PROGRESS IN BIOMEDICAL OPTICS AND IMAGING
Vol. 12, No. 20

Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues IX

Daniel L. Farkas
Dan V. Nicolau
Robert C. Leif
Editors

22–25 January 2011
San Francisco, California, United States

Sponsored and Published by
SPIE

Volume 7902

Proceedings of SPIE, 1605-7422, v. 7902

The papers included in this volume were part of the technical conference cited on the cover and title page. Papers were selected and subject to review by the editors and conference program committee. Some conference presentations may not be available for publication. The papers published in these proceedings reflect the work and thoughts of the authors and are published herein as submitted. The publisher is not responsible for the validity of the information or for any outcomes resulting from reliance thereon.

Please use the following format to cite material from this book:
Author(s), "Title of Paper," in *Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues IX*, edited by Daniel L. Farkas, Dan V. Nicolau, Robert C. Leif, Proceedings of SPIE Vol. 7902 (SPIE, Bellingham, WA, 2011) Article CID Number.

ISSN 1605-7422
ISBN 9780819484390

Published by
SPIE
P.O. Box 10, Bellingham, Washington 98227-0010 USA
Telephone +1 360 676 3290 (Pacific Time) · Fax +1 360 647 1445
SPIE.org

Printed in the United States of America.

Publication of record for individual papers is online in the SPIE Digital Library.

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Contents

xi *Conference Committee*
xiii *Introduction*

SESSION 1 CELL IMAGING I

7902 03 **Manipulating intracellular refractive index for contrast-enhanced digital holographic imaging of subcellular structures** [7902-01]
C. E. Rommel, C. Dierker, L. Schmidt, S. Przibilla, G. von Bally, B. Kemper, J. Schnekenburger, Univ. of Muenster (Germany)

7902 06 **Long-term time-lapse multimodal microscopy for tracking cell dynamics in live tissue** [7902-04]
B. W. Graf, M. C. Valero, E. J. Chaney, M. Marjanovic, M. D. Boppart, S. A. Boppart, Univ. of Illinois at Urbana-Champaign (United States)

SESSION 2 CELL IMAGING II

7902 08 **Multispectral imaging of the olfactory bulb activation: influence of realistic differential pathlength correction factors on the derivation of oxygenation and total hemoglobin concentration maps** [7902-06]
R. Renaud, H. Gurden, R. Chery, M. Bendhamane, C. Martin, F. Pain, Imagerie et Modélisation en Neurobiologie et Cancérologie, CNRS, Univ. Paris-Sud 11 (France)

7902 09 **Widefield in vivo spectral and fluorescence imaging microscopy of microvessel blood supply and oxygenation** [7902-07]
J. Lee, R. Kozikowski, M. Wankhede, B. S. Sorg, Univ. of Florida (United States)

7902 0A **Water deficit and salt stress diagnosis through LED induced chlorophyll fluorescence analysis in Jatropha curcas L. oil plants for biodiesel** [7902-08]
A. S. Gouveia-Neto, E. A. Silva, Jr., R. A. Oliveira, P. C. Cunha, E. B. Costa, T. J. R. Câmara, L. G. Willadino, Univ. Federal Rural de Pernambuco (Brazil)

SESSION 3 TISSUE IMAGING I

7902 0C **Quantifying thermal modifications on laser welded skin tissue** [7902-10]
H. Ö. Tabakoğlu, Fatih Univ. (Turkey); M. Gülsoy, Bogaziçi Univ, (Turkey)

7902 0D **Tumor cell differentiation by marker free fluorescence microscopy** [7902-11]
H. Schneckenburger, P. Weber, M. Wagner, M. Brantsch, P. Biller, Hochschule Aalen (Germany); P. Kioschis, Hochschule Mannheim (Germany); W. Kessler, Steinbeis-Hochschule Berlin (Germany)

