Photoacoustic Tomography Bridges Macroscopic, Microscopic

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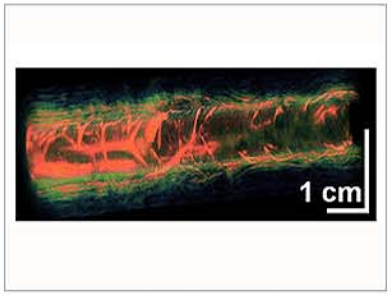
March 24, 2012 — Photoacoustic tomography (PAT) combines the best features of optical imaging and ultrasound to provide multiscale, multicontrast images of biological tissue, according to a review article published in the March 23 issue of *Science*.

Optical techniques produce images with quality resolution and strong contrasts, but only at tissue depths up to about 1 mm, as a result of photon scattering. "Ultrasound scattering is about 1000 times weaker than optical scattering," said lead author Lihong V. Wang, PhD, the Gene K. Beare Distinguished Professor of Biomedical Engineering in the School of Engineering and Applied Science at Washington University in St. Louis, Missouri, in a telephone interview with *Medscape Medical News*.



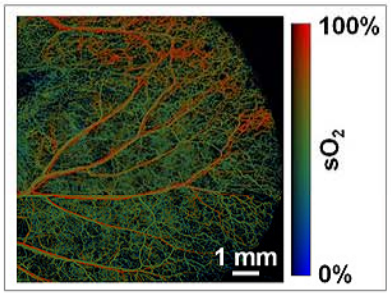
This image shows a rabbit's esophagus and adjacent internal organs. Photoacoustic colonoscopy would allow physicians to visualize not just superficial polyps but also deeper lesions. *Source: Joon Mo Yang/Liihong Wang*

In PAT, a pulsed laser is directed at the tissue of interest, causing it to heat slightly and expand. This thermoelastic expansion converts photons to ultrasound waves that are used to form speckle-free images with the resolution associated with the ultrasound wavelength, at tissue depths never before possible.

"In current practice, if we want to image organelles and cells, we use optical microscopy, and when we want to image tissues and organs, we use nonoptics [magnetic resonance imaging], X-ray [computed tomography], ultrasound, [positron emission tomography], or [single photon emission tomography]. Consequently, between the microscopic domain and the macroscopic domain, there is a large divide, which prevents us from correlating images acquired from different-length scales," Dr. Wang said.

"Photoacoustic tomography can bridge that gap. By looking at the same contrast mechanisms, it'll be much easier to correlate images acquired from different length scales," he added.

This technology provides anatomical, functional, metabolic, and molecular information.



The arteries (*red*) and veins (*green*) stand out clearly in a photoacoustic microscope image of a mouse ear. *Source: Joon Mo Yang/Liihong Wang*

PAT uses endogenous contrasts — DNA/RNA, hemoglobin, melanin, water, and lipid — to image differences in chemical composition. This capability may revolutionize early cancer detection by identifying the excessive oxygen metabolism typically seen in the earliest days of the disease. Melanin, which has broadband optical absorption from the ultraviolet to the near-infrared range, can be spectroscopically distinguished from hemoglobin based on optical absorption to aid diagnosis of melanoma.

Four clinical trials are currently in the works, according to a Washington University news release. In 1 trial, researchers are testing the ability of this technique to identify sentinel lymph nodes for breast cancer staging, with the hope that future lymph node biopsies will be done without surgery. The other clinical trials will examine the technique's usefulness in monitoring early chemotherapy response, imaging melanomas, and imaging the gastrointestinal tract.

"[PAT] will actually deliver on the promise of molecular imaging: an area with great potential, but so far little reality," said Reuben Mezrich, MD, PhD, professor of diagnostic radiology and nuclear medicine at the University of Maryland Medical Center in Baltimore, in an email interview with *Medscape Medical News*. Dr. Mezrich was not involved in the *Science* review. "Photoacoustic will enable researchers and clinicians to probe molecular activity by taking advantage of the interaction of light with endogenous and exogenous agents (many of which are already approved for human use) at reasonably good resolution (perhaps as high as 200 microns) relatively deep into the body," he said.

"Right now this technology is growing exponentially, so obviously there's still a lot to do," said Dr. Wang. "In my opinion, the priority is to demonstrate and validate this technology in the clinic, which is what we're doing right now, and convert this technology to commercial products so it will get into the hands of radiologists and physicians."

Dr. Wang and Dr. Mezrich agree that radiologists should be prepared to use this technology when it becomes available. "Radiologists should know it is coming, follow the research, and be ready to adapt it into practice as soon as vendors bring it to market. I don't believe there are significant hurdles for [US Food and Drug Administration] approval, so it might come quickly," said Dr. Mezrich.

"If we can convince commercial entities to commercialize this technology for clinical applications, physicians will find new applications that we're not even aware of," Dr. Wang concluded.

Dr. Wang has financial interests in Microphotoacoustics Inc and Endra Inc. The study was supported by grants from the National Institutes of Health. Dr. Mezrich has disclosed no relevant financial relationships.

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