Tissue and Blood Optical Clearing for Biomedical Applications

Dan Zhu
Bernard Choi
Elina Genina
Valery V. Tuchin
Tissue and Blood Optical Clearing for Biomedical Applications

Dan Zhu
Huazhong University of Science and Technology
Britton Chance Center for Biomedical Photonics
Wuhan National Laboratory for Optoelectronics
1037 Luoyu Lu
Wuhan 430074, China
E-mail: dawnzh@mail.hust.edu.cn

Bernard Choi
University of California, Irvine
Beckman Laser Institute
1002 Health Sciences Road
Irvine, California 92617, USA
E-mail: choib@uci.edu

Elina Genina
Saratov State University
Research-Educational Institute of Optics and Biophotonics
ul. Astrahanskaya 83
Saratov 410012, Russia
E-mail: eagenina@yandex.ru

Valery V. Tuchin
Saratov National Research State University
Research-Education Institute of Optics and Biophotonics
83 Astrakhanskaya str., Saratov 410012, Russia
and
Institute of Precision Mechanics and Control of the RAS
Saratov 410028, Russia
and
National Research Tomsk State University
Laboratory of Biophotonics
Tomsk 634050, Russia
E-mail: tuchinvv@mail.ru

Advanced optical methods pave the way to study the molecular and cellular structure and function of tissues in vivo or in vitro. However, the high scattering of turbid biological tissues limits the penetration of visible and near-infrared light, and the imaging resolution and contrast decrease as light propagates deeper into the tissue. Tissue optical clearing (TOC) techniques have an increasingly prominent role in biomedical imaging and applications. This special section on TOC includes one review and ten original papers.

Recently, TOC techniques have made major advances in three-dimensional reconstruction of thick tissue sections and intact organs. In the review paper, Silvestri et al. discuss TOC of fixed tissues from the perspective of the end user. They propose a taxonomy of clearing techniques based on matching the various TOC protocols with different optical microscopy techniques. This taxonomy will help researchers identify the protocol best suited to their studies.

A primary application of TOC of intact organs is in the field of neurobiology. Many exciting advances have been made in the visualization of cerebral structures, yet limitations remain with regards to the complexity of implementation of some protocols, and with the long incubation times required especially for imaging of entire organs. Yu et al. describe a rapid and prodium iodide-compatible optical clearing method for brain tissue. Drops of sorbitol, sucrose, and fructose can quickly render mouse brain samples transparent, and result in a threefold enhancement in imaging depth. This rapid optical clearing method is expected to enable optical imaging with sectioning and clearing, and provides a new approach for large-volume reconstruction.

Skin optical clearing continues to be a primary area of research. Feng et al. studied attention to the optical clearing potential of disaccharides with use of molecular dynamics simulations and ex-vivo and in-vivo experiments. Their results show that the two disaccharides exhibit a better optical clearing potential than fructose at the same concentration, and that the use of sucrose with optical coherence tomography (OCT) can achieve a more significant increase in imaging depth and signal intensity. Liopo et al. report on a two-step method for enhancement of light penetration through skin. This method involved pretreatment by hyaluronic acid prior to application of clearing agents (PEG and PPG), and resulted in a ~47-fold increases in transmission of red and near-infrared light and significantly enhanced contrast of optoacoustic images.

OCT is a common method used to evaluate the efficacy of TOC, and seven papers in this section involve use of different OCT approaches. Two papers describe the combination of

© 2016 Society of Photo-Optical Instrumentation Engineers (SPIE)
TOC and OCT to image the cutaneous microcirculation. Guo et al. report on the use of OCT angiography (Angio-OCT) to perform comprehensive evaluation of skin optical clearing in vivo. They performed simultaneous quantification of optical properties and imaging of blood flow and correlated the scattering coefficient with refractive-index matching. In combination with TOC, Angio-OCT demonstrates enhanced performance in imaging cutaneous hemodynamics with satisfactory spatiotemporal resolution and contrast. Enfield et al. applied correlation-mapping OCT to image vascular networks at the capillary level. With in-vivo topical application of a high-concentration fructose solution, they measured a 13% increase in OCT penetration depth, thereby enabling the visualization of vessel features at deeper depths within the tissue. Pires et al. used near-infrared OCT to evaluate the effect of a topically-applied optical clearing agent (OCA) to study melanoma in vivo and image the microvascular network with speckle variance and depth-encoded algorithms. After treatment with optical clearing for 250 min, they observed improved contrast resolution up to a depth of ~750 μm within the tumor. Based on these findings, optical clearing techniques are a promising adjuvant to clinical optical characterization of melanoma, such as assessing prognosis and treatment responses.

