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Editorial — The centennial celebration of Dr. Britton Chance

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To celebrate the scientific legacy and spirit of the late Dr. Britton Chance (1913–2010) and his 100th birthday, the Britton Chance International Symposium on Metabolic Imaging and Spectroscopy was held at the Perelman School of Medicine, University of Pennsylvania on June 18–19th, 2013. The symposium brought together over 200 physicists, engineers, biologists and clinicians from all over the world including Europe, Asia and North America. The latest research innovations and clinical progresses by optical, nuclear magnetic resonance (NMR) and nuclear medicine methods were presented and discussed extensively.

The life of Britton Chance spanned nearly a century and his contributions to various parts of human lives were recognized by numerous awards including the US National Medal of Science and an Olympic Gold Medal in sailing. Most importantly, his scientific contributions were characterized by an extraordinary range of research discoveries and innovations, as well as a tenacious pursuit of clinical translation of new technologies. In the 1930–1940s, he invented the miniature stop-flow instrument and made seminal contributions to our understanding of enzymatic kinetics, including the first experimental demonstration of the existence of Michaelis-Menten enzyme–substrate complex. In the 1950s, he invented the dual-beam spectrophotometer for his pioneering investigations of bioenergetics and the redox state in mitochondria. In the 1960s he first discovered the quantum-mechanical electronic tunneling process in biological systems. In the 1970s, he identified hydrogen peroxide released by the respiratory chain in mitochondria. In the late 1970s–1980s, he was a key player in developing *in vivo* NMR spectroscopy for bioenergetic studies and the use of synchrotron radiation to illuminate the structure–function relation of biomolecules. In the late 1980s–1990s, he became a founding father of biophotonics, particularly for biomedical research and clinical practice. In the 2000s, he focused on translating his inventions to clinical practice for improving human healthcare.

This special JIOHS issue includes 15 papers, both original research and review articles, in the field of biomedical photonics, with which we hope to commemorate and carry on the spirit and legacy of Britton Chance.

One of the most important scientific accomplishments by Britton Chance centered on oxygen transport and metabolism in living systems. To translate this information for human health care, quantifying blood oxygenation and flow in the mammalian body had been a very important task for Dr. Chance. He pioneered the development of the optical measurement techniques based on chromophores, e.g., NADH, hemoglobin and cytochromes that respond to oxygen levels. Tissue oxygenation/hypoxia and its relation

to diseases, such as stroke and cancer, was one of the main research interests of Dr. Chance. In this issue, Vaupel and Mayer review the critical issues in imaging tumor hypoxia due to diverse pathogenic mechanisms leading to hypoxia subtypes. Shi *et al.* present work on early identification of the cause of acute hypoxia based on the optical signal patterns of brain NADH fluorescence and cerebral blood flow (CBF) measured by techniques pioneered by Dr. Chance. This work may have significant clinical impact on determining the treatment plan for brain diseases such as stroke and hemorrhage. Lloyd *et al.* present about an alternative approach for oxygenation measurement in biosystems using phosphorescent Ru-embedded nanoparticles.

Understanding mitochondrial metabolism was a lifetime focus of the research of Britton Chance. His research group first observed the fluorescence of NADH and oxidized flavoproteins (Fp) from mitochondria and used them for assessing mitochondrial redox state in cells, tissues and organs. While the history of the research on NADH fluorescence has been well covered in the literature, Hassinen reviews in this issue the history with FP and redox ratios as mitochondrial redox indicators for intact tissue. Furthermore, Xu and Li summarize more recent applications of the Chance redox scanner for cancer diagnosis/prognosis in both animal models and human subjects as well as monitoring treatment response, metabolism and developmental processes. Xu *et al.* also present 3D sub-millimeter imaging of mitochondrial NADH, Fp, and the redox state of rat hearts under normal and overnight starvation conditions. For the first time, they report the observation of NADH decrease in heart tissue induced by dietary restriction. To understand biogeochemical cycles and biodiversity, Powers *et al.* report on the real-time *in situ* detection and quantification of bacteria in the arctic environment using the handheld field-portable fluorescence device that measures cellular NAD(P)H, flavins and a few other molecules in the bacteria.

Since 1990s, the technical development of near infrared (NIR) imaging and spectroscopy was another research focus of Britton Chance. In this issue, Yücel *et al.* present a novel targeted principle component analysis method that can reduce the motion artifacts in the NIR spectroscopy data without significantly filtering out true signals. To extract the spatial resolution information for heterogeneous physiological systems based on the optical data, mathematical models such as finite element and finite difference techniques have been utilized extensively. Guo *et al.* present a numerical method for fluorescence molecular tomography that takes advantage of simplified spherical harmonics approximation. In the past several decade, considerable work has gone into developing luminescent contrast agents to overcome the limitation of utilizing intrinsic fluorescence in the living tissue, such as penetration depth and variance in tissue morphology. The paper by Gainer and Romanowski reviews the state-of-the-art of upconverting lanthanide nanoparticles used for this purpose and describes a few which show favorable attributes.

Translating physical techniques to clinical practice for disease diagnosis and prognosis and helping patients has always been a pursuit of Britton Chance. In this issue, Andrews *et al.* describe the new application of optical coherence tomography (OCT) to evaluate the ischemic insult in kidney during transplantation. OCT can visualize tissue microstructure and quantify blood flow, and thereby provide new information for predicting transplant organ viability. Zhang *et al.* describe the application of near infrared spectroscopy (NIRS) as a potentially effective, real-time monitoring tool for patients with obstructive sleep apnea syndrome. They identified oscillatory brain hemodynamics associated with periodical apnea events in control patients, and these features disappeared when the patients were treated with the continuous positive airways pressure therapy.

This special issue also includes three commemorative articles on Britton Chance's life time and legacy. Kang vividly reflects her experience under the tutelage of Dr. Chance, including the daily life of Dr. Chance, and how his teaching has impacted and shaped her scientific career. She successfully applied the NIR techniques acquired from Dr. Chance to molecular sensing using nanotechnology. Liu *et al.* reflect on the life of Britton Chance from the perspective of longevity, discussing various factors in the life style of Dr. Chance that contribute to his longevity. With a scientometric approach, Li *et al.* review the scientific achievements of Dr. Chance, and illustrate his scientific impact by the detailed analyses on his annual publications and citations, top cited papers, coauthors, etc.

Lastly, we would like to acknowledge the support and help from Dr. Shoko Nioka and many other friends and colleagues who have contributed significantly to the Britton Chance Centennial Celebration.

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