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Unsedated imaging of human upper GI tract using tethered capsule endomicroscopy

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Introduction

Endoscopic examination of the upper gastrointestinal tract is costly, inconvenient, and typically requires that the patient be sedated.¹ Standard video endoscopy only provides macroscopic information so small, focal biopsies are excised in order to obtain a microscopic tissue diagnosis. Because there are few reliable visible cues for Barrett's esophagus and dysplasia, crucial diagnostic regions can be missed. In order to overcome these limitations of endoscopy, we have integrated a microscopic imaging technology into a tethered capsule that can be swallowed. This new method, which we term tethered capsule endomicroscopy, provides microscopic information from the entire esophagus as the pill passes through the GI tract.

Description of the Technology

Our tethered capsule endomicroscope (Fig. 1) implements a second-generation, high-speed form of optical coherence tomography (OCT) termed optical frequency domain imaging (OFDI).^{2, 3} OCT is a noninvasive diagnostic technique that provides cross-sectional images of tissue microstructure at a resolution of less than 10 μm .⁴ This technology has shown to be

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accurate for diagnosis of BE and dysplasia.^{5, 6} After the 11 × 25 mm transparent capsule is swallowed, light from the OFDI console is delivered to the tissue via an optical fiber that resides within the tether. Inside the capsule, the fiber is terminated by miniature optics that direct and focus the light in the esophageal wall. The device is connected to a rotary junction that spins the optical fiber and thus the optics within the capsule. OFDI data is collected while the optics rotate, providing cross-sectional images of the entire esophageal wall at a rate of approximately 20 frames per second. Three-dimensional images are obtained by compiling cross-sections as the capsule is propelled through the esophagus by peristalsis or by pulling the tether up towards the mouth.

Description of the Procedure

Patients are NPO for four hours prior to the procedure. After the capsule is swallowed with a sip of water, the OFDI imaging procedure starts. Similar to endoscopy, the position of the capsule in the esophagus can be determined using calibration marks on the tether, measured from the incisors. Circumferential OFDI cross-sections are displayed on the console's screen allowing the operator to visualize the esophageal microstructure in real time. After characteristic images of stomach are seen, the operator slowly pulls the capsule up using the tether and a second imaging pass is performed as the device moves proximally. Typically, we conduct 4 imaging passes per procedure (2 down and 2 up). After the final imaging pass, the capsule is pulled out through the mouth. The entire catheter is then disinfected for reuse.

Results

To date, we have enrolled 26 subjects in the tethered capsule endomicroscopy study, including 11 normal volunteers, 2 with GERD, 10 with BE, and 3 for the indication of eosinophilic esophagitis (Partners IRB protocol 2011-P-002619).² The capsule was swallowed by 24 subjects (92.3%), including 8 subjects with hiatal hernia and 1 subject who reported a history of a strong gag reflex. Two subjects were unable to swallow the capsule. A total of 5/26 (20%) patients had a weak gagging reflex during procedure, accompanied by coughing in 2 cases. High quality images, defined as those in which the capsule remained in close contact with at least 50% of the tissue, were obtained in total of 93.7% ± 10% of frames. For subjects with clinical history of hiatal hernia, we found that 89% ± 11% of all frames were in good contact with the capsule's surface. In the rare instances when gagging or coughs were observed, we noticed an expansion of the esophagus followed by its immediate contraction around the capsule. These events did not obscure or otherwise affect the quality of the images. There have been no complications of the tethered capsule endomicroscopy procedures, which on average lasted 5:17 ± 1:52 minutes.

Video Description

In the movie case shown here, the subject was a volunteer with no history of BE. A timer is displayed in the lower left hand corner of the video. The video shows the ease with which the capsule is swallowed, following a sip of water (00:26 – 00:30). Imaging commences after more water is swallowed (00:48). The real-time computer display of the OFDI images can be seen in the lower right hand corner of the video. At approximately 01:05, a reformatted version of the OFDI movie is displayed on the upper right portion of the video (picture-in-picture). The layered structure of the normal squamous mucosa can be clearly identified as the capsule descends the esophagus. A still image of this subject's normal squamous mucosa is shown in Figure 2a. After 01:25, the capsule leaves the esophagus as evidenced by characteristic rugae (folds in the mucosa) and pit and crypt architecture in the images. A still image of this subject's normal gastric mucosa is shown in Figure 2b. The first imaging pass ends around 01:40. The video then transitions to the final pull up pass at

03:25. Since the capsule now starts in the stomach, the rugae and pit and crypt architecture can be identified as the imaging starts (03:30 – 03:36). Once again, as we enter the squamous mucosa, the layered architecture is clearly identified and sustained during the entire pull up (03:37 – 03:53). Removal of the capsule occurs between 04:00 – 04:10 where it can be seen to be easily removed from the mouth. OFDI images showed no abnormalities in this subject.

