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Dynamics and Fluctuations in Biomedical Photonics VIII

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Editors

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Contents

- ix Conference Committee
- xi Introduction
- xiii *Report on the panel discussion on Harnessing biophotonics for better healthcare and the creation of an international microcirculation imaging lab*
M. J. Leahy, University of Limerick (Ireland); R. K. Wang, Univ. of Washington (United States); S. Foster, Sunnybrook Health Sciences Ctr. (Canada); E. Ritman, Mayo Clinic (United States); L. V. Wang, Washington Univ. in St. Louis (United States); W. Steenbergen, Univ. Twente (Netherlands); B. Tromberg, Beckman Laser Institute and Medical Clinic (United States); K. Larin, Univ. of Houston (United States); D. Duncan, Portland State Univ. (United States); V. Tuchin, Saratov State Univ. (Russian Federation); A. Liebert, Polish Academy of Sciences (Poland)

SESSION 1 CELL/TISSUE COMPLEX STRUCTURE AND DYNAMICS

- 7898 03 **Optical micro-angiography reveals depth-resolved muscular microcirculation (Invited Paper)** [7898-02]
Y. Jia, R. K. Wang, Univ. of Washington (United States)
- 7898 06 **Effect of hypothermic preservation on biological tissues in physiological solution** [7898-05]
M. G. Ghosn, Univ. of Houston (United States) and Baylor College of Medicine (United States); M. A. Mohamed, A. Mehralizad, M. Mashiatulla, S. Syed, Univ. of Houston (United States); F. Castro-Chavez, J. D. Morrisett, Baylor College of Medicine (United States); K. V. Larin, Univ. of Houston (United States), Baylor College of Medicine (United States), and Saratov State Univ. (Russian Federation)
- 7898 08 **The study of optical properties and proteoglycan content of tendons by PS-OCT** [7898-07]
Y. Yang, A. Rupani, A. Weightman, I. Wimpenny, Keele Univ. (United Kingdom); P. Bagnaninchi, The Univ. of Edinburgh (United Kingdom); M. Ahearne, Keele Univ. (United Kingdom)

SESSION 2 SPECKLE MEASURING AND IMAGING TECHNOLOGIES

- 7898 0A **Speckle-based measurement of the light scattering by red blood cells in vivo (Invited Paper)** [7898-09]
I. Fine, A. Kaminsky, Elfi-Tech Ltd. (Israel)
- 7898 0C **High-speed dynamic laser speckle imaging of changes of microcirculation in vivo** [7898-11]
J. Qin, L. An, R. Wang, Univ. of Washington (United States)
- 7898 0D **Measurement of directed blood flow by laser speckle** [7898-12]
E. R. Hirst, Industrial Research Ltd. (New Zealand); O. B. Thompson, Industrial Research Ltd. (New Zealand) and Auckland Bioengineering Institute, Univ. of Auckland (New Zealand); M. K. Andrews, Industrial Research Ltd. (New Zealand)

- 7898 OE **Is there a difference between laser speckle and laser Doppler in depth sensitivity?** [7898-13]
O. B. Thompson, Industrial Research Ltd. (New Zealand) and Auckland Bioengineering Institute, Univ. of Auckland (New Zealand); E. R. Hirst, M. K. Andrews, Industrial Research Ltd. (New Zealand)
- 7898 OF **A laser speckle contrast analysis (LSCA) study of the effect of curing irradiance on composite polymerization kinetics** [7898-14]
E. M. Wells-Gray, Oregon Health & Science Univ. (United States); S. J. Kirkpatrick, Michigan Technological Univ. (United States); D. D. Duncan, Portland State Univ. (United States)
- 7898 OG **Study on blood flow pulsation using laser speckle contrast imaging** [7898-15]
S. Yuan, The Univ. of Memphis (United States); Y. Chen, Univ. of Maryland, College Park (United States); C. Preza, The Univ. of Memphis (United States); C.-M. Tang, Univ. of Maryland School of Medicine (United States)

