HIGHLIGHTING THE SCIENCE, TECHNOLOGY, AND APPLICATION OF IMAGING

IMAGING AT ILLINOIS

THE NEXT GENERATION

Computational Imaging
Biomedical Imaging
Imaging Agents and Agent Chemistry

Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

http://www.imaging.beckman.illinois.edu/imaging2012

JUNE 1 2012
The University of Illinois at Urbana-Champaign has a long and rich history of significant achievements in imaging, from the early developments of ultrasound imaging and its bioeffects, to the development of magnetic resonance imaging by the late Paul Lauterbur, who received the Nobel Prize in Medicine in 2003 for his work in establishing this technique. With computational strengths at the National Center for Supercomputing Applications and over 150 faculty across many departments, colleges, and interdisciplinary institutes, Illinois is positioned to make major advances in imaging. Imaging, and the visualization of images, are pervasive elements in our data-rich lives, and the Imaging at Illinois, which began on our campus in 2008, is an effort to build a campus-wide, collaborative, integrated community of faculty, researchers, and students in imaging science, imaging technology, and the application, use, and interpretation of images.
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Beckman Institute for Advanced Science and Technology
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## Agenda

### Friday, June 1

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<td><strong>Poster set-up</strong> – East Atrium, Beckman Institute</td>
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<td><em>Robert Easter - President-designate, University of Illinois</em></td>
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<td><em>The role of serendipity in molecular imaging</em></td>
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<td><em>Sam Achilefu - Washington University, St Louis</em></td>
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<td><strong>Concurrent Session 1</strong></td>
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<td><strong>Biomedical Imaging</strong></td>
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<td><em>Session Chair: Brad Sutton – University of Illinois at Urbana-Champaign</em></td>
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<td><em>Interfacing with the brain through real-time fMRI</em></td>
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<td><em>Stephen LaConte - Virginia Tech</em></td>
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<td><em>Quantitative ultrasound: A promising new image mode for diagnostics and therapy monitoring</em></td>
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<td><em>Quantifying the mechanical properties of brain tissue with magnetic resonance elastography</em></td>
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<td><em>Curtis Johnson - University of Illinois at Urbana-Champaign</em></td>
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<td><em>Resolving axonal integrity of specific pathways with diffusion weighted imaging in MRI</em></td>
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<td><em>Joseph Holtrop - University of Illinois at Urbana-Champaign</em></td>
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<td><em>Ultra-compact PET/MR and SPECT/MR system with sub-500µm resolution</em></td>
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<td><em>Liang Cai - University of Illinois at Urbana-Champaign</em></td>
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### Concurrent Session 2
Room 4269, Beckman Institute

**10:00 am**

**Computational Imaging and Visualization**

Session Chair: **John Stone** - *Beckman Institute*

- Visualization of petascale molecular dynamics simulations
  **John Stone** - *University of Illinois at Urbana-Champaign*

- Imaging photosynthetic light harvesting
  **Johan Strumpfer** - *University of Illinois at Urbana-Champaign*

- Interactive visualization of protein folding process from molecular dynamics simulations
  **Yanxin Liu** - *University of Illinois at Urbana-Champaign*

- Molecular level visualization of the HIV-1 capsid
  **Juan R. Perilla** - *University of Illinois at Urbana-Champaign*

- Lattice microbes: computational imaging of whole cells
  **John Cole** - *University of Illinois at Urbana-Champaign*

**Noon - 2 pm**

**Lunch** - Room 1005, Beckman Institute

**Poster Session** - East Atrium

### Concurrent Session 3
Room 2269, Beckman Institute

**2:00 pm**

**Biological Imaging**

Session Chair: **Peter Wang** - *University of Illinois at Urbana-Champaign*

- Optical tweezers in the study of mechanobiology
  **Elliot Botvinick** - *University of California-Irvine*

- Simplicity of design principles underlying cis-regulatory plasticity of Shp2 conformation
  **Jie Sun** - *University of Illinois at Urbana-Champaign*

  *In vivo* optical trapping reveals that kinesin drags dynein
  **Ben Blehm** - *University of Illinois at Urbana-Champaign*

### Concurrent Session 4
Room 4269, Beckman Institute

**2:00 pm**

**Imaging Agents and Agent Chemistry**

Session Chair: **Wawrzyniec Dobrucki** - *Beckman Institute*

- PET imaging of tumor angiogenesis: antibodies and nanoparticles
  **Weibo Cai** - *University of Wisconsin-Madison*

