Ultrahigh speed endoscopic optical coherence tomography for gastroenterology

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Abstract: We describe an ultrahigh speed endoscopic swept source optical coherence tomography (OCT) system for clinical gastroenterology using a vertical-cavity surface-emitting laser (VCSEL) and micromotor imaging catheter. The system had a 600 kHz axial scan rate and 8 µm axial resolution in tissue. Imaging was performed with a 3.2 mm diameter imaging catheter at 400 frames per second with a 12 µm spot size. Three-dimensional OCT (3D-OCT) imaging was performed in patients with a cross section of pathologies undergoing upper and lower endoscopy. The use of distally actuated imaging catheters enabled OCT imaging with more flexibility, such as volumetric imaging in the small intestine and the assessment of hiatal hernia using retroflex imaging. The high rotational scanning stability of the micromotor enabled 3D volumetric imaging with micron scale volumetric accuracy for both en face OCT and cross-sectional imaging, as well as OCT angiography (OCTA) for 3D visualization of subsurface microvasculature. The ability to perform both structural and functional 3D OCT imaging in the GI tract with microscopic accuracy should enable a wide range of studies and enhance the sensitivity and specificity of OCT for detecting pathology.

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OCIS codes: (110.2350) Fiber optics imaging; (120.3890) Medical optics instrumentation; (120.5800) Scanners; (140.3600) Three-dimensional image acquisition; (140.7260) Vertical cavity surface emitting lasers; (170.2150) Endoscopic imaging; (170.2680) Gastrointestinal; (170.3880) Medical and biological imaging; (170.4500) Optical coherence tomography.

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1. Introduction

Optical coherence tomography (OCT) enables micron scale, cross-sectional and three dimensional (3D) imaging of tissue microstructure in real time [1–3] and can enable “optical biopsy”. The microstructure information of the tissue can be obtained with resolutions approaching that of excisional biopsy and histopathology, without the need to remove tissue specimens or apply additional contrast agents on the tissue [4–6]. Three-dimensional imaging can be conducted by performing a two-dimensional scan pattern at different transverse positions. Three-dimensional OCT (3D-OCT) enables powerful methods for visualizing tissue architecture. OCT has been investigated in numerous biomedical fields including ophthalmology [7], cardiology [8], gastroenterology [9], pulmonology [10], urology [11], and gynecology [12]. One particularly promising application for OCT imaging is...
gastroenterology. OCT can be readily integrated with a wide range of imaging devices such as fiber optic catheters and endoscopes to enable imaging inside the body [13]. Endoscopic OCT imaging of the human gastrointestinal (GI) tract has been investigated by several groups and studies have been performed in the esophagus and stomach [9, 14–21], large and small intestine [15, 17, 22–26], and bile duct [27, 28]. Multiple clinical studies were conducted and demonstrated the potential clinical utility of endoscopic OCT for detection of early malignancy [29, 30], evaluation of ablative therapies [31–33], and image guided biopsy [21].

Continuing advancements in imaging speed and quality allow a more comprehensive evaluation of tissue in real time, thereby improving the clinical utility of endoscopic OCT. Clinical utility is also improved through advanced imaging catheter designs. With better transverse resolution, more detailed tissue structure can be visualized. With larger scanning area, the detection of focal pathologies is improved. Faster and more stable beam scanning minimizes motion artifacts and image distortion. Improved device maneuverability enables acquisition of images in distal parts of the GI tract. One important advance is the use of a miniaturized distal scanner in the imaging catheter. Traditional imaging catheters using proximal rotary actuation can cover a large area with a simple scanner configuration and are currently used in most endoscopic OCT systems. However, the scanning uniformity and speed are limited because the proximal rotation is transmitted through a long torque cable to the distal imaging optics, which severely limits the ability to make sharp turns or retroflex the endoscope. Distal scanning methods using piezoelectric transducers (PZT) [34–36] or micro-electro-mechanical systems (MEMS) [37–40] enable micron precision scanning. Cellular-level OCT imaging of *ex vivo* human GI specimens and *in vivo* mouse colon were demonstrated using quadrupole PZT based imaging catheters, highlighting the scanning stability of distal actuated catheters [34]. These devices usually have limited imaging coverage because the scan area is limited by the catheter size. However, distal rotary scanning micromotors, combined with proximal pullback, can provide large imaging area while maintaining high speed and uniform rotation [41, 42]. Several endoscopic imaging studies using micromotor based catheters have been performed and speeds up to 3,200 frames per second (fps) have been demonstrated [43–45].