SESSION 3 IMAGING OF MICROVASCULATURE, BLOOD FLOW, AND MICROCIRCULATION

- 7898 OI **Role of microcomputed tomography in microvascular imaging (Invited Paper)** [7898-16]
E. L. Ritman, Mayo Clinic (United States)
- 7898 OK **Smart velocity ranging quantifiable optical microangiography** [7898-18]
Z. Zhi, R. K. Wang, Univ. of Washington (United States)
- 7898 OL **Multimodal diagnostic approach for functional imaging of tumor vascular network and blood microcirculation** [7898-19]
V. Kalchenko, N. Madar-Balakirski, Y. Kuznetsov, Weizmann Institute of Science (Israel); I. Meglinski, Univ. of Otago (New Zealand); A. Harmelin, Weizmann Institute of Science (Israel)
- 7898 OM **Correlation mapping: rapid method for retrieving microcirculation morphology from optical coherence tomography intensity images** [7898-20]
E. Jonathan, J. Enfield, Univ. of Limerick (Ireland); M. J. Leahy, Univ. of Limerick (Ireland) and Royal College of Surgeons (Ireland)
- 7898 ON **Development of an absorption-based tomographic system for mapping the human microvasculature** [7898-21]
P. M. McNamara, E. Jonathan, M. J. Leahy, Univ. of Limerick (Ireland) and Royal College of Surgeons (Ireland)
- 7898 OO **In-vivo three-dimensional Doppler variance imaging for tumor angiogenesis on chorioallantoic membrane** [7898-22]
W. Qi, Beckman Laser Institute, Univ. of California, Irvine (United States) and Univ. of California, Irvine (United States); G. Liu, Z. Chen, Beckman Laser Institute, Univ. of California, Irvine (United States)

SESSION 4 BLOOD PERFUSION IMAGING AND HEMODYNAMICS

- 7898 OR **Investigation of cerebral hemodynamic changes during repeated sit-stand maneuver using functional near-infrared spectroscopy** [7898-25]
H. Niu, The Univ. of Texas Southwestern Medical Ctr. and The Univ. of Texas at Arlington (United States) and Beijing Normal Univ. (China); L. Li, G. S. Bhavé, Z. Lin, F. Tian, B. Khosrow, The Univ. of Texas Southwestern Medical Ctr. and The Univ. of Texas at Arlington (United States); R. Zhang, Presbyterian Hospital of Dallas and The Univ. of Texas Southwestern Medical Ctr. (United States); H. Liu, The Univ. of Texas Southwestern Medical Ctr. and The Univ. of Texas at Arlington (United States)
- 7898 OS **Lag time changes between capillary blood glucose and in-vivo interstitial glucose levels by HATR-FTIR spectroscopy** [7898-26]
N. S. Eikje, MC Professional OÜ (Estonia)

