recommendations of 5-ASA use. The truth is many patients decide to stop their drugs when feeling well even if it is recommended to remain on 5-ASA to prevent relapse. Second, in this study we were measuring cumulative use so "user" patients did not have to consistently remain on the drug and many patients may wax and wane in their use. Third, the percentage use of 38, 13, and 6% at 1 year, 5 years, and 7.5 years cumulatively reflect use in Crohn's disease and ulcerative colitis combined. 5-ASA is not widely prescribed in Crohn's disease in Manitoba and its efficacy in Crohn's disease is minimal at best.

We do agree with the correspondents though that among the numerous studies addressing the issue of 5-ASA and CRC chemoprophylaxis, that none (sic) "have conclusively shown any impact of 5-ASAs on the risk of developing CRC". While our study may not be the definitive or final study on the issue, we hope that it adds sufficient weight to the body of research in this area that others share the views of ours and the correspondents that to date there is no conclusive evidence of 5-ASA preventing CRC. Rather than other authors writing about this topic as an accepted fact, we would hope they would accept that the concept of 5-ASA preventing CRC in IBD remains unproven.

CONFLICT OF INTEREST

Dr Charles Bernstein has consulted to Abbott Canada, Astra Zeneca Canada, Janssen Canada, and Shire Canada, received research grants from Abbott Canada and Prometheus Laboratories, and received an educational grant from Axcan Pharma. Drs Nugent and Blanchard have no conflicts to report.

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Low-Cost Endomicroscopy in the Esophagus and Colon

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SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg Video content online

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To the Editor: Confocal endomicroscopy is emerging as a safe, minimally invasive means of improving the accuracy of endoscopic screening and surveillance for Barrett's esophagus (1) and colorectal cancer (2). When used alongside "red-flag" techniques such as autofluorescence imaging or narrow-band imaging (NBI), endomicroscopy enables the gastroenterologist to evaluate the gastric or colonic mucosa with cellular level resolution in a real-time "optical biopsy" (3). Both endoscope-based and probe-based platforms have demonstrated improved diagnostic yield and very high preliminary accuracy compared with standard endoscopy in prospective, double-blind studies (4,5). However, the cost and learning curve associated with these systems limits their usage to a selected number of academic centers (3). To enable widespread translation of this promising technology, we developed a high-resolution microendoscope (HRME) in prototype form for under $5,000 (6,7). The instrument uses a 1-mm diameter probe, which passes through the working channel of a standard gastroscope or colonoscope; images are displayed at 15 frames-per-second at ×400 magnification. A light-emitting diode provides illumination at 445 nm, which is delivered through the probe to the tissue surface. The spatial resolution of the probe is 4.4 μm and the field-of-view is 720 μm in diameter. In this Letter, we present the first *in vivo* clinical applications of this technology in the upper and lower gastrointestinal tracts. We present a case involving surveillance and guided therapy of Barrett's esophagus, followed by three cases illustrating the characteristic features of normal, inflammatory, and adenomatous tissue in the colon. This study was approved by the Institutional Review Boards of Mount Sinai Hospital and Rice University.

Similar to several confocal endomicroscopy studies (3), the HRME uses fluorescent contrast agents, typically either topical acriflavine or proflavine. In the esophagus, this enables the discrete, evenly spaced nuclei of normal squamous mucosa to be distinguished from the glandular appearance of columnar metaplasia (**Figure 1a–d**). Barrett's metaplasia has previously been characterized on HRME by large glands with intact nuclear polarity, whereas high-grade dysplasia (HGD) exhibits crowded, irregular glands, and loss of nuclear polarity (6,8).

A 47-year-old male with longstanding reflux symptoms and Barrett's esophagus was referred for endoscopic evaluation. The patient underwent high-definition white-light endoscopy (**Figure 1e**) with NBI (**Figure 1f**), which revealed a 6-cm segment of Barrett's (Prague Classification C5M6) with several "NBI-abnormal" areas showing a distorted mucosal and vascular pattern. These areas were sprayed with 1–2 ml of 0.01% (w/v) proflavine and imaged with the HRME probe (see **Supplementary Video S1** online). HRME imaging revealed non-neoplastic epithelium in the majority of NBI-abnormal areas. However, focal HGD was noted in two separate areas in the proximal portion of the segment, evidenced by a proliferation of small irregular glandular structures (arrows in **Figure 1c** and **d**). The patient opted for and subsequently underwent endoscopic cryoablation of the Barrett's segment (**Figure 1g** and **h**).

