

Advances in Experimental Medicine and Biology 1232

Pan-Dong Ryu  
Joseph C. LaManna  
David K. Harrison  
Sang-Suk Lee *Editors*

# Oxygen Transport to Tissue XLI



Springer

# **Advances in Experimental Medicine and Biology**

Volume 1232

## **Series Editors**

Wim E. Crusio, *CNRS and University of Bordeaux UMR 5287, Institut de  
Neurosciences Cognitives et Intégratives d'Aquitaine, Pessac Cedex, France*

John D. Lambris, *University of Pennsylvania, Philadelphia, PA, USA*

Nima Rezaei, *Children's Medical Center, Tehran, University of Medical  
Sciences, Tehran, Iran*

More information about this series at <http://www.springer.com/series/5584>

Pan-Dong Ryu • Joseph C. LaManna  
David K. Harrison • Sang-Suk Lee  
Editors

# Oxygen Transport to Tissue XLI

 Springer

### *Editors*

Pan-Dong Ryu  
Department of Veterinary Pharmacology  
College of Veterinary Medicine  
Seoul National University  
Seoul, Republic of Korea

Joseph C. LaManna  
Department of Physiology and Biophysics  
School of Medicine  
Case Western Reserve University  
Cleveland, OH, USA

David K. Harrison  
Heilig-Kreuz-Strasse 19  
St. Lorenzen, Italy

Sang-Suk Lee  
Department of Oriental Biomedical  
Engineering  
Sangji University  
Wonju, Republic of Korea

ISSN 0065-2598

ISSN 2214-8019 (electronic)

Advances in Experimental Medicine and Biology

ISBN 978-3-030-34459-7

ISBN 978-3-030-34461-0 (eBook)

<https://doi.org/10.1007/978-3-030-34461-0>

© Springer Nature Switzerland AG 2020, Corrected Publication 2020

The chapters “Near-Infrared Spectroscopy Measured Cerebral Blood Flow from Spontaneous Oxygenation Changes in Neonatal Brain Injury”, “Developing a Model to Simulate the Effect of Hypothermia on Cerebral Blood Flow and Metabolism” and “Broadband NIRS Cerebral Evaluation of the Hemodynamic and Oxidative State of Cytochrome-c-Oxidase Responses to +Gz Acceleration in Healthy Volunteers” are licensed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>). For further details see license information in the chapter.

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

# The Heritage, Foundation, Mission and Legacy of ISOTT

Prior to the 1960s, it was almost unheard of for medical scientists and engineering scientists to collaborate on important medical research problems. It was during the 1960s that the concept of bioengineering was born. At that time, the research between Dr. Melvin H. Knisely's group at the Medical University of South Carolina and Dr. Duane F. Bruley's group at Clemson University focused on oxygen transport problems inspired the creation of ISOTT at the Clemson-Charleston founding meeting in 1973. In that same era, three of the traditional engineering disciplines, civil, mechanical, and electrical, were based primarily on physics and mathematics, and the fourth discipline, chemical engineering, was based on physics, chemistry, and mathematics. The fifth traditional discipline of engineering, bioengineering, was evolving and it was based on biology, in addition to the other basic sciences and mathematics.<sup>1</sup>

- The *heritage* of ISOTT lies directly in the established four traditional disciplines of engineering, the three basic sciences, the fundamental medical sciences, and mathematics. Until the 1960s, these disciplines were totally separate, except for rare instances, and not formalized as an approach to solving important medical problems.
- The *foundation* of our society was designed to bring teams of medical and engineering scientists together working on problems related to oxygen transport to tissues. The meetings were designed to promote inter- and cross-disciplinary research projects. Rather than break out into individual sessions, the meeting was to be held in one large venue that would hold all participants. This was done to enhance interactions and understandings of important medical issues related to oxygen transport to tissue.
- The mission of our society was conceived to promote collaboration between the medical sciences and engineering sciences to assemble more sophisticated teams

---

<sup>1</sup>Bruley, D.F., "Bioengineering: The Fifth Traditional Engineering Discipline," *Oxygen Transport to Tissue XIV*, Advances in Experimental Medicine and Biology, vol. 317, p. 3–6, 1992, Plenum Press

to understand and solve medical problems related to oxygen supply and utilization in human tissue.

- The legacy of ISOTT will be its pioneering involvement in the formalization of the fifth traditional discipline of engineering, bioengineering. Secondly, its leadership as a focused and international research society to formulate and solve crucial medical problems related to oxygen transport in human health makes it important in reducing human suffering and mortality.

The author has prepared this document to inform our new as well as older members of the planning that went into establishing a meaningful society that enhances medical research. He hopes that ISOTT was and will continue to be a unique and high-level research organization that inspires and supports collaborative research on oxygen-related issues.

D. F. Bruley  
Synthesizer, Inc.  
Ellicott City, MD, USA

# Preface

This volume is the publication of papers presented at the 46th annual meeting of the International Society on Oxygen Transport to Tissue (ISOTT) 2018 held in Seoul, Republic of Korea, from July 1 to July 5, 2018. It contains research results and perspectives on the transport of oxygen to tissues presented by the scientists in the multiple disciplines as did in the previous volumes. The papers in this book have been subjected to peer review by the leading experts in this area.

The meeting brought 122 participants including 30 students from 12 countries in Asia, Europe, and North America. The meeting was opened on Sunday July 1, 2018, with a welcome by Dr. Pan-Dong Ryu (President, ISOTT 2018), and followed by opening lecture of Dr. Kwang-Sup Soh, “Current Developments in the Primo Vascular System and Oxygen.” He overviewed the research on the system and its relation to oxygen transport. The lecture was followed by the cultural event “Hidden Wonders of Korea” providing an opportunity for the participants to experience Korean culture.

In the scientific sessions, various key aspects of “oxygen transport to tissue” were addressed, as in previous meetings. The themes of the 11 oral presentation sessions were oxygenation theory and methods, NIRS methods, oximetry methods, brain disease, tumor 1 and 2, brain oxygenation 1 and 2, blood vessels, special topics (primo vascular system), and complementary and alternative medicine. In these sessions, there were 41 oral presentations, 9 keynote lectures, and 1 Peter Vaupel Lecture. Dr. G. Multhoff delivered the Peter Vaupel lecture under the title “Hypoxia Compromises Anti-cancer Immune Responses.” A total of 56 posters were presented for two day sessions, and the contents of each poster were introduced in a 2-minute oral presentation in two poster flash sessions.