- Functional DNAs as selective agents for multi-target and multi-modal imaging and therapy
  **Yi Lu** - *University of Illinois at Urbana-Champaign*
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<td>3:30 pm</td>
<td><strong>Break</strong> - Room 1005, Beckman Institute</td>
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<td>4:00 pm</td>
<td><strong>Keynote Lecture</strong> – Auditorium, Beckman Institute</td>
<td>Multimodal imaging of remodeling post myocardial infarction: anatomy, physiology, and molecular targets&lt;br&gt;<strong>Albert Sinusas</strong> - Yale University</td>
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<td>4:45 pm</td>
<td><strong>Poster Awards, Closing Remarks, &amp; Future Directions</strong> - Auditorium, Beckman Institute</td>
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<td>5:00 pm</td>
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A variety of contrast mechanisms is available for imaging molecular processes in vivo by optical methods. At the core of molecular imaging is the need for in-depth understanding of key molecular processes involved in pathologic conditions of interest. This then allows for a logical design of molecular probes for detecting or reporting the functional status of specific molecular targets. Today, many molecular probes have been developed for preclinical and clinical studies using this scientific approach. Despite our best efforts to use scientific methods in the lab, unexpected results frequently occur. Although many such results are discarded, sometimes they give rise to the discovery of important molecular reporter systems. Two examples of recent unexpected but exciting findings in our lab will be used to illustrate the concept of serendipity in molecular optical imaging research.

Changes in the structure, geometry and eventually function of the left ventricle (LV) and atria occur following myocardial infarction (MI) and has been termed post-MI remodeling. The rate and degree of post-MI remodeling have been clearly indicated as independent predictors of morbidity and mortality. It is now well recognized that the process of post-MI myocardial remodeling that often leads to heart failure is associated with important changes within the myocardial extracellular matrix (ECM), and are associated with risk for ventricular and atrial arrhythmias. Matrix metalloproteinases (MMPs) and integrins are responsible for modulation of the remodeling process and could represent potential targets for non-invasive imaging of the molecular events that precede the structural changes. Defining the regional relationship between changes in LV and atrial geometry and mechanics in relation to MMP and integrin activation could lead to new mechanistic insights into these complex process and potentially new therapeutic approaches to prevent post-MI remodeling and risk for arrhythmias. Our multidisciplinary team has been developing high sensitivity targeted molecular imaging approaches and cine magnetic resonance (MR) imaging methods in order to quantify regional molecular events with structural changes post-MI. This combined molecular-mechanical approach will allow us to modify the adverse remodeling, and reduce risk and improve outcome.

The application of hybrid SPECT-CT, PET-CT, or PET-MR imaging systems will clearly improve the quantification of nuclear-based molecular imaging approaches. Targeted molecular imaging approaches not only complement existing imaging technology, but may predict late adverse myocardial remodeling, before the manifest as changes in physiological function or anatomical structure. Thus, molecular imaging of the cardiovascular system will enhance the development and application of truly personalized therapeutic regimens, and facilitate the monitoring of therapeutic efficacy and outcome.
Brain computer interfaces (BCIs) provide a powerful method for converting mental states into control signals to drive real-world devices. Thus BCIs have compelling applications for assistive technologies and rehabilitation protocols, and in the near future will likely have widespread impact on the public through computer gaming and the entertainment industry. Having a direct link with the brain also creates exciting new avenues to understand its function. In particular, real-time functional magnetic resonance imaging (rtfMRI), while unlikely to find applications for everyday gaming or as a living room keyboard in the near future, is currently the best technology available for non-invasive whole brain measurements in humans. Therefore rtfMRI is a critical complement to both more invasive and more portable technologies and has potentially singular advantages for rehabilitation, therapy, and basic scientific discovery. rtfMRI can track localized regions in the brain as well as decode brain states from distributed network activity. Based on this foundation, some important questions now are: How can rtfMRI be applied to further our understanding of how the brain works? and What are the translational potentials for rtfMRI for rehabilitation and therapy? The field is still in its infancy in addressing these questions. In a sense, developing a working BCI for a given interface and patient population is an important underpinning, but just the first step before embarking upon full-fledged rehabilitation studies.

