Dear Reviewers,

Thank you very much for your helpful comments, which are greatly appreciated and incorporated in the revised manuscript. Please find below our point by point answers:

Reviewer's code: 00188995

This study assesses the role of capsule colonoscopy in patients with incomplete colonoscopy. It is an interesting study. Comments are as follows –

1. It is expected that areas which were not seen during colonoscopy will have lesion in some cases and will be picked up on other modality. The choice of capsule colonoscopy needs to be justified as it is an expensive procedure. It would have been better if the patients also had CT or MR colonography to compare the yield of radiology imaging and endoscopic modality. We agree, that having more comparators as CT or MR colonoscopy could provide additional information on the diagnostic impact of different methods. However, in this study, feasibility of two preparation protocols (either the day following incomplete OC or within 30 days using complete new bowel prep) was evaluated. Hence, another procedure with the need for preceding bowel prep, would have added too many confounding factors. This issue has been included in the section on research perspectives.

2. As inability to take biopsy is limitation of both radiology imaging and CCE, the overall yield rate and cost would decide the choice between the two. This information is lacking in this study and hence the clinical implication of the findings is not clear. This is an important point. However, comparison of CCE with other methods was not part of our study. Demand for cost effectiveness analysis of CCE compared to other methods has been included in the research perspectives section of article highlights.

3. Some of the patients had previous abdominal surgery and some had adhesions as a cause of incomplete colonoscopy. Would CCE be a preferred modality in them? Although adhesions were supposed to be the cause of incomplete OC in some patients, no related clinical problems or capsule retention following CCE were observed. This point has been added in the discussion.

4. Complete CCE was reported in 65% patients which is another limitation of CCE. We agree, that a rate of 65% complete CCE is low. However, patients included in our study did not belong to a screening population but were highly selected by previously failed colonoscopy. Primary endpoint of the study was the ability of CCE to visualize colonic segments missed by colonoscopy. This could be achieved in 90% 97%, respectively

5. Minor point – in Abstract, Result – sentence 2 – Language correction is required (should be 'CCE visualized missed colonic…'). This sentence has been modified.

Reviewer's code: 03474672

Well written. This manuscript bring original findings, but some doubts that need to be answered.

Capsule colonoscopy has been approved by the FDA for imaging the proximal colon in patients with previous incomplete colonoscopies and more recently for patients who need colorectal imaging but who are not candidates for colonoscopy or sedation, or has a redundant colon or unfavorable anatomy. I suggest that these main indications should be emphasized in the introduction. This point has been added in the introduction.

Capsule colonoscopy is not approved by the FDA for screening average-risk persons. Advantages of capsule colonoscopy are the achievement of endoscopic imaging without an invasive procedure and avoiding the risks of colonoscopy. Disadvantages are that the bowel preparation is more extensive than that for colonoscopy and this difficulty should be described clearly in limitations, since it was a limitation in this study. We agree that bowel preparation is more extensive for colon capsule than for colonoscopy. This is a limitation of the method and was the reason to test the feasibility of a low volume preparation protocol and the possibility to perform CCE after colonoscopy without a complete repeated cleansing procedure. However, it must be stressed, that all patients included in our study had been scheduled for standard colonoscopy which had failed. Thus, CCE was performed as a ´rescue procedure´ to complement incomplete colonoscopy and not as a primary alternative to colonoscopy.

Also, because the logistics of performing same-day colonoscopy on patients with positive capsule studies are quite difficult, most patients with positive studies will require repreparation and colonoscopy on a separate day. In a large screening trial in 884 patients, capsule colonoscopy had 88% sensitivity for detecting patients with a conventional adenoma 6 mm in size but was ineffective for the detection of serrated lesions, and 9% of patients had technically failed examinations for inadequate cleansing or rapid transit of the capsule. Thank you for this very valuable comment. Potential uptake of colon capsule in a screening population would be definitely improved by the option to perform colonoscopy on the same day directly after CCE in case significant polyps were detected. However, patients in our selected study population all had previously incomplete colonoscopy performed by an experienced endoscopist. As another repeated colonoscopy would very likely fail again, other methods as device assisted colonoscopy seem more appropriate, in case relevant findings are detected by CCE. In these highly selected cases, repeated bowel prep might be tolerable to remove these difficult to reach lesions.

In this study I miss the polyps founded classifications, since it clearly impact in the method success. Polyps in this study have been classified by their size and number to stratify them as insignificant or significant. Patients with significant polyps ($\geq$ 6 mm or $\geq$ 3 polyps) were recommended to repeated colonoscopy or surgery. Systematic repeated endoscopy was not part of the protocol. Histology from device assisted colonoscopy or surgery was available from 3 patients with significant polyps at CCE. One patient with large polyp had a cecum carcinoma at surgery, one patient 3 tubular adenomas with low grade intraepithelial neoplasia (IEN), and a third patient had tubulo-villous adenoma with high grade IEN and hyperplastic polyps. In a forth patient, the polyp seen at CCE was confirmed at CT colonography but not removed due to high pulmonary risk for sedation.

Another concern is about the age of selected patient, since in the elderly we should pay attention in complications like capsule retention in diverticulosis disease. How many patients had diverticular

disease? Diverticula were detected by incomplete colonoscopy in 35/74 pts., and in 47/74 pts. by colon capsule endoscopy. However, diverticula were not considered as relevant findings in our study. These data have been added in the results section. In the present study, no capsule was retained due to diverticulosis. Although this theoretical risk cannot be totally excluded we are not aware of colon capsule or small bowel capsule retained in colonic diverticula. In our recent review on contraindications for capsule endoscopy in World Journal of Gastroenterology (https://www.wjgnet.com/1007-9327/full/v22/i45/9898.htm) we found only single reports of capsule retention in extra-colonic diverticula (e.g. Zenker´s, Meckel´s or duodenal diverticulum).

Another data missing are the better specifications about the capsule (size, generation, series). Specifications of the capsules have been added in the method section.

Reviewer's code: 00504462

Dear Sir, I want to congratulate your manuscript, as well as the quality for analyzing it, however, as you mention you have the limitation of not having randomized your patients.

Also, I have a question regarding the recruiting timing. Why did you stop the study in 2013? Were there any problem?
The study was terminated per protocol in 2013 when the predefined number (according to power analysis) of patients had been reached. There was no problem during conduction of the study.
Or Can you tell us why did it take almost 5 years to send it to publish?
Unfortunately, there was a delay due to some problems in manpower in finalizing the analysis and preparing the final manuscript.
And finally, if you did continue the research, you should have mentioned it.
The study has been closed per protocol as described in the manuscript.
Hope to hear from you soon. Sincerely

With kind regards,
Sincerely

Peter Baltes, MD