ISOTT 2018 hosted two evening get-togethers on the second and third days of the program. The July 2 event was held at Hoam Faculty House of Seoul National University, where various fusion dishes and beer and other refreshments were served. The July 3 get-together was held at a Korean food buffet restaurant (Nature Kitchen). This brought participants a time to mingle as well as a chance to sample various types of Korean foods popular among Seoulites. In addition, ISOTT 2018 offered two sight-seeing trips on the afternoon of July 4: one to visit historic sites,

including UNESCO World Heritage sites, and another to see dynamic new locations, including Seoul Sky Observatory.

The conference concluded on July 5 with the Annual General Meeting of ISOTT and an awards ceremony and banquet. At the awards ceremony, the Melvin H. Knisely Award was presented to Anne Riemann, the Dietrich W. Lübbers Award to Hamoon Zohdi, and the Britton Chance Award to Jingjing Jiang. In addition, six Duane F. Bruley Travel Awards were presented to junior scientists: Andrei Belten, Dries Hendrikx, Yuki Komuro, Aldo Di Costanzo Mata, Joshua Russell-Buckland, and Shun Takagi. After the Awards Ceremony, the evening ended with a banquet where participants could enjoy food, drinks, and jazz played on a “Piri,” a Korean traditional reed instrument, by crossover music group “Oriental Scholar.”

We like to thank all the participants of ISOTT 2018. We acknowledge the great work done by the members of the local organizing and working committees (Sungchul Kim, So Yeong Lee, Ku Youn Baik, Ji Yoon Lee, Chae Jeong Lim), the session chairs, and the student supporters. We thank the ISOTT officers, including Dr. Oliver Thews and Harold M. Swartz, for their invaluable advice and support during the preparation of ISOTT 2018. Finally, we also thank those of our participants who submitted their manuscripts and the reviewers who improved the quality and significance of those papers. All these efforts made this volume come to its fruition.

Wonju, Republic of Korea  
Seoul, Republic of Korea

Sang-Suk Lee  
Pan-Dong Ryu

# Acknowledgments

As the president of the 46th Annual Meeting of the International Society on Oxygen Transport to Tissue, held on July 1–5, 2018, in Seoul, Republic of Korea, I would like to gratefully acknowledge the generous support of our sponsors.



서울대학교 수의과대학  
College of Veterinary Medicine  
<http://vet.snu.ac.kr>

**OBELAB<sup>®</sup>**

<http://www.obelab.com>



<http://scitechkorea.com>



**BrainKorea21<sup>PLUS</sup>**

<http://vetgrad.snu.ac.kr>



국가마우스표현형분석사업단  
KOREA MOUSE  
PHENOTYPING CENTER

<http://www.mousephenotype.kr>



<http://www.bio-d.co.kr>



<http://www.kangstem.com>



WONKWANG UNIVERSITY MEDICAL CENTER, GWANGJU

**A.L.S CENTER**

<http://wkugh.com>

**KSPVS**

Korean Society of Primo Vascular System



**대한수의학회**

The Korean Society of Veterinary Science

<http://www.ksvs.or.kr>

# Panel of Reviewers

| Reviewer                | Affiliation                                                            |
|-------------------------|------------------------------------------------------------------------|
| Ku Youn Baik            | Kwangwoon University, Seoul, Republic of Korea                         |
| Gemma Bale              | University College London, UK                                          |
| Denis Bragin            | University of New Mexico, Albuquerque, USA                             |
| Ann Flood               | EPR Center at Dartmouth, Hanover, USA                                  |
| Howard Halpern          | University of Chicago, USA                                             |
| David Harrison          | Microvascular Measurements, St. Lorenzen, Italy                        |
| Peter Keipert           | PAREXEL, San Diego, USA                                                |
| Sungchul Kim            | Wonkwang University Gwangju Korean Medical Hospital, Republic of Korea |
| Sung Joon Kim           | Seoul National University, Republic of Korea                           |
| Joseph LaManna          | Case Western Reserve University, Cleveland, USA                        |
| Fredéric Lange          | University College London, UK                                          |
| Ji Yoon Lee             | CHA University, Seongnam, Republic of Korea                            |
| Sang-Suk Lee            | Sangji University, Wonju, Republic of Korea                            |
| So Yeong Lee            | Seoul National University, Republic of Korea                           |
| Lin Li                  | University of Pennsylvania, Philadelphia, USA                          |
| Timon Cheng-Yi Liu      | South China Normal University, Guangzhou, China                        |
| Subhabrata Mitra        | University College London, UK                                          |
| Gabriele Multhoff       | Technical University Munich, Germany                                   |
| Edwin Nemoto            | University of New Mexico, Albuquerque, USA                             |
| Daniel Ostojic          | University of Zurich, Switzerland                                      |
| Sally Pias              | New Mexico Tech, Socorro, USA                                          |
| Michelle Puchowicz      | University of Tennessee Health Science Centre, Memphis, USA            |
| Anne Reimann            | University of Halle, Germany                                           |
| Joshua Russell-Buckland | University College London, UK                                          |
| Pan-Dong Ryu            | Seoul National University, Republic of Korea                           |
| Gennadi Saiko           | Oxilight Inc., Toronto, Canada                                         |
| Kaoru Sakatani          | Nihon University School of Medicine, Tokyo, Japan                      |

(continued)

| Reviewer                        | Affiliation                                              |
|---------------------------------|----------------------------------------------------------|
| Felix Scholkmann                | University of Bern and University of Zurich, Switzerland |
| Oxana Semyachkina-Glushkovskaya | Saratov State University, Russia                         |
| Harold Swartz                   | EPR Center at Dartmouth, Hanover, USA                    |
| Ilias Tachtsidis                | University College London, UK                            |
| Shun Takagi                     | Doshisha University, Kyoto, Japan                        |
| Oliver Thews                    | University of Halle, Germany                             |
| Atsuhiko Tsubaki                | Niigata University, Japan                                |
| Peter Vaupel                    | University Medical Center, Mainz, Germany                |
| Martin Wolf                     | University of Zurich, Switzerland                        |
| Ursula Wolf                     | University of Bern, Switzerland                          |
| Sung-Joon Ye                    | Seoul National University, Republic of Korea             |