Mechanical properties of tissue have a long history as biomarkers for disease and pathology. Magnetic resonance elastography (MRE) is a non-invasive MRI technique used to investigate the mechanical properties of tissues in vivo. Our work focuses on MRE of the brain, which has been used to show a general global decrease in tissue viscoelasticity in neurodegenerative diseases. However, brain MRE is marked by inconsistent results throughout the field, owing to the complex mechanical nature of brain tissue and the difficulties associated with generating and imaging shear waves in the brain. In order to improve brain MRE results, we have developed a fast, high-resolution MRE acquisition capable of generating reliable results with the highest published spatial resolution. The improved resolution allows for MRE results to be interpreted at a local level, where the properties of structures in the white matter can be individually quantified. Such investigations can extend the capabilities of MRE for studying disorders in the human brain by identifying local variations in mechanical properties corresponding to specific regions of the brain.
Quantitative ultrasound: A promising new image mode for diagnostics and therapy monitoring

M. L. Oelze
Associate Professor
Department of Electrical and Computer Engineering
University of Illinois at Urbana-Champaign

Conventional ultrasound B-mode imaging is mainly qualitative in nature. While conventional imaging techniques, including ultrasound, may be sensitive to the detection of anomalous tissue features, the ability to classify these tissues often lacks specificity. As a result, a large number of biopsies of tissues with suspicious image findings are performed each year with a vast majority of these biopsies resulting in a negative finding. Quantitative ultrasound (QUS) imaging techniques can provide specific numbers related to tissue features that can increase the specificity of image findings leading to improvements in diagnostic ultrasound. QUS imaging techniques can encompass a wide variety of techniques including spectral-based parameterization, elastography, flow estimation and envelope statistics. Furthermore, a goal of QUS imaging techniques is to provide system- and operator-independent parameters related to tissue properties.

Different applications of QUS imaging techniques in diagnostic ultrasound will be discussed in this paper. Specifically, spectral-based techniques and envelope statistics at clinical frequencies and at high ultrasonic frequencies (> 15 MHz) will be examined for their abilities to improve diagnostic ultrasound. Spectral-based techniques include the estimation of the backscatter coefficient, estimation of attenuation, and estimation of scatterer properties such as the correlation length associated with an effective scatterer size and the concentration of scatterers. Envelope statistics include the estimation of the number density of scatterers and quantification of coherent to incoherent signals produced from the tissue.

Recent successes of QUS implementation for medical diagnostics will be discussed. Successful applications demonstrating the ability of QUS to improve medical diagnostics will include cancer detection and classification of solid tumors and lymph nodes, detection and quantification of fatty liver disease, and monitoring and assessment of thermal therapy on solid tumors.

Resolving axonal integrity of specific pathways with diffusion weighted imaging in MRI

Joseph Holtrop
Graduate Student
Department of Bioengineering
University of Illinois at Urbana-Champaign

Diffusion weighted imaging (DWI) with MRI is a technique that is used to look at restrictions in water diffusion. DWI has enabled measures of axon integrity to be made in vivo. However, DWI faces several challenges in improving the spatial resolution to delineate specific fiber pathways. By using a 3D multi-slab approach that takes advantage of a more SNR efficient data acquisition strategy, the resolution of diffusion weighted images can be improved.
Ultra-compact PET/MR and SPECT/MR system with sub-500µm resolution

Liang Cai
Graduate Student
Department of Nuclear, Plasma and Radiological Engineering
University of Illinois at Urbana-Champaign

In this presentation, we will discuss the development of high performance nuclear imaging systems (SPECT and PET) that can be operated inside MR scanners for simultaneous dual-modality in vivo imaging studies. The combined nuclear imaging and MR systems are constructed based on novel highly-pixelated semiconductor (CdTe and CZT) detectors developed in our laboratory. These detectors offer intrinsic resolutions of ranging from 350µm to 100 µm and an excellent energy resolution of around 3~4kev. In order to provide an ultrahigh resolution in 3-D imaging studies, a hybrid pixel-waveform readout (HPWF) method has also been developed to extract information from the cathode signal to deliver energy, timing and depth-of-interaction (DOI). With the high spatial resolution, excellent energy resolution, proper timing information and excellent MR compatibility provided by the imaging detectors, we are able to construct several ultra-compact PET/MR and SPECT/MR systems that offer a range of imaging capabilities well-beyond the current state-of-art. The technological development related to both the imaging detectors, and the combined SPECT/MR and PET/MR systems will be discussed.

NOTES:
One of the key strengths of the computer as an instrument for the study of biomolecular complexes is its ability to provide researchers with graphical views and quantitative information at a level of fidelity and accuracy limited only by the quality of the available structural information. Molecular dynamics simulations provide valuable atomic level details about the dynamics of biomolecules when combined with powerful molecular visualization and analysis tools. The size of biomolecular systems that can be studied in atomic detail has steadily increased from that of Lysozyme (40,000 atoms) in 1990 to the million-atom STMV virus capsid in 2006, to 100 million atom systems using petascale supercomputers becoming available later this year. We describe challenges involved in visualizing large and complex biomolecular systems and our use of advanced computer graphics algorithms and GPU-accelerated computational approaches for visualizing these structures.

