

Answers to reviewers 00183658

Question 1: To date, the diagnostic value of high-resolution micro-endoscopy is in the preclinical stage. Further randomized controlled trials are needed.

Answer: So far, the diagnostic value of HRME is still in preclinical stage, although it shows a good prospect of clinical application. Because HRME imaging equipment is not perfect enough, so it is not widely used in clinical. The practicability and diagnostic accuracy of HRME need further randomized controlled trials to validate and it plays an important role in the clinical application of HRME.

Question 2: Please discuss and add the limitations of high-resolution micro-endoscopy.

Answer: The limitations of HRME are as follows. First, HRME is a small-field-of-view imaging equipment and the field of imaging is only about 720 um, so it can not realize macroscopic imaging for lesions. Because of this limitation, HRME can only be used for further detailed check of the suspicious lesion after wide field endoscopic examination. Second, HRME is a microscopic imaging method, subtle movement in the process of imaging, such as breathing and heartbeat, could produce motion artifacts, so it is more difficult to handle HRME than white light endoscopy. Third, the lack of contrast agents is a major problem for HRME. Recently, more and more studies have examined specific contrast agents developed for certain molecules. These specific contrast agents can be used in HRME imaging and can obtain quantitative and qualitative data to improve the diagnostic rate for certain diseases. To date, no unified standard describes lesions observed during HRME, which limits the clinical application of this imaging technique. In the present study, we used HRME in the imaging of colon polyps, developed diagnostic criteria for different types of colon polyps, and laid a foundation for future research.

Question 3: Please also add the limitations of the study in the discussion section.

Answer :The limitations of this study are as follows. First, in this study we used HRME to image for ex vivo specimens of colon polyps, but we didn't make an in vivo study. Second, fluorescence imaging agents used in the study is proflavine hydrochloride, it can combine with the DNA and RNA in the nucleus. But proflavine hydrochloride is a kind of nonspecific fluorescence imaging agents, it cannot be used in targeted imaging of lesions. Finally, a part of specimens were used in the study came from biopsy, due to the small size of biopsy specimens, it is difficult to rinse off completely and it affected the imaging effect, thus influenced the outcome of the preliminary diagnosis.

Question 4:The authors should to recommend the readers “How to apply this knowledge for routine clinical practice?”

Answer :When we found lesions under white light endoscopy, we cannot judge the character of lesions right now. At this time, we can use HRME for lesions imaging, because of the instant histopathological characteristics of HRME, so we can make an accurate judgment for lesion properties at the first time and it will help doctors to make the best the choice of treatment.

Answers to reviewers 00041963

Question 1: prospective study should exclude from key words.

~~Answer: Keywords: high-resolution micro-endoscopy; colon polyps; pathology; diagnostic criteria.~~

Question 2: In object section gender, age and polyp diameters should replace to results section

Answer: Gender, age and polyp diameters are in results section now.

Question 3: Table -1 should re-arrange. HRME and pathological diagnosis be in columns and in rows type of polyps should be. This type will be better.

Answer: After re-arranging, the form of table-1 is the following table.

Table 1 Comparison between the results of HRME and those of the pathological examination

Pathological diagnosis	HRME diagnosis					Total
	Inflammatory	Hyperplastic	Tubular	Villous	Mixed	
Inflammatory	21	2	0	0	1	24
Hyperplastic	2	8	0	0	1	11
Tubular	0	1	14	1	3	19
Villous	0	0	1	6	1	8
Mixed	0	0	3	1	18	22
Total	23	11	18	8	24	84