7902 0E **Autofluorescence ratio imaging of human colonic adenomas** [7902-12]
K. Imaizumi, Kyoto Prefectural Univ. of Medicine (Japan) and Olympus Medical Systems Corp. (Japan); Y. Harada, N. Wakabayashi, Y. Yamaoka, P. Dai, H. Tanaka, T. Takamatsu, Kyoto Prefectural Univ. of Medicine (Japan)

7902 0F **Multimode optical imaging for translational chemotherapy: in vivo tumor detection and delineation by targeted gallium corroles** [7902-13]
J. Y. Hwang, Cedars-Sinai Medical Ctr. (United States) and Univ. of Southern California, Los Angeles (United States); Z. Gross, Beckman Research Institute (United States) and Technion-Israel Institute of Technology (Israel); H. B. Gray, Beckman Research Institute (United States); L. K. Medina-Kauwe, Cedars-Sinai Medical Ctr. (United States) and Univ. of California, Los Angeles (United States); D. L. Farkas, Univ. of Southern California (United States) and Spectral Molecular Imaging, Inc. (United States)

SESSION 4 TISSUE IMAGING II

7902 0G **Simultaneous dual modality optical and MR imaging of mouse dorsal skin-fold window chamber** [7902-14]
M. F. Salek, The Univ. of Arizona (United States) and College of Optical Sciences, The Univ. of Arizona (United States); M. D. Pagel, The Univ. of Arizona (United States); A. F. Gmitro, The Univ. of Arizona (United States) and College of Optical Sciences, The Univ. of Arizona (United States)

7902 0I **Multispectral line confocal imaging microscope for fluorescence applications** [7902-81]
M. M. Meyers, I. Ferreira, GE Global Research (United States); P. Fomitchov, GE Healthcare Lifesciences (United States); R. Filkins, GE Global Research (United States)

7902 0J **The new hyperspectral microscopic system for cancer diagnosis** [7902-17]
Y.-F. Hsieh, National Central Univ. (Taiwan); O.-Y. Mang, J.-C. Chiou, Y.-J. Lin, National Chiao-Tung Univ. (Taiwan); M.-H. Tsai, D.-T. Bau, C.-F. Chiu, G.-C. Teseng, N.-W. Chang, China Medical Univ. (Taiwan); W.-C. Kao, S.-D. Wu, National Taiwan Normal Univ. (Taiwan)

7902 0K **Polarization-sensitive digital dermoscopy for image processing-assisted evaluation of atypical nevi: towards step-wise detection of melanoma** [7902-84]
L. S. Yu, Windward School (United States); A. O. N. R. Joseph, Univ. of Southern California (United States); E. H. Lindsley, Spectral Molecular Imaging, Inc. (United States); D. L. Farkas, Univ. of Southern California (United States) and Spectral Molecular Imaging, Inc. (United States)

SESSION 5 MICRO IMAGING, MANIPULATION, PROBING I

7902 0L **Live atomic force microscopy imaging of laser microbeam assisted cellular microsurgery** [7902-18]
N. Ingle, S. K. Mohanty, The Univ. of Texas at Arlington (United States)

7902 0M **Monitoring single membrane protein dynamics in a liposome manipulated in solution by the ABELtrap** [7902-19]
T. Rendler, M. Renz, E. Hammann, S. Ernst, N. Zarrabi, M. Börsch, Univ. of Stuttgart (Germany)

7902 0N **Optical trapping forces on biological cells on a waveguide surface** [7902-20]
P. Løvhaugen, B. S. Ahluwalia, Univ. of Tromsø (Norway); T. R. Huser, Univ. of California Davis Medical Ctr. (United States) and Univ. of Tromsø (Norway); P. McCourt, O. G. Hellesø, Univ. of Tromsø (Norway)

7902 0O **2D freeform plasmonic trapping via spatial light modulator** [7902-21]
H.-W. Su, C.-Y. Lin, K.-C. Chiu, National Cheng Kung Univ. (Taiwan); H.-L. Tsai, Missouri Univ. of Science and Technology (United States); S.-J. Chen, National Cheng Kung Univ. (Taiwan)