We have also used the HRME during screening colonoscopy, where the ability to rapidly stratify benign polyps and precancerous adenomas is essential. In normal colonic mucosa, small uniformly spaced circular crypts, absent of glandular

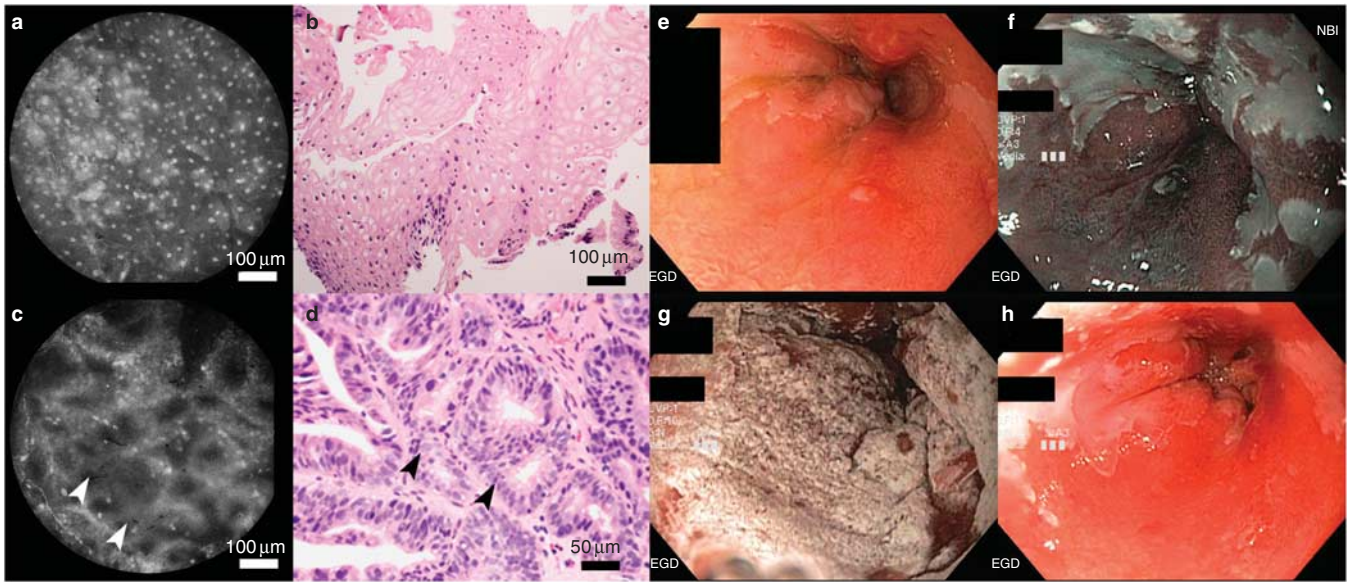
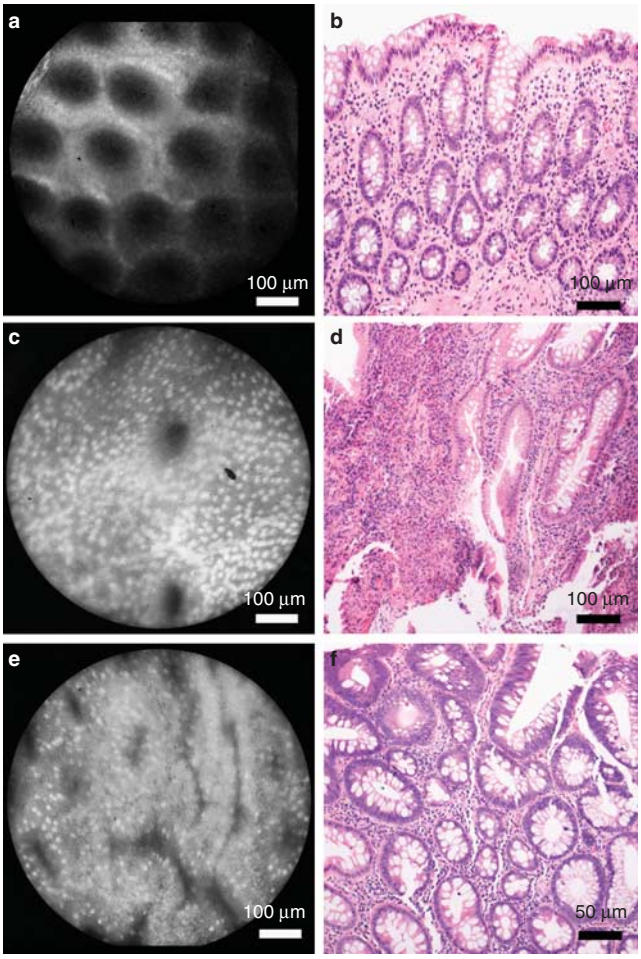


Figure 1. High-resolution microendoscope imaging in the esophagus. (**a**) Normal squamous mucosa and (**c**) Barrett's metaplasia with focal high-grade dysplasia (arrows) in a 47-year-old male undergoing endoscopic evaluation. (**b**, **d**) Histopathology sections (hematoxylin and eosin) corresponding to the locations imaged in (**a**) and (**c**), respectively. (**e**) High-definition white light and (**f**) narrow-band imaging view of the esophagus in the same patient. (**g**) White light view during and (**h**) post-cryotherapy treatment.



distortion or atrophy are readily apparent under HRME imaging (**Figure 2a**), and also seen in the corresponding histopathology (**Figure 2b**). Small, basally oriented nuclei are also apparent under HRME imaging. With inflammatory polyps, a dense population of inflammatory cells is commonly observed on HRME (**Figure 2c**), with only a few irregularly shaped and variably sized glands visible. Tubular adenomas (**Figure 2e**) are easily distinguished; glands appear as irregular structures with heterogeneous orientation, involving elongated, crowded cells, and enlarged nuclei.

