





SPIE TRANSLATIONAL BIOPHOTONICS 2014.

TECHNICAL PROGRAM

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Rice University, Bioscience Research Collaborative Houston, Texas, USA

Conference: 19-20 May 2014

SPIE. TRANSLATIONAL BIOPHOTONICS

Rice University, Bioscience Research Collaborative Houston, Texas, USA

19-20 MAY 2014

Welcome to Translational Biophotonics

On behalf of SPIE and the symposium organizers, we welcome you to Translational Biophotonics 2014. This new event is an interdisciplinary forum for collaboration and learning among top researchers, clinicians, and industrial partners in fields related to medicine and biophotonics.

This event includes both oral and poster presentations with a focus on optical diagnostics, image-guided intervention, novel microscopy techniques, new probes, and system design and implementation. Applications include cancer diagnostics, cardiovascular imaging, and detection of infectious disease.

We hope you enjoy the conference!



Tomasz Tkaczyk Rice University

ORGANIZING COMMITTEE

Brian E. Applegate, Texas A&M Univ. Kathrin Berkner, Ricoh Innovations, Inc. Jason M. Eichenholz, Open Photonics, Inc.

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SPIE and Bioscience Research Collaborative - Rice University would like to express its deepest appreciation to the symposium chairs, conference chairs, program committees, session chairs, and authors who have so generously given their time and advice to make this symposium possible.

The symposium, like our other conferences and activities, would not be possible without the dedicated contribution of our participants and members. This program is based on commitments received up to the time of publication and is subject to change without notice.

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INVITED SPEAKERS



Sharmila Anandasabapathy

The Mount Sinai Medical Ctr. Novel approaches to endoscopic screening cancer screening: challenges and experiences from China

Dana Brooks Northeastern Univ. Image analysis and machine learning for quantitative reading of confocal images of skin



Gerard Coté Texas A&M Univ.

Using micro and nanofluidics with surface enhanced Raman spectroscopy for in vitro blood based biomarker detection



Jason Eichenholz Open Photonics Inc.

Embracing open innovation: how engaging in collaborative development with companies can result in new sources of funding and accelerate the commercialization of your idea



Marc Feldman The Univ of Texas Health and Science Ctr. at San Antonio Clinical applications of OCT

R. Daniel Ferguson Physical Sciences Inc. Multimodal/adaptive optics imaging: bringing new perspectives to the clinic









Optical diagnostics for improved

pancreatic disease detection



Memorial Sloan-Kettering Cancer Ctr. Advances in confocal microscopy to improve patient care in cutaneous oncology: a Mohs surgeon's perspective

Aydogan Ozcan

Kishwer Nehal

Univ. of California Los Angeles Democratization of next-generation imaging, diagnostics, and measurement tools using mobile phones



Path, present and future, or, stromics and hectaplexing

Jeeseong Hwang

Technology

screening

Duke Univ.

quidance

Joseph Izatt

Richard Levenson

Univ. of California, Davis

National Institute of Standards and

Label-free hyperspectral microscopy

Real time volumetric swept source OCT

for ophthalmic imaging and surgical

for quantitative chemical mapping of single erythrocytes for malaria

John McDevitt Rice Univ.

Programmable bio-nano-chips customized for cardiac and cancer diagnostic applications

Mary-Ann Mycek Univ. of Michigan

INVITED SPEAKERS



David Piwnica-Worms

The Univ. of Texas MD Anderson Cancer Ctr.

Single-cell resolution imaging of apoptosis in vivo using cell-penetrating caspase-activatable peptides



Eric Potma Univ. of California, Irvine

resource settings

Nonlinear optical microscopy in the clinic



Rebecca Richards-Kortum Rice Univ. Point-of-care diagnostics for low-

Lihong Wang Washington Univ. in St. Louis Photoacoustic tomography: ultrasonically beating optical diffusion and diffraction



Siavash Yazdanfar

GE Global Research Translational biophotonics: perspectives from an industrial R&D center



Seok Hyun Yun Wellman Ctr. for Photomedicine, Harvard Univ. Brillouin light microscopy: translating ocular biomechanics into the clinic

Registration Desk Hours

Location: Auditorium (Foyer), BioScience Research Collaborative

Monday	7:30 AM to 4:30 PM
Tuesday	

Coffee Breaks and Lunches

Location: Auditorium, BioScience Research Collaborative

Morning and afternoon coffee/tea with light snacks and daily lunches will be served. Please see the program schedule for timing of daily breaks.

Poster Session and Reception

Location: Event Hall, Bioscience Research Collaborative

Monday 19 May5:00 to 6:30 PM

Conference participants are invited to attend the poster session and reception on Monday evening. Come view the posters, enjoy light refreshments, ask questions, and network with colleagues in your field. Authors of poster papers will be present to answer questions concerning their papers. Attendees are required to wear their conference registration badges to the poster sessions.

POSTER AUTHORS: Please set up your poster on Monday during the morning coffee break or the lunch break, and plan to stand by your poster during the poster session. Posters must be removed from the boards following the poster session as posters that remain on the boards will be discarded.

Internet Access

Location: BioScience Research Collaborative

WiFi internet access is available. Please see registration desk for instructions.

Get conference proceedings papers online during the meeting.

Beginning the first day of the conference, SPIE Translational Biophotonics pre-registered attendees will have online access to all proceedings papers related to this event as they are published. Papers can be accessed online through the SPIE Digital Library and all downloaded PDFs of papers are yours to keep. Event attendees who register after the pre-registration cutoff, or onsite, will receive access after the meeting.

TO ACCESS THE PROCEEDINGS (BEGINNING 19 MAY):

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Authors—papers submitted by the due date of 24 March will be available online during the meeting. Content submitted after the due date will be available as published.



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LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

Monday - Tuesday 19-20 May 2014 • Proceedings of SPIE Vol. 9155

SPIE Translational Biophotonics 2014

Conference Chair: Tomasz S. Tkaczyk, Rice Univ. (USA)

Program Committee: Brian E. Applegate, Texas A&M Univ. (USA); Kathrin Berkner, Ricoh Innovations, Inc. (USA); Jason M. Eichenholz, Open Photonics, Inc. (USA); Rongguang Liang, College of Optical Sciences, The Univ. of Arizona (USA); Michal E Pawlowski, Rice Univ. (USA); Mark C. Pierce, Rutgers, The State Univ. of New Jersey (USA); Milind Rajadhyaksha, Memorial Sloan-Kettering Cancer Ctr. (USA); Rebecca R. Richards-Kortum, Rice Univ. (USA)

MONDAY 19 MAY

OPENING REMARKS LOCATION: AUDITORIUM. BIOSCIENCE RESEARCH COLLABORATIVE

8:45 AM TO 9:00 AM

Session Chair: Tomasz S. Tkaczyk, Rice Univ. (USA)

SESSION 1 LOCATION: AUDITORIUM, BIOSCIENCE

RESEARCH COLLABORATIVE

MON 9:00 AM TO 11:00 AM

Biophotonic Tools in the Hands of Clinicians

Session Chair: **Gracie Vargas,** The Univ. of Texas Medical Branch (USA)

9:00 am: **Clinical applications of OCT** *(Invited Paper)*, Marc D. Feldman, The Univ. of Texas Health Science Ctr. at San Antonio (USA)......[9155-1]

10:00 am: Advances in confocal microscopy to improve patient care

SESSION 2 LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

MON 11:30 AM TO 1:00 PM

Microscopy in Clinical Applications

12:30 pm: Optical diagnostics for improved pancreatic disease		
detection (Invited Paper), Mary-Ann Mycek, Univ. of Michigan		
(USA)		
Lunch Break Mon 1:00 pm to 2:00 pm		

SESSION 3

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE MON 2:00 PM TO 3:30 PM

Diagnostic Imaging and Detection

Session Chair: Brian E. Applegate. Texas A&M Univ. (USA)

 2:00 pm: Real time volumetric swept source OCT for ophthalmic imaging and surgical guidance (Invited Paper), Joseph A. Izatt, Duke Univ. (USA)

 2:30 pm: Point-of-care diagnostics for low-resource settings (Invited Paper), Rebecca Richards-Kortum, Rice Univ. (USA)

Poster Previews

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

4:00 PM TO 5:00 PM

Session Chair: David Cuccia, Modulated Imaging, Inc. (USA)

Poster previews include:

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

Poster Session and Reception LOCATION: EVENT HALL:

BIOSCIENCE RESEARCH COLLABORATIVE

MON 5:00 PM TO 6:30 PM

Conference participants are invited to attend the poster session and reception on Monday evening. Come view the posters, enjoy light refreshments, ask questions, and network with colleagues in your field. Authors of poster papers will be present to answer questions concerning their papers. Attendees are required to wear their conference registration badges to the poster sessions.

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Wide spectral-range imaging spectroscopy of photonic crystal microbeads for multiplex biomolecular assay applications, Jianping Li, Hong Kong Baptist Univ. (Hong Kong, China) and Institute of Research and Continuing Education (Hong Kong, China)[9155-16]

Assessing pediatric postoperative chylothorax at the bedside using near-infrared fluorescence lymphatic imaging, Duraisamy Balaguru, I-Chih Tan, John C. Rasmussen, Renie Guilliod, John T. Bricker, Eva M. Sevick-Muraca, The Univ. of Texas Health Science Ctr. at Houston (USA)......[9155-17]

Dominant frequency analysis of prefrontal cortex: a study of resting-state functional optical topography, Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)[9155-23]

Periodontal disease diagnosis with swept-source Doppler optical coherent tomography, Cheng-Han Huang, Chia-Wei Sun, Ching-Cheng Chuang, National Chiao Tung Univ. (Taiwan)[9155-24]

 Confocal autofluorescence microscopy of inflamed biopsies to improve oral cancer detection, Anne Hellebust, Rice Univ. (USA); Jana M. Howe, Vijayashree S. Bhattar, Michelle D. Williams M.D., Ann M. Gillenwater M.D., The Univ. of Texas M.D. Anderson Cancer Ctr. (USA); Rebecca Richards-Kortum, Rice Univ. (USA)[9155-29]

Design and evaluation of confocal endoscope for early oral cancer detection, Joey M. Jabbour, Bilal H. Malik, Rodrigo Cuenca Martinez, Shuna Cheng, Javier A. Jo, Texas A&M Univ. (USA); Yi-Shing L. Cheng D.D.S., John Wright D.D.S., Texas A&M Health Science Ctr. (USA); Kristen C. Maitland, Texas A&M Univ. (USA)

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

Performance evaluation of fluorescence tomography in a Siemens Inveon multimodality scanner, Yujie Lu, Chinmay D. Darne, I-Chih Tan, Banghe Zhu, John C. Rasmussen, Eva M. Sevick-Muraca, The Univ. of Texas Health Science Ctr. at Houston (USA)........[9155-49]

Noninvasive monitoring of cholesterol in the blood vessels using THz TDS, Anna A. Ezerskaya, Igor V. Prozheev, Evgeniy A. Strepitov, Olga A. Smolyanskaya, National Research Univ. of Information Technologies, Mechanics and Optics (Russian Federation)...[9155-50]

In vivo microscopy for malaria diagnosis, Jennifer Burnett, Jennifer L. Carns, Rebecca Richards-Kortum, Rice Univ. (USA)[9155-51]

Quantitative "label-free" imaging of dynamic biological events, Katherine Creath, 4D Technology Corp. (USA) and The Univ. of Arizona (USA); Goldie L. Goldstein, 4D Technology Corp. (USA)[9155-57]