7902 0P **High-speed FRET screening for optical proteomics in a microfluidic format** [7902-22]
V. Visitkul, D. R. Matthews, G. E. Weitsman, M. D. Keppler, S. M. Ameer-Beg, Richard Dimbleby Lab. of Cancer Research, King's College London (United Kingdom)

SESSION 6 MICRO IMAGING, MANIPULATION, PROBING II

7902 0S **Hyphal responses of *Neurospora crassa* to micron-sized beads with functional chemical surface groups** [7902-25]
M. Held, C. Edwards, D. V. Nicolau, Univ. of Liverpool (United Kingdom)

7902 0U **Digital holographic microscopy combined with optical tweezers** [7902-27]
N. Cardenas, The Univ. of Texas at Arlington (United States); L. Yu, Nanoscope Technologies LLC (United States); S. K. Mohanty, The Univ. of Texas at Arlington (United States)

7902 0V **Dynamics of optically trapped red blood cells by phase contrast microscopy** [7902-28]
M. Potcoava, Colorado School of Mines (United States) and JILA, Univ. of Colorado and National Institute of Standards and Technology (United States); E. Hoover, K. Roth, G. Riccota, J. Squier, Colorado School of Mines (United States); R. Jimenez, JILA, Univ. of Colorado and National Institute of Standards and Technology (United States); D. W. M. Marr, Colorado School of Mines (United States)

7902 0X **Depth-targeted transvascular drug delivery by using annular-shaped photomechanical waves** [7902-30]
T. Akiyama, Keio Univ. (Japan); S. Sato, H. Ashida, National Defense Medical College (Japan); M. Terakawa, Keio Univ. (Japan)

SESSION 7 BIOMOLECULAR IMAGING

7902 0Y **Simultaneous measurements of fluorescence lifetimes, anisotropy, and FRAP recovery curves** [7902-31]
J. A. Levitt, P.-H. Chung, D. R. Alibhai, K. Suhling, King's College London (United Kingdom)

7902 10 **Validation of method for enhanced production of red-shifted bioluminescent photons in vivo** [7902-33]
J. Dragavon, S. Blazquez, Institut Pasteur (France); K. L. Rogers, The Walter & Eliza Hall Institute of Medical Research (Australia); C. Samson, Vanderbilt Univ. (United States); R. Tournebize, S. Shorte, Institut Pasteur (France)

7902 11 **Determination of the in vivo redox potential using roGFP and fluorescence spectra obtained from one-wavelength excitation** [7902-34]
S. Wierer, K. Elgass, S. Bieker, U. Zentgraf, A. J. Meixner, F. Schleifenbaum, Univ. of Tuebingen (Germany)

7902 12 **Impedance microflow cytometry for viability studies of microorganisms** [7902-82]
M. Di Berardino, M. Hebeisen, T. Hessler, A. Ziswiler, S. Largiadèr, G. Schade, Leister Process Technologies (Switzerland)

SESSION 8 CYTOMICS

7902 13 **Detection and isolation of rare cells by 2-step enrichment high-speed flow cytometry/cell sorting and single cell LEAP laser ablation** [7902-36]
M. D. Zordan, J. F. Leary, Purdue Univ. (United States)

7902 14 **The influence of selected antimicrobial peptides on the physiology of the immune system** [7902-37]
K. Gołąb, A. Mittag, A. Pierzchalski, J. Bocsi, Univ. of Leipzig (Germany); W. Kamysz, Medical Univ. of Gdańsk (Poland); A. Tarnok, Univ. of Leipzig (Germany)

7902 15 **Study of cell classification with a diffraction imaging flow cytometer method** [7902-39]
K. Dong, TEO Systems, Inc. (United States); K. M. Jacobs, East Carolina Univ. (United States); Y. Sa, Y. Feng, Tianjin Univ. (China); J. Q. Lu, East Carolina Univ. (United States); X.-H. Hu, TEO Systems, Inc. (United States) and East Carolina Univ. (United States)