Endomicroscopy has the potential to become an important clinical tool (9), but

Figure 2. High-resolution microendoscope (HRME) imaging in the colon. (**a**) HRME image of the normal colon in vivo, with corresponding histopathology from the same site (**b**). Note the appearance of small, uniformly spaced circular crypts, with small, basally oriented nuclei. (**c**) HRME image and (**d**) corresponding histopathology of an inflammatory polyp, presenting a dense population of inflammatory cells and few irregularly shaped glands. (**e**) HRME image and (**f**) corresponding histopathology of a tubular adenoma, revealing highly irregular and heterogeneously oriented glands, with elongated, crowded cells, and enlarged nuclei.

its overall impact on patient care may ultimately be limited by cost. HRME imaging provides real-time "optical biopsies" with many of the same diagnostically relevant features established for confocal endomicroscopy, yet costs significantly less than probe- and endoscope-based confocal platforms. Low-cost endomicroscopy may prove to be a more widely accessible adjunct to standard endoscopy for managing conditions, including Barrett's metaplasia and screening colonoscopy, by assisting the endoscopist in selecting sites for biopsy and/or guiding treatment.

CONFLICT OF INTEREST

Guarantor of the article: Sharmila Anandasabapathy, MD.

Specific author contributions: Designed and assembled HRME instrumentation, drafted the manuscript, and approved the final draft: Mark C. Pierce; operated HRME instrumentation and approved the final draft: Peter M. Vila; evaluated histopathology and HRME image data and approved the final draft: Alexandros D. Polydorides; designed the study, interpreted image data, and approved the final draft: Rebecca Richards-Kortum; designed the study, performed endoscopic image collection, interpreted image data, and approved the final draft: Sharmila Anandasabapathy.

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Potential competing interests: Rebecca Richards-Kortum holds patents related to endomicrosopy devices. The remaining authors declare no conflict of interest.

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Dysplastic Barrett's Esophagus in Cirrhosis: A Treatment Dilemma

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To the Editor: A 58-year-old man with non-alcoholic steatohepatitis-related Childs A cirrhosis presented with bleeding esophageal varices requiring band ligation. At the time of esophagogastroduodenoscopy (EGD), a 5 cm segment of Barrett's esophagus (BE) was identified with a focal area of nodularity and distorted mucosal pattern on narrow band imaging. The patient was referred to our service for reassessment and consideration of endoscopic therapy.

His other past medical history was remarkable for diabetes, obesity, hypertension, and dyslipidemia.

On review at our center, repeat blood work revealed an elevated international normalized ratio of 1.3 and thrombocytopenia with platelets of 98,000/l. At repeat EGD he was found to have grade 1 esophageal varices. The gastroesophageal junction was at 41 cm with circumferential Barrett's mucosa to 38 cm, where a 3 mm nodule was identified. The Barrett's mucosa extended for a further 2 cm in a non-circumferential distribution (C3M5) to 41 cm (**Figure 1**).

Endoscopic ultrasound confirmed multiple esophageal varices without any mediastinal lymphadenopathy (**Figure 2**). Using a standard gastroscope and the Cook 6-shooter band ligation device, the nodule together with visible varices within the Barrett's segment were ligated with a total of five bands deployed. The tip of the nodule was biopsied prior to withdrawal of the gastroscope. Histology revealed intestinal metaplasia with high-grade dysplasia (HGD).

He continued to have follow-up EGD with band ligation of visible Barrett's mucosa at 2- to 4-month intervals with a total of four procedures performed (**Figure 3**). At each endoscopy, following band ligation, the tips of pseudopolyps were biopsied with histology confirming multifocal HGD. He was maintained on pantoprazole 40 mg o.d.

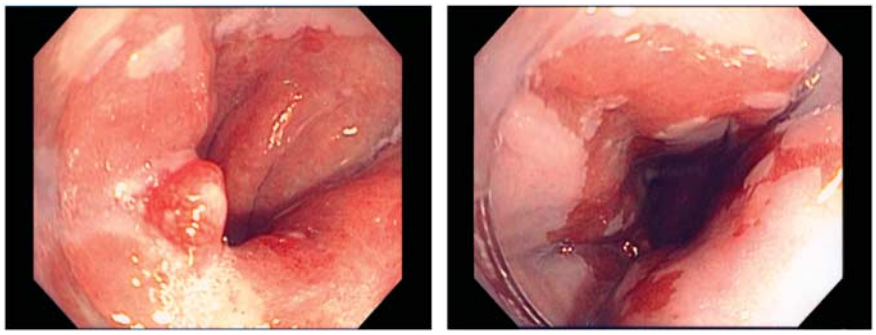

Figure 1. White light endoscopy revealing a nodular area in a short segment of Barrett's mucosa.