SESSION 5 SKIN OPTICS AND DYNAMICS

- 7898 OU **Ultra-high-sensitive optical micro-angiography provides depth resolved visualization of microcirculations within human skin under psoriatic conditions** [7898-28]
J. Qin, L. An, R. Wang, Univ. of Washington (United States)
- 7898 OV **Optical coherence tomography: imaging architect for dermal microdialysis in psoriasis** [7898-29]
M.-L. O'Connell, W. O'Connor, Univ. of Limerick (Ireland); B. Ramsay, Mid-Western Regional Hospital (Ireland); E. Guihen, Univ. of Limerick (Ireland); W. L. Ho, Mid-Western Regional Hospital (Ireland); M. J. Leahy, Univ. of Limerick (Ireland)
- 7898 OW **Finite element simulation of laser generated surface waves in layered skin model: effect of laser beam characteristics** [7898-30]
C. Li, Univ. of Dundee (United Kingdom) and Univ. of Washington (United States); S. Li, A. Letang, Z. Huang, Univ. of Dundee (United Kingdom); R. Wang, Univ. of Washington (United States)
- 7898 OX **In-vivo assessment of cleavage line orientation in human skin using optical coherence tomography** [7898-31]
J. Enfield, E. Jonathan, Univ. of Limerick (Ireland) and National Biophotonics and Imaging Platform Ireland (Ireland); M. J. Leahy, Univ. of Limerick (Ireland), National Biophotonics and Imaging Platform (Ireland), and Royal College of Surgeons (Ireland)
- 7898 OY **Measurements of adipose derived stem cell vitality with optical coherence phase microscopy** [7898-32]
P. O. Bagnaninchi, The Univ. of Edinburgh (United Kingdom); C. Holmes, McGill Univ. (Canada); N. Drummond, The Univ. of Edinburgh (United Kingdom); J. Daoud, M. Tabrizian, McGill Univ. (Canada)
- 7898 OZ **Finger tissue model and blood perfused skin tissue phantom** [7898-33]
V. V. Tuchin, Saratov State Univ. (Russian Federation) and Institute of Precise Mechanics and Control (Russian Federation); A. N. Bashkatov, E. A. Genina, V. I. Kochubey, V. V. Lychagov, S. A. Portnov, N. A. Trunina, Saratov State Univ. (Russian Federation); D. R. Miller, S. Cho, H. Oh, B. Shim, M. Kim, J. Oh, H. Eum, Y. Ku, D. Kim, Y. Yang, LG Electronics (Korea, Republic of)

POSTER SESSION

- 7898 10 **Monte Carlo simulation on how optical clearing technique influences predicting precision of non-invasive optical blood glucose sensing** [7898-34]
J. Jiang, W. Chen, L. Zhang, Tianjin Univ. (China); R. K. Wang, Oregon Health & Science Univ. (United States); K. Xu, Tianjin Univ. (China)
- 7898 11 **Quantifying low-frequency fluctuations in the laser Doppler flow signal from human skin** [7898-35]
M. S. Folgosi-Correa, G. E. C. Nogueira, Instituto de Pesquisas Energéticas e Nucleares (Brazil)
- 7898 12 **Depth-resolved optical imaging of hemodynamic response in mouse brain with microcirculatory beds** [7898-36]
Y. Jia, Univ. of Washington (United States); R. Nettleton, M. Rosenberg, E. Boudreau, Oregon Health & Science Univ. (United States); R. K. Wang, Univ. of Washington (United States)
- 7898 14 **Influence of cholesterol on non-invasive blood glucose sensing studied with NIR spectroscopy** [7898-38]
J. Jiang, L. Zhang, Q. Gong, K. Xu, Tianjin Univ. (China)
- 7898 15 **Classification of spiking events with wavelet neural networks** [7898-39]
A. I. Nazimov, A. N. Pavlov, Saratov State Univ. (Russian Federation)
- 7898 16 **High sensitive volumetric imaging of renal microcirculation in vivo using ultrahigh sensitive optical microangiography** [7898-41]
Z. Zhi, Y. Jung, Y. Jia, L. An, R. K. Wang, Univ. of Washington (United States)
- 7898 19 **Propagation of circular polarized light in a scattering medium influenced by optical clearing** [7898-45]
C. Macdonald, I. Meglinski, Univ. of Otago (New Zealand)
- 7898 1A **Determination of blood types using a chirped photonic crystal fiber** [7898-46]
A. V. Malinin, Saratov State Univ. (Russian Federation) and SPE LLC Nanostructured Glass Technology (Russian Federation); A. A. Zanishevskaja, Saratov State Univ. (Russian Federation); Yu. S. Skibina, Saratov State Univ. (Russian Federation) and SPE LLC Nanostructured Glass Technology (Russian Federation); I. Yu. Silokhin, SPE LLC Nanostructured Glass Technology (Russian Federation); V. V. Tuchin, Saratov State Univ. (Russian Federation) and Institute of Precise Mechanics and Control (Russian Federation); V. A. Dubrovskiy, A. A. Dolmashkin, Saratov State Medical Univ. (Russian Federation)
- 7898 1B **Study of optical clearing of blood by immersion method** [7898-47]
O. S. Zhernovaya, Univ. of Limerick (Ireland) and Saratov State Univ. (Russian Federation); E. Jonathan, Univ. of Limerick (Ireland); V. V. Tuchin, Saratov State Univ. (Russian Federation); M. J. Leahy, Univ. of Limerick (Ireland)
- 7898 1C **Full-field speckle correlation technique as applied to blood flow monitoring** [7898-48]
M. A. Vilensky, D. N. Agafonov, P. A. Timoshina, O. V. Shipovskaya, Saratov State Univ. (Russian Federation); D. A. Zimnyakov, Saratov State Technical Univ. (Russian Federation) and Institute of Precision Mechanics and Control (Russian Federation); V. V. Tuchin, Saratov State Univ. (Russian Federation) and Institute of Precision Mechanics and Control (Russian Federation); P. A. Novikov, Saratov State Univ. (Russian Federation)