Development of a spatial frequency domain imaging system platform, David J. Cuccia, Amaan Mazhar, Scott Dolin, Modulated Imaging, Inc. (USA); Steve Saggese, Advanced Coherent Technologies LLC (USA); Pierre Khoury, Modulated Imaging, Inc. (USA)....[9155-65]

 Improvement of tissue analysis and classification using optical coherence tomography combined with Raman spectroscopy, Ji Qi, Peter Liu, Kirill V. Larin, Wei-Chuan Shih, Univ. of Houston (USA)......[9155-69] Microfluidic label-free monitoring of DNA hybridization, Ji Qi, Jianbo Zeng, Fusheng Zhao, Wei-Chuan Shih, Univ. of Houston (USA)......[9155-70] Nanoporous gold disks for photothermal light harvesting and light-

TUESDAY 20 MAY

SESSION 4

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

TUE 8:30 AM TO 9:30 AM

Beyond Classical In-Vivo Detection: Other Translation Perspectives I

Session Chair: **Mark C. Pierce,** Rutgers, The State Univ. of New Jersey (USA)

8:30 am: **Democratization of next-generation imaging, diagnostics, and measurement tools using mobile phones** *(Invited Paper)*, Aydogan Ozcan, Univ. of California, Los Angeles (USA)......[9155-11]

SESSION 5

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE TUE 10:00 AM TO 11:30 AM

Beyond Classical In-Vivo Detection: Other Translation Perspectives II

Session Chair: Mark C. Pierce, Rutgers, The State Univ. of New Jersey (USA)

10:00 am: Using micro and nanofluidics with Surface Enhanced Raman Spectroscopy for in vitro blood based biomarker detection (Invited Paper), Gerard L Coté, Department of Biomedical Engineering, Texas A&M Univ. (USA); Jun Kameoka, Electrical and Computer Engineering, Texas A&M Univ. (USA); Haley Marks, Department of Biomedical Engineering, Texas A&M Univ. (USA).............[9155-13]

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

SESSION 6

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE TUE 12:30 PM TO 2:30 PM

Making it Real: Commercialization and Industry Perspectives

Session Chair: Michal E. Pawlowski, Rice Univ. (USA)

PANEL DISCUSSION

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE

3:00 PM TO 4:00 PM

Pathways to Successful Translation

Moderator: **Richard Levenson,** Univ. of California, Davis (USA)

Panelists:

Jeeseong Hwang, National Institute of Standards Technology; David Piwnica-Worms,

The University of Texas MD Anderson Cancer Center Milind Rajadhyaksha, Memorial Sloan-Kettering Cancer Ctr. Siavash Yazdanfar, GE Global Research

CLOSING REMARKS

LOCATION: AUDITORIUM, BIOSCIENCE RESEARCH COLLABORATIVE 4:00 PM TO 4:15 PM

Session Chair: Tomasz S. Tkaczyk, Rice Univ. (USA)

9155-1, Session 1

Clinical applications of OCT (Invited Paper)

Marc D. Feldman, The Univ. of Texas Health Science Ctr. at San Antonio (USA)

SPEAKER BIOGRAPHY: Dr. Feldman is a Professor of Medicine & Engineering at the University of Texas Health Science Center in San Antonio, where he is the Director, Cardiac Catheterization Laboratories, as well as the Joaquin G. Cigarroa, Jr. MD Distinguished Chair in Medicine. Dr. Feldman co-founded a company which was the basis of Volcano Corporation's Cardiovascular OCT program, and has co-authored more than 20 full length manuscripts related to Cardiology and OCT.

ABSTRACT: OCT has generated amazing images of human anatomy not available to physicians in clinical practice previously. However, these images have often not translated into altering physician decision making and hence clinical acceptance of OCT has been slow in certain clinical disciplines. The talk will focus on examples where clinical decision making may be impacted including cardiovascular applications such as identification of plaque erosion rather than thin capped fibroatheroma to avoid stenting during heart attacks, OCT interrogation of freshly deployed stents to improve patient outcomes, plaque composition by combining OCT with other optical techniques, nuclear sizing in Barrett's Esophagus to identify cancerous transformation, OCT guided refractive surgery for the eye, and OCT guided cataract surgery.

9155-2, Session 1

Novel approaches to endoscopic screening cancer screening: challenges and experiences from China (Invited Paper)

Sharmila Anandasabapathy, The Mount Sinai Medical Ctr. (USA)

BIOGRAPHY: Sharmila Anandasabapathy, MD is Chief of Endoscopy, Associate Professor of Medicine in the Division of Gastroenterology at the Mount Sinai Medical Center in New York. The recipient of a BA degree in English from Yale University and MD from the Albert Einstein College of Medicine, she completed an internal medicine residency at the Weill Cornell Medical Center, NY and a gastroenterology fellowship at Mount Sinai Medical Center, NY. After serving as Director of Endoscopic Ultrasound at Mount Sinai, she joined the faculty at the MD Anderson Cancer Center in Houston in 2005 and later returned to Mount Sinai as Director of Endoscopy, Division of Gastroenterology in 2008.

Her clinical and research interests embrace the development and validation of novel, low-cost approaches to gastrointestinal cancer screening. She works closely with Dr. Rebecca Richards-Kortum and the bioengineering group at Rice University on the development of novel optical imaging modalities for the early detection and minimally invasive treatment of esophageal malignancy.

Dr. Anandasabapathy currently is involved in 11 domestic and international funded clinical trials centered on the early detection of gastrointestinal neoplasia. She has several active clinical collaborations across multiple centers in China, India, Central America and West Africa. In July of 2014, she will be returning to Houston to serve as Director of Baylor's Global Innovation Center.

ABSTRACT: No abstract available.

9155-3, Session 1

Advances in confocal microscopy to improve patient care in cutaneous oncology: a Mohs surgeon's perspective (Invited Paper)

Kishwer S. Nehal M.D., Memorial Sloan-Kettering Cancer Ctr. (USA)

BIOGRAPHY: Kishwer Nehal, M.D. is Director of Mohs/Dermatologic Surgery and Attending Physician at Memorial Sloan-Kettering Cancer Center. She specializes in cutaneous oncology with expertise in surgical management of complex facial melanomas and high risk non-melanoma skin cancers. Her clinical research has facilitated real-time skin cancer diagnosis and surgical margin control with confocal microscopy. Dr. Nehal serves on the American Joint Committee on Cancer. She is Professor of Dermatology at Cornell University/Weill and program director of Procedural Dermatology/Mohs fellowship.

ABSTRACT: Reflectance confocal microscopy is a noninvasive imaging approach with optical sectioning and resolution that shows nuclear, cellular and architectural morphology. Basal cell carcinomas and melanocytic lesions can be detected in vivo with high sensitivity and specificity and confocal imaging could reduce number of benign biopsies. Imaging is being implemented to guide treatment of lentigo melanomas for improved margin control. With fluorescence confocal mosaicing microscopy, residual basal cell carcinomas can be detected in Mohs tissue ex vivo with high sensitivity and specificity and this approach is under study to guide surgical treatment at the bedside. These advances demonstrate potential for improved patient and cost-effective care in our new health care system.

9155-4, Session 1

Single-cell resolution imaging of apoptosis in vivo using cell-penetrating caspase-activatable peptides (Invited Paper)

David R. Piwnica-Worms M.D., The University of Texas MD Anderson Cancer Center (USA)

BIOGRAPHY: Dr. Piwnica-Worms is Professor and Chair, Department of Cancer Systems Imaging, and Deputy Head, Research Affairs, Division of Diagnostic Imaging at The University of Texas MD Anderson Cancer Center. Dr. Piwnica-Worms is a founding pioneer of the field of molecular imaging and has lead the way in creating genetically-encoded bioluminescent and radiotracer reporter systems for imaging signal transduction, protein-protein interactions, and transcriptional regulation of gene expression at scales ranging from single cells to cell populations to live animals in vivo. He also has spearheaded translational research directed toward imaging cell-penetrating peptides and radiopharmaceuticals in medical imaging applications.

ABSTRACT: Peptide probes for imaging apoptosis consist of a cell-penetrating peptide targeting moiety and a fluorophore-quencher pair flanking an effector caspase consensus sequence. Using TcapQ488, a new probe synthesized for compatibility with clinically-relevant imaging instruments, and real time imaging of a live rat model of RGC degeneration, fully characterized time- and dose-dependent probe activation and signal-to-noise ratios have been performed using a confocal scanning laser ophthalmoscope (Heidelberg Retinal Angiograph II). In vivo fluorescence fundus imaging revealed distinct single-cell probe activation indicating RGC apoptosis induced by intravitreal NMDA injection, confirmed in corresponding retinal flat mounts. Electroretinography following intravitreal probe injections showed no significant difference compared with control injections. These cell-penetrating peptide probes enable quantitative non-invasive RGC apoptosis detection in vivo. 9155-5, Session 2

Nonlinear optical microscopy in the clinic (Invited Paper)

Eric O. Potma, Univ. of California, Irvine (USA)

BIOGRAPHY: Dr. Eric O. Potma is an Associate Professor in the Department of Chemistry at the University of California, Irvine (UCI). He holds an adjunct position in the Beckman Laser Institute and Medical Clinic at UCI. His research group is active in developing nonlinear optical imaging techniques for the purpose of interrogating biological tissues and nanostructured materials.

ABSTRACT: The imaging capabilities of nonlinear optical (NLO) imaging techniques, such as two-photon excited fluorescence, second harmonic generation, and coherent Raman scattering, are extremely well suited for noninvasive and label-free examination of skin tissue. Yet, the translation of the technique into a clinical setting has met many challenges. Some of these challenges are purely technical in nature, and can be addressed with innovative engineering. In this contribution, we discuss several technologies that lower the barrier for the clinical implementation of NLO imaging.

9155-6, Session 2

Brillouin light microscopy: translating ocular biomechanics into the clinic (Invited Paper)

Seok Hyun Andy Yun, Wellman Ctr. for Photomedicine (USA)

BIOGRAPHY: Dr. Yun received a B.S. and Ph.D. in Physics. He is currently Associate Professor at Harvard Medical School and the Wellman Center for Photomedicine at Massachusetts General Hospital. His primary research interest is developing novel light-based technologies for biomedical applications. Besides problem-solving, Dr. Yun's research also embraces curiosity-driven project such as the biological cell lasers.

ABSTRACT: The loss of corneal mechanical stability is thought to play a critical role in keratoconus and post-LASIK ectasia. Corneal collagen crosslinking is a promising treatment by increasing corneal stiffness. We have developed a new technique, called Brillouin microscopy, to measure the elastic modulus of the cornea tissue with high spatial resolution. In this talk, I will present optical instrumentation, results of human pilot studies, and potential of this technique for translation into the clinic.

9155-7, Session 2

Optical diagnostics for improved pancreatic disease detection (*Invited Paper*)

Mary-Ann Mycek, Univ. of Michigan (USA)

BIOGRAPHY: Mary-Ann Mycek, Ph.D., is a Professor in the Biomedical Engineering Department in the College of Engineering and in the Medical School at the University of Michigan. She received her Ph.D. in Physics from U.C. Berkeley and her postdoctoral training in laser medicine at Massachusetts General Hospital and Harvard Medical School. The translational research program in her Biomedical Optical Diagnostics Laboratory includes basic (pre-clinical), applied (clinical), and computational research toward quantitative, non-invasive, optical sensing and imaging in living cells and tissues.

