OPTICAL COHERENCE TOMOGRAPHY

A Microscope in a Needle

A microscope small enough to fit into a needle creates many new possibilities for optics in medicine.

We have developed a range of optical coherence tomography (OCT) needle probes. Connected to an OCT scanner via a single mode fiber, the probes are constructed by fusing exact lengths of no-core fiber and graded-index fiber to focus a broadband light beam. We terminated the optics with angle-polished, gold-coated no-core fiber to deflect the beam. Encased in a needle (outer diameter 310 µm), these probes are capable of 3-D imaging.[1] However, the important developments of 2012 have been where we have taken these needle probes.

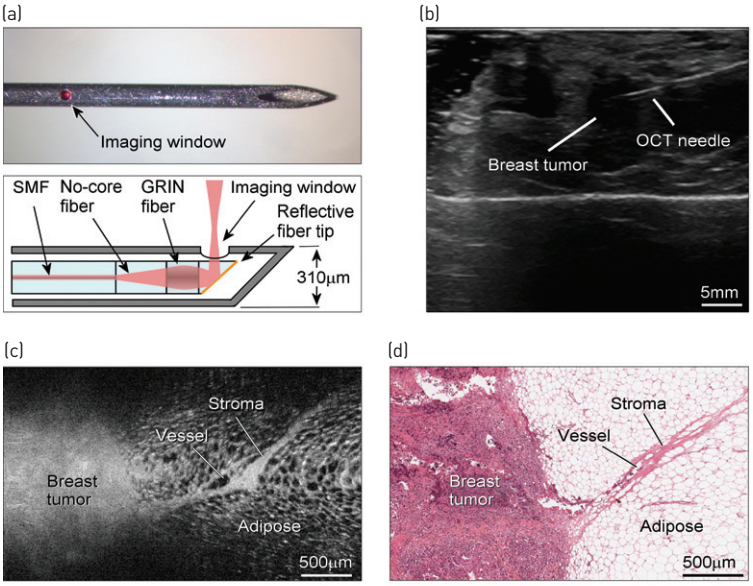
We have explored their use in breast cancer. The near-infrared backscatter of cancer is different to many types of healthy tissue, and OCT has the potential for surgical guidance. But OCT is limited by its image penetration depth, typically only 1 to 3 mm. By combining OCT needle probes with ultrasound guidance, we are able to take the light beam to the tumor.[2]

We have also developed needle probes as a new dynamic imaging technology in lungs.[3] Encasing the needle probe in a stationary outer sheath, the needle can be scanned at high rates, obtaining a time sequence of images. This has allowed physiologists to dynamically track the expansion and collapse of alveoli deep within the lung.

Unfortunately, all-fiber lenses tend to have small depth of focus (DOF), typically several hundred microns. We have addressed this by incorporating a miniature phase mask into the focusing optics, almost doubling the DOF.[4]

Constructing an image with these probes requires micrometer-scale position information, typically achieved by rigidly constraining the needle to translate and rotate with a set of motors. But clinical implementation demands a hand-held probe. We have taken steps towards this goal, combining an OCT needle probe with a magnetic tracking system.[5] Using signal processing techniques, we were able to achieve micrometer-scale resolution, sufficient to reconstruct OCT images.

This new generation of hand-held OCT needle probes has significant potential for intra-operative guidance, helping surgeons make better informed decisions of where to cut and where to avoid. OPN



(a) Photo and schematic of an OCT needle probe encased in a 30-gauge needle. (b) Ultrasound image showing an OCT needle probe scanning a human breast tumor sample. (c) *Ex vivo* OCT needle probe scan of a tumor margin taken from a 70-year old female patient with invasive ductal carcinoma. (d) Haematoxylin- and eosin-stained histological section of the same tumor margin.

We wish to thank the staff at Sir Charles Gairdner Hospital; Royal Perth Hospital; PathWest Laboratory Medicine; the School of Surgery, University of Western Australia; and the Centre for Neonatal Research and Education, University of Western Australia.

This work was supported by the Cancer Council Western Australia; National Breast Cancer Foundation, Australia; and the Raine Medical Research Foundation.

Visit **www.opnmagazine-digital.com** to view the video that accompanies this article.

Researchers

Robert A. McLaughlin (robert.mclaughlin@uwa.edu.au), **Bryden C. Quirk**, **Dirk Lorenser**, **Xiaojie Yang**, **Boon Y. Yeo**, **Andrea Curatolo**, **Kelsey M. Kennedy**, **Loretta Scolaro**, **Rodney W. Kirk** and **David D. Sampson**
University of Western Australia in Perth

References

1. D. Lorenser et al. Opt. Lett. **36**, 3894 (2011).
2. R.A. McLaughlin et al. IEEE J. STQE **18**, 1184 (2012).
3. R.A. McLaughlin et al. J. App. Phys. **113**, 967 (2012)
4. D. Lorenser et al. Opt. Lett. **37**, 1616 (2012).
5. B.Y. Yeo et al. Biomed. Opt. Exp. **3**, 1565 (2012).

