Respected Editor,

Thank you for the opportunity to submit the revised manuscript to your esteemed journal. Please find below our responses to individual comments from the reviewers and appropriate changes have been made in the manuscript.

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: The use of artificial intelligence (AI) in colonoscopy has gained extensive attention in current times. In the present review, the authors reported the preliminary ex-vivo experiences and summarized the promising results of the first randomized controlled trials. The content of the review is comprehensive, and the language of the manuscript needs minor polishing. I suggest this manuscript be minor revised.

Response: Thanks for the support! We have revised the entire manuscript for language improvement based on your comment.

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: Dear Sirs, Thank you for your invitation to review the this article. I think the authors correctly concluded that "the detection ability of AI systems is dependent on the inspection of the mucosa exposed by the endoscopist during the scope withdrawal, and an adequate technique is essential for its effective operating." However I cannot accept their approach to another task for AI - the improving in detection of hyperplastic polyps with low malignant potential It looks like a dream (point no. 2 in conclusion) that macroscopically we are able to recognize polyps with a malignant potency when even experienced pathologists differ in accuracy assessment of hyperplastic/ serrated polyps and even adenomas – not to mention dysplasia in small polyps. I would not like to argue with such opposite opinions but I think, the authors should balance their statement with other studies which have confirmed that we should not relay on "optical pathology" but rather histopathological diagnoses. I think that realistic assessment of tasks for AI, enables its real development. Therefore, the authors should not avoid limitations and clearly they define. I think the authors reached their goals and they provided an overview on the progress of AI. However, in the first sentence where they started paragraph ARTIFICIAL INTELLIGENCE (AI) they have written: "Artificial intelligence (AI) is the evolution of general software systems that provide an input and obtain an output through an algorithm." I would rather write that AI is a result of this evolution (because this is a process). The authors mentioned endoscopists' and other limitations which provoke interest in AI (written) in the first part of the article: cecal intubation rate (>95% in screening colonoscopies), withdrawal time > 6 minutes, bowel preparation. These parameters are also important for AI which is based on skills and quality of endoscopist's work. Therefore, I would mention that aspirational withdrawal time in some countries is recommended as >9 minutes Although the same assumption regarding withdrawal time was made in the authors' publication in "Gastroenetrology" but this measure in not well accepted in some countries. Therefore, it would be also very interested to know the results of their study for endoscopists whose withdrawal time was not shorter than 10 minutes (see British Society of Gastroenetology's guidelines

- Rees CJ et al. UK Key Performance Indicators & Quality Assurance Standards for Colonoscopy. http://dx.doi.org/10.1136/gutjnl-2016-312044). Also I am interested to know more about effect of CADe on individual endoscopist and know endoscopist's feedback retrospectively why they missed some polyps. Regarding future development it would be very welcome to employ AI for monitoring endoscopist if he assess sufficiently each colonic segment and then AI allows endoscopist to continue endoscopy with more distal segments.

Reviewer: " However I cannot accept their approach to another task for AI - the improving in detection of hyperplastic polyps with low malignant potential It looks like a dream (point no. 2 in conclusion) that macroscopically we are able to recognize polyps with a malignant potency when even experienced pathologists differ in accuracy assessment of hyperplastic/ serrated polyps and even adenomas – not to mention dysplasia in small polyps. I would not like to argue with such opposite opinions but I think, the authors should balance their statement with other studies which have confirmed that we should not relay on "optical pathology" but rather histopathological diagnoses. I think that realistic assessment of tasks for AI, enables its real development. Therefore, the authors should not avoid limitations and clearly they define. "

Response: Thank you for bringing up an important point! We clarified in the text (with appropriate references) accordingly.

R: "However, in the first sentence where they started paragraph ARTIFICIAL INTELLIGENCE (AI) they have written: "Artificial intelligence (AI) is the evolution of general software systems that provide an input and obtain an output through an algorithm." I would rather write that AI is a result of this evolution (because this is a process). "

Response: Thanks for the suggestion, we have rephrased it accordingly in the text on page 6, line 8 of the manuscript.