ABSTRACT: Our research in Biomedical Optics develops tools to quantitatively assess tissues in vivo, with a goal of impacting clinical care by creating non- and minimally-invasive optical diagnostic technologies. To investigate whether tissue optical spectroscopy could potentially aid in the detection of pancreatic disease, a prototype clinical optical diagnostic device was developed and employed in a series of pilot studies to optically probe human pancreatic tissues. The results suggest that quantitative tissue optical spectroscopy holds promise as a potential clinical method to improve the detection of pancreatic disease.

9155-8, Session 3

Real time volumetric swept source OCT for ophthalmic imaging and surgical guidance (Invited Paper)

Joseph A. Izatt, Duke Univ. (USA)

BIOGRAPHY: Joseph A. Izatt is Professor of Biomedical Engineering and Ophthalmology, and Program Director for Biophotonics at the Fitzpatrick Institute for Photonics at Duke University in Durham, North Carolina. He is also Chairman and Chief Science Officer at Bioptigen, Inc., a North Carolina startup company commercializing optical coherence tomography technology. Dr. Izatt is a Fellow of the American Institute for Medical and Biological Engineering (AIMBE), Society of Photo-Instrumentation Engineers (SPIE), and Optical Society of America (OSA). He serves as editor-in-chief of Biomedical Optics Express.

ABSTRACT: Optical coherence tomography (OCT) and its extensions employ combinations of spatial and spectral encoding techniques to obtain micron-scale measurements of structure and function in living tissues and organisms. OCT has become a standard of care in clinical ophthalmology and has shown significant potential for applications in cardiology, endoscopy, surgery, and developmental biology. We are developing next-generation OCT technologies customized for new applications in refraction correction, pediatric imaging, and retinal microsurgery. These technology advances allow for real time volumetric microstructural imaging in living patients, which we are deploying for hand-held and intrasurgical applications. Compact multi-modal combinations of OCT with confocal microscopy allow for imaging of individual retinal receptor cells without adaptive optics. Functional extensions of OCT for Doppler and speckle-variance based blood flow imaging provide imaging of capillary-level blood flow without contrast agents in living eyes. The lecture will review the current state of these technologies and provide an overview of selected applications.

9155-9, Session 3

Point-of-care diagnostics for low-resource settings (Invited Paper)

Rebecca Richards-Kortum, Rice Univ. (USA)

BIOGRAPHY: Rebecca Richards-Kortum is the Stanley C. Moore Professor and Chair of Bioengineering at Rice University. After receiving a B.S. in Physics and Mathematics from the University of Nebraska-Lincoln in 1985, she continued her graduate work at the Massachusetts Institute of Technology, where she received an MS in Physics in 1987 and a PhD in Medical Physics in 1990. She joined the faculty in Bioengineering at Rice University in 2005. In addition to being named a Howard Hughes Medical Institute Professor in 2002 and 2006, her awards include election to the US National Academy of Engineering (2008).

ABSTRACT: Half the world's children live on less than \$2/day and do not have access to basic medical technologies. This talk will describe efforts to engineer appropriate high-performance, low-cost biophotonics technologies to meet health needs in low-resource settings.

9155-10, Session 3

Photoacoustic tomography: ultrasonically beating optical diffusion and diffraction (Invited Paper)

Lihong V. Wang, Washington Univ. in St. Louis (USA)

BIOGRAPHY: Lihong Wang holds the Beare Distinguished Professorship at Washington University. His book entitled "Biomedical Optics" won the Goodman Award. He has published 365 journal articles with an h-index of 85 (>28,000 citations) and delivered 380 keynote/plenary/invited talks. His laboratory invented functional photoacoustic CT and 3D photoacoustic microscopy. He serves as the Editor-in-Chief of the Journal of Biomedical Optics. He was awarded OSA's C.E.K. Mees Medal, NIH Director's Pioneer Award, and IEEE's Biomedical Engineering Award.

ABSTRACT: Photoacoustic tomography (PAT), combining optical and ultrasonic waves via the photoacoustic effect, provides in vivo functional, metabolic, molecular, and histologic imaging. PAT has the unique strength of high-resolution imaging across the length scales of organelles, cells, tissues, and organs with consistent contrast. PAT has the potential to empower multiscale biology research and accelerate translation from microscopic laboratory discoveries to macroscopic clinical practice. PAT may also hold the key to the earliest detection of cancer by in vivo label-free quantification of hypermetabolism, the quintessential hallmark of cancer. Broad applications include imaging of the breast, brain, skin, esophagus, colon, vascular system, and lymphatic system in both humans and animals.

9155-16, Poster Session Monday

Wide spectral-range imaging spectroscopy of photonic crystal microbeads for multiplex biomolecular assay applications

Jianping Li, Hong Kong Baptist Univ. (Hong Kong, China) and Institute of Research and Continuing Education (Hong Kong, China)

The development of optically color-encoded microspheres has prompted suspension array to be a very competitive approach over traditional planar array; the reaction speed, multiplexing and throughput of molecular assays can be greatly increased for detecting and quantifying biomolecular analytes^[1]. No matter how the microbeads are color encoded, by photoluminance from organic dyes ^[2] or inorganic semiconductor nanoparticles ^[3], or by reflection from periodic photonic crystal structures ^[4], it is always indispensible to have an accurate and high-speed optical means for spectral decoding and hence realizing high-throughput detection. Two decoding methods are dominant in fulfilling this task: the first one is flow cytometry; and the other one is imaging spectroscopy ^[5]. In this manuscript, we present the design and implementation of an imaging spectrometer platform towards the fast color decoding purpose for high-throughput and multiplexed molecular assay.

Among the existing methods, imaging Fourier transform spectroscopy (IFTS) is well known for its signal collection advantage and Connes advantage ^[6]. However, conventional IFTS is more frequently used in IR spectral bands because it is easier in longer wavelengths to keep interferogram sampling accuracy while tracking its scanning mirror position, so that the fundamental Nyquist criterion can be satisfied ^[7]; the sampling mechanism for shorter wavelengths IFTS used to be very sophisticated, high-cost and bulky. In order to overcome this handicap and take better usage of its advantages for high-throughput multiplexed detection applications, we propose to use a simple optical beam-folding interferometric position-tracking technique ^[8] to aid another beam-folded continuous-scan interferometer to successfully extend the spectral range of an IFTS covering UV-Vis-NIR. The detailed construction and testing of the IFTS system were well documented in references ^[9, 10].

To evaluate the spectral and spatial performance of the IFTS system, we performed a series of system tests by measuring coherent (He-Ne laser) and incoherent (LEDs) light emitted from a multimode fiber end. The testing results have proved the following several good features of the system:

1. Benefited from the Connes advantage provided by the reference He-Ne laser driven interferometer, the spectral accuracy is proved to be extremely accurate, which eliminates the need of frequent spectral calibration usually required in other spectral imaging methods.

2. The system has tunable spectral resolution. The highest achieved can reach to ~0.4nm (9.78cm-1) at FWHM of the He-Ne laser line by capturing 4 thousands sample images in about 120 seconds. The acquisition time can be reduced to only ~20s when measuring low coherent LED light with same FOV but less number of interferogram frames.

3. The shortest detectable wavelength of the system is theoretically deduced to be 316.4nm. Test results have proved that the IFTS system had achieved a broad spectral coverage of about 350-1000nm from UVA to NIR, which is only limited by the spectral response of the CCD.

4. Test results have also shown the system spatial resolution can be diffraction-limited and a maximum image resolution of about 300?300pixels can be obtained. This image resolution may not necessarily be corresponding to a small field of view (FOV); a larger FOV can also be converted to smaller image resolution by CCD pixel binning at the price of spatial resolution sacrifice.

Different from other spectral imaging methods, the IFTS system possesses unique features of ease to tune spectral resolution and very broad spectral range, which make it very convenient and versatile for measurements without a priori

9155-16, Poster Session Monday (continued)

spectral characteristics of the samples. Moreover, the proposed IFTS system has very flexible reconfiguration ability to fit for both photoluminance and reflection measurements thanks to the parallel optical path inside.

Then we applied the proposed system on microspectroscopic reflection spectra measurement from white light illuminated silica colloidal crystal microbeads (SCCBs) [4]. Although the implementation of some RGB color image processing algorithms seemed to be a good solution for color reading, the color inhomogeneity intrinsically associated with the interior photonic crystal structure of these microbeads will be problematic in practice and consequently deteriorates the decoding accuracy. However, our method can remove this color ambiguity by detecting spectra from centers of the microspheres. As the spectral information is independent from the changes of experimental conditions (e.g. illumination color temperature variation), color recognition by imaging spectroscopy is much more accurate than by RGB color imaging. The measurement results have also demonstrated that a theoretical color decoding speed of 100beads/s had been achieved by using the system; larger values can also be expected as these beads are pretty large and their mean center-to-center distance is about 200µm. More of them can be imaged in larger FOVs under lower magnifications, while their centers can still be spatially resolved easily.

The good spectral resolving ability and fast acquisition speed demonstrated in the experiments shows the proposed IFTS system owns practical potential to become a new imaging platform for high-throughput suspension array-based biomolecular multiplex assays.

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9155-17, Poster Session Monday

Assessing pediatric postoperative chylothorax at the bedside using near-infrared fluorescence lymphatic imaging

Duraisamy Balaguru, I-Chih Tan, John C. Rasmussen, Renie Guilliod, John T. Bricker, Eva M. Sevick-Muraca, The Univ. of Texas Health Science Ctr. at Houston (USA)

ABSTRACT: Diagnostic imaging could aid decision making for timely management of chylothorax, of which the pathogenesis is poorly understood. Non-invasive near-infrared fluorescence lymphatic imaging was used on a 5-week-old infant, who developed chylothoraces after heart surgery, to determine whether thoracic duct ligation or pleurodesis would restore normal drainage. Images showed that lymph flow from feet stopped at groins. From left hand injection, no lymph flowed into the subclavian vein, but instead, into the left pleural space. Based on the imaging results, left pleurodesis was performed with the result of temporary reduction of chest tube drainage.

Depth sensitive oblique polarized reflectance spectroscopy of oral epithelial tissue

Maria K. Jimenez, The Univ. of Texas at Austin (USA); Sylvia F. Lam, Catherine F. Poh D.D.S., The BC Cancer Agency Research Ctr. (Canada); Konstantin V. Sokolov, The Univ. of Texas M.D. Anderson Cancer Ctr. (USA)

ABSTRACT: Identifying depth-dependent alterations associated with epithelial cancerous lesions can be challenging in the oral cavity where variable epithelial thicknesses and troublesome keratin growths are prominent. Spectroscopic methods with enhanced depth resolution would immensely aid in isolating optical properties associated with malignant transformation. Combining multiple beveled fibers, oblique collection geometry, and polarization gating, oblique polarized reflectance spectroscopy (OPRS) achieves depth sensitive detection. We report promising results from a clinical trial of patients with oral lesions suspected of dysplasia or carcinoma demonstrating the potential of OPRS for the analysis of morphological and architectural changes in the context of multilayer, epithelial oral tissue.