7902 16 **Flow cytometric separation of spectrally overlapping fluorophores using multifrequency fluorescence lifetime analysis** [7902-40]
P. L. Jenkins, New Mexico State Univ. (United States); J. P. Freyer, Los Alamos National Lab. (United States); M. S. Naivar, DarklingX , LLC (United States); A. Arteaga, J. P. Houston, New Mexico State Univ. (United States)

7902 17 **A CytometryML table of contents that describes relationships between elements based upon DICOM and flow cytometry standard** [7902-41]
R. C. Leif, S. H. Leif, Newport Instruments (United States)

SESSION 9 NEW IMAGING TECHNIQUES I

7902 1A **Adaptive optics in sectioning microscopes: the practical implementation** [7902-43]
J. Andilla, Imagine Optic SA (France); J. Ballesta, Imagine Optic Inc. (United States); R. Aviles-Espinosa, Instituto de Ciencias Fotonicas (Spain); X. Levecq, Imagine Optic SA (France)

7902 1C **Quantum cascade laser-based replacement for FTIR microscopy** [7902-45]
M. J. Weida, B. Yee, Daylight Solutions, Inc. (United States)

SESSION 10 NEW IMAGING TECHNIQUES II

7902 1G **Cellular spectroscopy: applications to cancer stem cell characterization** [7902-49]
G. Wiegand, H. Xin, A. Anderson, J. Mullinax, K. Jaiswal, NCI, National Institutes of Health (United States); A. Wiegand, Estuary Biophotonics, Inc. (United States); I. Avital, NCI, National Institutes of Health (United States)

SESSION 11 NEW IMAGING TECHNIQUES III

7902 1I **Characterizing collagen-based materials modified by glycation: a multiphoton optical image guided spectroscopy method** [7902-50]
Y.-J. Hwang, J. Granelli, C. Flores, J. Lyubovitsky, Univ. of California, Riverside (United States)

7902 1K **Validation of ALFIA: a platform for quantifying near-infrared fluorescent images of lymphatic propulsion in humans** [7902-52]
J. C. Rasmussen, M. Bautista, I-C. Tan, K. E. Adams, M. Aldrich, M. V. Marshall, The Univ. of Texas Health Science Ctr. at Houston (United States); C. E. Fife, E. A. Maus, L. A. Smith, The Univ. of Texas Health Science Ctr. at Houston (United States) and Memorial Hermann Hospital (United States); J. Zhang, X. Xiang, S. K. Zhou, Siemens Corporate Research (United States); E. M. Sevick-Muraca, The Univ. of Texas Health Science Ctr. at Houston (United States)

SESSION 12 IMAGE ANALYSIS, PROCESSING, AND QUANTIFICATION I

7902 1M **Metabolic remodeling of the human red blood cell membrane measured by quantitative phase microscopy** [7902-54]
Y. Park, KAIST (Korea, Republic of); C. Best, Univ. of Illinois at Urbana-Champaign (United States); T. Auth, Institute for Complex Systems (Germany); N. S. Gov, S. Safran, Weizmann Institute of Science (Israel); G. Popescu, Univ. of Illinois at Urbana-Champaign (United States)

7902 1O **Classification and discrimination of pediatric patients undergoing open heart surgery with and without methylprednisolone treatment by cytomics** [7902-56]
J. Bocsi, A. Mittag, A. Pierzchalski, Univ. of Leipzig (Germany); P. Osmancik, Charles Univ. and Univ. Hospital (Czech Republic); I. Dähnert, A. Tárnok, Univ. of Leipzig (Germany)

7902 1P **Computational efficient segmentation of cell nuclei in 2D and 3D fluorescent micrographs** [7902-57]
J. De Vylder, W. Philips, Ghent Univ. (Belgium)