Another method to enhance OCT performance is to improve the imaging engine. Higher axial line rates enable increased image sample density, broader swept source tuning range improves axial resolution, higher data acquisition speeds can increase imaging range, or higher output power, if necessary, can increase signal. With the development of Fourier domain OCT technologies, endoscopic OCT has been demonstrated with much higher imaging speed compared to time domain OCT [36, 46–50]. Using FDML swept laser sources, *in vivo* endoscopic 3D-OCT imaging in the rabbit and human GI tracts were demonstrated with axial scan rates of 100-500 kHz and axial resolutions of 7-20 µm [36, 51]. Short cavity swept lasers also enable high sweep rate operation [52, 53]. Although the sweep rate of short cavity lasers is limited compared to FDML lasers, short cavity lasers are less sensitive to intracavity dispersion and can usually achieve narrower instantaneous linewidth, which improves the sensitivity roll-off of the OCT imaging system and is especially important for long range imaging [52]. MEMS-tunable vertical cavity surface emitting lasers (VCSEL) [54] provide an extremely narrow instantaneous linewidth that supports a long imaging range. The micron-scale cavity length of VCSELS and the rapid MEMS response also allows long range, real time adjustability of both the sweep frequency and wavelength tuning range. Recently, imaging speeds of 1 MHz were demonstrated in the rabbit GI tract *in vivo* using a VCSEL based swept source OCT system [45]. The combination of high speed imaging and distal beam scanning with the micromotor catheter enabled volumetric endoscopic OCT angiography (OCTA) in the human GI tract for the first time [55].

In this study, we developed an ultrahigh speed endoscopic OCT imaging system for clinical gastroenterology using a high speed swept source and a micromotor imaging catheter, and performed endoscopic OCT imaging in the human GI tract with a 10-fold higher imaging speed and dramatically improved scanning stability compared to commercially available endoscopic OCT systems. The system achieved a 600 kHz axial scan rate and 8 µm axial...
resolution in tissue. 3D-OCT imaging was performed in patients with a cross section of pathologies undergoing upper and lower endoscopy. High quality volumetric data sets covering large areas in the GI tract not only enabled visualization of tissue structure in any orientation, but also provided functional information including 3D angiograms of vasculature.

2. Methods

2.1 Swept source endoscopic OCT system

Figure 1 shows a schematic of the ultrahigh speed endoscopic OCT system developed for this study. This system is similar to the endoscopic OCT system recently reported [45], but it is further engineered for clinical imaging. A portion of the laser output was coupled to a Mach-Zehnder interferometer (MZI) to calibrate the VCSEL frequency sweep. The MZI was dispersion balanced and set at 6.6 mm path difference, and fringes were detected by a 1 GHz dual-balanced optical clock generator (Thorlabs, Inc.) to clock the A/D and sample the OCT fringe signal at constant frequency intervals. The OCT system had a Michelson interferometer with two optical circulators and a 50/50 fiber-optic splitter (AC Photonics, Inc.) and the OCT signal was detected with a 1 GHz dual balanced detector (Thorlabs, Inc.). The optical clock signal triggered a 12 bit dynamic range A/D card (ATS9360 AlazarTech, Inc.). The A/D was rated at 1.8 GSPS, but could only be optically clocked up to ~1.1 GSPS. Since the VCSEL frequency sweep was nonlinear and acquisition was limited by the highest clocking speed, the average data acquisition speed was closer to 500 MSPS. The sample arm of the Michelson interferometer included a patient interface unit (PIU) that translated the distal micrometer of the catheter at a pullback speed of up to 2.8 mm/s. The PIU was attached to the proximal end of the imaging catheter for pulling back the torque cable in the catheter, which generated a longitudinal translation, resulting in a helical scan. Data acquisition, real-time processing, and display were performed by custom C++ based software [45].

![Schematic of endoscopic OCT imaging system using a swept source laser and micromotor imaging catheter (optics: blue; electronics: green). Left inset shows the principle of optical clock generation using the MZI output. Right inset shows the rotary scanning direction of the focused spot. C: circulator; MZI: Mach-Zehnder interferometer; RM: reference mirror; DA: differential amplifier; OC: optical clock; P: photodetector; PIU: patient interface unit.](image1)

2.2 VCSEL operating at 600 kHz axial scan rate

Figure 2(a) shows a schematic of the VCSEL swept laser (Praevium Research, Inc. and Thorlabs, Inc.) system and device structure. The VCSEL was optically pumped at 976 nm via a wavelength-division multiplexer (WDM) and the wavelength swept by electrostatic deflection of a MEMS tunable filter. The resonant frequency of the MEMS tunable filter was
approximately 325 kHz and it was driven with a sinusoidal waveform at 300 kHz. Both forward and backward wavelength sweeps were used to achieve an effective sweep rate of 600 kHz. The laser output was amplified with a semiconductor optical amplifier (SOA, Thorlabs, Inc.) and the average output power was 40 mW. Figure 2(b) shows the time integrated VCSEL output spectrum measured by an optical spectrum analyzer. The central wavelength was ~1310 nm and the total sweep range was 120 nm. Figure 2(c) shows the fringe signal from a Mach-Zehnder interferometer. The duty cycle was >90% with a 1.67 μs sweep duration and symmetric forward and backward sweeps.

