New high-speed 3-D imaging system holds potential for improved cancer screening

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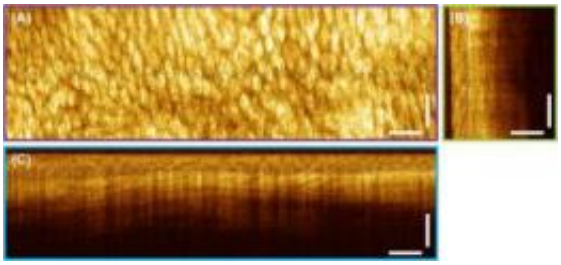

This is a 3-D OCT volumetric data set from an excised human colon specimen. (A) En face view showing regular organization of normal colon. (B and C) Cross-sectional views along two different directions showing sub-surface features. Two cross-sections are shown as examples, however multiple cross-sectional views can be extracted from the 3-D OCT data. Scale bar: 500um. Credit: Massachusetts Institute of Technology

Researchers at the Massachusetts Institute of Technology (MIT) have developed a new imaging system that enables high-speed, three-dimensional (3-D) imaging of microscopic pre-cancerous changes in the esophagus or colon. The new system, described in the Optical Society's (OSA) open access journal *Biomedical Optics Express*, is based on an emerging technology called optical coherence tomography (OCT), which offers a way to see below the surface with 3-D, microscopic detail in ways that traditional screening methods can't.

Endoscopy is the method of choice for cancer screening of the colon or

esophagus. In the procedure, a tiny camera attached to a long thin tube is snaked into the colon or down the throat, giving doctors a relatively non-invasive way to look for abnormalities. But standard endoscopy can only examine the surface of tissues, and thus may miss important changes occurring inside tissue that indicate cancer development.

OCT, which can examine tissue below the surface, is analogous to medical ultrasound imaging except that it uses light instead of sound waves to visualize structures in the body in real time, and with far higher resolution; OCT can visualize structures just a few millionths of a meter in size. Over the past two decades, OCT has become commonplace in ophthalmology, where it is being used to generate images of the retina and to help diagnose and monitor diseases like glaucoma, and has emerging applications in cardiology, where it's used to examine unstable plaques in blood vessels that can trigger heart attacks.

The new endoscopic OCT imaging system reported by OCT pioneer James G. Fujimoto of MIT and his colleagues, works at record speeds, capturing data at a rate of 980 frames (equivalent to 480,000 axial scans) per second—nearly 10 times faster than previous devices—while imaging microscopic features less than 8 millionths of a meter in size.

At such high speeds and super-fine resolution, the novel system promises to enable 3-D microscopic imaging of pre-cancerous changes in the esophagus or colon and the guidance of endoscopic therapies. Esophageal and colon cancer are diagnosed in more than 1.5 million people worldwide each year, according to the American Cancer Society.

"Ultrahigh-speed imaging is important because it enables the acquisition of large three-dimensional volumetric data sets with micron-scale resolution," says Fujimoto, a professor of electrical engineering and computer science and senior author of the paper.

"This new system represents a significant advance in real-time, 3-D endoscopic OCT imaging in that it offers the highest volumetric imaging speed in an endoscopic setting, while maintaining a small probe size and a low, safe drive voltage," says Xingde Li, associate professor at the Whitaker Biomedical Engineering Institute and Department of Biomedical Engineering at Johns Hopkins University, who is not affiliated with the research team.

In OCT imaging, microscopic-scale structural and pathological features are examined by directing a beam of light on a tissue and measuring the magnitude and echo time-delay of backscattered light. Because the amount of light that can be recaptured and analyzed decreases quickly with depth in tissue due to scattering, the technique can generally only be used to visualize sub-surface features to a depth of 1 to 2 millimeters. "However these depths are comparable to those sampled by pinch biopsies and unlike biopsy, information is available in real time," Fujimoto says. By using miniature fiber optic scanning catheters or probes, either on their own or in combination with standard endoscopes, colonoscopes, or laparoscopes, OCT imaging can be performed inside the body.

In collaboration with clinicians at the VA Boston Healthcare System and Harvard Medical School, the team is investigating endoscopic OCT as a method for guiding excisional biopsy—the removal of tissue for histological examination—to reduce false negative rates and improve diagnostic sensitivity.

"Excisional biopsy is one of the gold standards for the diagnosis of cancer, but is a sampling procedure. If the biopsy is taken in a normal region of tissue and misses the cancer, the biopsy result is negative although the patient still has cancer," notes Fujimoto, whose team is one of a number of research groups—including at Johns Hopkins University; the University of California, Irvine; Case Western University; and

Massachusetts General Hospital—that are actively pursuing the development of smaller, faster endoscopic OCT systems.

Endoscopic OCT requires miniature optical catheters or probes—just a few millimeters in diameter—that can scan an optical beam in two dimensions to generate high-resolution 3-D data sets. Scanning the beam in one transverse direction generates an image in a cross-sectional plane, whereas scanning the beam in two directions generates a stack of cross-sectional images—that is, a 3-D (or volumetric), image.

"This device development is one of the major technical challenges in endoscopic OCT because probes must be small enough so that they can be introduced into the body, but still be able to scan an optical beam at high speeds," Fujimoto says. "Increasing imaging speeds has also been an important research objective because high-resolution volumetric imaging requires very large amounts of data in order to cover appreciable regions of tissue, so rapid image acquisition rates are a powerful advantage."

The optical catheter developed by the MIT researchers and their collaborators uses a piezoelectric transducer, a miniature device that bends in response to electrical current, allowing a laser-light emitting optical fiber to be rapidly scanned over the area to be imaged.

So far, the device—which must be further reduced in size, Fujimoto notes, before it can be deployed with the standard endoscopes now used—has only been used in animal models and in samples of human colons that had been removed during surgical procedures; further development and testing of the technology is needed before it can be tested in human patients. "The ultimate clinical utility of new devices must be established by large clinical studies, which assess the ability of the technology to improve diagnoses or therapy," he says. "This is a much more complex and lengthy task than the initial development of the

technology itself."

More information: *Biomedical Optics Express*, Vol. 2, Issue 8, pp. 2438-2448 (2011) doi:10.1364/BOE.2.002438