ORIGINAL ARTICLE

Tethered capsule endomicroscopy for microscopic imaging of the esophagus, stomach, and duodenum without sedation in humans (with video)

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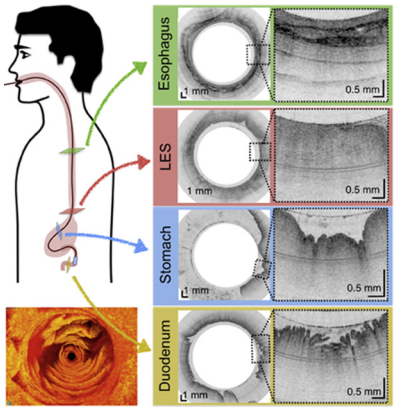
GRAPHICAL ABSTRACT



Background and Aims: Patients with many different digestive diseases undergo repeated EGDs throughout their lives. Tethered capsule endomicroscopy (TCE) is a less-invasive method for obtaining high-resolution images of the GI mucosa for diagnosis and treatment planning of GI tract diseases. In this article, we present our results from a single-center study aimed at testing the safety and feasibility of TCE for imaging the esophagus, stomach, and duodenum.

Methods: After being swallowed by a participant without sedation, the tethered capsule obtains cross-sectional, 10 μm–resolution, optical coherence tomography images as the device traverses the alimentary tract. After imaging, the device is withdrawn through the mouth, disinfected, and reused. Safety and feasibility of TCE were tested, focusing on imaging the esophagus of healthy volunteers and patients with Barrett's esophagus (BE) and the duodenum of healthy volunteers. Images were compared with endoscopy and histopathology findings when available.

Results: Thirty-eight patients were enrolled. No adverse effects were reported. The TCE device swallowing rate was 34 of 38 (89%). The appearance of a physiologic upper GI wall, including its microscopic pathology, was visualized with a tissue coverage of 85.4% ± 14.9% and 90.3% ± 6.8% in the esophagus of BE patients with and without endoscopic evidence of a hiatal hernia, respectively, as well as 84.8% ± 7.4% in the duodenum. A blinded comparison of TCE and endoscopic BE measurements showed a strong to very strong correlation ($r = 0.7$-0.83; $P < .05$) for circumferential extent and a strong correlation ($r = 0.77$-0.78; $P < .01$) for maximum extent (Prague classification). TCE interobserver correlation was very strong, at $r = 0.92$ and $r = 0.84$ ($P < .01$), for Prague classification circumferential (C) and maximal (M) length measurements, respectively.

Conclusions: TCE is a safe and feasible procedure for obtaining high-resolution microscopic images of the upper GI tract without endoscopic assistance or sedation. (Gastrointest Endosc 2018;■:1-11.)

(footnotes appear on last page of article)

EGD is the standard of care for diagnosing upper GI disease. EGD provides information about the macroscopic appearance of the surface of the mucosa but is unable to evaluate subsurface and microscopic alterations without requiring excisional biopsies. Despite recent technical improvements in endoscopes, white-light endoscopy-guided biopsies are subject to sampling errors in patchy diseases such as esophageal dysplasia in Barrett's esophagus (BE). EGD is an invasive procedure that often is undesirable by patients, because it requires a day-long effort considering the procedure itself, the requirements of sedation, and subsequent recovery.

These limitations of EGD suggest that there is room for improvement in upper GI tract diagnostics. For example, premalignant conditions such as BE are not screened for appropriately,[1] in part because of the lack of sufficiently accurate, well-tolerated, and cost-effective tests.[2] Celiac disease requires a timely and accurate tissue diagnosis before a patient is committed to a gluten-free diet.[3]

Imaging depth resolved, microscopic architecture (about 10-μm resolution) of the esophagus over large areas was introduced recently, by using a balloon catheter and optical coherence tomography (OCT) technology (also known as volumetric laser endomicroscopy).[4] This advanced imaging technology still requires some form of endoscopy and, as a result, has all of the associated limitations. Although improvements in patient comfort have been achieved with video endoscopy that uses a video capsule that can be swallowed and other forms of tethered capsule endoscopy,[5,6] these devices enable only macroscopic visualization of the mucosal surface. A new technology termed tethered capsule endomicroscopy (TCE) was developed recently that implements the imaging capabilities of OCT in a tethered capsule that can be swallowed and is reusable (Fig. 1A). Early results obtained with TCE for imaging BE were reported previously.[7-9]

The aim of this study was to test the safety and feasibility of TCE for imaging the esophagus, stomach, and duodenum. Additionally, we compared TCE and EGD findings for BE assessment.

METHODS

TCE

TCE technology consists of an OCT imaging console and a tethered capsule (Fig. 1A).[7,8] The tethered capsule has a diameter ranging from 11 to 12.8 mm and a length of 24 to 24.8 mm (Appendix 1, available online at www.giejournal.org), which is comparable to the size of a video endoscopy capsule, and a flexible, 2 m-long tether that connects it to an OCT imaging console. The custom-built OCT imaging console, like an endoscopy processor, is responsible for light generation, collection of information from the probe, and image processing and display. The OCT TCE technology provides images at a frame rate of 20 frames per second (2048 A-lines per frame and 2048 points for each A-line), with 10-μm axial (depth) resolution in tissue and 35-μm resolution along the lateral axis in 2-dimensional cross-sections.[10] Resolution in the longitudinal direction (image spacing or spatial separation between cross-sections) depends on the velocity of the capsule and is controlled by the operator. The imaging console was approved for clinical use previously by the Massachusetts General Hospital (MGH) Biomedical Engineering department.[11,12] Nineteen TCE catheters were manufactured at MGH and were used in these studies. Each capsule was used an average of 4 ± 3 times.

Study design

The first pilot study was approved by the Partners Institutional Review Board (IRB-2011-P002619) in February 2012, aimed at imaging healthy volunteers. This study was extended to include patients with BE. A subset of 4 participants was re-enrolled to test performance of different generations of the devices (Appendix 1, available online at www.giejournal.org). Thus, the total number of TCE procedures was larger than the total number of patients. Swallowing rate and procedure preference statistics were calculated after we excluded re-enrolled participants. In August 2013, a study conducted to investigate the use of TCE to image the duodenum was approved for healthy volunteers (IRB-2013-P001405).

Patients and/or participants

Healthy volunteers were recruited by public announcement on the MGH Web site. The inclusion criteria for healthy volunteers included age ≥18 years and the absence of a known digestive disease history. Patients with BE were recruited from the MGH Gastrointestinal Unit. For all study participants, the exclusion criteria were known esophageal strictures, intestinal strictures, dysphagia, prior GI surgery, or history of intestinal Crohn's disease.

Clinical procedure

Participants required minimal preparation before TCE, which included fasting for 4 hours. Clear liquids were allowed up until 2 hours before the procedure. After the capsule was swallowed, patients were free to talk normally and were asked to occasionally sip water. During the TCE procedure, patients were seated in a comfortable position, with the exception of the studies in which patient positioning (eg, lateral decubitus) was used to navigate the capsule to the pylorus. The participants were informed that they could stop the procedure at any time. In order to ensure the collection of the best quality data in each patient, the GI tract was imaged in multiple passes (Fig. 1B) before capsule removal by pulling the tether out. During the procedure, OCT images were displayed in real time on the screen.