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Clinical near-infrared spectroscopy and imaging of the brain

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The *Journal of Biomedical Optics* (JBO) was founded in 1996. In the fourth issue of 1996 and in the subsequent first issue of 1997, JBO published a Special Section on Near Infrared Spectroscopy and Imaging of Tissues, guest edited by Marco Ferrari, David T. Delpy, and David A. Benaron.[1] The special section included 12 articles on fetal- and infant-brain oximetry, muscle oximetry, and breast spectroscopy. In 2016, JBO celebrates its 20th anniversary. Throughout these two decades, JBO papers reported the tremendous progress in this field. A new Special Section on Clinical Near Infrared Spectroscopy and Imaging in JBO (including 7 reviews and 8 original articles) and this parallel Special Section on Clinical Near-Infrared Spectroscopy and Imaging of the Brain in *Neurophotonics* highlight these achievements.

The discovery of the medical near infrared spectroscopy (NIRS) goes back to 1977,[2] when Frans Jöbsis reported that the relatively high degree of transparency of brain tissue in the near infrared range enables real-time noninvasive detection of hemoglobin (Hb) oxygenation using transillumination spectroscopy. Brain and muscle oximetry and functional NIRS[3] (fNIRS) represent the most established clinical and/or basic research areas, but additional applications to other tissues and organs are emerging.

This *Neurophotonics* special section includes 6 reviews and 8 original articles. In the last 20 years the clinical applications of brain oximetry have consistently increased. Gorm Greisen, one contributor of the 1996 special section,[1] and his coauthors wrote an Outlook article focusing on the potential of cerebral tissue oximetry for clinical use to improve the outcome of preterm infants. They present a research agenda with three parallel components: randomized clinical trials, pathophysiologic studies to quantify the effectiveness of clinical interventions, and improved instrumentation. Moreau et al. investigate the feasibility of using frequency-domain NIRS to study adult brain oxygenation in the first few hours of stroke onset. The authors highlight the current technical limitations and future challenges in the development of this unique bedside monitoring tool for stroke. In the 1996 JBO special section,[1] Claudia Robertson in collaboration with Britton Chance reported the use of NIRS to identify traumatic intracranial hematoma in 305 patients. In the present issue Robertson's group (Sen et al.) reviews the recent advances in the clinical applications of NIRS in traumatic brain injury.

Papers from four different groups were published in 1993 demonstrating the ability of fNIRS to non-invasively measure Hb changes coupled with brain activation in humans.[3] In 2014 *Neuroimage* dedicated a special issue to commemorate the first 20 years of fNIRS research, including 9 reviews and 49 contributed papers.[4] In the present special section, 10 of the 15 articles are dedicated to various aspects of fNIRS in infants and adults.

In their commentary article, Tachtsidis and Scholkmann highlight a significant problem that needs to be considered and addressed when performing fNIRS, namely the possibility of inadvertently measuring systemic hemodynamic responses in superficial layers that are not due to neurovascular coupling. They summarize the possible physiological origins of these issues and suggest ways to avoid and remove them.

fNIRS has been largely applied on infants, although motion artifacts are difficult to prevent. Barker et al. propose a new method for correction of motion artifacts and serial correlations for real-time fNIRS suitable for infant studies. Emberson et al. isolate the effects of surface vascular signals in infant neuroimaging using short-distance optical channels.

Goodwin et al. identify and optimize the factors affecting the quality of NIRS data from alert upright infants. It is demonstrated that a light-weight comfortable probe, a stimulus and rest protocol that maximizes attention, and adequate optical contact are essential for acquiring infant NIRS data.

The lack of a diagnostic index is a problem that needs to be overcome in the diagnostics of autism spectrum disorder. Yanagisawa et al. propose an auxiliary diagnosis index for autism spectrum disorder based on fNIRS during working memory and nonworking memory tasks.

