Esophageal-guided biopsy with volumetric laser endomicroscopy and laser cautery marking: a pilot clinical study

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Background: Biopsy surveillance protocols for the assessment of Barrett's esophagus can be subject to sampling errors, resulting in diagnostic uncertainty. Optical coherence tomography is a cross-sectional imaging technique that can be used to conduct volumetric laser endomicroscopy (VLE) of the entire distal esophagus. We have developed a biopsy guidance platform that places endoscopically visible marks at VLE-determined biopsy sites.

Objective: The objective of this study was to demonstrate in human participants the safety and feasibility of VLE-guided biopsy in vivo.

Design: A pilot feasibility study.

Setting: Massachusetts General Hospital.

Patients: A total of 22 participants were enrolled from January 2011 to June 2012 with a prior diagnosis of Barrett's esophagus. Twelve participants were used to optimize the laser marking parameters and the system platform. A total of 30 target sites were selected and marked in real-time by using the VLE-guided biopsy platform in the remaining 10 participants.

Intervention: Volumetric laser endomicroscopy.

Main Outcome Measurements: Endoscopic and VLE visibility, and accuracy of VLE diagnosis of the tissue between the laser cautery marks.

Results: There were no adverse events of VLE and laser marking. The optimal laser marking parameters were determined to be 2 seconds at 410 mW, with a mark separation of 6 mm. All marks made with these parameters were visible on endoscopy and VLE. The accuracies for diagnosing tissue in between the laser cautery marks by independent blinded readers for endoscopy were 67% (95% confidence interval [CI], 47%-83%), for VLE intent-to-biopsy images 93% (95% CI, 78%-99%), and for corrected VLE post-marking images 100% when compared with histopathology interpretations.

Limitations: This is a single-center feasibility study with a limited number of patients.

Conclusion: Our results demonstrate that VLE-guided biopsy of the esophagus is safe and can be used to guide biopsy site selection based on the acquired volumetric optical coherence tomography imaging data. (Clinical trial registration number: NCT01439633.) (Gastrointest Endosc 2014;79:886-96.)

(footnotes appear on last page of article)

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Barrett's esophagus (BE) and associated dysplasia is a microscopic disease that is usually diagnosed by histopathologic analysis of tissues that are excised during an endoscopic biopsy procedure.[1] Because endoscopy alone may not be sufficient to distinguish BE from irregular z lines[2] or to identify dysplasia and intramucosal carcinoma and because the involved area is frequently much larger than the size of a biopsy specimen, endoscopic biopsy specimens

are taken at random locations, with the hope of excising areas that contain the most severe disease.[3-5] This technique is subject to significant sampling error, which leads to diagnostic uncertainty and suboptimal patient management.[3,5]

A new imaging paradigm recently has been developed that aims to reduce sampling error by acquiring comprehensive volumetric microscopic images of the entire esophagus.[6,7] Currently, this technique uses optical coherence tomography (OCT) technology to obtain 10-μm–resolution, cross-sectional images of the esophageal wall.[8-10] Prior studies have shown that this technique can accurately identify BE and dysplasia.[11-14] To create a 3-dimensional microscopic image of the esophagus, the OCT laser beam is helically scanned over a long length of esophagus (approximately 6.0 cm) in 1 to 2 minutes by miniature optics that are in the center of a 2.5-cm diameter, transparent balloon-centering catheter (Fig. 1).[6,15] Early clinical results using this imaging method demonstrate that it is a safe and effective procedure for obtaining comprehensive microscopic mapping of esophageal diseases in vivo.[6]

An important clinical application of this imaging approach, which has been termed volumetric laser endomicroscopy (VLE),[16] is guiding the selection of higher yield biopsy sites based on the microscopic image data. However, biopsies cannot be excised during the scan because the dataset is continuously acquired through the balloon while it is inflated. In order to realize VLE-guided biopsy, we have developed a technique that places visible marks on the esophagus that delineate tissues corresponding to image regions of interest that are selected during the scan.[17] These marks are created by transient, high-power laser transmission through the balloon catheter's optics.[17] After the balloon catheter is removed, the tissue between the marks is biopsied.[17] The objective of this study was to demonstrate in human participants the safety and feasibility of VLE-guided biopsy in vivo and to describe our first human experience with this newly developed biopsy guidance platform.

Take-home Message

- Volumetric laser endomicroscopy (VLE) is an imaging technique for obtaining microscopic images of the entire distal esophagus.
- In this article, the authors show that VLE-guided biopsy using laser cautery marking is feasible and safe in vivo.

METHODS

OCT VLE imaging system and balloon catheter

A schematic of the VLE imaging system and balloon-centering catheter is shown in Figure 1. The imaging system obtains microscopic images using optical frequency domain imaging (OFDI), a second-generation, high-speed form of OCT technology.[7] OFDI images were acquired at a rate of 40,000 axial scans (A-lines, depth-resolved reflectivity profiles) per second.[6] Each cross-sectional esophageal image contained 4096 A-lines; the resultant cross-sectional frame rate was 10 per second. The power, center wavelength, and tuning range used for OFDI imaging were 30 mW, 1350 nm, and 140 nm, respectively. The axial resolution was 7 μm in tissue. The balloon-centering catheter had a guidewire provision, an inflated diameter of 2.5 cm, and an imaging window length of 6.0 cm (Fig. 1).[6] Optics centered in the balloon catheter provided a minimum transverse spot diameter of 40 μm (full-width, half-maximum) that was located approximately 0.5 mm outside the inflated balloon's surface. The optics were translated at a rate of 1.0 mm per second, providing a cross-sectional image spacing of 100 μm. In order to fit images of each esophageal cross-section on the computer monitor, images were displayed in real time using a compressed (5:1) study aspect ratio. The 1:1 full aspect ratio images were stored for future offline assessment.

Marking laser

The 1450-nm wavelength cautery-marking laser light was coupled into an optical fiber that was multiplexed into the balloon-centering catheter's optical fiber via a light combiner. By combining the marking and imaging lasers and launching them through the same optical catheter, it is possible to simultaneously image and mark the esophagus at any point within the imaging window of the balloon catheter (360 degrees, 2.5 cm diameter × 6-cm long balloon). As with the 1350 nm OFDI light, after transmission through the catheter's optics, the cautery-marking laser's light was focused to an about 40-μm spot approximately 0.5 mm outside of the inflated balloon. Different cautery-marking optical powers were tested in the patients, including 280 and 410 mW. A foot pedal was used to actuate a shutter that allowed the cautery-marking laser light to be transmitted to the patient for a preset duration of 2 seconds (Fig. 1). Prior studies have shown that laser illumination with these parameters produces thermally mediated damage that is predominantly limited to the mucosa in vivo.[17]

Guided biopsy procedure

A flowchart of the guided biopsy procedure is depicted in Figure 2A. After informed consent, patients undergoing surveillance for BE and meeting the study inclusion and exclusion criteria were enrolled in the study. A total of 22 patients were enrolled. The Partners Institutional Review Board approved the study (Protocol 2010P000553). The VLE balloon-centering catheter was placed at the gastroesophageal junction over the guidewire and inflated to a pressure of approximately 0.5 atmospheres (Fig. 2B). To ensure correct balloon placement, an initial scout scan was performed, and, if necessary, the balloon was deflated and repositioned. Helical imaging of the