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Dynamics and Fluctuations in Biomedical Photonics VIII

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

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

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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.

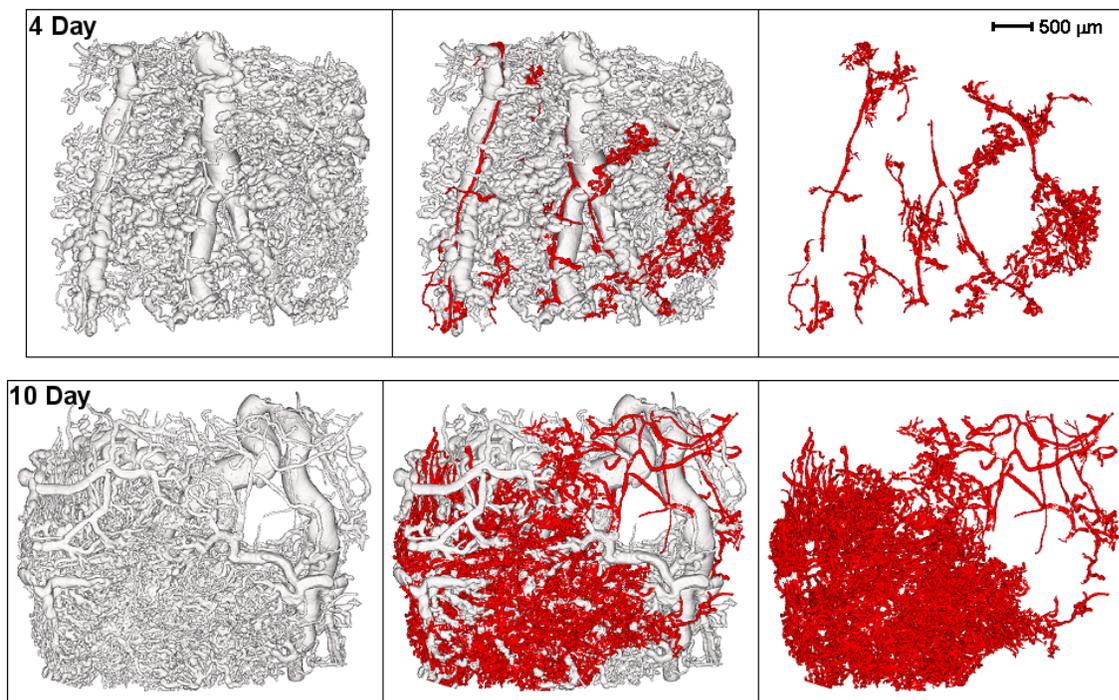


Figure 1. Micro-CT imaging during angiogenesis (vessel growth) in the mouse ear after local injection of the growth factor VEGF. The sequence of images demonstrates that vessels below a certain diameter can be segmented out, in this case $\leq 36 \mu\text{m}$ to specifically identify the growing vessels (source: Ritman, E. L., Proceedings of SPIE Volume: 7898, CID 789801).

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.