- 7898 1D **Saturation thresholds of evoked neural and hemodynamic responses in awake and asleep rats** [7898-49]
J. L. Schei, A. S. Van Nortwick, P. C. Meighan, D. M. Rector, Washington State Univ. (United States)

Author Index

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Session Chairs

Keynote Session

Donald D. Duncan, Portland State University (United States)

- 1 Cell/Tissue Complex Structure and Dynamics
Valery V. Tuchin, Saratov State University (Russian Federation)
- 2 Speckle Measuring and Imaging Technologies
Donald D. Duncan, Portland State University (United States)
- 3 Imaging of Microvasculature, Blood Flow, and Microcirculation
Martin J. Leahy, University of Limerick (Ireland)
- 4 Blood Perfusion Imaging and Hemodynamics
Ruikang K. Wang, University of Washington (United States)
- 5 Skin Optics and Dynamics
Kirill V. Larin, University of Houston (United States)

Panel Discussion on Harnessing Biophotonics for Better Healthcare and the Creation of an International Microcirculation Imaging Lab

Martin J. Leahy, Moderator, University of Limerick (Ireland)
Donald D. Duncan, Portland State University (United States)
Stuart Foster, Sunnybrook Health Sciences Center (Canada)
Kirill V. Larin, University of Houston (United States)
Adam Liebert, Polish Academy of Sciences (Poland)
Erik L. Ritman, Mayo Clinic (United States)
Wiendelt Steenbergen, Universiteit Twente (Netherlands)
Bruce Tromberg, Beckman Laser Institute and Medical Clinic (United States)
Valery V. Tuchin, Saratov State University (Russian Federation)
Lihong V. Wang, Washington University in St. Louis (United States)
Ruikang K. Wang, University of Washington (United States)

Introduction

These proceedings are from the Dynamics and Fluctuations in Biomedical Photonics VIII conference, held 22–24 January 2011 at the SPIE Photonics West symposium in San Francisco, California. The two-day conference featured 34 oral and 14 poster presentations from leading international research groups.

The goal of the conference was to gather essentially different groups of leading researchers such as biophysicists, medical doctors and physicians, mathematicians, optical and laser engineers, along with students, to report the current state of the art and to facilitate future progress in the development of optical and laser technologies based on dynamics and fluctuations approaches (such as speckle-based coherence imaging, microcirculation analysis using various optical techniques and methods, dynamics of molecular diffusion, including nanoparticles, etc.) towards biomedical science and clinical applications. These approaches should be useful for diagnosis and therapy of devastating life-threatening diseases such as those of the heart, cancer, vascular, mental illness, and many others that manifest as a breach of the living organism's auto-control systems at the level of molecule, cell, organ, or organism as a whole. We hope that this volume will contribute to the development of such interdisciplinary fields of science and applications as dynamics and structures of living systems, biomedical optics and laser medicine, and that it will be helpful for scientists, medical doctors, engineers and students.

