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Light and sound - emerging imaging techniques for inflammatory bowel disease

Dear reviewers,

we gratefully appreciate your careful review and critical suggestions. We hope to answer your ideas for improvement with the appropriate changes to our manuscript.

Kind regards,

Ferdinand Knieling

Maximilian Waldner

Reviewer 1:

Comments Pages 12-13 : The authors could insist on the accuracy of confocal laser endomicroscopy for assessing mucosal healing in IBD (Mace V et al., J Gastroenterol Hepatol 2015), and intraepithelial neoplasia (Sharma P, Gastrointest Endosc 2011). The authors could also cite and comment on a very recent paper by Haas K et al (World J Radiol 2016) on the current imaging guidelines in pediatric and adult IBD patients.

Author response: Thanks for your suggestions, citations and comments have been included in the appropriate sections of the text.

The text should be checked for typos (including page 3, "core tip", lines 1 and 5; page 11 paragraph "ultrasound molecular imaging" line 5 ; pages 13 and 14, second paragraphs (patterns ; dyes) ; page 15, second paragraph lines 4, 8, 11 ; page 15 second-last line..).

Author response: Text has been corrected and double-checked by a native speaker.

Reviewer 2:

Many technologies listed in the review are not widely available even in IBD specialized tertiary centers. Moreover, some technologies are not proved to be useful for diagnostic or surveillance purposes. So that this review seems to be a mere list of technologies applicable for a lot of intestinal diseases.

Author response: We integrated a comment in the introduction, especially stating that these modalities could be applied to many more disease entities. In the following sentence we try to limit the topic highlight to inflammatory bowel diseases. To our understanding we included technologies, which have been applied or are about to translate into clinical use. You are correct that these might not be widely available but we try to give an outlook into future applications.

It would be useful to read in the different paragraphs on what occasion in IBD each technology could be applied, to have a more in-depth analysis of the various arguments. For example, the search for granuloma formation in Crohn's disease is a

challenging question. In the major part of cases CD is not diagnosed on the basis of granuloma finding, and microscopic endoscopic technologies unlikely may improve the diagnosis. The paragraphs 'Clinical evidence and translation of endoscopic techniques' and 'Clinical evidence and translation of ultrasound techniques' seem an oversimplification and are difficult to read.

Author response: Paragraphs have been divided and we added specific titles for each sub-section to more easily follow the different topics.

It is stated that the new techniques are useful for surveillance and detection of dysplasia in IBD. I agree for this statement, but the new techniques are equally important in finding colon cancer in IBD, especially in cases with a large number of pseudopolyps.

Author response: We added the term "cancer" to clarify that these approaches might not only serve in terms of surveillance. The paragraph is now named "Surveillance, detection of precursor lesion and colon cancer".

I believe that the figures 1 and 2 do not add anything to the work and should be removed. Table 1, Recommendations and state-of-the-art in IBD imaging. As it is, the statements included in the table are not acceptable. For each statement a reference should be added.

Author response: To our understanding the figures should serve as an overview to the reader going hand-in-hand with a more detailed description in the text. The statements in Table 1 are excerpts from international guidelines; references have been added in the header.

The text should be checked for typographical errors.

Author response: Text has been corrected and double-checked by a native speaker.