Multi-protein, many million-atom structures provide a great challenge for scientific visualization. By using GPU-accelerated surface calculations this challenge is addressed in VMD while simultaneously enabling visualization of structures spanning three orders of magnitude.
Interactive visualization of protein folding process from molecular dynamics simulations

Yanxin Liu
Graduate Student
Theoretical and Computational Biophysics Group
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

Protein folding is a process by which a protein acquires its functional structure and is related to many neurodegenerative diseases. Molecular dynamics simulation of protein folding has the potential to reveal the folding process with unprecedented temporal and spatial resolutions. I will present the successful folding of a five-helix bundle protein from molecular dynamics simulation, the largest protein folded in silico. The challenges in both simulation and visualization will be discussed throughout a live demo of the protein folding trajectory using VMD.

Molecular level visualization of the HIV-1 capsid

Juan R. Perilla, Ph.D.
Postdoctoral Research Associate
Theoretical and Computational Biophysics
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

HIV-1 genome is encased in a protein shell arranged in a helical assembly crucial for the virus success. Here we present at atomic level the HIV-1 capsid using data from NMR, X-ray and Cryo-EM along with computational modeling.
Lattice Microbes: computational imaging of whole cells

John Cole
Graduate Student
Theoretical and Computational Biophysics Group
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

Lattice Microbes is a stochastic simulation software package for modeling reaction networks in realistic cellular environments. It is unique amongst competitors for its ground-up design emphasis on parallel GPU computing, enabling as much as two orders of magnitude speed-up in simulating large biochemical reaction networks in crowded inhomogeneous conditions. As evidence mounts that spatial localization arising from molecular crowding can play an important role in many biochemical processes in vivo, realistic models of the cellular environment based on advanced imaging techniques like cryoelectron tomography take on a greater necessity. Understanding the microscopic details of crowding-based effects such as anomalous diffusion and compartmentalization requires powerful visualization capabilities. The popular molecular dynamics visualization software VMD offers us a window into these phenomena.

A plugin for visualizing Lattice Microbes trajectories in VMD has been developed to allow even novice users to view the diffusion and interaction of chemical species in their simulations. The new QuickSurf representation in particular lends clarity to course-grained models of molecular crowding. Here we demonstrate some of the visualization capabilities of VMD for Lattice Microbes, exploring continuous and course-grained representations of molecular crowding, as well as trajectories from simulations of the lac genetic switch in realistic in vivo conditions based on cryoelectron tomogram data.

NOTES:
Many advances in biology and medicine are driven by the availability of new diagnostic tools. Our research focuses on the engineering of novel microscopy instrumentation and the application of these new tools to study biomedical problems. The problems tackled in my laboratory range from understanding the structure/function of single proteins, nature's smallest machines, to the development of a new non-invasive optical method for cancer diagnosis. The available research topics in my laboratory can be categorized into molecular, cellular and tissue levels.

Our lab implements optical tweezers to study mechanics in cell signaling and function. We combine optical tweezers microrheology for the measurement of ECM stiffness and a simple shear gradient device to test the role of local stiffness in cell differentiation and function.
Protein functions are largely determined by conformations. However, it remains an enigma on the design principles of modular arrangement within proteins for the conformational regulation. Here we show that a protein tyrosine phosphatase Shp2 displays an unexpected plasticity of conformational regulations. An antagonistic combination of contextual amino acid sequence and position of two regulatory phosphotyrosines (e.g. favorable position combined with adverse sequence) governs their competitiveness for the cis-interaction of the same SH2 domain within Shp2. The trans-interaction between these phosphotyrosines and a neighboring protein Grb2 can tune the Shp2 cis-interactions and conformations. Swapping the contextual sequences at the two tyrosine sites resulted in the loss of Shp2 conformational plasticity and the reprogramming of downstream ERK signaling. Thus, a simple antagonistic combination of sequence and position leads to a cis-regulatory plasticity of Shp2 conformation, which can serve as a basic design principle for natural and synthetic proteins with tunable conformations.

In vivo optical trapping reveals that kinesin drags dynein

Benjamin H. Blehm, Ph.D.
Postdoctoral Research Associate
Department of Physics
University of Illinois at Urbana Champaign

Kinesin and dynein are fundamental components of intracellular transport, but their interactions when simultaneously present on cargos are unknown. We have built an optical trap that can be calibrated in vivo to measure forces in living cells. By comparing directional stall forces in vivo and in vitro, we found that cytoplasmic dynein is active during both minus- and plus-end directed motion, while kinesin(s) is only active in the plus direction. In vivo, we found that outward (=plus-end) stall forces range from 2-7 pN, significantly less than the 5-7 pN stall force measured in vitro for single kinesin molecules. In vitro measurements on beads with both kinesin-1 and dynein bound revealed a similar distribution, implying that an interaction between two opposite polarity motors causes this difference. Finally, inward (=minus-end) stalls in vivo were 2-3 pN, higher than the 1.1 pN stall force of a single dynein, implying multiple active dynein.