SESSION 13 IMAGE ANALYSIS, PROCESSING, AND QUANTIFICATION II

7902 1Q **A novel method for multiparameter physiological phenotype characterization at the single-cell level** [7902-58]
L. Kelbauskas, S. Ashili, J. Houkal, D. Smith, A. Mohammadreza, K. Lee, A. Kumar, Arizona State Univ. (United States); Y. Anis, Cairo Univ. (Egypt); T. Paulson, Fred Hutchinson Cancer Research Ctr. (United States); C. Youngbull, Y. Tian, R. Johnson, M. Holl, D. Meldrum, Arizona State Univ. (United States)

7902 1R **Determination of the PSI/PSII ratio in living plant cells at room temperature by spectrally resolved fluorescence spectroscopy** [7902-59]
K. Elgass, Univ. of Tuebingen (Germany); M. Zell, V. G. Maurino, Univ. of Cologne (Germany); F. Schleifenbaum, Univ. of Tuebingen (Germany)

POSTER SESSION

7902 1T **Heating device for 96-well microtiter culture plates** [7902-61]
T. Bruns, C. Berchtold, H. Schneckenburger, Hochschule Aalen (Germany)

7902 1U **The study of the correlation properties on RBC flickering using double-path interferometric quantitative phase microscopy** [7902-62]
S. Lee, J. Y. Lee, C.-S. Park, Gwangju Institute of Science and Technology (Korea, Republic of); D. Y. Kim, Yonsei Univ. (Korea, Republic of)

7902 1V **Real time diagnosis of bladder cancer with probe-based confocal laser endomicroscopy** [7902-63]
J.-J. Liu, K. Wu, W. Adams, S. T. Hsiao, K. E. Mach, A. H. Beck, K. C. Jensen, J. C. Liao, Stanford Univ. School of Medicine (United States) and Veterans Affairs Palo Alto Health Care System (United States)

7902 1W **High speed fluorescence lifetime measurement by dual channel waveform measurement** [7902-64]
Y. Won, D. Y. Kim, Gwangju Institute of Science and Technology (Korea, Republic of)

7902 1X **Transillumination of subcutaneous adipose tissues using near-infrared hyperspectral imaging in the 1100-1800 nm wavelength range** [7902-65]
K. Ishii, A. Kitayabu, Y. Kobayashi, N. Honda, Osaka Univ. (Japan); K. Awazu, Osaka Univ. (Japan), Univ. of Fukui (Japan), and Kyoto Univ. (Japan)

7902 1Y **Developments of pulse-laser-assist optical tweezers (PLAT) for in vivo manipulation** [7902-66]
S. Maeda, T. Sugiura, K. Minato, Nara Institute of Science and Technology (Japan)

7902 20 **Differentiating human cervical dysplastic and normal tissue through wavelet domain characterization of intrinsic fluorescence** [7902-68]
R. Gudibande, GMR Institute of Technology (India); M. Mozumder, R. Singh, Indian Institute of Technology Kanpur (India); P. K. Panigrahi, Indian Institute of Science Education and Research Kolkata (India); S. Gupta, Univ. of California, Riverside (United States); A. Pradhan, Indian Institute of Technology Kanpur (India)

7902 21 **Infrared spectroscopic imaging of kidney tumor tissue** [7902-69]
V. Sablinskas, Vilnius Univ. (Lithuania); G. Steiner, E. Koch, Dresden Univ. of Technology (Germany); J. Ceponkus, M. Pucetaite, S. Strazdaite, V. Urboniene, F. Jankevicius, Vilnius Univ. (Lithuania)

7902 22 **Automated optical cell detection, sorting, and temperature measurements** [7902-71]
J. Kindt, M. Naqbi, T. Kiljan, W. Fuller, W. Wang, Colorado State Univ. (United States); D. W. Kisker, eOptra LLC (United States); K. L. Lear, Colorado State Univ. (United States)

