

## REVISION

### Major Compulsory Revisions:

- 1. Due to the major drawbacks of CCE, the inability to take biopsies and the procedural costs, it seems that CCE could not take more advantages than MRI (or CT)-applied virtual colonoscopy, as the latter procedure would be cheaper and the possibility of high quality images.*

The aim of our review is to delineate the potential and the scientific data of CCE. It is beyond the aim of this review to propose National screening programs which are set up on basis of performance of all diagnostic tests that are available, prevalence of disease, and societal/economic considerations. None of the tests are 100% accurate and none are for free.

But in fact we doubt that high quality MRI- or CT-imaging might equal endoscopic visualization of the colon in many respects, e.g. small polyps, flat lesions, inflammatory mucosal lesions and others.

As a minimal invasive diagnostic or screening test the inability of CCE to perform therapeutic interventions or take biopsies is not per se a major limitation. Obtaining histopathological material always comes with a higher invasiveness of the method used, that's the same with endoscopy.

- 2. In the Introduction section, FDA approval has been granted for CCE basing on data from a 16-site clinical trial involving 884 patients that assessed the safety and effectiveness of CCE in detecting adenomas at least six millimeters in size. Therefore, how about polyps at the size of 5 mm, of which would be missed by CCE? Five-mm adenomatous polyps should be removed if detected.*

Thank you for this remark. Of course should neoplastic and premalignant lesions be removed, and adenomas <5 mm are to be detected and resected. The above mentioned trial is not available as a full published paper yet, so it is hard to analyze the methods of this study. As far as we understand this study today, all polyps - including those less than 5 mm in size - were noted but analysis in comparing the golden standard of colonoscopy was differentiated for size of polyps.

- 3. In the Colon capsule endoscopy – technical features and safety paragraph, an additional energy saving feature has been introduced to CCE-2 which captures only 14 frames per minute until small bowel images are detected. Please check again only 14 or 4 frames per minute?*

Because of the slower peristaltic activity of the colon, the transit time of the capsule in the colon is relatively long that might overuse the limited battery power of the capsule. To transfer the capsule optimally through the small bowel and colon, a laxative (booster) is ingested to accelerate the transit of the capsule through the small bowel into the colon (hence the name booster). Automatic detection of the small bowel mucosa triggers the timing of booster ingestion and is signaled to the patient by the data recorder. This is optimized by the CCE-2 device.

Cp. Gastrointest Endosc 2012;76:1170-4.

4. Title of table 2 showed the complication rates reported from studies involving both first and second generation colon capsules; however, most complications from colonoscopy-related not by CCE?

Yes that's true; most complications are from colonoscopy and not related to CCE as mentioned in the text and the subtext of the table.

5. Suggest authors to add the accuracy rate of individual study into table 4.

Accuracy is a combined assessment tool of diagnostic tests; sensitivity and specificity are given in the table.

6. The potential capsule retention would be another obstacle for patients suspected with malignancy; however, colorectal cancer is the major disease that we must treat in our patients. The actual role of CCE would be significantly affected in clinical practice. Furthermore, with the introduction of colonoscopy by IV anesthesia, the case numbers in whom conventional colonoscopy cannot be or has been incompletely performed would be significantly decreased.

For colonic malignancy, capsule retention is of little concern; retention cases have not been reported so far. In all cases in whom CRC screening results in detecting malignancy, treatment would anyway remove the capsule even if retained...

7. In Summary paragraph, its acceptance among patients and accuracy for the detection of pathologic findings has been studied for a variety of indications including the detection of polyps and adenomatous lesions as well as for monitoring inflammatory bowel disease. For ulcerative colitis, CCE would be fine whereas for Crohn's disease complicated with lumen stenosis, CCE would probably lead to the capsule retention as patients with malignancies.

Capsule retention is a concern in symptomatic Crohn's disease patients, but might be easily overcome by use of the patency capsule that can safely predict passage of the capsule endoscope.