

Dear Reviewer#1,

Thank you very much for your interest and effort, as well as for the extremely constructive comments regarding the revision of our manuscript. We have analyzed your recommendations with all due seriousness and attention, and we appreciate your observations that lead us to improve the quality and content of the manuscript. In the following, we provide you with point-by-point responses to the revision you sent us.

Comment 1. Explain complex terminologies like Atrous Spatial Pyramid Pooling, dual attention gate, and reverse attention mechanism in simpler terms or with schematic representations. Provide a more in-depth comparative table summarizing the performance metrics of the reviewed models (e.g., Dice Score, IOU, precision, inference time).

Response 1. Atrous Spatial Pyramid Pooling is a deep-learning technique used in semantic segmentation networks, dual attention gate is a mechanism for image segmentation, reverse attention is a mechanism for image segmentation used in difficult regions. For metrics, I have completed Table 2 for a better understanding.

Comment 2. Include systematic reviews or meta-analyses on AI in CRC detection to strengthen the literature base.

Response 2. I have included reviews and meta-analysis in this work as proven by the following references: 53, 60, 67, 68, 78, 80, 82, 83, 109, 130, 131, 132, 133, 134, 165.

Comment 3. The manuscript should elaborate more on how AI models are being validated or used in clinical trials, including FDA-approved tools or ongoing studies. Discuss regulatory, ethical, and patient-centered challenges in deploying AI-powered colonoscopy tools in real-world settings.

Response 3. I have reviewed the whole manuscript and added several comments on this subject, described in the following chapters - REAL-LIFE AI-ASSISTED GUIDELINES ACCORDING TO RECOMMENDATIONS OF WORLDWIDE MAJOR

ASSOCIATIONS, STATE OF THE ART, CLINICAL AND ECONOMIC IMPACT OF IMPLEMENTING AI and LIMITATIONS, data is structured and in a more systematic manner in Table 4.

Comment 4. Expand the analysis of limitations such as lack of generalizability across demographics, sensitivity to low-quality data, and integration with endoscopic hardware. Address reproducibility and explainability issues in black-box models, which remain major barriers to clinical adoption.

Response 4. I have developed the entire chapter of Clinical and Economic impact of Implementing AI for this matter.

Comment 5. Language and grammar require attention; ensure all sentences are concise and scientifically appropriate.

Response 5. I have requested a collaborator of mine that works for several years in a London Hospital and improved grammar and language.

Comment 6. Figures or visual summaries of model architectures and performance comparisons will enhance reader understanding.

Response 6. I have added some tables for this purpose.

Comment 7. The term "craining" in the attention-based model description should be corrected to "training."

Response 7. Corrected.

Comment 8. Ensure consistency in abbreviations, such as using CRC uniformly instead of alternating with CCR.

Response 8. Corrected.

Comment 9. The introduction statistics should cite GLOBOCAN 2022 properly and contextualize them regionally. The manuscript offers a valuable overview of AI-enhanced colonoscopy techniques but requires major revisions to enhance its clarity, scientific soundness, and relevance. Incorporating up-to-date references, refining the introduction, and improving technical descriptions will significantly strengthen the impact of this work.

Response 9. I have rephrased the entire Introduction chapter and I have modified the GLOBOCAN citation. I have added several up-to-date references.

With best regards,

Cătălin Andrei Duței

Corresponding author

Dear Reviewer#2,

Thank you for reviewing our manuscript and for your helpful comments, which were extremely useful in improving the quality of our work, in accordance with WJG standards. We provide the following punctual responses to your observations.

Comment 1. Need to work on the flow of the text. Some minor grammar and spelling issues identified. For example, page 11 "et al," "when to address them [via] surgery"
For example, "

Response 1. We have revised the entire text and have collaborated with a fellow doctor from UK to accomplish a more fluent writing; we have corrected the spelling and grammar errors encountered. We have carefully scanned the text and have corrected the mentioned grammar and spelling errors. We have rephrased part of the paragraphs, in order to be more concise and have more flow in reading. We understand the background data section may provide too much details, thus we have reduced the non-necessary scientific definitions of biomarkers and other definitions.