Besides skin, the optical clearing of the gastrointestinal tract, cochlea, and teeth are reported on in this section. Liang et al. applied the mixture of liquid paraffin and glycerol to reduce attenuation of pig and guinea pig esophagus ex vivo, and enhance the imaging depth of spectral-domain OCT at 800 nm. With swept-source OCT, Lee et al. studied the effectiveness of decalcification using ethylenediaminetetra-acetic acid (EDTA) as an optical clearing method to enhance depth-resolved visualization of internal soft tissues of cochlea. They showed that mouse and guinea pig cochlear samples required decalcification for 7–14 days to obtain optimal optical clearing results. In addition, Kang et al. imaged extracted teeth with natural occlusal lesions with OCT with and without the addition of a transparent vinyl polysiloxane impression material (VPS) currently used in vivo. They showed that OCAs can be used to improve the ability of OCT to visualize subsurface lesions and the dentin—enamel junction under sound and demineralized enamel.

As a more fundamental application of TOC, Mueller matrix polar decomposition (MMPD) is affected by the refractive index matching process, which is one of the major mechanisms of TOC. Chen et al. studied the interaction of TOC with polarization measurements, using Monte Carlo simulations with anisotropic tissue-mimicking models. The depth-resolved polarization features indicate that the refractive index matching process increases the depth of polarization measurements and may lead to higher contrast between tissues of different anisotropies in deeper layers. Furthermore, MMPD-derived polarization parameters can enable qualitative characterization of the refractive index matching process.

In conclusion, we thank all authors for their contribution to this special section. As we look forward, we believe that optical clearing will enhance biomedical optical imaging performance and can make significant contributions in the fields of light-based diagnostic and biomedical imaging techniques.

Dan Zhu. PhD is a professor and vice-director of the Biomedical Photonics Division of Wuhan National Laboratory at Huazhong University of Science and Technology. She has authored more than 100 papers in the field of tissue optics imaging. For years, she has been focusing on optical clearing of tissue in vivo and in vitro for improving optical imaging. She serves as the vice president and secretary general of the Biomedical Photonics Committee of the Chinese Optical Society.

Bernard Choi. PhD, is an associate professor of biomedical engineering and surgery at University of California, Irvine, a core faculty member of the Beckman Laser Institute, affiliated faculty member of the Edwards Lifesciences Center for Advanced Cardiovascular Technology, and visiting scientist at CHOC Children's Hospital. He has held several leadership roles in international optics societies, and he is a Fellow of SPIE. He has published more than 100 peer-reviewed papers and two book chapters.

Elina A. Genina is an associate professor of the Departments of Optics and Biophotonics of Saratov National Research State University, Russia. She received her PhD in biophysics in 2002. She is an author of more than 100 peer-reviewed publications and six book chapters on biomedical optics, and she holds 6 patents. For many years, she has been a scientific secretary of the Saratov Fall Meeting. Her research interests include biomedical optics, tissue optical clearing, biomedicall diagnostics, and laser therapy.

Valery V. Tuchin is a professor and head of optics and biophotonics at Saratov National Research State University and several other universities and institutions. His research interests include tissue optics, laser medicine, tissue optical clearing, and nanobiophotonics. He is a fellow of SPIE and OSA, has been awarded Honored Science Worker of the Russia, SPIE Educator Award, FIDtPro (Finland), Chime Bell Prize of Hubei Province (China), and Joseph W. Goodman Book Writing Award (OSA/SPIE).