OPTICAL COHERENCE TOMOGRAPHY

Time Reversal Optical Tomography

There has been a surge of interest in diffuse optical tomography (DOT) that uses near-infrared light to detect, localize and diagnose maladies such as breast cancer and brain injury.[1] Scattering and light attenuation limit the resolution and accuracy of DOT methods that use small differences in optical properties to distinguish lesions from normal tissue. Researchers need a DOT approach that can, for example, quickly reconstruct images to detect and map tumors at early growth stages and determine if they are malignant or benign.[2]

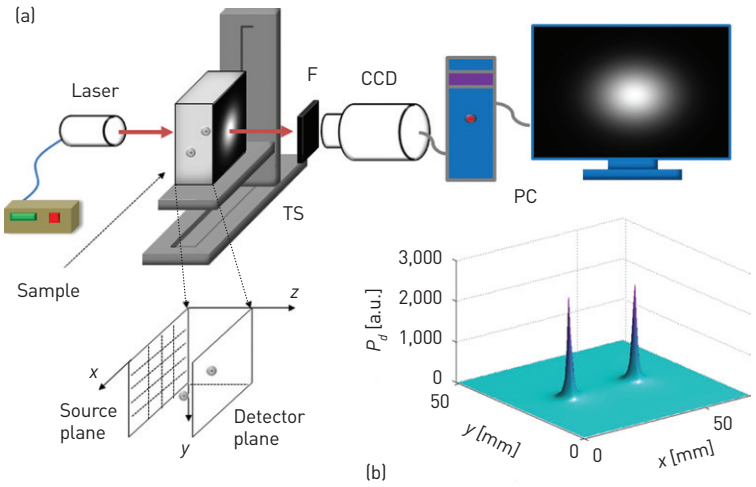
Time reversal optical tomography (TROT) extends the use of TR imaging and a subspace-based method of multiple signal classification (MUSIC) from acoustic and radar imaging to optical imaging.[3,4,5] TROT uses a multisource illumination and multi-detector signal acquisition scheme to acquire multiple angular views of the sample.

The perturbation in light intensity distribution due to the targets is extracted from the data and organized in a matrix K. The leading eigenvalues of the TR matrix, $T = K^{\dagger}K$, correspond to the targets whose locations are determined using MUSIC, along with Green's functions for light propagation in the sample.

We first tested the efficacy of TROT using a 60-mm-thick slab of Intralipid-20 percent suspension in water and 9-mm diameter glass spheres as absorptive or scattering targets. We filled the glass spheres with ink dissolved in the suspension to provide absorptive targets, and with a higher concentration of Intralipid to provide scattering targets. We chose the optical properties and size of the sample and targets to emulate average values for breast tissue and small tumors. We found that TROT could retrieve the location of a single target with millimeter accuracy and resolve two targets when their adjacent surfaces were only 4-mm apart.

Another experiment involved a realistic breast model composed of *ex vivo* breast tissue with two pieces of embedded tumors; TROT accurately located the positions of both the tumors. We have extended TROT for locating fluorescent targets.

TROT is non-iterative and faster than other iterative DOT approaches. It is particularly suited for detecting point-like targets. OPN



(a) F = signal transmitting narrow-band filter; TS = translation stage; CCD = charge coupled device; and PC = computer. Continuous wave 790-nm diode laser light illuminates the front of the sample cell. Diffusely transmitted light from the opposite face is collected by a camera lens through F and sensed by a CCD camera. The sample cell is step-scanned across the laser beam in a 2-D *x-y* array of grid points using the computer-controlled TS. (b) A TROT-generated pseudo image of two absorptive targets at z = 30.5 mm plane when the targets are separated by 27.6 mm.

Researchers

Binlin Wu, **Wei Cai** and **Swapan K. Gayen** (gayen@sci.ccny.cuny.edu)
City College and Graduate Center of the City University of New York, N.Y., U.S.A.

References

1. A.P. Gibson et al. Phys. Med. Biol. **50**, R1 (2005).
2. N. Kroman et al. Int. J. Cancer **105**, 542 (2003).
3. B. Wu et al. Opt. Express **19**, 21956 (2011).
4. M. Fink et al. Rep. Prog. Phys. **63**, 1933 (2000).
5. A.J. Devaney. IEEE Trans. Antenn. Propag. **53**, 1600 (2005).

