Dear Dr. Bonino and Dr. Singh,

Thank you for considering our original narrative review article “Artificial Intelligence in Gastroenterology: A Narrative Review” for resubmission as a publication in *Artificial Intelligence in Gastroenterology.*

We have revised our manuscript to address reviewer comments and address their individual issues below.

Sincerely,

Jonathan Galati, MD
Internal Medicine | PGY-3
NYU Langone Health

Comment:
Add the term "depth convolution neural network" as the full name of "DCNN".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Esophagogastroduodenoscopy section, add the full name of the "AUC".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Esophagogastroduodenoscopy section, the authors said "The CADe obtained excellent results in the two external validation groups (97.2%, 91.9%) regarding biopsy site". What does "97.2%, 91.9%" mean?

Response:
Thank you for your comment. The 97.2% and 91.9% refers to the CADe system’s ability to identify the optimal site for biopsy in two external validation sets. We have made the following change to our manuscript:

“In two external data sets (external validation data set 4 and 5), the CADe identified the optimal biopsy site in 97.2% of cases and 91.9% of cases respectively”

Comment:
In the Esophagogastroduodenoscopy section, add the full name of the "AUROC".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Esophagogastroduodenoscopy section, the authors said "…Yasuda et al. used linked color imaging. (LCI) …". This sentence should be revised as "…Yasuda et al. used linked color imaging (LCI) …".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Wireless Capsule Endoscopy section, the authors said "… and accuracy of 91.2%, 85." This sentence should be revised as "… and accuracy of 91.2%85".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Wireless Capsule Endoscopy section, the authors used the word "non-bleeding" or "nonbleeding". Please keep them consistent in format.

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
Why not explain the "BBPS" and "MES" in the Colonoscopy section?

Response:
Thank you for your recommendation. We included the following statements in our manuscript to better explain BBPS and MES.

“Building upon their experience with ENDOANGEL, Zhou *et al*. created a new system using two DCNNs: DCNN1 filtered unqualified frames while DCNN2 classified images by Boston Bowel Preparation Scale (BBPS) scores[113]. The BBPS is a validated rating scale for assessing bowel preparation quality[114]. Colonic segments are assigned scores on a scale from 0 to 3.

Colonic segments unable to be evaluated due to the presence of solid, unremovable stool are assigned a score of 0 whereas colonic segments that are able to be easily evaluated and contain minimal to no stool are assigned a score of 3[114]. Zhou *et al.*'s DCNN2 classified images into two categories: well-prepared (BBPS score 2-3) or poorly prepared (BPPS score 0-1)."

"The most commonly used endoscopic scoring system in these studies is the Mayo Endoscopic Score (MES). Physicians assign scores on a scale from 0 to 3 based on the absence or presence of erythema, friability, erosions, ulceration and bleeding[122]. A score of 0 indicates normal or inactive mucosa whereas a score of 3 indicates severe disease activity[122]. In 2018, Ozawa *et al.* published the first study to use a DCNN to classify still images obtained from patients with UC into MES-0 vs MES 1-3 and MES 0-1 vs MES 2-3[120]."

Comment:
In the Colonoscopy section, add the full name of the "DNUC".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
In the Colonoscopy section, the authors said "With respect to histologic remission, DNUC had had a sensitivity of 92.4%…". This sentence should be revised as "With respect to histologic remission, DNUC had a sensitivity of 92.4%…".

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
The word "EACH" should be revised as "EAC" in the Table 1.

Response:
Thank you for this recommendation. We have included this change in our manuscript.

Comment:
Too many Key Words, reduce to less than 6.

Response:
Thank you for this recommendation. We have reduced the number of Key Words in our manuscript.

Comment:
The paper's contribution needs to be stated clearly.

Response:
Thank you for this recommendation. We have included the following statements in the manuscript:

"Author Contributions: JSG, SAG: manuscript concept and design. JSG, RJD, MO: obtaining and interpreting literary sources, drafting of manuscript. JSG, SAG: revision of manuscript. All authors read and approved the final version of the manuscript."