2.3 Micromotor imaging catheter

Figure 3 shows the schematic of the imaging catheter used in the study, which is similar to the published previously design [45]. The spot size was 12 μm (full width at half maximum, FWHM) in tissue with a Rayleigh range of ~350 μm. By pulling the micromotor and optical assembly from the proximal end of the torque coil during the rotary image acquisition, a helical scanning pattern could be performed. The catheter had a 3.2 mm outer diameter and 18.2 mm rigid length and could pass through a 3.7 mm endoscope working channel. The micromotor could rotate uniformly with an imaging frame rate from 20 fps to 1,200 fps. In this study, a frame rate of 24,000 rpm (400 fps) and a pullback speed of 2 mm/s were used to
acquire the 3D-OCT data sets. The total length of the torque coil and sheath for the prototype catheter was ~2 meters.

2.4 Study protocol

This study was conducted at the Veterans Affairs Boston Healthcare System (VABHS) and the study protocol was approved by institutional review boards (IRB) of the VABHS, Harvard Medical School and Massachusetts Institute of Technology. Patients undergoing surveillance endoscopy and colonoscopy for indications such as Barrett’s esophagus (BE), gastric antral vascular ectasia (GAVE), radiation proctitis (RP) and inflammatory bowel disease (IBD) were enrolled in this study. After obtaining written informed consent, patients underwent standard esophagogastroduodenoscopy (EGD) or colonoscopy procedures. For EGD, a high-definition (HD) dual-channel endoscope (GIF-2TH180, Olympus) was used allowing acquisition of simultaneous co-registered biopsy with the OCT images. For colonoscopy, a HD colonoscope (CF-H180AL, Olympus) was used. Immediately following diagnostic endoscopy, regions of interest (ROIs) were imaged with OCT by introducing the disinfected OCT imaging catheter in the endoscopic field of view through the instrument channel and gently placing it in contact with each ROI. After OCT data acquisition, clinically indicated regions were biopsied or resected and underwent standard histological processing and pathology examination.

2.5 OCT structural imaging

The ultrahigh speed system enabled the acquisition of very large data sets, which cover large areas of tissue with dense spatial sampling. The system acquired circumferential, cross-sectional images at 400 frames per second (fps) with a total of 1,500 axial scans per cross-sectional image. Total acquisition time was 8 seconds for each volumetric data set, corresponding to a volume size of 10 mm x 16 mm x 2.4 mm (rotary x pullback x axial directions) in tissue. The acquired OCT fringes consisted of ~800 samples and axial scans were obtained with 1,024-point Fourier transform. The pixel spacing was 6.7 μm x 5 μm x 4.8 μm in the rotary x pullback x axial directions, respectively. Images were generated by computing the logarithm of the axial scan magnitude. Post-processing and image visualization were performed using Matlab software (Mathworks, Inc.) and 3D rendering software (Amira, Visage Imaging, Inc.). Structural OCT images were reconstructed and displayed in Cartesian coordinates using a sepia color table. Each image frame was flattened according to the surface of the imaging catheter sheath before 3D volume rendering to enable en face visualization at a given depth in the tissue. The micromotor imaging catheter provides stable scan so the sheath surface is consistent along the whole pullback. Hence the sheath detection can be done in single frame and the flattening can be applied on all other frames in the same data set. In this study, the sheath surface contour was determined manually in one frame and flattening was performed in each data set by vertically shifting the pixels according to the user-defined contour. This process could also be automated using segmentation software. The cross-sectional images displayed are averaged in the transverse directions over 20 μm and en face images are averaged over 20 μm volumetric data to improve signal and reduce noise.

2.6 OCT angiography

In addition to structural information, OCT can also provide information on vasculature. Several methods have been previously developed to generate vascular information using phase changes (Doppler signal) of the OCT signal due to moving erythrocytes [56, 57]. Doppler methods allow quantitative measurement of blood flow. However, conventional Doppler methods are not sensitive to blood flow perpendicular to the OCT beam, limiting the ability to visualize vessels [58, 59]. Other methods can image vasculature by generating motion contrast using OCT signal intensity changes from moving erythrocytes [60, 61]. These methods can enable 3D imaging of microvasculature and are known as OCT angiography (OCTA). In this study we used amplitude-based OCT angiography, which measures intensity decorrelation (Fig. 4) to generate microvasculature contrast [62, 63]. Decorrelation (D) is
defined as the variation of the OCT intensity between multiple, sequentially acquired images at a given voxel. This decorrelation signal intensity is generated by erythrocytes, which move within, or pass through, the cross-sectional OCT image plane at a particular voxel. Voxels with high intensity variation between consecutive cross-sectional images yield higher D values and are associated with flowing erythrocytes. Conversely, voxels associated with static tissue yield lower D values due to lower intensity variations between consecutive images. In this study, intensity thresholding was applied on all OCT intensity images to remove the speckle in the background prior to calculating the decorrelation. Two consecutive frames were used to calculate the decorrelation and decorrelation images were constructed and displayed in Cartesian coordinates using an inverse grayscale (higher decorrelation is displayed as black). Each image frame was flattened relative to the surface of the catheter sheath, to enable en face visualization at a given tissue depth. En face OCT angiograms were generated by averaging the volumetric OCTA data set over 20 μm depth at different depth levels.

