Response to reviewers' comments

Dear Editors, dear Reviewers,

We wish to express our appreciation to the Editors and Reviewers for their insightful comments, which have helped us significantly to improve our manuscript. According to the suggestions, we have thoroughly revised our manuscript and its final version is enclosed. Point-by-point responses to the comments are listed below.

Round 1

Reviewer # 05355683

1. Full terminology should be given for "ADR" in Core tip section.

Response: As requested, full terminology was provided for ADR in Core tip section

2. "This intelligence can extend to the algorithm becoming agnostic to manual data input and it can learn unsupervised by developing its own rules and classifiers [16,17]." The word of "unsupervised" is confusing as in most cases, supervised machine learning was actually used by telling the machine the normal and abnormal cases in the training phase.

Response: We are very grateful for this precious suggestion. As You suggested, we corrected the sentence accordingly: This intelligence can extend to the algorithm becoming agnostic to manual data input and it can learn by developing its own rules and classifiers [16,17].

3. More study details and discussions should be provided regarding Randomized Clinical Trials.

Response: We are very grateful for this precious suggestion. As You suggested, we enriched the section 3 and 4, therefore providing more details regarding randomized controlled trials in both the sections.

4. More technical details of those systems, such as WavSTAT, should be provided, so the readers could know more about what AI techniques and foundations are behind

those systems.

Response: We are very grateful for this precious suggestion. As You suggested, we enriched the manuscript accordingly: "Kuiper et al used a system called WavSTAT for real-time optical diagnosis based on laser-induced autofluorescence spectroscopy on 87 patients with 207 small (< 10 mm) colorectal lesions.During colonoscopy, the endoscopists tried to differenciate real-time adenomas vs non-adenomas as a low or high confidence call. Then, all lesions were analyzed using the system. Histopathology was used as the reference standard. The accuracy and negative predictive value (NPV) of WavSTAT were 74.4% and 73.5% respectively for WavSTAT alone, while they were 79.2% and 73.9% respectively combining WavSTAT with high resolution endoscopy[37]. The study concluded that it did not fulfill the American Society of Gastrointestinal Endoscopy (ASGE) performance thresholds for the assessment of diminutive and small lesions.Rath et al used the WavSTAT4 optical biopsy forceps system designed by Spectrascience Inc, San Diego, California, USA. for prediction of histology using laser-induced autofluorescence spectroscopy (LIFS) on 27 patients with 137 diminutive (≤ 5 mm) polyps [38]. The accuracy was 84.7% along with sensitivity of 81.8%, specificity of 85.2% and NPV of 96.1%. They concluded that this new WavSTAT4 systemhad the potential to meet the ASGE thresholds for the "resect and discard" strategy."

Reviewer # 05122080
1. The notion of interval carcinoma in the introduction section can be broadened
Response: In accordance with Your comment, we added the notion of interval colorectal cancer carcinoma in the introduction section

2. Definitions of AI, deep learning, deep network, ground truth can be also explained by means of a figure interlacing these concepts.
Response: In accordance with Your comment, we added a figure in which is showed the interlacing of the aforementioned concepts

3. A comparative table in the "How could artificial intelligence help in polyp

characterization?" section can be added.

Response: Dear reviewer, many thanks for Your comment. We added a comparative table about the role of AI on chacterization of colonic polyps.

Many thanks again,

Yours Sincerely,
Emanuele Sinagra

Round 2

Dear Editor We corrected the aforementioned file (58311) according to the reviewer's comment, and in particular: - we mentioned the figure 1, already submitted to the f6 publishing system, in the section "what is artificial intelligence"? - we added the two tables in the submitted file - we corrected the spelling errors and the other typos Sincerely Yours Emanuele Sinagra