The conference was organized into several sessions: Cell/Tissue Complex Structure and Dynamics; Speckle Measuring and Imaging Technologies; Imaging of Microvasculature, Blood Flow, and Microcirculation; Blood Perfusion Imaging and Hemodynamics; Skin Optics and Dynamics; and a poster session. Most of the sessions featured invited talks. The special features of this year's conference were keynote lecture by Prof. Vladimir P. Zharov from the Univ. of Arkansas for Medical Sciences entitled "In-vivo multiplex photoacoustic Raman flow cytometry with magnetic sorting," and special panel discussion on "Harnessing biophotonics for better healthcare and the creation of an international microcirculation imaging lab," [described in detail below and beginning page xiii]. Both of these sessions drew significant attention from the audience and resulted in wide discussions of these topics.

The keynote lecture delivered by Prof. Vladimir P. Zharov described recent advances in development and application of multimodal (photoacoustic, photothermal, Raman) flow cytometry technology for real-time in-vivo detection and, most importantly, thermo-destruction of circulating tumor cells in lymph system. Vladimir Zharov is the director of the Phillips Classic Laser & Nanomedicine Laboratories and a Professor of Biomedical Engineering (BME) at the University of Arkansas for Medical Sciences, USA. He is the author of five books, 40 patents,

and more than 200 papers in the field of laser spectroscopy, biophotonics, and nanobiotechnology and recipient of many international prizes and awards, including the State Prize from the Russian Science Foundation and the U.S. Maiman Award. The lecture described in detail the development of the multimodal flow cytometry platform (which includes multicolor laser arrays, high speed signal acquisition algorithms, molecular contrast nanoagents and multiplex targeting) followed by examples from animal studies of detection and destruction of circulating tumor cells, which could prevent the occurrence of tumor metastasis.

The oral sessions and corresponding poster session of the conference featured four invited talks and overall 48 presentations which described, among others, advanced theoretical, computational, and experimental studies in dynamics of microcirculation within skeletal muscles, tissue structural characterization, speckle-based measurement of the light scattering by RBCs, the origin of laser speckle contrast imaging, and the role of microcomputed tomography in microvascular imaging. The reader is encouraged to browse the table of contents of this issue to learn about different methods and techniques developed and applied to study complex problems of dynamics and fluctuations in biological systems on the scale ranging from cell to the whole body.

The conference chairs would like to thank the members of the technical program committee for their help in organizing the conference. We sincerely appreciate the support of the SPIE and the conference staff. Finally, we would like to thank all of the conference attendees and authors for their contributions and participation, especially the invited speakers, which helped to make this meeting a success.

Valery V. Tuchin
Donald D. Duncan
Kirill V. Larin
Martin J. Leahy
Ruikang K. Wang

Report on the panel discussion on Harnessing Biophotonics for Better Healthcare and the Creation of an International Microcirculation Imaging Lab

Martin J. Leahy, Univ. of Limerick (Ireland), Ruikang Wang, Washington Univ. (United States), Stuart Foster, Sunnybrook Health Sciences Ctr. (Canada), Erik Ritman, Mayo Clinic (United States), Lihong Wang, Washington Univ. in St. Louis (United States), Wiendelt Steenbergen, Univ. Twente (Netherlands), Bruce Tromberg, Beckman Laser Institute and Medical Clinic (United States), Kirill Larin, Univ. of Houston (United States), Donald Duncan, Portland State Univ. (United States), Valery Tuchin, Saratov State Univ. (Russian Federation), Adam Liebert, Polish Academy of Sciences (Poland)

A special panel, organized and moderated by Prof. Martin J. Leahy, was assembled with the leading researchers in microcirculation imaging who discussed how to bring biophotonics developments to the clinic. The discussion focused on microcirculation imaging as a case study and covered the state of the art, recent developments, the interrelationships between techniques, and the possible clinical applications likely to succeed.