Mihara and Miyai review the research on fNIRS application in neurorehabilitation. Topics include potential advantages and shortcomings of fNIRS for investigating the neural mechanism of functional recovery after brain damage and as therapeutic tool for rehabilitation including brain-computer interface and neurofeedback. Peng et al. first review the recent use of multichannel continuous electroencephalography (EEG) combined with fNIRS in epilepsy research and then describe applications to study focal seizures and interictal epileptiform discharges. Chalia et al. use simultaneous EEG and diffuse optical tomography (DOT) to investigate whether bursts of EEG activity in infants with hypoxic ischemic encephalopathy are associated with an observable cerebral hemodynamic response. DOT reveals patient-specific spatial distributions of the hemodynamic response that may be indicative of a complex pattern of cortical activation underlying discontinuous EEG activity that is not readily apparent in scalp EEG.

Fantini et al. provide a comprehensive description of principles, methods, and clinical requirements of cerebral blood flow and cerebral autoregulation measurements and highlight the potentially important role that noninvasive optical methods can play in the assessment of neurovascular health.

Diffuse correlation spectroscopy (DCS) measurements of blood flow rely on the sensitivity of the temporal autocorrelation function of diffusively scattered light to red blood cell mean square displacement. Boas et al. offer, for the first time, theoretical support for the empirically accepted ability of the DCS blood flow index to quantify tissue perfusion.

Cassano et al. review the use of near-infrared and red radiation (photobiomodulation, PBM) for treating major depressive disorder. PBM appears to be a promising treatment for depression that is safe and well-tolerated. However, large randomized controlled trials are still needed to establish the safety and effectiveness of this new treatment.

The guest editors believe that this special section and the parallel special section in JBO are valuable reading for scientists both inside and outside the biomedical optics community. Readers will get a glimpse of how NIRS technologies impact medicine today and what can be expected from developments of tomorrow's technologies. In the coming years, current generations of NIR instruments will migrate along the translational path toward clinical adoption as both the product engineering and use protocols are refined. However, while many aspects of NIRS technology have been tested for limits such as resolution, quantitative accuracy, field-of-view, depth sensitivity, wearability, portability and integration with other modalities, many of these individual demands are at odds with other performance measures. For example, the solutions to several performance specifications positively correlate with instrument weight and thus work against wearability. Thus the phase-space for optimizing and engineering real world NIRS instruments remains immense. In summary, NIRS has already provided many valuable insights in clinical research. While NIRS is on the verge of entering everyday clinical routine, the innovation yet to come is still brighter.

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Marco Ferrari is a biochemistry professor at the Department of Physical and Chemical Sciences, L'Aquila University, Italy. He has pioneered clinical applications of NIRS of the adult and infant muscle and brain, and has given substantial contributions to the wider NIRS scientific community. His recent research activity is focused on the study of the cerebral cortex hemodynamic changes upon cognitive and motor tasks of different complexity by using functional near-infrared spectroscopy (fNIRS). He has been a member of the editorial board of *Journal Biomedical Optics* since 1996.

Joseph P. Culver is a professor of radiology at Washington University. He obtained a PhD in physics at the University of Pennsylvania for work in ultrafast infrared laser spectroscopy. As a postdoc he developed diffuse optical tomography systems for imaging breast cancer and imaging cerebral hemodynamics in animals. His lab explores ways of leveraging optical measurements for neuroimaging, with a focus on development of diffuse optical tomography techniques for mapping human brain function.

Yoko Hoshi is a professor in the Department of Biomedical Optics at Hamamatsu University School of Medicine. She graduated from Akita University School of Medicine and got her medical license in 1981, and received a PhD at Hokkaido University in 1990. She is a pediatrician (a child neurologist), while she has also been participating in developing NIRS and research in cognitive neuroscience, mainly neural mechanisms of emotion generation and emotion regulation. Her recent research interest is developing time-domain diffuse optical tomography.

Heidrun Wabnitz is a senior scientist in the Department of Biomedical Optics at Physikalisch-Technische Bundesanstalt (PTB) in Berlin. She received her Dr. rer. nat. degree from Friedrich Schiller University in Jena. Her fields of work included picosecond spectroscopy of molecules and time-resolved laser scanning microscopy. She joined PTB in 1991, where she focused on medical optical imaging, in particular optical mammography and optical brain imaging. She is active in the development of time-domain instrumentation, modeling and data analysis, performance characterization of instruments, and clinical applications.