algorithm. Or the authors need to consider elaborating on the endoscopy suite requirement to update local hardware for AI and ways to circumvent that. A cloud-based AI can help with that issue. It is impossible to update local hardware at all endoscopy suites. Other options are to purchase industry equipment and attach them to existing endoscopy hardware. These can be discussed under limitations.

Authors' reply: We thank the reviewer for raising this interesting point. We are actually unaware of cloud based AI systems as of today. However, we have included a small paragraph on the implementation of an AI system in an endoscopy suite. Summarising, there is often no need at all to update local hardware apart from actually acquiring the AI system. Some endoscope manufacturers are indeed implementing AI systems in their new hardware systems, but other AI systems are independent and work alongside any kind of scope/hardware brand. It will probably be up to the centres to decide which is the best and more convenient way of implementing AI in their suite.

3. More summary tables will be appreciated by the readers. But the authors have done well in summarizing the studies in the text of the manuscript.

Authors' reply: We agree and have added a summary table for better readability.

Reviewer #2:

Specific Comments to Authors: This is a review on the role of artificial intelligence in the field of colonoscopy and polyp recognition and analysis. The paper is very well written and addresses nearly all the relevant aspects of this new and exciting technology. Few comments for consideration:

1. The definition of interval colon cancer, better described as post-colonoscopy colon cancer, used in the introduction is not optimal. Please replace with “cancer that is identified before the next recommended screening or surveillance examination”

Authors' reply: Thank you for the comment. This has now been corrected.

2. Suggested change: “While mucosal exposure depends on the endoscopist’s examination technique” AND QUALITY OF THE PREPARATION. Although the endoscopist’s technique may be able to correct for deficiencies in the preparation at times, it cannot do so when the preparation is poor and/or when large amount of solid or adherent stools are seen.

Authors' reply: We appreciate the remark and we amended our manuscript following your suggestion.

3. In the Characterization of Colorectal neoplasia section a reference is missing: Among the considerable number of retrospective studies, similar pooled results were found [refer].

Authors' reply: Thank you for noticing that out. The respective reference has now been added.

4. It may be useful if the authors can discuss further the potential drawbacks of this technique including increased reliance on technology affecting performance and training, replacing quality improvement strategies to improve human eye recognition and training, potential harm in non-expert hands (reliance on technology) especially given the one and done ADR issue, etc.

Authors' reply: We agree with the reviewer and have added a section addressing these issues.

Round-2

Reviewer

TABLE 1 needs footnotes and citations/ references to each of the AI system listed. Otherwise the authors have answered all the relevant questions.

Authors' reply: we have revised our manuscript according to your comment. Please find the revised manuscript including a Table attached. Thank you