\[ D(x,z) = 1 - \frac{A_0(x,z)A_{0+1}(x,z)}{\frac{1}{2} \Delta s(x,z) + \frac{1}{2} \Delta s_{11}(x,z)} \]

Fig. 4. Flow chart showing the OCT angiography algorithm. Motion contrast from erythrocytes flowing in blood vessels (right) is detected by calculating the intensity decorrelation D, between consecutive cross-sectional intensity images (left). The OCTA image was displayed using a reverse grayscale lookup table (right).

3. Results

3.1 System performance

Axial resolution was measured using a metallic mirror in the imaging catheter focal plane and a fiberoptic neutral density (ND) filter in the sample arm. The mirror generated a reflection at an adjustable position from the imaging catheter, while the ND filter provided −35 dB of double-pass attenuation to prevent detector saturation. Figure 5(a) shows the linear point spread function (PSF) at an imaging depth of 1.43 mm. The PSF is symmetric and has an 11 μm FWHM in air, corresponding to an 8 μm axial resolution in tissue. The PSF sidelobes were less than 10% without spectral shaping. The MZI was set to a path mismatch of 6.6 mm to generate a maximum optical clock frequency of 1.04 GHz, corresponding to a 3.3 mm imaging range in air, sufficient for endoscopic imaging applications.

Fig. 5. (a) Linear PSF measured at imaging depth of 1.43 mm. Axial resolution is 11 μm in air or 8 μm in tissue. (b) Log PSFs at different delays. No significant roll off observed across the imaging depth range.
System sensitivity was measured as the ratio of the peak signal value of the PSF at a short imaging depth (~0.5 mm) to the standard deviation of the system noise floor recorded with the sample arm blocked. Optical power from the imaging catheter was ~20 mW (without ND filter). The measured sensitivity was 101 dB. The theoretical shot-noise limited sensitivity is 107 dB and the estimated system losses were ~5dB arising from the losses in the optics, PIU, mirror reflectivity, and backcoupling, which accounted for the difference between measured and theoretical sensitivity. Sensitivity roll off for the full system was measured by translating the mirror in the reference arm and recording the PSFs as shown in Fig. 5(b). There was no significant sensitivity roll off across the entire imaging depth, indicating the narrow linewidth of the VCSEL and that the detection and A/D bandwidth was sufficient to support the maximum ~500 MHz frequency of the OCT signal.

3.2 Normal human GI tract

Figure 6 shows a representative volumetric OCT data set obtained from the normal human esophagus. The images in Fig. 6 have been axially cropped to remove the catheter sheath and portions beyond the penetration depth of light in tissue. Figure 6(a) shows an en face OCT image at a tissue depth of 240 µm, corresponding to the center of the lamina propria layer. The en face OCT of the normal esophagus is featureless due to the overlying homogeneous squamous epithelium layer. The small, hyposcatte ring regions (indicated by red arrows) are glandular structures, which can be distinguished from vessels because they are isolated features in the 3-D volume. Artifacts due to the cardiac motion can be observed in the en face OCT as periodic bulk motion artifacts, which are difficult to avoid in upper GI tract imaging. The inset shows an endoscopic video capture obtained prior to endoscopic OCT imaging. The esophageal mucosa appears pale-pink, smooth and homogeneous, consistent with normal squamous tissue. Figure 6(b) shows a cross-sectional image along the pullback direction at the position indicated by the green dashed line in Fig. 6(a). The typical well-defined layered architecture of the normal esophagus can be appreciated throughout the length of pullback. Figure 6(c) shows a cross-sectional image along the rotary direction at the position indicated by the blue dashed line in Fig. 6(a), which also shows a regular layered structure. Since the stable scan provides much better frame-by-frame alignment, it is easier to distinguish blood vessels in the lamina propria and submucosa layers (first and second hyperscattering layers in Figs. 6(b) and 6(c)) from the glandular structures between the squamous epithelium and lamina propria, based on their shadows in the axial direction and interconnectivity across multiple cross-sectional images. Figure 6(d) shows an en face OCT from the same data set at an imaging depth of 500 µm, corresponding to the submucosa layer. The shadow of vessels from the lamina propria layer and the vessels in the submucosa layer can be clearly appreciated. Figure 6(e) shows corresponding histology of normal esophageal squamous mucosa. Good correlation is observed between the histology and cross-sectional OCT images. The epithelium, lamina propria, muscularis mucosa, submucosa, and muscularis propria are visible as well-separated and distinct layers with alternating hypo- and hyperintensity in the OCT image (Fig. 6(f)). The histology shows only the epithelium and lamina propria layers, highlighting the depth limitations of standard pinch biopsy.

