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Volumetric Mapping of Barrett's Esophagus and Dysplasia With *en face* Optical Coherence Tomography Tethered Capsule

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To the Editor

Dysplasia in Barrett's Esophagus (BE) is patchy (1) and sometimes missed by random biopsies. Optical coherence tomography (OCT) can image large areas of the esophagus; however, slow imaging speeds in earlier studies limited visualization to cross-sections. Cross-sectional OCT detected high-grade dysplasia with sensitivity/specificity of ~80% (2,3). Tethered OCT capsules were demonstrated for cross-sectional imaging in unsedated screening to detect BE (4,5). Our group recently developed ultrahigh-speed OCT for *en face* and angiographic imaging, using micromotor probes in patients (6,7) and large field-of-view tethered capsule devices in swine (8). Narrow-band imaging (NBI) visualizes surface mucosal patterns to detect dysplasia, but multi-center trials reported suboptimal dysplasia detection (9). In this report, we demonstrate an ultrahigh-speed OCT tethered capsule enabling large field-of-view, subsurface *en face*, and cross-sectional volumetric imaging of BE and dysplasia. Subsurface *en face* OCT provides complementary information to cross-sectional OCT and NBI.

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CONFLICT OF INTEREST

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The OCT prototype instrument was 20× faster than commercial OCT instruments (3). Imaging was performed using ~30 mm long×12 mm diameter tethered capsules (Figure 1c), with micromotor scanning at 300 frames per second. The semi-rigid tether enabled the capsule to be introduced into the esophagus of sedated patients prior to introducing the endoscope for examination and biopsy/resection. The tether could be pulled/pushed to volumetrically map the esophagus.

Eighteen patients were imaged with different resolutions and pull/push speeds to optimize the imaging protocol; three were imaged with the optimum protocol presented here. One patient, a 68-year-old male with dysplasia history and treatment-naïve C4M5 segment is presented, the other two patients had non-dysplastic BE. After sedation, the capsule was advanced to the gastro-esophageal junction under OCT guidance. The capsule was pulled back ~24 cm in ~20 s to acquire an OCT volume, advanced to acquire a second volume, then withdrawn (Supplementary Video 1 online). The endoscope was then introduced for standard examination.

A slightly raised lesion at 6 o'clock, ~1 cm distal to the squamo-columnar junction (SCJ) appeared irregular on NBI and was removed with endoscopic mucosal resection (EMR). Histopathology showed extensive low-grade dysplasia. The EMR region was registered using OCT capsule fiducials and endoscopic landmarks such as the SCJ. In the EMR region, cross-sectional OCT showed atypical glandular architecture, dilated glands, layer effacement, and surface signal intensity higher than subsurface (Figure 1d, Supplementary Video 2), which are OCT features associated with dysplasia (3). Subsurface *en face* OCT at 200 and 400 μm depths exhibited irregular mucosal patterns and dilated glands respectively (Figure 2a, b, Supplementary Video 2), which are features associated with dysplasia on NBI (9) and OCT. Near the SCJ, cross-sectional OCT showed layered BE (Figure 1e, f, Supplementary Video 3), while *en face* OCT at 200 μm depth (Figure 2c, Supplementary Video 3) exhibited regular circular and ridged/villous mucosal patterns, features of non-dysplastic BE.

The registered cross-sectional and *en face* views facilitated interpretation of the OCT data. The near-vertical columnar epithelium of crypts was associated with high optical scattering and transmission, producing bright vertical features in OCT cross-sections, which were projected to deeper depths in *en face* OCT. Conversely, the crypt lumen and lamina propria between crypts were associated with low optical scattering, producing dark vertical features in cross-sections and *en face* OCT. These effects imply that *en face* OCT visualizes the integrated effect of light transmission and backscattering. Disruption of vertical crypt architecture by dysplasia increased OCT signal at shallow depths and attenuated signals at deeper depths in both cross-sectional and *en face* OCT.

The study was limited because the full esophageal circumference was not imaged; non-contact regions appeared dark in the *en face* images. Nonuniform longitudinal capsule actuation from manual pull/push, respiratory/cardiac motion, or peristalsis produced *en face* image distortion. Motion artifacts were ameliorated by the ultrafast imaging speed and ~1

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cm/s longitudinal pull/push (~300 frames/cm), which yielded smoother motion than slower pull/push speeds. OCT reading was not blinded to histopathology. The EMR was smaller than the OCT field-of-view, therefore many OCT regions were histologically unverified.

Introducing the capsule with a semirigid tether prior to endoscopy was well tolerated with no adverse events and enabled endoscopic/histology correlation with OCT findings. The semirigid tether preserved capsule orientation, enabling registration to endoscopic views. These capabilities will facilitate larger studies correlating OCT with histology. Imaging can also be performed with a soft tether in non-sedation screening/surveillance.

En face OCT capsule imaging enables rapid mapping of the esophagus. *En face* features at shallow depths corresponded with known NBI features, while subsurface *en face* views visualized gland morphology. Cross-sectional and *en face* views were intrinsically co-registered and showed features of BE and dysplasia. *En face* capsule OCT provides information that is complementary to cross-sectional OCT and NBI, and promises to improve sensitivity/specificity for detecting dysplasia.

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Figure 1.

(a) *En face* OCT obtained by averaging from ~200 to 280 μm below esophageal surface. Only the distal 12 cm out of 24 cm data is shown. Dark regions are due to noncontact of the capsule with the esophagus. Scale bar 1 cm. (b) Representative cross-section (blue) from EMR region (red). Scale bar 1 mm. (c) Photograph of capsule. Scale bar 1 cm. (d) Enlargement (pink) from (b) showing layer effacement, surface signal greater than subsurface, and multiple dilated glands (arrows). (e) Cross-section (brown) showing layered BE, which is likely non-dysplastic. (f) Cross-section (yellow) showing the squamo-columnar junction at a tongue of BE. Inset scale bars 1 mm.

Figure 2.

(a) *En face* OCT (red) enlarged from Figure 1a (averaged from ~200 to 280 μm depth) showing the region from which EMR was taken, with irregular mucosal patterns (circled). (b) Deeper *en face* OCT from same region as (a) (averaged from ~400–480 μm depth) showing dilated glands (arrows). (c) *En face* OCT (green) from Figure 1a (~200 to 280 μm depth) showing regular circular and ridged/villous mucosal patterns (circled), likely non-

dysplastic BE. Inset scale bars 1 mm. **(d)** EMR histopathology showing LGD. **(e)** Endoscopic NBI image of EMR region.

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