**Technical Reviewer**

|                      |                            |
|----------------------|----------------------------|
| Laraine Visser-Isles | Rotterdam, the Netherlands |
| Eileen Harrison      | St. Lorenzen, Italy        |

# ISOTT Participants at the Seoul National University



## Local Organizing Committee

Pan-Dong Ryu  
Hyeon-Min Bae  
Ku Youn Baik  
Hee Young Kim  
Sungchul Kim  
Sung Joon Kim  
Sang-Suk Lee  
So Yeong Lee  
Ji Yoon Lee  
Su Ho Park  
Sung-Joon Ye  
Chae Jeong Lim

## Scientific Committee

Pan-Dong Ryu, Seoul National University, Republic of Korea  
Sungchul Kim, Wonkwang University, Republic of Korea  
Sang-Suk Lee, Sangji University, Republic of Korea  
Terence Leung, University College London, UK  
Lin Li, University of Pennsylvania, USA  
Sally Pias, New Mexico Tech, USA  
Eiji Takahashi, Saga University, Japan  
Oliver Thews, Martin Luther University Halle-Wittenberg, Germany  
Martin Wolf, University of Zurich, Switzerland

# ISOTT Officers and Executive Committee

## **President**

Name: Pan-Dong Ryu  
Country: Republic of Korea  
Telephone: (+82) 2-880-1254  
Fax: (+82) 2-879-0378  
Email: pdryu@snu.ac.kr

## **Past President**

Name: Oliver Thews  
Country: Germany  
Telephone: (+49) 345 557-4048  
Fax: (+49) 345 557-4019  
Email: oliver.thews@medizin.uni-halle.de

## **Presidents-Elect**

Name: Edwin M. Nemoto  
Country: USA  
Telephone: (+1) 505-272-5990  
Fax: (+1) 505-272-6091  
Email: Enemoto@salud.unm.edu

## **Secretary**

Name: Oliver Thews  
Country: Germany  
Telephone: (+49) 345-557-4048  
Fax: (+49) 345-557-4019  
Email: oliver.thews@medizin.uni-halle.de

**Treasurer**

Name: Peter Keipert

Country: USA

Phone: (+1) 858-699-4789

Fax: (+1) 858-792-7489

Email: peterkeipert@gmail.com

**Chairman, Knisely Award Committee**

Name: Duane F. Bruley

Country: USA

Telephone: (+1) 410-313-9939

Fax: F: (+1) 410-313-9939

Email: bruley33@verizon.net

**Executive Committee**

Boris Epel (USA)

Edwin M. Nemoto (USA)

Sally Pias (USA)

Michelle A. Puchowicz (USA)

Anne Riemann (Germany)

Kaoru Sakatani (Japan)

Harold M. Swartz (USA)

Ursula Wolf (Switzerland)

Karen A. Yilmaz (USA)

# ISOTT Award Winners

## The Melvin H. Knisely Award

The Melvin H. Knisely Award was established in 1983 to honor Dr. Knisely's accomplishments in the field of the transport of oxygen and other metabolites and anabolites in the human body. Over the years, he has inspired many young investigators, and this award is to honor his enthusiasm for assisting and encouraging young scientists and engineers in various disciplines. The award is to acknowledge outstanding young investigators. It was first presented during the banquet of the 1983 annual conference of ISOTT in Ruston, Louisiana. The award includes a Melvin H. Knisely plaque and a cash prize.

## Melvin H. Knisely Award Recipients

|      |                                |
|------|--------------------------------|
| 1983 | Antal G. Hudetz (Hungary)      |
| 1984 | Andras Eke (Hungary)           |
| 1985 | Nathan A. Bush (USA)           |
| 1986 | Karlfried Groebe (Germany)     |
| 1987 | Isumi Shibuya (Japan)          |
| 1988 | Kyung A. Kang (Korea/USA)      |
| 1989 | Sanja Batra (Canada)           |
| 1990 | Stephen J. Cringle (Australia) |
| 1991 | Paul Okunieff (USA)            |
| 1992 | Hans Degens (the Netherlands)  |
| 1993 | David A. Benaron (USA)         |
| 1994 | Koen van Rossem (Belgium)      |
| 1995 | Clare E. Elwell (UK)           |
| 1996 | Sergei A. Vinogradov (USA)     |
| 1997 | Chris Cooper (UK)              |
| 1998 | Martin Wolf (Switzerland)      |

|      |                                    |
|------|------------------------------------|
| 1999 | Huiping Wu (USA)                   |
| 2000 | Valentina Quaresima (Italy)        |
| 2001 | Fahmeed Hyder (Bangladesh)         |
| 2002 | Geofrey De Visscher (Belgium)      |
| 2003 | Mohammad Nadeem Khan (USA)         |
| 2004 | Fredrik Palm (Sweden)              |
| 2005 | Nicholas Lintell (Australia)       |
| 2006 | –                                  |
| 2007 | Ilias Tachtsidis (UK)              |
| 2008 | Kazuto Masamoto (Japan)            |
| 2009 | Rossana Occhipinti (USA)           |
| 2010 | Sebastiano Cicco (Italy)           |
| 2011 | Mei Zhang (USA)                    |
| 2012 | Takahiro Igarashi (Japan)          |
| 2013 | Malou Friederich-Persson (Sweden)  |
| 2014 | David Highton (UK)                 |
| 2015 | Alexander Caicedo Dorado (Belgium) |
| 2016 | Sally Pias (USA)                   |
| 2017 | Felix Scholkmann (Switzerland)     |
| 2018 | Anne Riemann (Germany)             |

## **The Dietrich W. Lübbers Award**

The Dietrich W. Lübbers Award was established in honor of Professor Lübbers' long-standing commitment, interest, and contributions to the problems of oxygen transport to tissue and to the society. This award was first presented in 1994 during the annual conference of ISOTT in Istanbul, Turkey.