Ultrahigh speed endoscopic OCT can also be used to investigate portions of the GI tract that are difficult to access with proximal rotary catheters. Figure 7 shows a volumetric OCT data set of the terminal ileum (TI). Accessing the TI requires advancing the colonoscope through several sharp bends of the colon, hence it is particularly difficult to use a proximal rotary actuated imaging catheter to examine this anatomical location. However, the micromotor catheter obviates the need to rotate the entire torque cable assembly. Proximal pullback is still required, but this can be performed more easily than rapid rotary actuation. Therefore, the micromotor probe is especially useful to image the left colon, TI, hiatal hernia, gastric antrum and duodenum, which require multiple bends of the endoscope. Figure 7(a) shows an en face OCT at a 50 µm depth, corresponding to the surface of the ileum villi. The en face OCT of the terminal ileum surface shows similar structure to that observed in the endoscopic view (inset) but with high magnification, allowing better evaluation of
morphology. Figure 7(b) shows another en face OCT at a 300 µm depth, corresponding to the base of the ileum villi. The round, crypt-like structure can be distinguished in the en face image, showing the transverse cross-section of the villi.

Fig. 6. Volumetric OCT data of the normal esophagus. (a) En face OCT image at 240 µm depth. The inset shows an endoscopic view of the esophagus obtained prior to endoscopic OCT imaging. (b) Cross-sectional image along the pullback direction. (c) Cross-sectional image along the rotary direction. (d) En face OCT image at 500 µm depth. (e) Corresponding pinch biopsy histology taken from the imaged region, where a gland can be identified under the squamous epithelium. (f) Enlarged view of the cross-sectional image along the pullback direction. SE: squamous epithelium; LP: lamina propria; MM: muscularis mucosa; SM: submucosa; MP: muscularis propria. Red arrows: glandular structures. Blue arrows: Vessels.
Most of the villi in the data set are tilted due to the pressure from the imaging catheter, which also occurs in other imaging modalities that require direct tissue contact. Figures 7(c) and 7(d) show cross-sectional images along the pullback and rotary directions, respectively. The tilted villous structure can be observed in the cross-sectional images. Peyer’s patches can be observed in Fig. 7(c) as the thick, hyposcattering structure between the hyperscattering lamina propria and submucosa layers. Figure 7(e) shows corresponding pinch biopsy histology, with normal terminal ileum, consistent with the OCT images.

![Image of OCT images](image_url)

**Fig. 7.** Volumetric OCT of the terminal ileum. (a) En face OCT image at 50 µm depth shows typical villi structure. The inset shows the endoscopic view of the terminal ileum with the OCT imaging catheter in contact with the ileum wall. (b) En face OCT image at 300 µm depth shows numerous glandular structures under the tissue surface. (c) Cross-sectional image along the pullback direction. (d) Cross-sectional image along the rotary direction. (e) Corresponding biopsy histology of the terminal ileum. Red arrow: ileum glands. Blue arrows: Peyer’s patches.

### 3.3 Pathologies in the GI tract

Figure 8 shows a representative volumetric OCT data set obtained from a patient with dysplastic Barrett’s esophagus (BE). Figure 8(a) shows an en face OCT image at 70 µm depth. The en face OCT shows the subsurface crypt architecture with branching features. The features of these mucosal surface patterns (pit pattern), such as size, branching, heterogeneity are used as diagnostic markers in both the upper and lower GI tracts [64, 65]. Motion artifacts due to heartbeat and breathing can also be observed, similar to Fig. 6. The inset shows an endoscopic video capture obtained prior to OCT imaging. The non-dysplastic part of the BE mucosa is dark red, inflamed, and irregular, which makes it difficult to identify the dysplastic
region from the endoscopic image. Figure 8(b) shows an en face OCT image at 170 µm depth, to evaluate the subsurface features of the BE region. The crypt structure in the distal region is different (more branching) from that in the proximal region (more round), suggesting that these two regions contain different types of BE. Figures 8(c)-8(e) show cross-sectional OCT images of the BE region along the pullback and rotary directions.

