

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4988-revised.doc).

Title: Beyond white light endoscopy: the role of optical biopsy in inflammatory bowel disease

Author: Julia Liu, Aldona Dlugosz, Helmut Neumann.

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4988

The manuscript has been improved according to the suggestions of editor and reviewers. We believe we have satisfactorily addressed all their comments.

Editor comments:

1. We have provided the following information requested by the editor: running title, authors' affiliations, corresponding author, author contributions, abstract, keywords, and core tip.
2. We have changed the headings 1 and 2 to the requested format.
3. We changed the bibliography format to the World Journal of Gastroenterology format.

Below is a list of point-by-point response to each reviewer's comments.

Reviewer 1:

The paper deals with a review on confocal laser endomicroscopy and endocytoscopy. Both techniques have been extensively described, the data on the possible application discussed in detail. The paper is enjoyable and acceptable as it is, providing minor changes. First, there is the need of figures about the number of papers present in literature, the number of them reviewed, the date of beginning and end of PUBMED (or other) search. For each paper mentioned the level of evidence should be made explicit.

We appreciate the reviewer's comment about how all the papers present in the literature on the topic of optical biopsies in IBD. Unfortunately, the literature on the use of optical biopsy for inflammatory bowel disease (IBD) is limited, with only randomized controlled trials for dysplasia detection (2 studies), thus making a systematic review nearly an impossible task. Therefore, we structured this review as a general review of the use of optical biopsy in IBD based on our published experiences and not a systematic review.

We have included the results of a recent a systematic review on CLE for dysplasia detection in the appropriate section.

Secondly, in my opinion, there is not any comment on the cost of the procedure itself, the training of the endoscopists , the need of a pathologist or a pathologist formation, the necessity (sometimes legal) to also perform routine histology. These limitations are the true drawbacks that so far influenced the diffusion of the optical biopsy and the lack of comparison data on large series.

We have inserted the relevant information regarding the cost of procedure, training of endoscopists and recommendations regarding histology under the technical aspect of optical biopsy, as requested by the reviewer.

Review 2:

COMMENTS TO AUTHORS The authors have written on a very interesting topic. Although the subject is of great interest, for the lay, non-technological, readership (people like me) simpler descriptions are needed and this remains my main reservation about the manuscript. At the start I wish to see the history or idea behind development of CLE and EC. Why were they developed and needed at all. The authors have mentioned this in the manuscript but these points need to come in the beginning. I wish to know how technically difficult or applicable it can be in my day to day practice. What expertise is needed ? Can I set up such a system with two people scoping in say a remote area of Africa with one staff member or do I need a mucosal specialist with availability of a full-fledged lab for my use. The technical description on the two techniques reads like a brochure specifications advert and needs to be improved. Also a brief description on pros and cons of the two techniques is also needed. Re clinical applications, a general appraisal of the grades and types of mucosal disease followed by disease description should follow.

The technical aspect of optical biopsy is quite technical as it is a detailed description of the performance of the technique of optical biopsy. We have tried to make it as simple as possible, and incorporated most of our published experiences in the text. Since endocytoscopy is currently a prototype instrument, and not clinically available, we did not attempt to compare the two techniques in detail.

Again in the order of hierarchy although IBD forms my main practice too, perhaps dysplasia should come first. The individual disease sections need to be shortened – the IBD section for eg is considerably long. The section on 'Research applications' needs to be more punchy. I am not very excited to be able to see one too many bacteria in the

mucosa – this will not be a great reason for me to start adopting and learning about these techniques.

Although we appreciate the reviewers' suggestions, this review only focuses on optical biopsy in IBD and not other conditions, as it was written specifically for an issue dedicated to IBD.

Reviewer #3:

To: Professor Lian-Sheng Ma Editorial board World Journal of Gastroenterology Title: "Beyond white light endoscopy: the role of optical biopsy in inflammatory bowel disease (IBD)" Dear Editor, We have read through the manuscript and we think that some lacking news should be better re-evaluated: 1) Although this is not a systematic review, the manuscript should be better organized: a. What kind of database did the authors used? b. Which were the key-words adopted? c. How many articles/studies did they find? d. What inclusion/exclusion criteria did they adopt in order to consider or not a literature study in their research? e. How many articles did they excluded? f. How many physicians did perform the evaluation of the articles considered?

As we explained in the response to Reviewer # 1's first comment, the literature on the use of optical biopsy for specific conditions such as inflammatory bowel disease (IBD) is limited, with only two randomized controlled trials for dysplasia detection in IBD, thus making systematic review nearly an impossible task. Therefore, we structured this review as a general review of the use of optical biopsy in IBD based on our published experiences and not a systematic review.

2) A flow chart resembling the main steps of the evaluation of literature background, inclusion/exclusion criteria, number of studies considered/excluded, should be provided.

Please see response to comment #1. We have included the results of a recent a systematic review on CLE for dysplasia detection in the appropriate section.

3) A table gathering all the main characteristics of the studies considered, their outcomes, their results, etc should be provided in order to easily recognize the features of the present works.

Please see response to comment #2.

Reviewer #4:

You can add figure and photos. Also you should add more your experience in this review.

We have included figures and photos where appropriate. This review is largely based on our published experiences with optical biopsy in IBD.