## **Dietrich W. Lübbers Award Recipients**

|      |                           |
|------|---------------------------|
| 1994 | Michael Dubina (Russia)   |
| 1995 | Philip E. James (UK/USA)  |
| 1996 | Resit Demir (Germany)     |
| 1997 | Juan Carlos Chavez (Peru) |
| 1998 | Nathan A. Davis (UK)      |
| 1999 | Paola Pichiule (USA)      |
| 2000 | Ian Balcer (USA)          |
| 2001 | Theresa M. Busch (USA)    |
| 2002 | Link K. Korah (USA)       |
| 2003 | James J. Lee (USA)        |

|      |                                    |
|------|------------------------------------|
| 2004 | Richard Olson (Sweden)             |
| 2005 | Charlotte Ives (UK)                |
| 2006 | Bin Hong (China/USA)               |
| 2007 | Helga Blockx (Belgium)             |
| 2008 | Joke Vanderhaegen (Belgium)        |
| 2009 | Matthew Bell (UK)                  |
| 2010 | Alexander Caicedo Dorado (Belgium) |
| 2011 | Malou Friederich-Persson (Sweden)  |
| 2012 | Maria Papademetriou (UK)           |
| 2013 | Nannan Sun (China/USA)             |
| 2014 | Felix Scholkmann (Switzerland)     |
| 2015 | Shun Takagi (Japan)                |
| 2016 | Gemma Bale (UK)                    |
| 2017 | Ben Jones (UK)                     |
| 2018 | Hamoon Zohdi (Switzerland)         |

## **The Britton Chance Award**

The Britton Chance Award was established in honor of Professor Chance's long-standing commitment, interest, and contributions to the science and engineering aspects of oxygen transport to tissue and to the society. This award was first presented in 2004 during the annual conference of ISOTT in Bari, Italy.

## **Britton Chance Award Recipients**

|      |                                    |
|------|------------------------------------|
| 2004 | Derek Brown (Switzerland)          |
| 2005 | James Lee (USA)                    |
| 2006 | Hanzhu Jin (China/USA)             |
| 2007 | Eric Mellon (USA)                  |
| 2008 | Jianting Wang (USA)                |
| 2009 | Jessica Spires (USA)               |
| 2010 | Ivo Trajkovic (Switzerland)        |
| 2011 | Alexander Caicedo Dorado (Belgium) |
| 2012 | Felix Scholkmann (Switzerland)     |
| 2013 | Tharindi Hapuarachchi (UK)         |
| 2014 | Anne Riemann (Germany)             |
| 2015 | Wenhao Xie (China)                 |
| 2016 | Linda Ahnen (Switzerland)          |
| 2017 | Helene Isler (Switzerland)         |
| 2018 | Jingjing Jiang (Switzerland)       |

## The Duane F. Bruley Travel Awards

The Duane F. Bruley Travel Awards was established in 2003 and first presented by ISOTT at the 2004 annual conference in Bari, Italy. This award was created to provide travel funds for student researchers in all aspects of oxygen transport to tissue. The awards signify Dr. Bruley's interest in encouraging and supporting young researchers to maintain the image and quality of research associated with the society. As a cofounder of ISOTT in 1973, Dr. Bruley emphasizes cross-disciplinary research among basic scientists, engineers, medical scientists, and clinicians. His pioneering work constructing mathematical models for oxygen and other anabolite/metabolite transport in the micro-circulation, employing computer solutions, was the first to consider system nonlinearities and time dependence, including multidimensional diffusion, convection, and reaction kinetics. It is hoped that receiving the Duane F. Bruley Travel Award will inspire students to excel in their research and will assist in securing future leadership for ISOTT.

## The Duane F. Bruley Travel Award Recipients

- 2004 Helga Blockx (Belgium), Jennifer Caddick (UK), Charlotte Ives (UK), Nicholas Lintell (Australia), Leonardo Mottola (Italy), Samin Rezanian (USA/Iran), Ilias Tachtsidis (UK), Liang Tang (USA/China), Iyichi Sonoro (Japan), Antonio Franco (Italy)
- 2005 Robert Bradley (UK), Harald Oey (Australia), Kathy Hsieh (Australia), Jan Shah (Australia)
- 2006 Ben Gooch (UK), Ulf Jensen (Germany), Smruta Koppaka (USA), Daya Singh (UK), Martin Tisdall (UK), Bin Wong (USA), and Kui Xu (USA)
- 2007 Dominique De Smet (Belgium), Thomas Ingram (UK), Nicola Lai (USA), Andrew Pinder (UK), Joke Vanderhaegen (Belgium)
- 2008 Sebastiano Cicco (Italy)
- 2009 Lei Gao (UK), Jianting Wang (USA), Obinna Ndubizu (USA), Joke Vanderhaegen (Belgium)
- 2010 Zareen Bashir (UK), Tracy Moroz (UK), Mark Muthalib (Australia), Catalina Meßmer (USA), Takashi Eriguchi (Japan), Yoshihiro Murata (Japan), Jack Honeysett (UK), Martin Biallas (Switzerland)
- 2011 Catherine Hesford (UK), Luke S. Holdsworth (UK), Andreas Metz (Switzerland), Maria D. Papademetriou (UK), Patrik Persson (Sweden), Felix Scholkmann (Switzerland), Kouichi Yoshihara (Japan)
- 2012 Allann Al-Armaghany (UK), Malou Friederich-Persson (Sweden), Tharindi Hapuarachchi (UK), Benjamin Jones (UK), Rebecca Re (Italy), Yuta Sekiguchi (Japan), Ebba Sivertsson (Sweden), Andre' Steimers (Germany)
- 2013 Allann Al-Armaghany (UK), Gemma Bale (UK), Alexander Caicedo Dorado (Belgium), Luke Dunne (UK)
- 2014 Geraldine De Preter (Belgium), Benjamin Jones (UK), Stefan Kleiser (Switzerland), Nassimsadat Nasser (Switzerland), Marie-Aline Neveu (Belgium), Shinsuke Nirengi (Japan), Takuya Osawa (Japan)