Fig. 8. Volumetric OCT data set of dysplastic Barrett’s esophagus. (a) En face OCT image at 70 µm depth. The inset shows endoscopic view of the dysplastic BE using NBI, which shows dark-red, inflamed, and irregular surface feature similar to non-dysplastic BE. (b) En face OCT at 170 µm depth. (c) Cross-sectional image along the pullback direction. (d) Cross-sectional image along the rotary direction in the BE region with branching pit pattern. (e) Cross-sectional image in the BE region with round pit pattern. (f) Corresponding histology from the imaged region, diagnosed as focal high grade dysplasia. (g) Enlarged view of the cross-sectional image along the rotary direction. Red arrows: BE glands.

The layered architecture characteristic of the normal esophagus is absent, and the surface OCT signal is stronger than the subsurface OCT signal, indicating incomplete surface
maturation and suggesting the area may be dysplastic BE according to previously suggested diagnostic criteria [29]. Figure 8(f) shows histology of an endoscopic mucosal resection (EMR) specimen taken at the imaged location. This histology was diagnosed as BE with extensive low grade dysplasia and focal high grade dysplasia. These results demonstrate for the first time that ultrahigh speed endoscopic OCT enables visualization of 3D tissue architecture in both en face and cross-sectional OCT images. En face OCT may be important for improving the sensitivity and specificity of image guided biopsy of dysplastic BE.

Figure 9 shows a volumetric OCT data set obtained from a patient with radiation proctitis (RP). RP is a form of chronic inflammation of the lower GI tract which is common complication of radiation therapy used to treat prostate cancer, occurring in some form in approximately 10-15% of patients [66]. Figure 9(a) shows an en face OCT image of the recto anal junction (RAJ) at 240 µm depth, corresponding to the bottom of the epithelial layer. Unlike the normal squamous epithelial layer observed in the normal anus, the en face OCT shows a large number of subsurface structures, similar to the vessel structures observed in the endoscopic view shown in the inset. Figures 9(b) and 9(c) show cross-sectional images along the pullback and rotary directions indicated by the green and blue dashed lines in Fig. 9(a). The shadow of vessels from the lamina propria layer can be clearly appreciated, consistent with previous 3D-OCT imaging studies of RP [25, 26]. The patient was scheduled to receive radiofrequency ablation (RFA) treatment after the OCT imaging [67], so there was no clinical indication to take biopsies in the region and comparison between histology and OCT cannot be performed in this case.

Fig. 9. Volumetric OCT data set of radiation proctitis near the recto-anal junction. (a) En face OCT image at 240 µm depth shows numerous subsurface vasculature structures. The inset shows an endoscopic view of radiation proctitis near the recto-anal junction, with rectum distal and anal canal proximal in the field of view. (b) Cross-sectional image along the pullback direction. (c) Cross-sectional image along the rotary direction. Red arrows: vessels.
Gastric antral vascular ectasia (GAVE), also known as watermelon stomach, is a condition associated with dilated small blood vessels [68–70]. GAVE results in chronic GI bleeding and can cause anemia as well as occult blood in the stool. GAVE occurs in the antrum, the most distal part of the stomach, such that the endoscope must be retroflexed and bend more than 90° to evaluate the region [71]. Figure 10 shows a volumetric OCT data set obtained from a patient with GAVE. Figure 10(a) shows an en face OCT at a 150 µm depth, corresponding to the top surface of the gastric pits in the antrum. The OCT data set was acquired on the edge of one watermelon stripe, such the lower side of the en face OCT shows randomly distributed dark spots, which can be the fibrin thrombi in the lamina propria, while the upper half of the en face OCT shows relatively normal gastric pit pattern. The inset shows the endoscopic view with the OCT imaging catheter placed on the GAVE region. The typical watermelon stripes can be clearly distinguished in the endoscopic view. Figures 10(b) and 10(c) show cross-sectional images along the pullback and rotary directions. Multiple dilated, hyposcattering, but transparent glandular structures can be observed within the submucosa layer of the GAVE region. The imaged GAVE site was biopsied immediately after the OCT imaging for histological comparison. Figure 10(d) shows the corresponding histology, diagnosed as GAVE. In this case, the depth of standard pinch biopsy does not include the dilated glands observed in the cross-sectional OCT images, which are consistently observed deep in the submucosa layers. The much larger coverage of OCT imaging suggests that it can be used as an imaging-guided biopsy tool to minimize the sampling errors of pinch biopsy.