R: "The authors mentioned endoscopists' and other limitations which provoke interest in AI (written) in the first part of the article: cecal intubation rate (>95% in screening colonoscopies), withdrawal time > 6 minutes, bowel preparation. These parameters are also important for AI which is based on skills and quality of endoscopist's work. Therefore, I would mention that aspirational withdrawal time in some countries is recommended as >9 minutes Although the same assumption regarding withdrawal time was made in the authors' publication in "Gastroenetrology" but this measure in not well accepted in some countries. Therefore, it would be also very interested to know the results of their study for endoscopists whose withdrawal time was not shorter than 10 minutes (see British Society of Gastroenetology's guidelines - Rees CJ et al. UK Key Performance Indicators & Quality Assurance Standards for Colonoscopy. http://dx.doi.org/10.1136/gutjnl-2016-312044).

Response: Thanks for the suggestion, we totally agree on the importance of colonoscopy quality measurements in AI assisted colonoscopies, as underlined in the conclusions. We also better highlighted the importance of adequate intestinal preparation. As far as withdrawal time is concerned, none of the published studies had a withdrawal time > 10 minutes, and sub-group analysis are not reported for such a topic; The study from our group (Repici et al, Gastroenterology 2020) has a higher withdrawal time in CADe group (7.2 min vs 7 min) and it is by far the one with higher ADR (54.8%). However, we did not stress on this point because of the paucity of data and any conclusions at this point would be purely speculative.

R: "Also I am interested to know more about effect of CADe on individual endoscopist and know endoscopist's feedback retrospectively why they missed some polyps. Regarding future development it would be very welcome to employ AI for monitoring endoscopist if he assess sufficiently each colonic segment and then AI allows endoscopist to continue endoscopy with more distal segments."

Response: Thanks for the suggestion, of course this is a very interesting topic because it would allow the endoscopist a 'self-assessment" and consequently a continuous improvement in his clinical practice; unfortunately, considering personal feedback as a not replicable measure, we would consider the impact of Artificial Intelligence on differently skilled endoscopist as a surrogate measure helping us to understand how it help us in everyday practice. Data are still lacking so far, however our group, after having reported data among experienced endoscopists (Repici et al. Gastroenterology 2020), is replicating the study among endoscopists still in training (NCT04260321). On the other side, we explored the effects on endoscopists of false positive activation in a recent study and we briefly added in the text our findings.

Reviewer #3:
Scientific Quality: Grade A (Excellent)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (High priority)
Specific Comments to Authors: The authors deliver a very well written and comprehensive manuscript about artificial intelligence for the detection of colorectal lesions. The article methodically goes through this technology and its progress in field of colorectal polyp detection. 1- in the section about artificial intelligence, it would be helpful to add a figure to demonstrate the different layers of the neural network. (inut layer, hidden layers, output layers). 2- future needs section: It would be helpful to mention the current application of these different AI systems commercially throughout the world (for e.g. Medtronic system is rolled out in Europe for commercial use, FDA has not approved any AI system in US yet, etc..)

R: in the section about artificial intelligence, it would be helpful to add a figure to demonstrate the different layers of the neural network. (inut layer, hidden layers, output layers).

Response: Thanks for the suggestion, we added an explicative figure as requested.

R: future needs section: It would be helpful to mention the current application of these different AI systems commercially throughout the world (for e.g. Medtronic system is rolled out in Europe for commercial use, FDA has not approved any AI system in US yet, etc..)

Response: Thank you for the suggestion, we have specified this in table 3.

Reviewer #4:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: Very well written manuscript. To improve it 1. Explain the differences between the 2 available systems 2. Reference 26 is incomplete

R: Explain the differences between the 2 available systems

Response: Thanks for the suggestion, we have clarified this and explained the differences more appropriately (pages 6 and 7).

R: Reference 26 is incomplete

Response: Thank you for this point, we have corrected the reference.