The discussion was opened by Martin Leahy (U Limerick) with a general introduction and overview. This was followed by a series of two-minute presentations by the panelists on each of the leading approaches to microcirculation imaging to stimulate the discussion. Wiendelt Steenbergen (U Twente) provided an overview of the point measurement and 2D imaging techniques. In a contribution from the floor, Moor Instruments verified that laser Doppler perfusion imaging attained FDA diagnostic approval for burn depth assessment in 2008 – more than 30 years from the first report of laser Doppler perfusion monitoring by Mike Stern and 15 years from the first report of laser Doppler perfusion imaging by Wardell and Nilsson.

Erik Ritman (Mayo Clinic) demonstrated the ability of micro CT to provide exquisite detail of the microvascular architecture of small animals (see Figure 1) although in most cases the procedure was lethal due to the use of a polymer such as Microfil to fill the vessels or use of osmium tetroxide to stain the vessel walls. Nonetheless, this technique possibly provides the most robust registration of images in terms of recording the dimensions in a verifiable way since it is least sensitive to the likely impact of refractive index type variations which light and sound are susceptible to. It was therefore considered by the panel to be a possible gold standard against which the other devices could be tested. This leads to the concept of a standard phantom which might be imaged by several techniques in order to provide evidence of and confidence in techniques which might be used for quantitative microvascular imaging. Such a standard would be an important function of an International Microcirculation Imaging Lab. Due to the lack of intrinsic contrast between blood and soft tissue, it is necessary to inject a heavy element such as iodine to provide contrast for haemodynamic studies in the living animal. Prof. Ritman also illustrated recent developments in micro-CT based on the imaging of coherent x-ray scatter and on x-ray phase shift caused by local electron density distributions (reflecting molecular bond type in some cases) which provide greater inherent image contrast than x-ray attenuation.

Stuart Foster (U Toronto) mentioned high frequency ultrasound and photoacoustics illustrating how these techniques were positioned for clinical success using Figure 2. The salient point was that beyond the proper technical development of any imaging technique, it must meet a clear clinical need which is currently inadequately served.

Kirill Larin (U Houston) then introduced the 3D optical techniques showing how confocal fluorescence could provide wonderful detail in e.g. mammalian vascular development, but was unable to see much beyond 100 μm from the surface. Prof Larin then showed how optical coherence tomography (OCT) could see more than 1000 μm into the tissue and by use of the Doppler effect velocity information could also be extracted. Ricky Wang (U Washington) demonstrated that the limitation of the Doppler effect where vessels were aligned at an unfavorable angle for Doppler could be imaged by the optical

micro-angiography (OMAG) technique. Prof. R. Wang then showed how the OMAG technique could non-invasively register similar microvascular detail in the mouse brain as the invasive micro CT discussed earlier. Martin Leahy introduced cross-correlation OCT (ccOCT) as an elegant solution for quickly and efficiently determining microvascular morphology in mice and humans. Lihong Wang (St. Louis) described the state of the art in photoacoustic imaging including the ability to quantitatively determine blood oxygen saturation in the smallest capillaries of the human vascular system.

A short discussion, initiated by Adam Liebert (Polish AS), considered the merits of a transatlantic collaboration in the development of a microcirculation imaging lab. It was generally agreed that a transatlantic alliance would enhance the independence, credibility, and scope of the lab and that funding could be sought simultaneously from NIH and FP7 for such a development.

Figure 1. Micro-CT imaging during angiogenesis (vessel growth) in the mouse ear after local injection of the growth factor VEGF. The sequence of images demonstrates that vessels below a certain diameter can be segmented out, in this case $\leq 36 \mu\text{m}$ to specifically identify the growing vessels (source: Ritman, E. L., Proceedings of SPIE Volume: 7898, CID 78980I).

Preclinical Imaging

Clinical Imaging

Successful Product	Micro-ultrasound	Multiphoton Microscopy	Photoacoustic Imaging
Solves a problem for the market place	★	★	?
Simple to operate	★	★	?
Workflow easy	★	★	?
Low cost	★	★	?
Quantitative	★	★	?
Operates in realtime	★	★	?
Registered to 3D anatomy	★	★	?

Figure 2. Microcirculation Imaging: Commercial Realities; Stuart Foster tests the attributes of photoacoustic imaging against established techniques.