

Dear Board of Editors

Thank you very much for the valuable comments and thorough revision. We have revised the manuscript (manuscript ID 56576 *Fluorescence guided intraluminal endoscopy in the gastrointestinal tract: a systematic review*), and we hope to meet your expectations. Please view our revisions in the uploaded manuscript as well as the point by point responses in this document. Editor/referee comments are marked by **bold** and our response in plain text. Additional text added in the revised manuscript as in this document is marked by **red**.

Reviewers' comments:

Reviewer #1:

**Specific Comments to Authors: Olivia Engholt Mortensen and colleagues aimed to explore the feasibility of fluorescence endoscopy and evaluate its use in diagnosing and evaluating gastrointestinal disease. And they found that the use of fluorescence endoscopy was a promising method adding precisely diagnostic value in the early development of neoplasms and tumors, adenomas, assessment of tumor invasion within the gastrointestinal tract and adding therapeutic value within the field of gastrointestinal diseases. I think the review is useful and helpful. Furthermore, no obvious errors were found in this paper. I think this paper can be accepted.**

We are very grateful to the reviewer for the kind remarks, thank you!

Reviewer #2:

**Specific Comments to Authors: Title: suitable. Abstract: Suitable Introduction: Reference to support the first phrase in paragraph one.**

Thank you for noticing this error, we have now added a reference to support the phrase.

**Methods: Which key words the authors used in the search strategy? Results: Suitable Discussion: Suitable Conclusion: suitable**

We have listed the key words in table 1. We have now added “**The key words used in the search strategy is shown in table 1**”. We are very grateful to the reviewer for the remarks, thank you!

Science Editor:

**1 Scientific quality: The manuscript describes a systematic review of the fluorescence guided intraluminal endoscopy in the gastrointestinal tract. The topic is within the scope of the WJGE.**

We are very pleased to hear that. Thank you!

**(1) Classification: Grade A and Grade B; (2) Summary of the Peer-Review Report: The authors aimed to explore the feasibility of fluorescence endoscopy and evaluate its use in diagnosing and evaluating gastrointestinal disease. And they found that the use of fluorescence endoscopy was a promising method adding precisely diagnostic value in the early development of neoplasms and tumors, adenomas, assessment of tumor invasion within the gastrointestinal tract and adding therapeutic value within the field of gastrointestinal diseases. The review is useful and helpful. Furthermore, no obvious errors were found in this paper;**

We are very grateful to the reviewers for the kind remarks.

**and (3) Format: There are 3 tables and 2 figures. A total of 45 references are cited, including 12 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 provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the PRISMA Checklist form. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study is without financial support. The topic has not previously been published in the WJGE. The corresponding author has not published articles in the BPG. This manuscript is the resubmission of Manuscript No. 53661 (Rejected).**

We have provided the Non-Native Speakers of English Editing Certificate.

**5 Issues raised: (1) Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;**

Thank you for your reminder. We have now arranged the figures in PowerPoint. We will attach a Word file as well with the text supporting the figures.

**(2) I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text;**

Thank you for your reminder. We have now written the article highlight:

#### *Research background*

Different studies have investigated the use of fluorescence based endoscopy systems where the white light has been supplemented by infrared light and the use of relevant fluorophores.

Fluorescence endoscopy is among the recent advances within the field of fluorescence-guided surgery and cancer-specific imaging.

#### *Research motivation*

The aim of this systematic review was to evaluate both the diagnostic and therapeutic value of fluorescence-guided flexible intraluminal endoscopy. Angiogenesis and neovascularization are important factors in tumor invasion, and as mucosal and submucosal vessels are not visible to the naked eye, but after intravenous injection of a fluorophore and illumination by infrared light, profound structures can be visualized.

#### *Research objectives*

Fluorescence endoscopy can be used within the detection the early development of neoplasms and tumors, adenomas, assessment of tumor invasion within the gastrointestinal tract. Those qualities are a part of the recent advances within the field of fluorescence-guided surgery and cancer-specific imaging.

#### *Research methods*

The research method was a data analysis. We followed the PRISMA guidelines for this systematic review. The research covered five databases; Pubmed, Scopus, Web of Science, Embase, and the Cochrane Collection. Authors screened title and abstract for inclusion, subsequently full-text for inclusion according to eligibility criteria listed in the protocol. The risk of bias was assessed for all studies according to the Newcastle-Ottawa Scale. The authors extracted the data and reported the results in both text and tables.

### *Research results*

We included seven studies in the systematic review after screening a total of 2769 papers. Four studies evaluated the usefulness of fluorescence endoscopy in assessing tumor invasion. Three of the four studies reported an exceptional diagnostic accuracy in assessing tumor invasion, thus representing better visualization and more correct diagnosis by fluorescence endoscopy compared with the conventional endoscopy. The relationship between the endoscopic findings, tumor invasion, and tumor vascularity was evaluated in two studies showing a significant correlation. The use of fluorescence endoscopy is a promising method.

### *Research conclusions*

This systematic review explored the diagnostic and therapeutic value of fluorescence endoscopy. This study proposes fluorescence endoscopy as a method, which can increase those values, in the context of what is already known. This systematic review reflects a high clinical applicability, and fluorescence endoscopy is a method, that builds on the approach of tumor vascularity. This is the hypothesis of this systematic review and how this cooperate with the diagnostic and therapeutic value.

*Research perspectives*

More studies are needed to utilize the feasibility of fluorescence endoscopy compared with other endoscopic methods exploring the diagnostic and therapeutic value in different clinical issues.

**and (3) please don't include any \*, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP < 0.05, bP < 0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP < 0.05 and dP < 0.01 are used, and a third series of P values is expressed as eP < 0.05 and fP < 0.01. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.**

We thank the reviewer for all these correct observations and remarks, and we have corrected it all accordingly. We used "\*" in table 1 as it is exactly how we did the search string in e.g. Pubmed

Editorial Office Director:

**I have checked the comments written by the science editor.**

We thank the Editorial Office Director for reviewing our manuscript.

Company Editor-in-Chief:

**I have reviewed the Peer-Review Report, the full text of the manuscript and the relevant ethics documents, all of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revisions. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors.**

We thank the Company for the remarks and for reviewing our manuscript, thank you.

Hope that we with these corrections will meet the expectations of reviewers and editors.

On behalf of all authors

Best Regards,

**Olivia E. Mortensen**

Dept. of Surgical Gastroenterology

Copenhagen University Hospital - Rigshospitalet

Inge Lehmanns Vej 7

2100 Copenhagen Ø

Denmark

Mail: [olivia.mortensen@yahoo.com](mailto:olivia.mortensen@yahoo.com)

Tlf: +45 30 30 17 51