- 2015 Nannan Sun (China), Gemma Bale (UK), Chenyang Gao (China), Guennadi Saiko (Canada), Kuangyu Shi (Germany), Phong Phan (UK), Chae Jeong Lim (Korea)
- 2016 Isabel De Roever (UK), Yuya Enokida (Japan), Jingjing Jiang (Switzerland), Frédéric Lange (UK), Andreas J. Metz (Switzerland), Shun Takagi (Japan)
- 2017 Luca Giannoni (UK), Jingjing Jiang (Switzerland), Alexander Kalyanov (Switzerland), Zuzana Kovacsova (UK), Nassim Nasser (Switzerland), Maheen Faisal Siddiqui (UK), Shun Takagi (Japan), Yusuke Tsuruno (Japan), Lina Xu (Germany), Hamoon Zohdi (Switzerland)
- 2018 Andrei Belten (Canada), Dries Hendrikx (Belgium), Yuki Komuro (Japan), Aldo Di Costanzo Mata (Switzerland), Joshua Russell-Buckland (UK), and Shun Takagi (Japan)

## **Kováč Lecture**

The Kováč Lecture is presented periodically to honor a career dedicated to oxygenation research. Arisztid Kováč was a world-renowned cardiovascular physiologist and one of the early leaders of ISOTT. This lecture is dedicated to his remarkable scientific and teaching career.

## **Kováč Lecture Recipients**

- 2011 John Severinghaus  
2012 Peter Vaupel  
2014 Edwin Nemoto

## **Peter Vaupel Lecture**

The Peter Vaupel Lecture is presented to honor a career dedicated to oxygenation research. Peter Vaupel is a world-renowned tumor pathophysiologist and one of the early leaders of ISOTT. This lecture is dedicated to his remarkable scientific and teaching career.

## **Peter Vaupel Lecture Recipients**

- 2018 Gabriele Multhoff

# Contents

## Part I Brain Oxygenation and Function

|                                                                                                                                                             |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| <b>Near-Infrared Spectroscopy Measured Cerebral Blood Flow from Spontaneous Oxygenation Changes in Neonatal Brain Injury</b> . . . . .                      | 3  |
| Gemma Bale, Nathan Taylor, Subhabrata Mitra, Aleh Sudakou, Isabel de Roever, Judith Meek, Nicola Robertson, and Ilias Tachtsidis                            |    |
| <b>Nonlinear Transfer Entropy to Assess the Neurovascular Coupling in Premature Neonates</b> . . . . .                                                      | 11 |
| Dries Hendrikx, Liesbeth Thewissen, Anne Smits, Gunnar Naulaers, Karel Allegaert, Sabine Van Huffel, and Alexander Caicedo                                  |    |
| <b>Reference Value of Brain Tissue Oxygen Saturation in Newborns Immediately After Birth</b> . . . . .                                                      | 19 |
| Ryota Kato, Shigeharu Hosono, and Syori Takahashi                                                                                                           |    |
| <b>Changes in Brain Tissue Oxygenation and Metabolism During Rewarming After Neonatal Encephalopathy are Related to Electrical Abnormality</b> . . . . .    | 25 |
| Subhabrata Mitra, Gemma Bale, Isabel de Roever, Judith Meek, Nicola J. Robertson, and Ilias Tachtsidis                                                      |    |
| <b>Impact of Skull Thickness on Cerebral NIRS Oximetry in Neonates: An <i>in silico</i> Study</b> . . . . .                                                 | 33 |
| D. Ostojic, J. Jiang, H. Isler, S. Kleiser, T. Karen, M. Wolf, and F. Scholkmann                                                                            |    |
| <b>Resuscitation with Drag Reducing Polymers after Traumatic Brain Injury with Hemorrhagic Shock Reduces Microthrombosis and Oxidative Stress</b> . . . . . | 39 |
| Denis E. Bragin, Olga A. Bragina, Marina V. Kameneva, and Edwin M. Nemoto                                                                                   |    |

|                                                                                                                                                                                    |     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| <b>Anodal Transcranial Direct Current Stimulation Improves Impaired Cerebrovascular Reactivity in Traumatized Mouse Brain</b> .....                                                | 47  |
| Olga A. Bragina, Oxana V. Semyachkina-Glushkovskaya,<br>Edwin M. Nemoto, and Denis E. Bragin                                                                                       |     |
| <b>Comparative Analysis of Simultaneous Transcranial Doppler and Perfusion Computed Tomography for Cerebral Perfusion Evaluation in Patients with Traumatic Brain Injury</b> ..... | 55  |
| Alex Trofimov, Artem Kopylov, Michael Dobrzeniecki,<br>Anatoly Sheludyakov, Dmitry Martynov, Kseniia Trofimova,<br>Darya I. Agarkova, and Denis E. Bragin                          |     |
| <b>Meningeal Lymphatic Pathway of Brain Clearing From the Blood After Haemorrhagic Injuries</b> .....                                                                              | 63  |
| O. Semyachkina-Glushkovskaya, N. Navolokin, A. Shirokov,<br>A. Terskov, A. Khorovodov, A. Mamedova, M. Klimova, E. Rafailov,<br>and J. Kurths                                      |     |
| <b>Relationship Between Cerebral Oxygenation and Skin Blood Flow at the Frontal Lobe during Progressive Hypoxia: Impact of Acute Hypotension</b> .....                             | 69  |
| Masahiro Horiuchi, Junko Endo, and Yoko Handa-Kirihra                                                                                                                              |     |
| <b>Cerebral Autoregulation During Active Standing Test in Juvenile Patients with Instantaneous Orthostatic Hypotension</b> .....                                                   | 77  |
| Wakako Ishii, Yukihiro Fujita, Tadayasu Kawaguchi, Kaori Kimura,<br>Ayumi Fukuda, Tatsuo Fuchigami, and Ichiro Morioka                                                             |     |
| <b>Cerebral Blood Oxygenation Changes in Juvenile Patients with Delayed Orthostatic Hypotension During an Active Standing Test</b> .....                                           | 85  |
| T. Kawaguchi, Y. Fujita, W. Ishii, K. Kimura, A. Fukuda, T. Fuchigami,<br>and I. Morioka                                                                                           |     |
| <b>Relationship Between Cognitive Dysfunction and Systemic Metabolic Disorders in Elderly: Dementia Might be a Systematic Disease</b> .....                                        | 91  |
| Y. Komuro, K. Oyama, L. Hu, and K. Sakatani                                                                                                                                        |     |
| <b>Relationship Between Cerebral Blood Oxygenation and Electrical Activity During Mental Stress Tasks: Simultaneous Measurements of NIRS and EEG</b> .....                         | 99  |
| Y. Nagasawa, M. Ishida, Y. Komuro, S. Ushioda, L. Hu, and K. Sakatani                                                                                                              |     |
| <b>Right-Left Asymmetry of Prefrontal Cerebral Oxygenation: Does it Depend on Systemic Physiological Activity, Absolute Tissue Oxygenation or Hemoglobin Concentration?</b> .....  | 105 |
| Felix Scholkmann, Hamoon Zohdi, and Ursula Wolf                                                                                                                                    |     |