7902 23 **Modeling and tissue parameter extraction challenges for free space broadband fNIR brain imaging systems** [7902-72]
E. Sultan, K. Manseta, A. Khwaja, Drexel Univ. (United States); L. Najafizadeh, A. Gandjbakhche, K. Pourrezaei, National Institutes of Health (United States); A. S. Daryoush, Drexel Univ. (United States)

7902 24 **Microfluidic isolation and manipulation of microscopic objects using optical trap with geometric distortion** [7902-73]
S. Shivalingaiah, S. K. Mohanty, The Univ. of Texas at Arlington (United States)

7902 25 **Development of a stigmatic imaging mass spectrometer using laser desorption/ionization** [7902-74]
K. Awazu, Osaka Univ. (Japan), Univ. of Fukui (Japan), Kyoto Univ. (Japan), and Japan Science and Technology Agency (Japan); H. Hazama, H. Nagao, H. Yoshimura, J. Aoki, Osaka Univ. (Japan) and Japan Science and Technology Agency (Japan); K. Fujii, Osaka Institute of Technology (Japan) and Japan Science and Technology Agency (Japan); K. Masuda, Suntory Institute for Bioorganic Research (Japan) and Japan Science and Technology Agency (Japan); T. Tashima, Japan Science and Technology Agency (Japan); M. Toyoda, Osaka Univ. (Japan) and Japan Science and Technology Agency (Japan); Y. Naito, Graduate School for the Creation of New Photonics Industries (Japan) and Japan Science and Technology Agency (Japan)

7902 29 **Sensing and enumerating rare circulating cells with diffuse light** [7902-79]
E. Zettergren, D. Vickers, M. Niedre, Northeastern Univ. (United States)

Author Index

Conference Committee

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Keynote Presentation
Dan V. Nicolau, University of Liverpool (United Kingdom)

1 Cell Imaging I
Daniel L. Farkas, Cedars-Sinai Medical Center (United States)

2 Cell Imaging II
Daniel L. Farkas, Cedars-Sinai Medical Center (United States)

3 Tissue Imaging I
Daniel L. Farkas, Cedars-Sinai Medical Center (United States)

4 Tissue Imaging II
Daniel L. Farkas, Cedars-Sinai Medical Center (United States)

5 Micro Imaging, Manipulation, Probing I
Dan V. Nicolau, University of Liverpool (United Kingdom)

6 Micro Imaging, Manipulation, Probing II
Dan V. Nicolau, University of Liverpool (United Kingdom)

7 Biomolecular Imaging
Dan V. Nicolau, University of Liverpool (United Kingdom)

8 Cytomics
Robert C. Leif, Newport Instruments (United States)

9 New Imaging Techniques I
Robert C. Leif, Newport Instruments (United States)

10 New Imaging Techniques II
Robert C. Leif, Newport Instruments (United States)

11 New Imaging Techniques III
Robert C. Leif, Newport Instruments (United States)

12 Image Analysis, Processing, and Quantification I
Robert C. Leif, Newport Instruments (United States)

13 Image Analysis, Processing, and Quantification II
Dan V. Nicolau, University of Liverpool (United Kingdom)

Introduction

Believing in Seeing, *Vingt ans après*

As chairs for an exciting interdisciplinary conference featuring new advances in optical bioimaging, we feel blessed to just organize/introduce the talks and edit the resulting proceedings, while aiming for the highest quality in both. Thematically, we try to cast a wide net, resulting in the title Imaging, Manipulation and Analysis of Biomolecules, Cells and Tissues. The roman numeral IX following the title implies that this is our ninth year, but in fact it is our twentieth. This usually is a milestone, and calls for a look back, with an eye on distilling something useful for planning purposes, especially since "the best way to predict the future is to create it" (to underscore the differences between disciplines, this quote is attributed to Dennis Gabor, Alan Key, or Peter Drucker, depending on one's background and readings being in physics, computers or business, respectively).