Fig. 10. Volumetric OCT data set of the antrum with GAVE. (a) En face OCT image at 150 µm depth shows large glandular structures under the GAVE region. Inset shows the endoscopic view of the antrum with the OCT imaging catheter on the GAVE region. (b) Cross-sectional image along the pullback direction. (c) Cross-sectional image along the rotary direction. (d) Corresponding histology of the antrum, which was diagnosed as GAVE. Red arrow: Large glands in the GAVE region. Blue arrow: watermelon stripe.
3.4 Endoscopic OCT angiography

The ultrahigh speed micromotor endoscopic OCT system provides extremely high pixel density and excellent frame-to-frame scanning stability, necessary for OCT angiography (OCTA). Figure 11 shows an endoscopic OCTA generated from OCT structural data of normal esophagus shown in Fig. 6. Figure 11(a) shows the en face OCT intensity image at a depth corresponding to the lamina propria layer, which contains a large number of blood vessels including arteries, veins, and capillaries. Vascular features are difficult to identify in the structural OCT image; only larger vessels can be distinguished as lower intensity contours. Figures 11(b) and 11(c) show cross-sectional OCT images along the pullback and rotary directions at positions indicated by the dashed lines in Fig. 11(a). Figure 11(d) shows an en face OCTA obtained from the same data set at the same depth as Fig. 11(a). OCTA dramatically enhances the contrast of microvasculature and thus the vessel network in the LP layer can be clearly visualized. Some artifacts can be observed as lines along the rotary and pullback directions due to parasitic motion of the OCT catheter from heartbeat as well as artifacts from thickness variations of the catheter sheath. Figures 11(e) and 11(f) show cross-sectional endoscopic OCTA images along the pullback and rotary directions. Most of the vascular features are in the LP layer, consistent with the morphology of normal esophagus, while the high signal in the submucosa layer is caused by decorrelation effects, where the OCT beam diverges and the spot size becomes too large to resolve individual vessels.

![Fig. 11.](image)

Fig. 11. Endoscopic OCT angiography of the normal esophagus. (a) En face OCT image at 240 μm depth, corresponding to the LP layer. Cross-sectional OCT images along (b) the pullback direction and (c) rotary directions. (d) En face OCTA in the LP layer from the same OCT data set. Cross-sectional OCT angiograms (e) along the pullback and (f) rotary directions.

4. Discussion

The micromotor catheter enables high speed scanning with low driving voltage and is less sensitive to catheter bending, resulting in more stable scanning than proximally actuated rotary catheters. Polarization artifacts are less than in proximally actuated catheters because the optical fiber does not twist during actuation. However, if the polarization state of the incident beam to the tissue is not circular, it will still rotate when incident on the tissue because the polarization is reflected from a 90 degree rotating mirror. Therefore, if the tissue has polarization dependent backscattering, this may produce polarization artifacts in the images. The VCSEL light source has both very high sweep rate and broad wavelength tuning range, providing high axial line rate for in vivo imaging and good axial resolution. With the high speed data acquisition, the system can support sufficient imaging depth range with ultrafast line rate. In this study, the effective laser scan repetition rate is 600 kHz and the micromotor rotation speed is 400 Hz (24,000 rpm), so each frame contains 1,500 lines over the circumferential scanning range of 10 mm, corresponding to an axial scan spacing of ~6.7 μm at the catheter surface. The pullback speed was 2 mm/s, corresponding to a frame-to-
frame spacing of 5 μm. The maximum optical clock frequency is ~1.04 GHz supporting an imaging depth range of 3.3 mm in air, or 2.4 mm in tissue. The range was limited by the A/D card performance and can be improved using higher speed detection and data acquisition.

Clinical ultrahigh speed OCT imaging was performed in patients with a cross section of GI pathologies who were scheduled for upper and lower endoscopy. The high spatial sampling density and high optical resolution of ultrahigh speed endoscopic OCT enabled acquisition of dense 3D data sets. 3D OCT data enables the generation of cross-sectional images, which are registered to en face tissue features, as well as high-magnification en face visualization of tissue layers. Cross-sectional OCT images correlated well with histology from the imaged area, and showed tissue structures in the deeper layers such as muscularis mucosa and submucosa where pinch biopsy typically cannot reach. OCT not only generates en face images similar to chromoendoscopy, NBI or CLE, but also enables en face images at different depths to be extracted from the same data set. Although the OCT resolution in the current study is less than CLE, it can be scaled to the few micron level at the expense of depth of field. Furthermore, OCT and OCT angiography have the advantage that they do not require exogenous contrast. The micromotor imaging catheter enabled endoscopic OCT imaging of structures in the GI tract that are difficult to access using previous generation catheters, which promises to facilitate new clinical applications. Furthermore, OCT angiography enables visualization of 3D microvasculature without requiring exogenous contrast, augmenting the diagnostic capability of endoscopic OCT. The ability to volumetrically visualize subsurface vasculature and structure in the GI tract is a unique feature of endoscopic OCT compared to CLE and NBI, which promises to improve detection of premalignant pathology in the GI tract.