|                                                                                                                                                                                                     |            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Effect of Gum Chewing on PFC Activity During Discomfort Sound Stimulation. . . . .</b>                                                                                                           | <b>113</b> |
| M. Konno, K. Nakajima, T. Takeda, Y. Kawano, Y. Suzuki, and K. Sakatani                                                                                                                             |            |
| <b>Effect of Mastication Muscle Activity on Prefrontal Cortex NIRS Measurement: A Pilot Study . . . . .</b>                                                                                         | <b>121</b> |
| Kazunori Nakajima, Tomotaka Takeda, Maho Saito, Michiyo Konno, Yoshiaki Kawano, Yoshihiro Suzuki, Masayasu Nishino, Yoshiaki Matsuda, Keiichi Ishigami, and Kaoru Sakatani                          |            |
| <b>Part II Tumor Oxygenation and Metabolism</b>                                                                                                                                                     |            |
| <b>Hypoxia Compromises Anti-Cancer Immune Responses . . . . .</b>                                                                                                                                   | <b>131</b> |
| Gabriele Multhoff and Peter Vaupel                                                                                                                                                                  |            |
| <b>‘Oxygen Level in a Tissue’ – What Do Available Measurements Really Report? . . . . .</b>                                                                                                         | <b>145</b> |
| H. M. Swartz, P. Vaupel, B. B. Williams, P. E. Schaner, B. Gallez, W. Schreiber, A. Ali, and A. B. Flood                                                                                            |            |
| <b>Clinical and Statistical Considerations when Assessing Oxygen Levels in Tumors: Illustrative Results from Clinical EPR Oximetry Studies . . . .</b>                                              | <b>155</b> |
| A. B. Flood, P. E. Schaner, P. Vaupel, B. B. Williams, B. Gallez, E. Y. Chen, A. Ali, T. Liu, V. H. Lawson, W. Schreiber, and H. M. Swartz                                                          |            |
| <b>Fatal Alliance of Hypoxia-/HIF-1<math>\alpha</math>-Driven Microenvironmental Traits Promoting Cancer Progression. . . . .</b>                                                                   | <b>169</b> |
| Peter Vaupel and Gabriele Multhoff                                                                                                                                                                  |            |
| <b>Quantification of Tumor Oxygenation Based on FMISO PET: Influence of Location and Oxygen Level of the Well-Oxygenated Reference Region. . . . .</b>                                              | <b>177</b> |
| M. Lazzeroni, I. Toma-Dasu, A. Ureba, F. Schiavo, N. Wiedenmann, H. Bunea, B. Thomann, D. Baltas, M. Mix, C. Stoykow, A. Sörensen, and A. L. Grosu                                                  |            |
| <b>Pathways of Oxygen Diffusion in Cells and Tissues . . . . .</b>                                                                                                                                  | <b>183</b> |
| Sally C. Pias                                                                                                                                                                                       |            |
| <b>Part III Muscle Oxygenation and Sports Medicine</b>                                                                                                                                              |            |
| <b>Effect of Exercise Duration on Post-Exercise Persistence of Oxyhemoglobin Changes in the Premotor Cortex: A Near-Infrared Spectroscopy Study in Moderate-Intensity Cycling Exercise. . . . .</b> | <b>193</b> |
| Atsuhiko Tsubaki, Shinichiro Morishita, Yuta Tokunaga, Daisuke Sato, Weixiang Qin, Sho Kojima, and Hideaki Onishi                                                                                   |            |

|                                                                                                                                                                         |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| <b>Relationship Between Muscle Oxygen Saturation and Exercise Load in Patients with Malignant Hematopoietic Disease</b> . . . . .                                       | 201 |
| Tatsushi Wakasugi, Shinichiro Morishita, Katsuji Kaida, Yusuke Itani, Kazuhiro Ikegame, Norihiko Kodama, Hiroyasu Ogawa, Yoshihiro Fujimori, and Kazuhisa Domen         |     |
| <b>Comparison of the Effects of Continuous and Intermittent Exercise on Cerebral Oxygenation and Cognitive Function</b> . . . . .                                       | 209 |
| Yuya Ichinose, Shinichiro Morishita, Rio Suzuki, Gaku Endo, and Atsuhiko Tsubaki                                                                                        |     |
| <b>Relationship Between Exercise Capacity and Muscle O<sub>2</sub>Hb Saturation in Patients Before Hematopoietic Stem-Cell Transplantation</b> . . . . .                | 215 |
| Shinichiro Morishita, Tatsushi Wakasugi, Katsuji Kaida, Yusuke Itani, Kazuhiro Ikegame, Hiroyasu Ogawa, Yoshihiro Fujimori, and Kazuhisa Domen                          |     |
| <b>Differences in Muscle O<sub>2</sub> Dynamics During Treadmill Exercise Between Aerobic Capacity-Matched Overweight and Normal-Weight Adults</b> . . . . .            | 223 |
| Shun Takagi, Ryotaro Kime, Taishi Midorikawa, Masatsugu Niwayama, Shizuo Sakamoto, and Toshihito Katsumura                                                              |     |
| <b>Cerebral Oxygenation Dynamics of the Prefrontal Cortex and Motor-Related Area During Cardiopulmonary Exercise Test: A Near-Infrared Spectroscopy Study</b> . . . . . | 231 |
| Sho Kojima, Shinichiro Morishita, Weixiang Qin, and Atsuhiko Tsubaki                                                                                                    |     |
| <b>Reduced Optical Path Length in the Vastus Lateralis During Ramp Cycling Exercise.</b> . . . .                                                                        | 239 |
| Tasuki Endo, Ryotaro Kime, Tsubasa Watanabe, Sayuri Fuse, Norio Murase, Yuko Kurosawa, and Takafumi Hamaoka                                                             |     |
| <b>Improvements in Skeletal Muscle Can Be Detected Using Broadband NIRS in First-Time Marathon Runners.</b> . . . .                                                     | 245 |
| Siana Jones, Matthew Kinsella, Camilla Torlasco, Pardis Kaynezhad, Isabel de Roever, James C. Moon, Alun D. Hughes, and Gemma Bale                                      |     |
| <b>Comparison of Two NIRS Tissue Oximeters (Moxly and Nimo) for Non-Invasive Assessment of Muscle Oxygenation and Perfusion.</b> . . . .                                | 253 |
| Felix Scholkmann and Andrea Scherer-Vrana                                                                                                                               |     |