We are fortunate to work in an area of science and technology that is evolving very fast, to the point that it even justifies a new name: biophotonics. Many exciting advances in the field came from other areas of technology that were developed by target-oriented, extremely well-funded people in space exploration, telecommunications, defense, and nanotechnologies, to name a few. Other exceptional tools, such as femtosecond lasers, enabled new (but brilliantly long-predicted) approaches including multiphoton excitation microscopy. We had the first talks on this in our conference, but very quickly, it grew into its own very successful conference. The same applies to other fast-developing areas such as optical coherence tomography and its applications, and fluorescent proteins and their family (which brought our field the ultimate scientific recognition, Nobel Prizes to Drs. R. Tsien, O. Shimomura and M. Chalfie).

Perhaps even more importantly, biophotonics is on the brink of changing some important clinical areas by the new approaches it brings to major unmet needs. This is an evolution in the right direction because twenty years ago engineering-oriented meetings, such as those organized by SPIE tended to accentuate the technical virtuosity, with usually the last slide stating something along the lines of "and this could be useful in cancer research". Nowadays, presentations are not only more polished and continuing to advance the technologies, but they also focus much better on major challenges and the large set of requirements that need to be simultaneously met in order to achieve something meaningful. The application areas range from cancer (the perennial "grand challenge" on which progress has not been impressive) and cardiovascular disease, the biggest killers in our society, to areas that were not even in existence when we got started two decades ago: stem cells and cellular therapies, high throughput screening/sequencing, molecular diagnostics, and so on. Indeed, amazing results have been demonstrated in the lab (and reported in our conference through the

years): single molecules visualized in action (in a dish), whole genomes sequenced by optical means, cells moved around by laser beams into interesting action, entire (small) organisms imaged in 4D and sorted by features, single cancer cells captured in their first step towards setting up metastatic colonies (in small animals, in vivo), and many more. There is much cleverness deployed and promising many trends in these, and it is almost unfair to single out a few. Therefore, let us focus here on something of more general translational significance; how and when will all this yield something that will save lives and improve the human condition? More specifically, how do we go from impressive performance in the laboratory (femtosecond temporal and nanometer spatial resolution, molecular specificity) to equally impressive results in the clinic?

Complex disease will not yield to reductionist approaches, and molecular-specificity cellular-resolution imaging in the patient will be needed to effectively address such a challenge. This cannot (yet) be done, mostly because markers (such as quantum dots), big lasers, and other intense tools cannot be brought into the clinic except for ex vivo analyses. It is safe to predict, though, that if it can ever be done, optical imaging is likely to lead the way, as (a) light is a very powerful investigational tool and (b) all other medical imaging methods (x rays, MRI, ultrasound, etc.) seem severely limited in spatio-temporal performance and even specificity. It is vastly more difficult to image in a patient than in a dish, and not only for regulatory reasons; however, some of the necessary elements are already out there, being improved, fine-tuned, and sometimes unveiled at our conferences. For inspiration, let us think Mars Rover: we can image today dust on the Red Planet far better than we can image inside a human being who is in serious need in our best hospital. This does not feel right, and points the way towards where we should focus our efforts in the next twenty years. Luckily, there is a great supply of talented young scientists ready to do this, hopefully supported by enlightened governments, businesses, and unconventional sources. Let us hope that the results will be no less spectacular than those imagined by early science fiction, such as the influential sixties movie Fantastic Voyage, where a minified interdisciplinary group of scientists navigate in the body to the site of a life-threatening problem, and eliminate it with focused laser blasts. We have to keep believing in seeing: with lab-derived smart tools, at the right location (in the body), with performance far exceeding that of the human eye. This should allow finding problems early, guiding intervention, and achieving better outcomes, while also saving significantly on the cost of healthcare.

Daniel L. Farkas
Robert C. Leif
Dan V. Nicolau
(with thanks to **Bruce Tromberg** who co-chaired our first conference)