Intradermal administration of fluorescent contrast agents for delivery to axillary lymph nodes

John C. Rasmussen, The Univ. of Texas Health Science Ctr. at Houston (USA); Funda Meric-Berstam, Savitri Krishnamurthy M.D., The Univ. of Texas M.D. Anderson Cancer Ctr. (USA); I-Chih Tan, Banghe Zhu, The Univ. of Texas Health Science Ctr. at Houston (USA); Jamie L. Wagner, Gildy V. Babiera, Elizabeth A. Mittendorf, Eva M. Sevick-Muraca, The Univ. of Texas M.D. Anderson Cancer Ctr. (USA)

ABSTRACT: In this proof-of-concept study we seek to demonstrate the delivery of fluorescent contrast agent to the tumor-draining lymph node basin following intraparenchymal breast injections and intradermal arm injection of micrograms of indocyanine green in 20 breast cancer patients undergoing complete axillary lymph node dissection. Individual lymph nodes were assessed ex vivo for presence of fluorescent signal. In all, 88% of tumor-negative lymph nodes and 81% of tumor-positive lymph nodes were fluorescent. These results indicate that future studies utilizing targeted fluorescent contrast agents may demonstrate improved surgical and therapeutic intervention. 9155-20, Poster Session Monday

Handheld system for multispectral fluorescence lifetime imaging (FLIM) with real-time image processing

Shuna Cheng, Texas A&M Univ. (USA)

ABSTRACT: A handheld system for simultaneous multispectral FLIM is presented aiming for oral cancer imaging. The handheld system consists of a 7x13x5 cm3 box with a rigid probe (1.7 cm diameter, 14 cm length). Up to three spectral bands can be simultaneously detected. Online lifetime calculation is accomplished by comparing time-resolved decay against a lookup table of computer-generated decay of convolving instrument response with single exponential decays. A maximum pixel rate of 30 kHz was demonstrated. The system was validated by standard dyes and tissue (in vivo hamster cheek pouch, ex vivo human oral biopsy and in vivo human oral mucosa).

9155-21, Poster Session Monday

Dentin hypersensitivity diagnosis based on polarization sensitive optical coherence tomography (PS-OCT)

Yao-Sheng Hsieh, National Taiwan Univ. (Taiwan); Cheng-Han Huang, National Chiao Tung Univ. (Taiwan); Shyh-Yuan Lee D.D.S., National Yang-Ming Univ. (Taiwan) and Taipei Veterans General Hospital (Taiwan); Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)

ABSTRACT: The dentin-enamel junction (DEJ) is an interface that joins two distinct calcified tissues, enamel and dentin. In addition, the DEJ has been associated with oral problems such as dentin hypersensitivity. Dentin hypersensitivity is one of the most common clinical problems that cause patient distress. This study presents two dimension images with polarization sensitive optical coherence tomography (PS-OCT). Strong polarization property difference could be observed because of the reason that enamel is composed of defective carbonate-rich apatite crystals that are arranged in enamel rods or prisms that lie nearly perpendicular to the DEJ and dentin consists of dentinal tubules containing odontoblastic processes.

9155-22, Poster Session Monday

Wide-field endoscopic fluorescence imaging for gastrointestinal tumor detection with glucose analogue

Yun He, Tsinghua Univ. (China); **Yawei Qu,** General Hospital of Chinese Armed Police Forces (China); **Jing Bai,** Department of Biomedical Engineering, Tsinghua University (China); **Haifeng Liu,** General Hospital of Chinese Armed Police Forces (China)

ABSTRACT: The lack of functional information and targeted imaging in conventional white-light endoscopy leads to a high miss-rate of gastrointestinal tumor. The combination of near-infrared fluorescence imaging and endoscopy presents a promising approach. Here we introduce a new endoscopy method employing a home-made flexible wide-field epi-fluorescence endoscope, that can be inserted through the biopsy channel of a gastrointestinal endoscope, with the glucose analogue 2-DeoxyGlucosone as the near-infrared fluorescent probe. System characterization indicates a good sensitivity and linearity over a large field of view. Its capability of tumor identification and location is demonstrated with in-vivo imaging of xenografted tumor model.

Dominant frequency analysis of prefrontal cortex: a study of resting-state functional optical topography

Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)

ABSTRACT: Brain functional connectivity in resting-state by using functional optical topography (fOT) measurement has become one of important approach to understanding the organization of the human brain. The prefrontal cortex (PFC) is thought to play an important role in "higher" brain functions such as personality and emotion that may associated with several mental disorders. We propose a method of dominant frequency mapping to analyze resting-state fOT data, which refers to the spontaneous neural activity. The fOT method can provide high potential to be the ideal choice for resting-state functional studies in the fields of developmental and clinical neuroscience that can apply to several mental disorders diagnosis.

9155-24, Poster Session Monday

Periodontal disease diagnosis with swept-source Doppler optical coherent tomography

Cheng-Han Huang, Chia-Wei Sun, Ching-Cheng Chuang,

National Chiao Tung Univ. (Taiwan)

This study describes periodontal disease diagnosis based on swept-source Doppler optical coherence tomography (SS-DOCT). The periodontitis is one of the highest prevalence oral diseases among ages. The blood flow of gingival micro-vessel could be an indicator for periodontal disease diagnosis. The information of blood velocity is contained in the phase of the reconstructed signal and can be obtained through Hilbert transformation of A-scan signal of OCT. In SS-DOCT, the k-trigger was applied for phase stabilization. The experimental result demonstrates the Doppler image of gingiva with periodontal disease.

9155-25, Poster Session Monday

Usefulness of simultaneous electroencephalography near-infrared spectroscopy in diagnosis of neurological disorders

Dai-Chen Lu, Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)

ABSTRACT: Near-infrared spectroscopy (NIRS) is a noninvasive neuroimaging tool for measuring evoked functional changes of brain oxygenation. Electroencephalography (EEG) coherence can be used to evaluate the functionality of cortical connections and to obtain information of regional cortical activity. Coregistration of EEG-NIRS is a recent technique that was used to analyze the changes in both electrical and local hemodynamic activities of human brain. This coregistration is useful to avoid misleading interpretation of NIRS, especially in the diagnosis of neurological disorders. In this research, we investigate a approach to the analysis of enhance accuracy of NIRS by EEG for physiological activities in mental focus task.

9155-26, Poster Session Monday

Oxygenation dynamic monitoring using time-resolved diffuse optical imaging system with time division multiple access

Chen-Wun Ciou, Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)

ABSTRACT: We present the experimental results of in-vivo oxygenation dynamic monitoring based on a time-resolved diffuse optical imaging (TRDOI) system. The TRDOI was performed with picosecond diode lasers (dual-wavelength near-infrared source) and a fast-gated single-photon avalanche diode (SPAD) that coupled to a time-correlated single-photon counting electronics. The TRDOI enables depth-resolved estimation of changes in absorption by using moment calculation of the times-of-flight of photons (DTOFs). The oxygenation dynamic image of local tissue can be measured in clinical diagnosis.

9155-27, Poster Session Monday

Study on functional electrical stimulation therapy for knee osteoarthritis complicating quadriceps muscular atrophy with near-infrared spectroscopy measurement

Wei-Long Kao, Ching-Cheng Chuang, Chia-Wei Sun, National Chiao Tung Univ. (Taiwan)

ABSTRACT: With an aging population and growing obesity, the prevalence of knee osteoarthritis is also increasing. Functional electrical stimulation (FES) therapy has been proven to prevent muscle atrophy due to pain. FES is a technique that uses electrical currents to activate nerves innervating extremities. Generally, FES therapy was applied on patient based on the patient's subjective feeling and experience without objective basis for measuring the assessment. Near-infrared spectroscopy (NIRS) is a noninvasive technique to monitor tissue oxygenation status. In this research, we use NIRS to find the best pulse width and frequency of FES therapy. This method can find the optimal course of FES treatment for different individuals.

Point of care pathology with miniature microscopes for early detection and surgical guidance

Michael J. Mandella, Stanford Univ. School of Medicine (USA); Steven Y. Leigh, Danni Wang, Ye Chen, Daphne Meza, Yu Wang, Stony Brook Univ. (USA); Christopher Glazowski, Gary Peterson, Sanjeewa Abeytunge, Milind Rajadhyaksha, Memorial Sloan-Kettering Cancer Ctr. (USA); Jonathan T. C. Liu, Stony Brook Univ. (USA)

ABSTRACT: Miniature dual-axis confocal (DAC) microscopes are being developed for various clinical applications, including the early detection of oral cancers and for guiding brain tumor resection. We will discuss the design of MEMS-scanned DAC microscopes, the analysis and optimization of DAC microscope performance, and preclinical tests with phantoms and animal models. A translational strategy for oral-cancer detection and brain-tumor resection in humans will also be described.

Confocal autofluorescence microscopy of inflamed biopsies to improve oral cancer detection

Anne Hellebust, Rice Univ. (USA); Jana M. Howe, Vijayashree S. Bhattar, Michelle D. Williams M.D., Ann M. Gillenwater M.D., The Univ. of Texas M.D. Anderson Cancer Ctr. (USA); Rebecca Richards-Kortum, Rice Univ. (USA)

ABSTRACT: Inflammatory lesions often appear visually similar to precancerous lesions, making inflammation a common source of false positives during visual autofluorescence examination. While the relationship between inflammation and cancer is complex, the ability to distinguish between the two would aid in observation of high risk patients and provide a tool to reduce false positives in low-prevalence patient populations. To help us understand the biological origins of changes in optical properties of oral tissue with inflammation, confocal microscopy was used to assess changes in epithelial and stromal optical properties from fresh tissue oral biopsies with inflammation.

9155-30, Poster Session Monday

Rapid multiplexed molecular phenotyping of ex vivo and in vivo tissues with targeted SERS NPs

Yu Wang, Altaz Khan, Madhura Som, Steven Y. Leigh, Danni Wang, Ye Chen, Stony Brook Univ. (USA); Patrick Z. McVeigh, Brian C. Wilson, Univ. of Toronto (Canada); Jonathan T. C. Liu, Stony Brook Univ. (USA)

ABSTRACT: We are developing a miniature fiber-optic spectral-detection device and topical-staining protocol to rapidly detect multiplexed surface-enhanced Raman scattering (SERS) nanoparticles (NPs) targeted to cell-surface biomarkers in fresh tissues. Ex vivo and in vivo experiments were performed to optimize our strategy for the rapid detection of multiple cell-surface biomarkers following a brief (5 min) topical application of SERS NPs on tissues. The simultaneous detection and ratiometric quantification of targeted and nontargeted NPs allows for an unambiguous assessment of molecular expression that is insensitive to nonspecific variations in NP concentrations, potentially enabling point-of-care surgical guidance or early disease detection.

9155-31, Poster Session Monday

Design and evaluation of confocal endoscope for early oral cancer detection

Joey M. Jabbour, Bilal H. Malik, Rodrigo Cuenca Martinez, Shuna Cheng, Javier A. Jo, Texas A&M Univ. (USA); Yi-Shing L. Cheng D.D.S., John Wright D.D.S., Texas A&M Health Science Ctr. (USA); Kristen C. Maitland, Texas A&M Univ. (USA)

ABSTRACT: Early detection of oral cancer significantly reduces morbidity and mortality. The current standard of care is biopsy and histopathological diagnosis. We present the design and development of a novel rigid reflectance confocal endoscope probe towards the early assessment of the oral mucosa in vivo and in real time. The endoscope tip has an outer diameter of 6.5 mm, and a focus tunable lens is used for axial scanning. The system has a 7 Hz frame rate, 0.7 numerical aperture, 500 micron field of view, and subcellular lateral and axial resolution.