Comment 2. Background data regarding traditional screening methods and various innovative attempts" This section could be condensed further as it feels a bit tangential and technical The background seems more scientific than what a clinician needs to know about the topic at hand: (For example, CA19-9 (UniProtKB ID: Q969X2) is a tetra-saccharide that can bind to the O-glycans on the cell surface of tumor cells like pancreatic adenocarcinoma. Another example of CRC biomarker is CA125 (UniProtKB ID: Q8WX17), but both lack specificity, as they are also found to be related to endometriosis. DNA-based molecular biomarkers are based on the detection of methylated DNA in the stool. In one study, researchers combined the fecal immunohistochemistry testing (FIT) and multi-targeted stool DNA test (mt-sDNA) for the detection of hypermethylated DNA [30]) [Table 1. Trials using CAde system for colorectal lesions] could be broken down further to study, algorithm used, number of patients, and outcome for better organization and flow [Table 2. The Comparison between ileo-colonoscopy and CCE [128-138]] is a good comparison Also, I wonder if

[Real-life AI-assisted guidelines according to recommendations of worldwide major associations] section could be summarized in a table for easier flow. Otherwise, very good review of the topic with comprehensive updates. In summary: AI is transforming colorectal cancer (CRC) screening across multiple stages of diagnosis and treatment. It enhances noninvasive tests like FIT by refining thresholds and improving patient risk stratification. AI also helps patients prepare for colonoscopy with personalized guidance, leading to better outcomes. During colonoscopy, AI improves adenoma detection rates (ADR) through real-time image analysis and accurate polyp characterization, reducing missed precancerous lesions and avoiding unnecessary procedures. Post-screening, AI supports treatment decisions, aids surgical planning, and improves safety by guiding lymph node removal and minimizing overtreatment. Additionally, when paired with AI, technologies like colonic capsule endoscopy may provide effective alternatives for screening in underserved populations.

Response 2. We have cut down on the scientific details of biomarkers and tumoral markers mentioned in the text. We have re-organized Table 1 with the provided data. We have introduced some new chapters and we have organized the [Real-life AI-assisted guidelines according to recommendations] in a table with clear data and specific observations in each case.

With best regards,

Cătălin Andrei Duței

Corresponding author

Round 2:

Thank you for your interest and support in reviewing our manuscript entitled *Could artificial intelligence-powered colonoscopies change the future of colorectal cancer screening?*, submitted for publication in the WJG. We would like to thank you for your time and valuable comments on our manuscript. We much appreciate your effort to read and ponder the data we provide in regard to AI influence in colorectal cancer screening. Through your questions, you have pointed out precisely some issues that still need clarifying.

Comment 1. The manuscript presents valuable insights; however, some clarifications are needed. Could author explain the following;

Comment 1.I. How reliable and generalizable are AI-driven bowel preparation scoring systems across diverse patient populations and healthcare settings?

Response 1.I. AI intervention is a very debatable and controversial field in healthcare, as it interferes with numerous steps of the screening in general. Whether it is as reliable as it is promising, we definitely need further research, further learning and established, clear protocols for such step.

Comment 1.II. What factors contribute most significantly to discrepancies between AI-generated and provider-recommended preparation protocols, and how can these be minimized?

Response 1.II. In bowel preparation scoring, for example, AI needs to be provided with more specific data, concerning the geographic regions, patient variability – race, diet, lifestyle factors, medication and comorbidities. Protocols and instructions provided by a medical specialist tend to adjust better to each patient, also by offering further clarifications depending on the level of understanding.

Comment 1.III. Can AI models be optimized to deliver preparation instructions that are patient-specific, culturally sensitive, and tailored to different literacy levels?

Response 1.III. AI-generated protocols tend to be more objective and generalized – an issue that could be addressed by offering a first-hand questionnaire to better characterize the patient type. The good thing of AI is that it can be optimized by continuously teaching it every language level, literacy grade and cultural specificities until it is able to adjust the information provided according to each patient, covering eventual discrepancies.

Comment 1.IV. What role does AI play in addressing barriers such as diet restrictions, medication adjustments, or timing conflicts during bowel preparation?

Response 1.IV. To exploit most of its capacities, AI plays a crucial role by being able to offer a detailed timing to patients for their medication administration, diet restriction (for example, through a potential application), even using a personal phone, and finally objective instructions following a feedback loop in real time, after bowel preparation.

Comment 2. Furthermore, the authors have cited outdated references. To meet the standards of the scientific community and ensure the credibility of the research work, it is recommended that the authors cite references that are not older than five years. Updated references were suggested to enhance the credibility of the manuscript and meet the required standards. Older studies may reflect out-dated research and detract from the novelty of the work.

Response 2. We have analyzed the references comments and, in our defense, we consider that mentioning older protocols and older AI use gives a good insight about how it has started and how much it has evolved in time. We took your suggestions into consideration and completed the text with the appropriate data, although we did not mention those studies that were slightly beyond our subject field - CRC screening.

With best regards,

Cătălin Andrei Duței
Corresponding author