OPTICAL COHERENCE TOMOGRAPHY

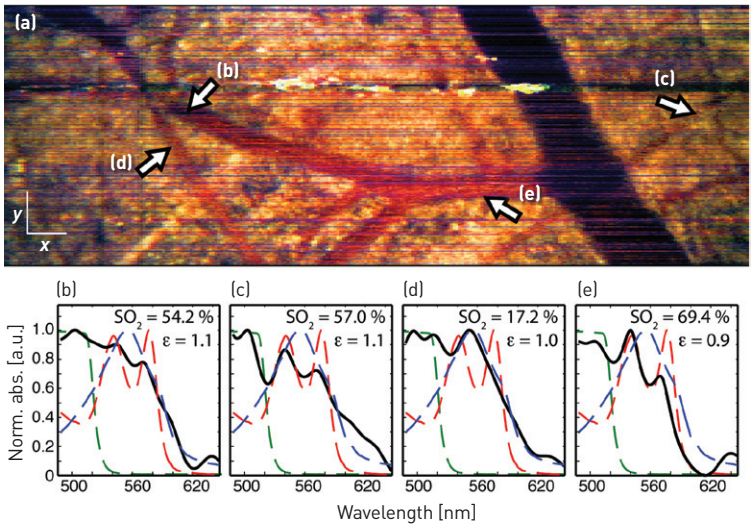
True Color Molecular Imaging with METRiCS OCT

Being able to assess, structure and quantify the molecular content of biological samples *in vivo* is paramount to improving our understanding of many diseases. To this end, we have developed molecular imaging true-color spectroscopic optical coherence tomography (METRiCS OCT), which derives functional information from the spatially resolved spectral content of scattered and absorbed light.[1]

The main working principle behind METRiCS OCT is spectroscopic OCT (SOCT), which provides the same noninvasive, high-resolution tomographic imaging capabilities as OCT with the addition of spectral information at each voxel of the sampled volume.[2] We use a wide spectral bandwidth laser source centered in the visible spectrum, thus allowing quantification of hemoglobin oxygenation (SO_2),[3] providing contrast from other readily available absorbers and enabling a true-color tomographic representation of samples.

In addition, METRiCS OCT uses a novel method for assessing spatially resolved spectral information. This method, termed dual window (DW), uses two short-time Fourier transforms with carefully chosen windows to reconstruct a time-frequency distribution and achieve high spatial and spectral resolution.[4] DW has also been shown to avoid the artifacts associated with other commonly used time-frequency methods, thereby providing spectra with high fidelity.

To demonstrate the capabilities of METRiCS OCT, we acquired images from an *in vivo* CD1 nu/nu normal mouse dorsal skinfold window chamber model. Our results demonstrate that both endogenous and exogenous chromophores—from Hb and sodium fluorescein (NaFS), respectively—provide unique colorimetric contrast. The figure illustrates the full potential of the method. As it shows, the rich spectral content allows quantification of each species—specifically, SO_2 and the ratio between Hb and NaFS ($\varepsilon \equiv$ NaFS/Hb).



(a) En-face (*x*-*y*) METRiCS OCT image using exogenous contrast and spectral profiles. Arrows indicate points where spectra were extracted. White *x* and *y* scale bars are 100 µm. (b-e) Spectral profiles from points as noted by arrows in (a). Measured spectral profiles (black) are superposed with the theoretical oxy (dashed red) and deoxy (dashed blue) Hb normalized extinction coefficients and normalized absorption of NaFS (dashed green). Also shown are the SO_2 levels and the relative absorption of NaFS with respect to total Hb ($\varepsilon \equiv$ NaFS/Hb). All spectra were selected from depths immediately beneath each corresponding vessel.

Adapted from F. E. Robles et al. Nature Photon. **5**, 744–7 (2011).

We believe that METRiCS OCT has the potential to become an incisive tool for many applications, including basic research into tumor development (e.g., angiogenesis and hypoxia); the diagnosis of ophthalmologic pathologies (retinal microvasculature perfusion and oxygenation) and cancer; and the delivery and monitoring of therapeutic agents. A recent continuation of this work has shown that plasmonic nanoparticles also provide useful colorimetric contrast.[5] This is an important step forward, particularly for the implementation of this method to deliver and monitor therapeutic agents. OPN

Researchers

Francisco E. Robles and **Adam Wax** (a.wax@duke.edu)
Duke University, Durham, N.C., U.S.A.

References

1. F. E. Robles et al. Nature Photon. **5**, 744 (2011).
2. D. Huang et al. Science **254**, 1178 (1991).
3. F. Robles et al. Biomedical Opt. Express **1**, 310 (2010).
4. F. Robles et al. Opt. Express **17**, 6799 (2009).
5. Y. Li et al. Biomedical Opt. Express **3**, 1914 (2012).