#### **Part IV Cell Metabolism and Tissue Oxygenation**

|                                                                                                               |     |
|---------------------------------------------------------------------------------------------------------------|-----|
| <b>Effects of Pulsed Magnetic Field on the Hemolysis of Erythrocytes Exposed to Oxidative Stress.</b> . . . . | 263 |
| Hyoje Ahn, Kyunghun Shin, and Hyunsook Lee                                                                    |     |

|                                                                                                                                                                                                                                                             |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| <b>Role of Microtubule-Associated Factors in HIF1<math>\alpha</math> Nuclear Translocation</b> . . . . .                                                                                                                                                    | 271 |
| Hyun Jik Lee and Ho Jae Han                                                                                                                                                                                                                                 |     |
| <b>Extracellular Acidosis Regulates the Expression of Inflammatory Mediators in Rat Epithelial Cells</b> . . . . .                                                                                                                                          | 277 |
| A. Riemann, S. Reime, M. Gießelmann, and O. Thews                                                                                                                                                                                                           |     |
| <b>Part V Methodology of O<sub>2</sub> Measurements</b>                                                                                                                                                                                                     |     |
| <b>Reducing False Alarm Rates in Neonatal Intensive Care: A New Machine Learning Approach</b> . . . . .                                                                                                                                                     | 285 |
| D. Ostojic, S. Guglielmini, V. Moser, J. C. Fauchère, H. U. Bucher, D. Bassler, M. Wolf, S. Kleiser, F. Scholkmann, and T. Karen                                                                                                                            |     |
| <b>Development of an IoT-Based Monitoring System for Healthcare: A Preliminary Study</b> . . . . .                                                                                                                                                          | 291 |
| M. Ishida, S. Ushioda, Y. Nagasawa, Y. Komuro, Z. Tang, L. Hu, T. Tamura, and K. Sakatani                                                                                                                                                                   |     |
| <b>Developing a Model to Simulate the Effect of Hypothermia on Cerebral Blood Flow and Metabolism</b> . . . . .                                                                                                                                             | 299 |
| Joshua Russell-Buckland and Ilias Tachtsidis                                                                                                                                                                                                                |     |
| <b>Validation and Comparison of Monte Carlo and Finite Element Method in Forward Modeling for Near Infrared Optical Tomography</b> . . . . .                                                                                                                | 307 |
| Jingjing Jiang, Wuwei Ren, Helene Isler, Alexander Kalyanov, Scott Lindner, Di Costanzo Mata Aldo, Markus Rudin, and Martin Wolf                                                                                                                            |     |
| <b>Development of a Cuff-Less Blood Pressure Monitoring System and Its Application</b> . . . . .                                                                                                                                                            | 315 |
| S. Ushioda, Y. Nagasawa, M. Isida, Y. Komuro, Z. Tang, L. Hu, T. Tamura, and K. Sakatani                                                                                                                                                                    |     |
| <b>Usefulness of a New Device to Monitor Cerebral Blood Oxygenation Using NIRS During Cardiopulmonary Resuscitation in Patients with Cardiac Arrest: A Pilot Study</b> . . . . .                                                                            | 323 |
| Tsukasa Yagi, Tsuyoshi Kawamorita, Keiichiro Kuroshima, Eizo Tachibana, Kazuhiro Watanabe, Nobutaka Chiba, Tadashi Ashida, Wataru Atsumi, Satoshi Kunimoto, Shigemasa Tani, Naoya Matsumoto, Yasuo Okumura, Atsuo Yoshino, and Kaoru Sakatani               |     |
| <b>Application of Peripheral Near Infrared Spectroscopy to Assess Risk Factors in Patient with Coronary Artery Disease: Part 1</b> . . . . .                                                                                                                | 331 |
| Tsuyoshi Kawamorita, Keiichiro Kuroshima, Tsukasa Yagi, Eizo Tachibana, Shonosuke Sugai, Satoshi Hayashida, Kazuki Iso, Korehito Iida, Wataru Atsumi, Satoshi Kunimoto, Yasuyuki Suzuki, Shigemasa Tani, Naoya Matsumoto, Yasuo Okumura, and Kaoru Sakatani |     |