In vivo molecular contrast OCT imaging of methylene blue in a zebrafish embryo

Wihan Kim, Brian E. Applegate, Texas A&M Univ. (USA)

ABSTRACT: Developing molecular contrast for Optical Coherence Tomography (OCT) holds the promise of micron scale resolution molecular imaging at depths up to 2 mm. In particular, the imaging of FDA approved dyes such as methylene blue (MB) could lead to more rapid adoption for clinical applications since the regulatory burden would be substantially reduced. We have introduced a 663 nm diode laser into an otherwise typical 830 nm spectral-domain OCT system by inserting a dichroic mirror into the sample arm of the OCT system. This relatively simple and inexpensive modification has enabled in vivo imaging of MB in a zebrafish embryo. The embryo was stained by immersing it in a 0.01% solution of MB for 6 hours. For reference, sentinel lymph node identification using MB prior to breast cancer surgery requires the injection of a 1% MB solution. In vivo images were acquired with a total power on the sample of 2.8 mW split equally between the pump and probe, well below the ANSI limit for skin. As expected, volumetric images show accumulation of MB in the pronephric ducts, which is the primary excretory organ. Gaining molecular contrast in OCT images from an FDA approved dye such as MB could find use both as a research tool and clinically to enhance the contrast of OCT images.

Simplified transient absorption ultrasonic microscope for achieving optically resolved photoacoustic imaging

Scott P. Mattison, Brian E. Applegate, Texas A&M Univ. (USA)

ABSTRACT: Recent advances in photoacoustic microscopy (PAM) using transient absorption have enabled subcellular transverse and axial resolutions through optical sectioning. This technique, called transient absorption ultrasonic microscopy (TAUM), is based on pump-probe spectroscopy and required the setup and maintenance of co-propagating pump and probe beams carefully aligned with a set time delay. The pump and probe were modulated at different frequencies enabling the detection of the pump-probe (optically sectioned) signal at the sum and difference frequencies. Here we describe a more efficient design that uses a single modulated beam to obtain the same subcellular resolution. The introduction of a modulation frequency on the pulsed laser source frequency encodes the PAM signal at the fundamental frequency and the TAUM signal at the second harmonic of the modulation. The TAUM signal is shifted to the second harmonic because it is a two photon process. This design is conceptually equivalent to setting the time delay between the pump and probe to zero and modulating both at the same frequency in our previous system design. This modification allows for collection of photoacoustic images with optical sectioning in both the axial and transverse imaging planes with the simple addition of a modulation frequency to the optical pathway of an existing PAM system. The imaging capabilities of this system are validated by capturing a 3-D volume of individual erythrocytes in a blood smear with an axial resolution of 1 μ m and a lateral resolution of 0.5 μ m.

9155-34, Poster Session Monday

Modulated alignment dual-axis (MAD) confocal microscopy for deep optical sectioning in tissues

Steven Y. Leigh, Ye Chen, Jonathan T. C. Liu, Stony Brook Univ. (USA)

ABSTRACT: A strategy is presented to enable optical-sectioning microscopy with improved contrast and imaging depth using low-power (0.5 mW) diode laser illumination. This method is a modification to the DAC microscope architecture in which intersecting illumination and collection beams significantly improve the spatial-filtering and optical-sectioning performance of confocal microscopy, we propose that modulating the spatial alignment of the dual-axis beams at a frequency f, such the focal volume signal of the microscope is modulated at 2f, further provides nearly an order-of-magnitude improvement in optical-sectioning contrast. Lock-in detection is used to remove the unmodulated background light, thereby enhancing our ability to image deeply within highly scattering tissues.

Cost-effective fluorescence microscope for point of care read out of bead-based assays

Alessandra J. Forcucci, Zachary A. Crannell, Ina Pavolova, Michal E. Pawlowski, Rebecca Richards-Kortum, Tomasz S. Tkaczyk, Rice Univ. (USA)

ABSTRACT: Many new platforms have been developed for multiplexed bioassays that rely on imaging targeted fluorescent beads labeled with different fluorescent dyes (e.g. Luminex). These systems typically rely on macroscale readers that are too bulky and expensive for use at the point-of-care. We developed a compact modular fluorescence microscope that can be used for multiplexed, bead-based assays that would reduce cost and support point-of-care applications. The microscope is composed of 3D-printed plastic modules that can be modified depending on the application. The objective and tube lens module houses a 4x, 0.25 NA infinity-corrected microscope objective and tube lens with manual focus adjustment capability. We successfully validated system performance with synthetic and non-synthetic targets.

9155-36, Poster Session Monday

Development and optimization of a line-scanned dual-axis confocal (LS-DAC) microscope for high-speed pathology

Danni Wang, Ye Chen, Daphne Meza, Yu Wang, Jonathan T. C. Liu,

Stony Brook Univ. (USA)

ABSTRACT: We have developed a line-scanned dual-axis confocal (LS-DAC) microscope with subcellular resolution suitable for real time diagnostic imaging at shallow depths. This design serves as a benchtop prototype for a handheld version of the LS-DAC intended for rapid point-of-care pathology. We have assessed the performance trade-offs between the LS-DAC and a point-scanning dual-axis confocal (PS-DAC) microscope via diffraction-theory analysis, Monte-Carlo simulations, and characterization experiments with phantoms and fresh tissues. In addition, we are exploring the use of a sCMOS detector array and rapid 3D deconvolution to improve the sensitivity and resolution of our LS-DAC microscope.

9155-37, Poster Session Monday

Excitation of fluorescence in the mouse lung using an internal diffusing fiber source and whole-animal optical imaging

Fatemeh Nooshabadi, Bilal H. Malik, Mark Wierzbicki, Duncan J. Maitland, Texas A&M Univ. (USA); Hee-jeong Yang, Jeffrey D. Cirillo, Texas A&M Health Science Ctr. (USA); Kristen C. Maitland, Texas A&M Univ. (USA)

ABSTRACT: Whole-body optical imaging of animal models is a new technique to study bacterial infection dynamics in vivo. However, interaction of light with tissue components diminishes the ability to detect small populations of cells deep inside the animal body, such as in the lung. We have integrated a diffusing fiber fluorescence excitation source into a whole-animal optical imaging system to physically transmit the excitation light to the fluorescent target and potentially increase fluorescence excitation efficiency deep in the animal. Integration of these technologies has the potential to allow for higher sensitivity detection of early infection, enhancing the ability to assess new therapeutic agents.

9155-38, Poster Session Monday

The identification of main molecules in chicken fascia and skin at spectral lines in-vitro

Olga A. Smolyanskaya, Igor V. Prozheev, Anna A. Ezerskaya, Evgenij A. Strepitov, Nikolay S. Balbekin, National Research Univ. of Information Technologies, Mechanics and Optics (Russian Federation)

ABSTRACT: The chicken fascia and skin spectra was obtained in-vitro by using THz time-domain spectroscopy. The spectral lines of main bio-molecules including amino acids were matched with spectral lines of the samples. Several substances were identified in chicken fascia and skin such as tryptophan, D-glucose, adenosine diphosphate, valine and reticulin. This spectral lines including amino acids connects with oscillation modes which conditioned chemical reactions, hydration processes and conformation changes of molecules in skin. The spectral lines of amino acids and other molecules, taking part in metabolic processes, was found at fascia and skin spectra. It is really important to develop THz diagnostic setup with maximal sensitivity and selectivity. It seems very promising to design metamaterial filters for improve the method sensitivity. It can allow us to use that method for precise skin diagnosis.

9155-39, Poster Session Monday

Multimodal foveated endomicroscope for the detection of esophageal adenocarcinoma in Barrett's esophagus

Adam Shadfan, Tomasz S. Tkaczyk, Rice Univ. (USA)

ABSTRACT: A foveated endomicroscope is proposed that improves upon current detection methods of esophageal adenocarcinoma (EAC) in Barrett's Esophagus (BE) such as the Seattle Protocol and the use of small field-of-view (FOV) high-resolution endoscopes. This objective mimics the human eye by utilizing a large FOV to provide browsing of BE segments, which can then be inspected for EAC with the high-resolution center of the FOV. The non-invasive device is integrated with a confocal microscope and hyperspectral camera to observe changes to morphological structures and biochemical signatures of the cells, further improving upon current techniques and reducing the number of biopsies taken.

9155-40, Poster Session Monday

Assessing lymphatic response to treatments in head and neck cancer using near-infrared fluorescence imaging

I-Chih Tan, Ron J. Karni, John C. Rasmussen, Eva M. Sevick-Muraca,

The Univ. of Texas Health Science Ctr. at Houston (USA)

ABSTRACT: Care for head and neck (HN) cancer could be improved with better mapping of lymphatic drainage pathways in HN region as well as understanding the effect of the cancer treatments on lymphatics. In this study, near-infrared fluorescence imaging was used to visualize the lymphatics in human subjects diagnosed with HN cancer before and after treatments. Imaging results showed the lymphatic architecture and contractile function in HN. Reformation of lymphatics during the course of cancer care was also seen in the longitudinal imaging. It allowed us to better understand the lymphatics in HN cancer patients.

Nonlinear optical imaging of the basement membrane in hamster model of oral carcinogenesis

Rahul Pal, Jinping Yang, Gracie Vargas, The Univ. of Texas Medical Branch (USA)

ABSTRACT: Survival rate of oral cancers depend on the stage of diagnosis and mostly early and pre-neoplastic alterations go unnoticed due to the lack of proper screening. Multiphoton Autofluorescence and Second Harmonic Generation Microscopy have provided noninvasive real-time information of tissue microarchitecture with subcellular resolution. We have utilized a combination of these nonlinear optical imaging techniques to assess tissue morphology in a hamster model of oral carcinogenesis and identified alterations in the basement membrane in (pre)neoplasia of the disease. Our data suggests irregularities basement membrane, along with cellular morphology could be used in delineating normal and inflamed tissue from dysplasia.

9155-42, Poster Session Monday

Phase-sensitive optical coherence tomography in the middle ear using an akinetic swept laser source

Jesung Park, Texas A&M Univ. (USA); John S. Oghalai M.D., Stanford Univ. (USA); Brian E. Applegate, Texas A&M Univ. (USA)

ABSTRACT: Hearing loss is a common sensory problem observed in all age groups with various risk factors, and causes critical impairment to the quality of life. Auditory processing in the middle ear changes sound waves to a mechanical vibration by the movement of the tympanic membrane (TM) and the ossicles. Monitoring the morphological structure and mechanical vibration of the middle ear is a crucial diagnostic approach for conductive hearing loss. Phase-sensitive OCT can visualize the morphological structures of the middle ear and measure its mechanical vibration. We developed a fiber-based phase-sensitive OCT system with an akinetic swept laser source for the measurement of mechanical vibration in the middle ear. The akinetic swept laser is electronically tuned and precisely controls sweeps without any mechanical movement, which results in minimal phase instability. The swept source was operated with a wavelength 1550 nm, sweep rate of 140 kHz, and provided picometer-scale phase sensitive OCT, we acquired the structures and vibrations of the middle ear of an ex vivo mouse model with high-speed real-time performance with field programmable gate array (FPGA) architecture.