"While other narrative reviews have been published regarding the use of artificial intelligence in esophagogastroduodenoscopy, WCE and colonoscopy, this narrative review goes a step further by providing a granular and more technical assessment of the literature."

Comment:
It may be helpful to identify the target audience for the paper, given the rather technical nature of research topic.

Response:
Thank you for this recommendation. We have included the following statement in the introduction section of our manuscript:

"As such, this narrative review is intended for medical providers and researchers who are familiar with the use of artificial intelligence in esophagogastroduodenoscopy, WCE and colonoscopy and are interested in obtaining an in-depth review in a specific area."

Comment:
The conclusion section needs to include some recommendations for practitioners based on the findings, if appropriate.

Response:
Thank you for this recommendation. We have included the following statement in the conclusion section of our manuscript:

“Medical providers at all levels of training should prepare to incorporate artificial intelligence systems into routine practice.”

Comment:
A very important part of the current manuscript that is missing is an outlook for the future of the field. I think the paper is of very little value if it just lists the results of existing research. The authors should point out the future trends in the field based on the current status of the existing research and the research priorities that deserve the researchers' attention.

Response:
Thank you for this recommendation. We have included an additional section in our manuscript title “Future Direction”. Please see below for the included section.

“Future Directions:
Artificial intelligence is in the very early stages for medicine, but especially in gastroenterology and endoscopy. AI will help is in the area of “augmentation” and “automation”. Augmentation like what is happening with polyp detection and interpretation. Automation by eliminating electronic paperwork, such as the use of natural language processing for procedure documentation. Artificial intelligence systems have repeatedly been shown to be effective at identifying gastrointestinal lesions with high sensitivity, specificity and accuracy. While lesion detection is important, this is only the beginning of AI’s utility in esophagogastroduodenoscopy, WCE and colonoscopy.

After refining their AI systems for lesion detection, several groups discussed in this narrative review were able to add additional functions to their AI systems. In BE, ESCC and gastric cancer, several AI systems were capable of predicting tumor invasion depth. Within IBD, AI systems were able to generate endoscopic disease severity scores. One group was able to train their CADe to recommend neoplasia biopsy sites in BE[13]. Additional efforts should be dedicated to developing these functions, testing them in real-time and having the AI system provide management recommendations when clinically appropriate.

Additional areas in need of future research are using AI systems to make histologic predictions, to assist with positioning of the endoscopic ultrasound (EUS) transducer and interpretation of EUS images, to detect biliary diseases and make therapeutic recommendations in endoscopic retrograde cholangiopancreatography (ERCP), and, in combination with endoscopic mechanical attachments, to improve colorectal cancer screening and surveillance. While endoscopists may perform optical biopsies of gastrointestinal lesions to predict histology and make real-time management decisions, these predictions are highly operator-dependent and often require expensive equipment that is not readily available. Thus, developing an AI system capable of performing objective optical biopsies, especially in WLE, would preserve the quality of

histologic predictions, be cost effective, and avoid the risks associated with endoscopic biopsy and resection.

Similarly, EUS is highly operator-dependent, requiring endoscopists to place the transducer in specific positions to obtain adequate views of the hepatopancreatobiliary system. Research should focus on using AI systems to assist with appropriate transducer positioning and perform real-time EUS image analysis[185-193].

Presently, several clinical studies are actively recruiting patients to evaluate the utility of AI systems in ERCP. Of particular interest is the diagnosis and management of biliary diseases. Some groups are planning to use AI to classify bile duct lesions and provide biopsy site recommendations[194]. One group is planning to use an AI system in patients requiring biliary stents to assist with biliary stent choice and stent placement[195]. It will be interesting to see how AI performs in these tasks as successes could pave the way for future studies investigating the utility of AI systems to make real-time management recommendations.

While this narrative review focused on the use of AI in colonoscopy, of growing interest is the use of endoscopic mechanical attachments in colonoscopy to assist with polyp detection in colorectal cancer screening and surveillance. Independently, AI systems and endoscopic mechanical attachments are known to increase ADR and PDR. Few studies have investigated how combining AI with endoscopic mechanical attachments impacts ADR and PDR. Future research should examine the impact that combining these modalities has on ADR and PDR.”