A trade-off between the transverse resolution and scanning speed was made in the system in order to meet different imaging requirements. For structural OCT imaging, a transverse resolution of 15 μm to 30 μm is sufficient to image tissue structures over a larger area, while transverse resolution 5 μm to 10 μm can show more detailed en face features, but trade off depth of field and require higher data density. The confocal parameter is quadratically proportional to the transverse resolution, so transverse resolution and signal intensity away from the focal plane degrade faster with shorter confocal parameter and limit the imaging depth in the volumetric data sets. For OCT angiography, the sampling density must be high enough to avoid excessive intensity decorrelation between consecutive frames which would increase noise, so the axial scan density and frame spacing needs to be at least two times smaller than the transverse resolution. In order to obtain good sensitivity in OCT angiography, the imaging catheter should either have a focal spot with larger transverse resolution or slower 2D scanning speed. However this reduces the imaging area given a fixed acquisition time. In this study, the transverse resolution was set to be ~12 μm in tissue, which was sufficient to resolve glandular structures while satisfying the criteria to sufficient OCT angiography sensitivity given the frame spacing of 5 μm.

The performance of the current prototype can be further improved. The micromotor scanning in the rotary direction is highly repeatable, however there are motion artifacts when the motor and optics are distally pulled back along the longitudinal direction. This can be a limiting factor in the image quality when using a long catheter because of the friction between the catheter cable and sheath along its length. The effects of friction may be reduced by choosing different torque coils or sheath materials. Furthermore, motion artifacts introduced by the heartbeat and breathing of patients typically occur in upper GI imaging and cause distortion in the en face OCT images. Current practice during OCT imaging is to place the imaging on top of the region of interest and deflate the GI tract to minimize the motion. It is possible to further reduce the motion by increasing the imaging speed (both rotation and pullback). A balloon catheter design may provide more stable positioning but is still susceptible to displacement of the imaging plane if the imaging optics flex within the balloon and the dilated balloon may compress the tissue structure [72]. Both bulk motion and non-uniform rotation of the motor has detrimental effects on OCT angiography imaging. The source of the bulk motion in the upper GI tract is mainly from cardiac motion. Pronounced
cardiac motion can be observed in the data sets especially when the imaging is conducted at the more proximal part of the esophagus, which is anatomically closer to heart. Cardiac motion can be observed in the OCTA images as vertical streaks with high decorrelation signal as noted in Fig. 11(d). The effects of bulk motion on OCTA images can be somewhat reduced by applying histogram-based correction methods [73–76], provided that the fluctuations in longitudinal position due to cardiac motion does not cause consecutive B-scans to become non-overlapped in the pullback direction. Non-uniform rotation distortion (NURD) causes consecutive B-scans to become distorted or lose registration in the transverse direction, causing errors in the decorrelation. Since NURD tends to occur throughout all frames, its effect is an overall increase of the decorrelation noise for the entire data set. NURD can be particularly severe if rotary optical components are not precisely balanced on the motor shaft, which causes excitation of parasitic vibrational modes of the motor or optics. In this study, the rotation performance of the micromotor imaging catheter was relatively good, hence NURD correction was not required. However, since it is challenging to fabricate micromotor based catheters which are precisely balanced, our group has recently developed a NURD correction algorithm based on the fiducial markers located on the micromotor catheters [77], which is effective at correcting the NURD and can improve the OCTA signal to noise. We have also found that correction of NURD improves the structural OCT images by removing artifacts in the en face OCT images, improving visualization of the fine mucosal surface patterns.

Finally, the rigid length of the distal catheter, including the micromotor and optics was 18.2 mm and the outer diameter is ~3.2 mm. The imaging catheter can be inserted through a therapeutic endoscope with a 3.7 mm diameter working channel, but is still too large to be introduced through the 2.8 mm working channel of most commonly used EGD endoscopes. The endoscope working channel has a sharp radius bend at the proximal end, which requires either a short rigid length or a smaller catheter outer diameter. Therefore, the size of the catheter must be reduced in order to enable use with the more common 2.8 mm working channel endoscopes. Alternately, the catheter could be used with a daughter scope carried on the side of a standard endoscope.

5. Conclusions

We demonstrated an ultrahigh speed endoscopic OCT imaging system for clinical gastroenterology with 400 fps frame rate using a micromotor imaging catheter, VCSEL light source and high speed data acquisition system. The system achieves 400 frames per second with 600 kHz axial line rate, 11 µm axial resolution, 11 µm transverse resolution and 3.3 mm imaging depth range in air, corresponding to 8 µm axial resolution, 12 µm transverse resolution, and 2.4 mm imaging depth range in tissue. In this pilot study, in vivo high imaging speed was demonstrated in the human GI tract, demonstrating next generation tissue visualization methods for clinical gastroenterology, including en face features similar to chromoendoscopy, narrow band imaging and confocal endomicroscopy, volumetric imaging in difficult to reach regions, and OCT angiography (OCTA) which enables 3D visualization of microvasculature. These capabilities promise to facilitate a wide range of new investigations as well as to enhance the ability of endoscopic OCT to detect GI pathologies.

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