9155-43, Poster Session Monday

A simple optofluidic platform for label-free cell-surface marker screening

Mustafa A. Mir, Olivia Scheideler, Lydia L. Sohn, Univ. of California, Berkeley (USA)

ABSTRACT: Current technologies for cell surface marker screening such as flow cytometry and florescence microscopy, though indispensable, are not well suited for deployment in low resource or point-of-care settings. Recently, node-pore sensing (NPS) has emerged as a microfluidic platform for label-free cell surface marker screening. In NPS the transit time of individual cells being flowed through an antibody-functionalized microchannel are measured. Cells that express surface markers corresponding to a functionalized region are delayed due to specific, transient interactions with the surface. In this manner, the presence or absence of a particular surface marker is determined with single cell resolution. Here we show that by measuring the transit time optically as opposed to electrically, the abilities of NPS can be extended. We demonstrate this approach through measurements on human breast cancer cells. The technology presented here could potentially be deployed in low-resource settings as a diagnostic tool. 9155-44, Poster Session Monday

Improvements in frequency-domain based NIRF optical tomography modality for preclinical studies

Chinmay D. Darne, Eva M. Sevick-Muraca,

The Univ. of Texas Health Science Ctr. at Houston (USA)

ABSTRACT: Herein we present recent improvements in system design and performance evaluation of near-infrared fluorescence (NIRF) frequency-domain photon migration (FDPM) system developed for small animal fluorescence tomography and installed within a commercial micro-CT/PET scanner. We improved system performance by increasing signal-to-noise ratio (SNR) through use of high powered rf modulation, novel data collection scheme, and data discrimination based on the associated noise levels. Noise characteristics show improvement with these techniques and are currently being employed to improve 3-D fluorescence for tomographic reconstructions in phantoms before incorporating into hybrid scanner.

9155-47, Poster Session Monday

Performance evaluation of integrating detectors for near-infrared fluorescence molecular imaging

Banghe Zhu, John C. Rasmussen, Eva M. Sevick-Muraca,

The Univ. of Texas Health Science Ctr. at Houston (USA)

ABSTRACT: Although there has been a plethora of devices advanced for clinical translation, there has been no standards to compare and determine the optical device for fluorescence molecular imaging. In this work, we compare different CCD configurations using a solid phantom developed to mimic pM – fM concentrations of near-infrared fluorescent dyesin tissues. Our results show that intensified CCD systems (ICCDs) offer greater contrast at larger signal-to-noise ratios (SNRs) in comparison to their un-intensified CCD systems operated at clinically reasonable, sub-second acquisition times. Furthermore, we compared our investigational ICCD device to the commercial NOVADAQ SPY system, demonstrating different performance in both SNR and contrast.

9155-48, Poster Session Monday

Study on temperature effect of microcirculation using near-infrared laser Doppler system

Chun-Jung Huang, Ching-Cheng Chuang, Chia-Wei Sun,

National Chiao Tung Univ. (Taiwan)

ABSTRACT: Microcirculation presents in the small vasculature embedded within tissue and it deals with the circulation of blood from the heart to arteries, veins and capillaries. The microcirculation could response the physiological condition of human. In this study, we built a near-infrared laser Doppler system for microcirculation detection. The near-infrared diffuse photon penetrates deeper tissue and reveals the information of microcirculation. We propose the far-infrared illumination as a contactless physiological intervention for laser Doppler measurement. The optical assessment shows an interpretation of tissue microcirculation change with oxygenation dynamics.

9155-49, Poster Session Monday

Performance evaluation of fluorescence tomography in a Siemens Inveon multimodality scanner

Yujie Lu, Chinmay D. Darne, I-Chih Tan, Banghe Zhu, John C. Rasmussen, Eva M. Sevick-Muraca, The Univ. of Texas Health Science Ctr. at Houston (USA)

ABSTRACT: A tri-modal (PET/CT/Optical) small animal tomographic imaging system was developed by integrating our advanced non-contact intensified CCD (ICCD) frequency-domain fluorescence imaging components into a Siemens Inveon scanner. We performed a performance evaluation of the developed imaging system by using the developed regularization-free high-order radiative-transfer-based reconstruction algorithm and custom solid phantoms. Our results show that frequency-domain photon migration (FDPM) fluorescence tomography can achieve better tomographic images with less artifacts and more precise fluorescent source localization compared to the continuous-wave counterpart. The developed multimodal tomographic imaging system provides a powerful tool for translational biomedical research.

9155-50, Poster Session Monday

Noninvasive monitoring of cholesterol in the blood vessels using THz TDS

Anna A. Ezerskaya, Igor V. Prozheev, Evgeniy A. Strepitov, Olga A. Smolyanskaya,

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ABSTRACT: Several models of atherosclerosis have been investigated. It can allow diagnosing atherosclerosis in the layers under the skin. Moreover, the typical reflection lines for lipid components of atherosclerotic plaque were identified. This set of lines positioned as suitable for diagnostics on selected frequencies.

9155-51, Poster Session Monday

In vivo microscopy for malaria diagnosis

Jennifer Burnett, Jennifer L. Carns, Rebecca Richards-Kortum, Rice Univ. (USA)

ABSTRACT: High-quality malaria diagnostics are critical to measure the efficacy of prevention and treatment efforts and to avoid misdiagnosis and over treatment. Conventional malaria diagnostics requires the collection of a finger-prick blood sample, which is stained and analyzed under a microscope. This method has varying performance from technician to technician, and is dependent on the quality of the prepared blood smear. Our approach is to detect malaria infected blood cells as they circulate in vivo, avoiding the generation of biohazards and the need for a trained specialist. This concept was evaluated in a mouse model using a portable, homebuilt microscope system.

9155-52, Poster Session Monday

Phantom tissue elastic properties assessment using hyperbolic modulation in dynamic spatial frequency domain imaging (DSFDI)

Jose E. Calderon, David Serrano, Univ. de Puerto Rico Mayagüez (USA)

ABSTRACT: Identification of mechanical properties of phantom tissue are important for biomedical research of laser photo therapeutic applications. Using a non-contact pattern illumination Spatial Frequency Domain Imaging technique, we evaluated the effectiveness to correlate the changes in the elastic properties subjected to photothermolysis. The illumination of modulated patterns correlated to scattering and absorption optical properties of the interrogated target were contrasted against resulting elastic modulus and ultimate tensile strength of material. Method include a CCD Camera with a 30X lens, a digital marrow display projector, and prototype Arduino UNO microcontroller with sensors where orchestrated using a desktop computer with parallel computing capabilities under Mathematica 9.0 (Wolfram Research) software and processing by a Graphic Processing Unit (GPU) GeForce 6300 from NVidia. Phantom Tissue was Siloxane with Achiote extract and Titanium Dioxide serving as absorption and scattering agents respectively. A controlled 465 nm +/- 20% blue 2 watts laser diode induced the thermal shock at for 2 seconds at 5 Hz and 50 millisecond pulse duration over a 50 mm diameter interrogating area. Elastic properties where determine using a tensionmeter Model ESM301. Image captured the structured illumination from modulated asymptote of hyperbolic and based ratio ellipsoid from 1 to 2Pi and from 0 to 1 respectively. Quantitative analysis from correlation between specimen UTS, PL and YS correlation of 0.7. Histogram showed standard deviation of 20 percent. Qualitative data shows potential non-contact technique to determine elastic properties of phantom. Further research needed under enhanced pattern illumination resolution.

9155-54, Poster Session Monday

Device for monitoring blood oxygenation levels in the tibia

Joseph L Hollmann, Paula Arambel, Northeastern Univ (USA); Judith Plet, University of Technology of Compiègne (France); Sandra Shefelbine, Stacey Markovic, Mark J Niedre, Charles A DiMarzio, Northeastern Univ (USA)

ABSTRACT: Osteoporosis is a common side effect of spinal cord injuries. Blood perfusion in the bone provides an indication of bone health and may help to evaluate therapies addressing bone loss. Current methods for measuring blood perfusion of bone use dyes and ionizing radiation, and yield qualitative results.

We present a device capable of measuring blood oxygenation in the tibia. The device illuminates the skin directly over the tibia with a white light source and measures the diffusely reflected light in the near infrared spectrum. Multiple source-detector distances are utilized so that the blood perfusion in skin and bone may be differentiated.

9155-55, Poster Session Monday

Automated frame selection process for analyzing high resolution microendoscope images

Ayumu Ishijima, Sharon Mondrik, Richard A Schwarz, Rice University (USA); Nadarajah Vigneswaran, The University of Texas School of Dentistry (USA); Ann M Gillenwater, The University of Texas MD Anderson Cancer Center (USA); Rebecca Richards-Kortum, Rice University (USA)

ABSTRACT: We developed an automated frame selection algorithm for high resolution microendoscope images. The algorithm rapidly selects a representative frame with minimal motion artifact from a short video sequence, enabling fully automated image analysis at the point-of-care. The performance of the algorithm was evaluated by comparing automatically selected frames to manually selected frames using quantitative image parameters. The implementation of fully automated high-resolution microendoscopy at the point-of-care has the potential to reduce the number of biopsies needed for accurate diagnosis of precancer and cancer in low-resource settings, where there may be limited infrastructure and personnel for standard histologic analysis.

9155-56, Poster Session Monday

Automated layer segmentation in retinal OCT images

Jonathan Luisi, David Briley, Adam Boretsky, Massoud Motamedi,

The Univ. of Texas Medical Branch (USA)

ABSTRACT: SD-OCT is a valuable diagnostic tool in both clinical and research settings. The depth-resolved intensity profiles generated by light backscattered from discrete layers of the retina provide a non-invasive method of investigating progressive diseases and injury within the eye. This study demonstrates the application of steerable convolution filters which automatically separate gradient orientations to identify edges and delineate tissue boundaries. The edge maps were recombined to measure thickness of individual retinal layers. This technique was successfully applied to monitor changes in retinal morphology in a mouse model of laser-induced choroidal neovascularization (CNV) and human data from age-related macular degeneration patients.

9155-57, Poster Session Monday

Quantitative "label-free" imaging of dynamic biological events

Katherine Creath, 4D Technology Corp. (USA) and The Univ. of Arizona (USA); Goldie L. Goldstein, 4D Technology Corp. (USA)

ABSTRACT: The ability to view cells' direct response before, during and after exposure to a treatment or drug is an important means to discovering reaction mechanisms and morphology changes. One new method that is providing new insight into dynamic cellular morphology is quantitative phase microscopy. This label-free imaging modality shows great utility in its ability to examine optical thickness and volume changes, directly proportional to dry cell mass over a range of timescales [1]. This paper describes new and recent research related to measuring optical thickness via a quantitative phase microscope and using it to study small populations of beating cardiac myocytes' and their response to a drug. Additional measurements are shown of blood flow in a 3-day old zebrafish and vesicle motion within actin fibers in myoblasts.

9155-62, Poster Session Monday

Hand-held multi-modal imaging probe for oral cancer diagnosis

Laura M. Higgins, Mark C. Pierce, Rutgers, The State Univ. of New Jersey (USA)

ABSTRACT: We present the design, characterization, and preliminary in vivo testing of a hand-held probe for simultaneous optical coherence tomography (OCT) and high-resolution epi-fluorescence (HRF) imaging. OCT provides cross-sectional imaging of tissue micro-architecture to a depth of approximately 2 mm, while HRF provides high-resolution en face imaging over a 0.75 mm square field-of-view. The optical design delivers OCT and HRF beams along a common optical path, allowing simultaneous, real-time display of co-registered images. The probe is designed to permit assessment of the oral mucosa, using HRF to identify abnormal lesions within the epithelium and OCT to determine depth of sub-mucosal involvement.