|                                                                                                                                                                                                                                                            |            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Broadband NIRS Cerebral Evaluation of the Hemodynamic and Oxidative State of Cytochrome-c-Oxidase Responses to +Gz Acceleration in Healthy Volunteers. . . . .</b>                                                                                      | <b>339</b> |
| F. Lange, G. Bale, P. Kaynezhad, R. D. Pollock, A. Stevenson, and I. Tachtsidis                                                                                                                                                                            |            |
| <b>Time-Resolved NIROT ‘Pioneer’ System for Imaging Oxygenation of the Preterm Brain: Preliminary Results. . . . .</b>                                                                                                                                     | <b>347</b> |
| A. Di Costanzo-Mata, J. Jiang, S. Lindner, L. Ahnen, C. Zhang, S. Sánchez-Majos, M. Wolf, E. Charbon, and A. Kalyanov                                                                                                                                      |            |
| <b>Application of Peripheral Near Infrared Spectroscopy to Assess Risk Factors in Patient with Coronary Artery Disease: Part 2 . . . . .</b>                                                                                                               | <b>355</b> |
| Keiichiro Kuronuma, Tsuyoshi Kawamorita, Tsukasa Yagi, Eizo Tachibana, Shonosuke Sugai, Satoshi Hayashida, Kazuki Iso, Korehito Iida, Wataru Atsumi, Satoshi Kunitomo, Yasuyuki Suzuki, Shigemasa Tani, Naoya Matsumoto, Yasuo Okumura, and Kaoru Sakatani |            |
| <b>Optimization of Band Selection in Multispectral and Narrow-Band Imaging: An Analytical Approach. . . . .</b>                                                                                                                                            | <b>361</b> |
| Guennadi Saiko and Andrei Betlen                                                                                                                                                                                                                           |            |
| <b>Fabrication and Optical Characterization of Gelatin-Based Phantoms for Tissue Oximetry . . . . .</b>                                                                                                                                                    | <b>369</b> |
| G. Saiko, X. Zheng, A. Betlen, and A. Douplik                                                                                                                                                                                                              |            |
| <b>Two-Photon Autofluorescence Imaging of Fixed Tissues: Feasibility and Potential Values for Biomedical Applications . . . . .</b>                                                                                                                        | <b>375</b> |
| Lin Z. Li, Marissa Masek, Ting Wang, He N. Xu, Shoko Nioka, Joseph A. Baur, and Timothy M. Ragan                                                                                                                                                           |            |
| <b>Part VI Special Topics</b>                                                                                                                                                                                                                              |            |
| <b>Acute Anemia Induces Erythropoiesis in Rat Organ Surface Primo-Vascular Tissue . . . . .</b>                                                                                                                                                            | <b>385</b> |
| Yiming Shen, Chae Jeong Lim, So Yeong Lee, and Pan-Dong Ryu                                                                                                                                                                                                |            |
| <b>Analysis and Differential Expression of Primo Genes Using RNA-Seq and qRT-PCR Experiments . . . . .</b>                                                                                                                                                 | <b>393</b> |
| Jun-Young Shin, Jong-Ok Ji, Sang-Heon Choi, Da-Woon Choi, Ye-Jin An, Jae-Hyeok Seo, Jong-Gu Choi, Min-Suk Rho, Ji Yoon Lee, Sujung Yeo, and Sang-Suk Lee                                                                                                   |            |
| <b>Acupuncture Inhibits the Increase in Alpha-Synuclein in Substantia Nigra in an MPTP- Induced Parkinsonism Mouse Model . . . . .</b>                                                                                                                     | <b>401</b> |
| Sujung Yeo, Jongbeom Song, and Sabina Lim                                                                                                                                                                                                                  |            |

|                                                                                                                                         |     |
|-----------------------------------------------------------------------------------------------------------------------------------------|-----|
| <b>On the Biomarkers of Alzheimer’s Disease</b> .....                                                                                   | 409 |
| Timon Cheng-Yi Liu, Tao Zheng, Rui Duan, Ling Zhu,<br>and Quan-Guang Zhang                                                              |     |
| <b>Effective Murine Model Induction for Niche Study in Immune<br/>Cells Against Leukemia</b> .....                                      | 415 |
| Dae Yong Kim, Sarah Lee, Dong Yu Kim, and Ji Yoon Lee                                                                                   |     |
| <b>Correction to: Improvements in Skeletal Muscle<br/>Can Be Detected Using Broadband NIRS in First-Time<br/>Marathon Runners</b> ..... | C1  |
| <b>Index</b> .....                                                                                                                      | 421 |

**Part I**  
**Brain Oxygenation and Function**

# Near-Infrared Spectroscopy Measured Cerebral Blood Flow from Spontaneous Oxygenation Changes in Neonatal Brain Injury



Gemma Bale, Nathan Taylor, Subhabrata Mitra, Aleh Sudakou, Isabel de Roever, Judith Meek, Nicola Robertson, and Ilias Tachtsidis

**Abstract** Neonates with hypoxic-ischaemic (HI) brain injury were monitored using a broadband near-infrared spectroscopy (NIRS) system in the neonatal intensive care unit. The aim of this work is to use the NIRS cerebral oxygenation data ( $HbD$  = oxygenated-haemoglobin – deoxygenated-haemoglobin) combined with arterial saturation ( $SaO_2$ ) from pulse oximetry to calculate cerebral blood flow (CBF) based on the oxygen swing method, during spontaneous desaturation episodes. The method is based on Fick's principle and uses  $HbD$  as a tracer; when a sudden change in  $SaO_2$  occurs, the change in  $HbD$  represents a change in tracer concentration, and thus it is possible to estimate CBF. CBF was successfully calculated with broadband NIRS in 11 HIE infants (3 with severe injury) for 70 oxygenation events on the day of birth. The average CBF was  $18.0 \pm 12.7$  ml  $100\text{ g}^{-1}\text{ min}^{-1}$  with a range of 4 ml  $100\text{ g}^{-1}\text{ min}^{-1}$  to 60 ml  $100\text{ g}^{-1}\text{ min}^{-1}$ . For infants with severe HIE (as determined by magnetic resonance spectroscopy) CBF was significantly lower ( $p = 0.038$ ,  $d = 1.35$ ) than those with moderate HIE on the day of birth.

**Keywords** Near-infrared spectroscopy · Cerebral blood flow · Neonatal brain injury · Hypoxic-ischaemic encephalopathy · Clinical

---

G. Bale (✉) · N. Taylor · I. de Roever · I. Tachtsidis  
Medical Physics and Biomedical Engineering, University College London, London, UK  
e-mail: [g.bale@ucl.ac.uk](mailto:g.bale@ucl.ac.uk)

S. Mitra · J. Meek · N. Robertson  
Institute for Women's Health, University College London, London, UK

A. Sudakou  
Nalecz Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw, Poland