Discussion

Capsule orientation

At the present time, we have not attempted to use the capsule to detect the circumferential location of an esophageal lesion. If this feature is required for diagnosis and subsequent management of certain esophageal pathologies, we can incorporate a position sensor into the capsule so that the device can be oriented with respect to its anatomic location and rotation within the esophagus.

Gag reflex

While we were able to successfully administer the capsule in most subjects, including a patient with a history of strong gag reflex and additional four patients that experienced a weak gagging reflex, we recognize that in some subjects a strong or weak gag reflex may make swallowing difficult. Since the size of our capsule is similar to that of other swallowable devices in clinical use, we do not anticipate that the success rates for swallowing the tethered capsule endomicroscope will be significantly different than that for video capsule endoscopy or manometry capsules.

Potential risks

Given the similarities in sizes and operating procedures of tethered capsule endomicroscopy and video capsule endoscopy (VCE), we believe the potential risks of the technologies to be comparable. Only few cases of aspiration of VCE have been reported, mostly in older patients. Retention has been reported as 2%, mainly in patients with strictures.⁷ In our tethered capsule study, strictures are exclusion criteria, and the capsule can be withdrawn using the tether; thus retention and aspiration are highly unlikely.

Take Home Message

Tethered capsule microscopy is a new method for obtaining three-dimensional microscopic image information from the GI tract. In addition to the conditions investigated to date, tethered capsule endomicroscopy can potentially be used to study other esophageal disorders such as bleeding, varices, erosions, and esophagitis, and for atrial ablation follow up. The procedure does not require sedation, can be performed in a few minutes, and the device can be retrieved and sterilized. These features of tethered capsule microscopy will likely make it a useful new screening tool for upper gastrointestinal diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Thota PN, Zuccaro G Jr, Vargo JJ 2nd, et al. A randomized prospective trial comparing unsedated esophagoscopy via transnasal and transoral routes using a 4 mm video endoscope with conventional endoscopy with sedation. *Endoscopy*. 2005; 37:559–65. [PubMed: 15933930]
2. Gora MJ, Sauk J, Carruth RW, et al. Tethered capsule endomicroscopy enables less-invasive imaging of gastrointestinal tract microstructure. *Nature Medicine*. 2013; 19:238–240.
3. Yun SH, Tearney GT, Vakoc BJ, et al. Comprehensive volumetric optical microscopy in vivo. *Nature Medicine*. 2006; 12:1429–1433.
4. Drexler W, Fujimoto JG. State-of-the-art retinal optical coherence tomography. *Progress in Retinal and Eye Research*. 2008; 1:450–88.
5. Poneris JM, Brand S, Bouma BE, et al. Diagnosis of specialized intestinal metaplasia by optical coherence tomography. *Gastroenterology*. 2001; 120:7–12. [PubMed: 11208708]
6. Evans JA, Poneris JM, Bouma BE, et al. Optical coherence tomography to identify intramucosal carcinoma and high-grade dysplasia in Barrett's esophagus. *Clinical Gastroenterology and Hepatology*. 2006; 4:38–43. [PubMed: 16431303]
7. Rondonotti E, Herrerias JM, Pennazio M, et al. Complications, limitations, and failures of capsule endoscopy: a review of 733 cases. *Gastrointestinal Endoscopy*. 2005; 62:712–716. [PubMed: 16246685]

Figure 1.
Photograph of the whole tethered capsule endoscopy catheter with the capsule adjacent to a penny for scale.

Figure 2. Tethered capsule endomicroscopy images obtained from a healthy volunteer *in vivo* showing (a) the architectural morphology of the normal esophageal wall, including the squamous epithelium (E), muscularis mucosa (MM), lamina propria (L), submucosa (S), inner muscularis (IM), outer muscularis (OM) and myenteric plexus (MP) and (b) the stomach with characteristic glandular 'pits' (arrowheads). The blue asterisk indicates a multiple reflection artifact. Tick marks 1 mm; scale bars 0.5 mm.