9155-64, Poster Session Monday

Super-resolution optical microscopy with standard clinical H&E stains: bringing definition to diagnostics

Arnold Vainrub, The Univ. of Texas Medical Branch (USA)

ABSTRACT: Emerging super-resolution (SR) optical microscopy has yet to be innovatively applied in clinical pathology. We recorded and compared conventional transmission images and SR images using microscopic samples. We found that standard H&E or Diff-Quick stains of bacteria, cells, and tissue sections provide high-contrast SR images in both reflected and fluorescent light modes. In SR images the lateral resolution is over ten times sharper than with transmission microscopy and the optical sectioning is substantially improved due to a shorter focus depth. Histological details are seen on a size scale of 0.1 to 2 microns, opening up possibilities for a 2D and 3D assessment of sub-cellular morphology on a much smaller scale than could previously be achieved. The results are illustrated by images of bacteria, leukocytes, and mouse retina sections.

Our structured-illumination microscopy (SIM) system built at UTMB provides super-resolution imaging of pathology slides in transmitted, reflected and/or fluorescent light modes. The lateral and axial resolutions of 0.09 microns and 0.25 microns, respectively, double the diffraction limit of resolution in conventional optical microscopy. Our SIM system is based on a popular Nikon Eclipse Ti microscope, but is compatible with many manufacturers' commercial microscopes. Two key developments achieve super-resolution. First, the hardware is upgraded to a custom designed and homebuilt structured illuminator. Second, customized software reconstructs 2D or 3D super-resolution images from a set of experimental images obtained via specific illumination patterns.

9155-65, Poster Session Monday

Development of a spatial frequency domain imaging system platform

David J. Cuccia, Amaan Mazhar, Scott Dolin, Modulated Imaging, Inc. (USA); Steve Saggese, Advanced Coherent Technologies LLC (USA); Pierre Khoury, Modulated Imaging, Inc. (USA)

ABSTRACT: Quantitative characterization of tissue structure and function is one of the most challenging problems in medical imaging. To this end, we present development of a robust and user-friendly platform Spatial Frequency Domain Imaging (SFDI) system for wide-field mapping of optical properties and chromophores. We will present: 1) Design and fabrication of a clinic-ready hardware platform with increased field-of-view (20cm x 15cm), spectral multiplexing (11 wavelengths), improved stability (<0.5% drift/hr) and enhanced ease of use (cart-mounted instrumentation); 2) Development of clinic-friendly software with automated analysis and refined algorithms; 3) Development of internal and external verification and validation procedures; 4) In-vivo evaluations to establish benchmarks of performance and sensitivity for quantitative hemoglobin and water parameter recovery. Application areas include research in chronic wound healing, pressure sore staging, burn assessment, reconstructive surgery, and preclinical studies. This work was developed with support from SBIR/STTR grants W81XWH11C0108 (TATRC), R43-RR025985 (NCI), and R42GM077713 (NIGMS).

Hyperspectral Raman imaging (HSRI) for multiplexed molecular imaging

Ji Qi, Jingting Li, Yulu Sung, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: Raman scattering and Surface-enhanced Raman scattering (SERS) have been employed to encode multiple "color channels" for multiplexed molecular imaging. In Raman scattering, molecular information are encoded in various endogenous vibrational features. In SERS, different labels are used to tag plasmonic nanoparticles such as nanospheres and nanoshells. Raman spectroscopic microscopy systems are needed to acquire full Raman spectra. Spectroscopic pattern matching and/or unmixing is then employed for correct channel assignment. Compared to fluorescence, Raman and SERS have the potential advantage of higher multiplexing capacity (i.e., more "color channels"), single excitation wavelength, and no photobleaching. However, current Raman spectroscopic microscopy systems are very slow.

Recently, we have developed a hyperspectral Raman imaging (HSRI) system for simultaneously collecting Raman spectra from multiple points [1-3]. This scheme is realized by multiple-point laser active-illumination using a spatial light modulator coupled with wide-field imaging. We have acquired full Raman spectra from as many as ~200 laser spots (equivalent to ~500 diffraction limited imaging pixels) within 1 second without mechanical scanning, inside a 100x100 ?m2 field of view. Such throughput is significantly higher than state-of-the-art commercial systems.

9155-68, Poster Session Monday

Monolithic nanoporous gold disks with large specific surface area, tunable plasmon resonance, and high-density, internal plasmonic hot-spots

Jianbo Zeng, Fusheng Zhao, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: Plasmonic metal nanostructures have shown great potential in sensing, photovoltaics, imaging and biomedicine, principally due to enhancement of the local electric field by light-excited surface plasmons, the collective oscillation of conduction band electrons. Thin films of nanoporous gold have received a great deal of interest due to the unique 3-dimensional bicontinuous nanostructures with high specific surface area. However, in the form of semi-infinite thin films, nanoporous gold exhibits weak plasmonic extinction and little tunability in the plasmon resonance, because the pore size is much smaller than the wavelength of light. Here we show that by making nanoporous gold in the form of disks of sub-wavelength diameter and sub-100 nm thickness, these limitations can be overcome. Nanoporous gold disks not only possess large specific surface area but also high-density, internal plasmonic "hot-spots" with impressive electric field enhancement, which greatly promotes plasmon-matter interaction as evidenced by spectral shifts in the surface plasmon resonance. In addition, the plasmonic resonance of nanoporous gold disks can be easily tuned from 900 to 1850 nm by changing the disk diameter from 300 to 700 nm. Furthermore, nanoporous gold disks can be fabricated as either bound on a surface or as non-aggregating colloidal suspension with high stability.

9155-69, Poster Session Monday

Improvement of tissue analysis and classification using optical coherence tomography combined with Raman spectroscopy

Ji Qi, Peter Liu, Kirill V. Larin, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: Optical coherence tomography (OCT) provides significant advantages of high-resolution (approaching the histopathology level) real-time imaging of tissues without use of contrast agents. Based on these advantages, the microstructural features of tumors can be visualized and detected intra-operatively. However, it is still not clinically accepted for tumor margin delineation due to poor specificity and accuracy. In contrast, Raman spectroscopy (RS) can obtain tissue information at the molecular level, but does not provide real-time imaging capability. Therefore, combining OCT and RS could provide synergy. To this end, we present a tissue analysis and classification method using both the slope of OCT intensity signal versus depth and the principle components from the RS spectrum as the indicators for tissue characterization. The goal of this study was to understand prediction accuracy of OCT and combined OCT/ RS method for classification of optically similar tissues and organs. Our pilot experiments were performed on mouse kidneys, livers, and small intestines. The prediction accuracy with five-fold cross validation of the method has been evaluated by the support vector machine method. The results demonstrate that tissue characterization based on the OCT/RS method was superior compared to using OCT structural information alone. This combined OCT/RS method is potentially useful as a noninvasive optical biopsy technique for rapid and automatic tissue characterization during surgery.

9155-70, Poster Session Monday

Microfluidic label-free monitoring of DNA hybridization

Ji Qi, Jianbo Zeng, Fusheng Zhao, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: Label-free sensing of trace biomolecules such as DNA and pathogens such as viruses would enable powerful amplification-free biosensing Surface-enhanced Raman spectroscopy (SERS) has been widely used for molecular detection and identification by exploiting the localized surface plasmon resonance effect when the target molecules are near gold or silver nanostructures. However, effective and robust SERS assays have yet become a reality for trace detection.

Recently, we have developed a SERS substrate by shaping nanoporous gold thin films into monolithic submicron disks, called nanoporous gold disks (NPGD). NPGD provides an effective surface area larger than its geometrical area and a SERS enhancement factor larger than 100 million ^[1]. Here we present examples of NPGD-based SERS label-free biosensing at the single-molecule level.

Nanoporous gold disks for photothermal light harvesting and light-gated molecular release

Greggy M. Santos, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: Nanoporous gold disks (NPGDs) with 400 nm diameter, 75 nm thickness, and 13 nm pores exhibit large specific surface area and effective photothermal light harvesting capability. A potential application is demonstrated by light-gated, multi-step molecular release of pre-adsorbed R6G fluorescent dye on arrayed NPGDs. Through the use of time-resolved temperature mapping, the spatial and temporal characteristics of photothermal heating in NPGD arrays is successfully demonstrated for both aqueous and air ambient environments. By applying a thermodynamic model to our experimental data, we determined the photothermal conversion efficiency at 56% for NPGD arrays. As a potential application, light-gated, multi-stage release of pre-adsorbed R6G dye molecules from NPGD arrays has been demonstrated. The results establish the foundation that NPGDs can be employed for photothermal light harvesting and light-gated molecular release.

9155-72, Poster Session Monday

Surface-enhanced Raman spectroscopy for label-free, multiplexed, molecular sensing and imaging

Ming Li, Jing Lu, Wei-Chuan Shih, Univ. of Houston (USA)

ABSTRACT: We report a novel surface-enhanced Raman spectroscopy (SERS) approach for label-free, multiplexed, molecular sensing and large-area, high-resolution molecular imaging on a surface. In this technique, nanoporous gold disk SERS substrates are physically brought to the surface where analytes of interested were pre-deposited, followed by SERS acquisition. This technique features simple sample preparation, low cost, and high reproducibility, which could lead to SERS-based sensing and imaging for point-of-care and forensics applications.

9155-11, Session 4

Democratization of next-generation imaging, diagnostics and measurement tools using mobile phones (Invited Paper)

Aydogan Ozcan, Univ. of California, Los Angeles (USA)

BIOGRAPHY: Dr. Aydogan Ozcan is the Chancellor's Professor at UCLA leading the Bio- and Nano-Photonics Laboratory at the Electrical Engineering and Bioengineering Departments. Dr. Ozcan holds 22 issued patents (all of which are licensed) and >15 pending patent applications and is also the author of one book and the co-author of more than 350 peer reviewed research articles in major scientific journals and conferences. Dr. Ozcan is a Fellow of SPIE and OSA, and has received major awards including the Presidential Early Career Award for Scientists and Engineers (PECASE), SPIE Biophotonics Technology Innovator Award, SPIE Early Career Achievement Award, ARO Young Investigator Award, NSF CAREER Award, NIH Director's New Innovator Award, ONR Young Investigator Award, IEEE Photonics Society Young Investigator Award and MIT's TR35 Award for his seminal contributions to near-field and on-chip imaging, and telemedicine based diagnostics. http://innovate.ee.ucla.edu/

ABSTRACT: In this presentation I will discuss some of the emerging applications and the future opportunities and challenges created by the use of mobile phones and their embedded components for the development of next-generation imaging, sensing, diagnostics and measurement tools. The massive volume of mobile phone users, which has now reached ~7 billion, drives the rapid improvements of the hardware, software and high-end imaging and sensing technologies embedded in our phones, transforming the mobile phone into a cost-effective and yet extremely powerful platform to run e.g., biomedical tests and perform scientific measurements that would normally require advanced laboratory instruments. This rapidly evolving and continuing trend will help us transform how medicine, engineering and sciences are practiced and taught globally.

9155-12, Session 4

Image analysis and machine learning for quantitative reading of confocal images of skin (Invited Paper)

Dana H. Brooks, Northeastern Univ. (USA)

BIOGRAPHY: Dana H. Brooks is Professor of Electrical and Computer Engineering, Northeastern University, co-founder of the Biomedical Signal Processing, Imaging, Reasoning, and Learning (B-SPIRAL) group there, and PI of the

Estimation Core of the Center for Integrative Biomedical Computing at University of Utah. His research includes application of signal and image processing and machine learning to medical and biological imaging.

ABSTRACT: Reflectance and fluorescence confocal microscopy are increasingly being applied in the clinic for noninvasive detection of skin cancer with high sensitivity and specificity. Expert clinicians reliably use confocal microscopy to guide biopsy and surgery and thus impact patient care. However, images are currently read purely by visual inspection, leading to variability in detection accuracy, especially with non-expert clinicians. We are developing machine learning and image analysis algorithms to enable a more quantitative and objective approach, potentially leading to tools to assist with reading images as well as for clinician training.

9155-13, Session 5

Using micro and nanofluidics with Surface Enhanced Raman Spectroscopy for in vitro blood based biomarker detection (Invited Paper)

Gerard L Coté, Department of Biomedical Engineering, Texas A&M Univ. (USA); **Jun Kameoka,** Electrical and Computer Engineering, Texas A&M Univ. (USA); **Haley Marks,** Department of Biomedical Engineering, Texas A&M Univ. (USA)

BIOGRAPHY: Gerard L. Coté holds the Charles H. & Bettye Barclay Professorship, is the Head of the Department of Biomedical Engineering, and the Interim Director of the Center for Remote Health Technology at Texas A&M University. His research focuses on optically-based biomedical sensing. He is the coauthor of over 250 publications, co-holder of several U.S. patents, and co-founder of three medical device companies. He is a Fellow of four societies including IEEE, AIMBE, BMES, and SPIE.

ABSTRACT: In this presentation we will discuss the development of a point-of-care optofluidic device that uses gold nanoparticle-based surface enhanced Raman spectroscopy (SERS) for detection of blood biomarkers. SERS approaches have been successfully used for detection of analytes due to the large enhancements provided by the interaction between the light, gold particles, and analyte. However, SERS approaches developed for use to accurately quantify an analyte have suffered from a lack of repeatability. We will describe our SERS optofluidic device with functionalized nanoparticles that helps to overcome these problems and will show results with a focus on blood toxins and cardiac biomarkers.

9155-14, Session 5

Label-free hyperspectral microscopy for quantitative chemical mapping of single erythrocytes for malaria screening (Invited Paper)

Jeeseong Hwang, National Institute of Standards and Technology (USA)

BIOGRAPHY: Jeeseong Hwang is a research biophysicist at NIST. He has investigated biophysical aspects of immune response of human cells using super-resolution microscopy and other laser-based optical techniques. His recent research focuses on nanobiophotonics for quantitative biophysics and medical imaging. Contributions to professional societies include the IEEE-Nanotechnology, SPIE BiOS, and the ISO. He received many awards including a US/DoC Silver Medal and the Washington Academy of Sciences Award in Biological Sciences.

ABSTRACT: We have developed an absorption spectroscopy-based hyperspectral microscope capable of resolving the distribution of different types hemoglobins in single erythrocytes infected by Plasmodium farciparum (Pf) malaria parasites. A spectrum of multi-component scene can be described as a linear superposition of spectra of "pure" individual substances called "endmembers." The identification these endmembers were demonstrated and validated using physics-based endmember extraction algorithms and abundance map calculation algorithms applied to the hyper-spectral data cubes. This method may be applied to a variety of diagnostics assays to screen blood-borne pathogens at a single cell sensitivity at the early stage.

9155-15, Session 5

Programmable bio-nano-chips customized for cardiac and cancer diagnostic applications (Invited Paper)

John McDevitt, Rice Univ. (USA)

BIOGRAPHY: John T. McDevitt is the Brown-Wiess Professor of Chemistry and Bioengineering at Rice University and is a pioneer in the development of "programmable bio-nano-chip" technologies. Since joining Rice in 2009, McDevitt's group has focused primarily on development of portable diagnostic devices that have potential to replace high-cost, lab-based, time-consuming diagnostic tests for both resource scarce settings where traditional laboratory measurements are not practical as well as for developed countries that are seeking to reduce health care costs. McDevitt's recent research has been supported by major programs funded by the National Institute of Dental and Craniofacial Research (NIDCR) division of the National Institutes of Health (NIH), the Bill and Melinda Gates Foundation, Cancer Prevention Research Institute of Texas (CPRIT), the National Aeronautics and Space Administration (NASA) and the United Kingdom's Home Office Scientific Development Branch. McDevitt and his team have written more than 170 peer-reviewed scientific manuscripts and have contributed to more than 150 patents and patent applications. This work was recognized with the "Best of What's New Award" in the Medical Device Category for 2008 by Popular Science as well as for the "Best Scientific Advances Award" in 1998 by the Science Coalition. Dr. McDevitt's individual honors include the Presidential Young Investigator Award, the 2010 California Polytechnic Distinguished Alumni Award and the Exxon Education Award. McDevitt now serves as the Principal Investigator for 6 major clinical trials and 2 clinical pilot studies all involving the programmable bio-nano-chip. Through these clinical efforts mini-sensor ensembles are being developed for major diseases in the areas of cardiac heart disease, trauma, drugs of abuse, oral cancer, ovarian cancer and prostate cancer. With CPRIT funding McDevitt has recently established the "Texas Cancer Diagnostics Pipeline" and serves at the Director for the newly formed "Early Disease Detection Gulf Coast Consortium Cluster" thereby creating a network of over 100 clinical researchers devoted to next generation of affordable diagnostics. McDevitt has served as the Scientific Founder for several companies in areas related to medical microdevice technologies.

ABSTRACT: Biological sensing using chip-based devices has become very popular in past two decades due to the strong potential impact on clinical care. However, lack of standard modular testing platform for multiplexed and multiclass analyte testing is major barrier for field. With this perspective in mind, McDevitt group has sustained concerted efforts to move multiplexed and multiclass biosensing onto single modular programmable bio-nano-chip (p-BNC) platform. This talk will focus on customization of p-BNC systems for major cardiac and cancer applications whereby the approach is now being validated through 6 major clinical trials involving over 5000 patients and 10 clinical sites.

9155-59, Session 6

Path, present and future, or, stromics and hectaplexing (Invited Paper)

Richard M. Levenson M.D., Univ. of California, Davis (USA)

BIOGRAPHY: Richard Levenson, MD, FCAP, is Professor and Vice Chair for Strategic Technologies in the Department of Pathology and Laboratory Medicine, UC Davis. He trained in medicine at University of Michigan and pathology at Washington University, and is Board-certified in Anatomic Pathology. He previously served as VP of Research at Cambridge Research and Instrumentation (now part of PerkinElmer), focusing on multispectral imaging and instrument systems development.

ABSTRACT: There is competition between tissue-extract-based proteomic and nucleic acid analyses that are precise and highly multiplexed (tens to thousands of analytes) but are largely devoid of spatial context, and microscopic imaging-based assays (like immunohistochemistry) that can have resolution down to the subcellular scale, but can deliver only modest levels of multiplexing. Novel instrumentation, reagents, and importantly, software (including machine learning and dimensionality reduction), can help deliver reliable assessments of pure morphology-associated features as well as efficient visualizations of highly multiplexed (~100 analytes), spatially resolved, molecular phenotypes. Attention to the microenvironment in addition to the epithelial compartment is likely to be rewarding.

9155-60, Session 6

Translational biophotonics: perspectives from an industrial R&D center (Invited Paper)

Siavash Yazdanfar, GE Global Research (USA)

BIOGRAPHY: Siavash Yazdanfar manages the Applied Optics Laboratory at GE Global Research, where he is responsible for a portfolio of optics research ranging from biomedical optics to advanced lighting. Since joining GE in 2005, he has supported or led numerous projects funded both internally and externally, including work in fluorescence image guided surgery, nonlinear microscopy, and high throughput automated microscopy. He has translated two projects to clinic, developing surgical and endoscopic instrumentation for first-in-man studies, and contributed to recently commercialized technology in digital and molecular pathology. He has published 37 peer reviewed journal articles, five book chapters and 17 U.S. patents.

ABSTRACT: In this presentation, I will describe optical technologies, developed by scientists at GE Global Research, which have advanced from benchtop research to clinical application. The first of these is a technology for based on high-resolution microscopy of molecular biomarkers, allowing for imaging up to 60 biomarkers in pathology samples, through the combination of high-throughput optical microscopy, microfluidics and multiplexed immunofluorescence. Coupled with analytical tools for visualization and quantitative image processing, this system opens new possibilities in molecular pathology. A second area of development is in fluorescence imaging, to allow for improved visualization of critical structures during surgery and endoscopy, through the use of molecular contrast agents and dedicated optical imaging hardware.

9155-61, Session 6

Multimodal/adaptive optics imaging: bringing new perspectives to the clinic (Invited Paper)

R. Daniel Ferguson, Physical Sciences Inc. (USA)

ABSTRACT: We will describe some recent progress in two distinct areas of translational R&D at PSI with a common thread: combining high resolution in vivo imaging using the complementary modalities of scanning confocal microscopy and OCT. The principle benefits of such imaging combinations arise most naturally when each mode informs and guides the other, providing both large scale structural perspective and local cellular detail. The result can be quicker and more efficient appreciation of the nature and extent of pathology in clinical examination and diagnosis. The PSI systems currently in the most advanced state of development include multimodal Adaptive Optics (AO) SLO/OCT instruments for retinal imaging and a hand-held combined reflectance confocal microscopy/OCT probe for skin imaging. A recent addition to the AO family of systems is a compact clinical prototype device currently being tested at Boston Children's Hospital, while the newest RCM/OCT instrument will be soon moved to Shriners Hospital to be tested on patients with skin burns. Lessons learned about instrument development for the clinical environment and preliminary clinical results will be discussed.

9155-66, Session 6

Embracing open innovation: how engaging in collaborative development with companies can result in new sources of funding and accelerate the commercialization of your idea (Invited Paper)

Jason M. Eichenholz, Open Photonics, Inc. (USA)

BIOGRAPHY: Jason M. Eichenholz Ph.D. is the CEO and founder of Open Photonics Inc and CTO of OPI's first spin out, MicroVapor Devices. Prior to starting OPI Jason was the Photonics Divisional Technology Director at Halma PLC responsible for driving innovation, technology and strategy development for multiple Halma companies. Prior to that he was CTO and on the board of directors of Ocean Optics and Director of Strategic Marketing at Newport/Spectra-Physics.

ABSTRACT: The OPI Photonic HorizonsTM grant program is a completely new peer reviewed, R&D funding initiative. It serves as the framework to facilitate collaboration between researchers and inventors and companies with pathways to bring them to the market.

The grant program is specifically designed to enable researchers and inventors to prove out their new ideas, develop prototypes, and partner with existing companies to bring these products to market. We help researchers commercialize their ideas.

Working in partnership with some of the top research institutions around the world, our open innovation and crowd sourced teams come together as a new ecosystem to find new technology, product ideas and markets.

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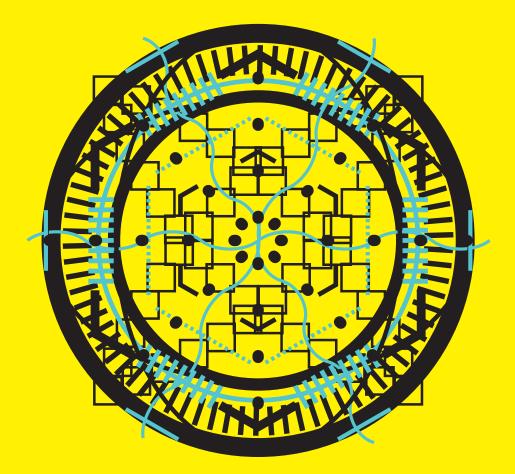
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