NOTES:
PET imaging of tumor angiogenesis: antibodies and nanoparticles

Weibo Cai
Assistant Professor
Department of Radiology and Medical Physics
University of Wisconsin - Madison

CD105 (also called “endoglin”) is considered one of the best markers for tumor angiogenesis. Comparing to CD31, which is expressed on both normal and tumor vasculature, CD105 is only over-expressed on proliferating tumor endothelial cells, thereby truly representing tumor angiogenesis. High CD105 expression correlates with poor prognosis in more than 10 solid tumor types, underscoring its clinical potential as a prognostic, diagnostic, and therapeutic vascular target in cancer. In this talk, I will present our recent work on the development of positron emission tomography (PET) and dual-modality PET/optical imaging agents targeting CD105, based on antibodies, antibody fragments, and nanomaterials.

Functional DNAs as selective agents for multi-target and multi-modal imaging and therapy

Yi Lu
Professor
Department of Chemistry
Department of Materials Science and Engineering
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign

Modern biology and medicine require advanced imaging tools. To meet the requirement, a number of new imaging techniques have been developed using known affinity agents such as RGD peptide as a proof of concept. To make these imaging technologies truly useful to researchers in biological and medical fields, one needs to develop imaging agents that are highly selective toward real targets in the researchers’ laboratory. Despite recent progress, designing those imaging agents based on a single class of molecules for a broad range of targets with high selectivity remains a significant challenge. Until today, antibodies are the main choice. Due to their large size, high costs and low stability, antibodies may not be suitable as imaging agents for many applications. In addition, antibodies are not effective against small molecular targets, targets too toxic to raise antibodies, or conditions not optimal for antibody functions. We have been able to use in vitro selection to obtain functional DNA (DNA with specific binding and enzymatic activities, also called DNAzymes and aptamers) that can bind both small and large molecular targets specifically, and used negative selection strategy to improve the selectivity. By labeling the resulting functional DNA with fluorophore/quencher, gold nanoparticles, quantum dots, or supermagnetic iron oxide nanoparticles, we have developed new classes of fluorescent, colorimetric and smart MRI contrast agents for a broad range of targets, with detection limit down to 11 ppt, and up to millions-fold selectivity. A novel approach of using an inactive variant of functional DNA to tune the concentration dynamic range to match those in the biological systems is also demonstrated. Recent results will be presented.
Precisely size controlled drug-silica nanoconjugate for cancer therapy

Li Tang
Graduate student
Materials Science and Engineering
University of Illinois at Urbana-Champaign

Drug delivery nanomedicine, exemplified by micelles and nanoparticles roughly in the size range of 1-200 nm, have attracted much interest in the past 2-3 decades as alternative modalities for cancer treatment. The size of these drug delivery vehicles has been strongly correlated with their in vivo biodistribution, penetration in tumor tissue, and intracellular trafficking. It potentially has significant impact on their antitumor efficacy. However, it is challenging to make nanomedicine in large quantities with controlled particle size and narrow particle size ranges, in particular for nanomedicine smaller than 100 nm. Here we report a novel drug delivery platform based on drug-silica nanoconjugates (drug-Si NCs) that can be controlled fabricated at nearly any desired size between 20 and 200 nm, with extremely narrow particle size distribution, in multi-gram scale within a few hours. Several in vitro and in vivo studies demonstrated that the sizes of the drug-Si NCs have huge impact on biodistribution, tumor penetration, cell uptake and overall antitumor efficacy; the drug-Si NCs with size under 50 nm outperform their counterparts with larger sizes, showing great promise in cancer therapy and diagnosis.

Imaging the LAT-1 amino acid transporter with Zr-89 immunoPET

Oluwatayo (Tayo) Ikotun, Ph.D.
Postdoctoral Associate
Mallinckrodt Institute of Radiology
Washington University School of Medicine

The L-type amino acid transporter 1 (LAT 1) is upregulated in a variety of cancers including breast, non-small cell lung cancer, glioma, ovarian, colon, and prostate cancers and is thought to be the target of many amino acids used for tumor imaging, including O-[(2-[(18)F]-fluoroethyl)]-L-tyrosine ([F-18]FET) and 6-[(18)F]-fluoro-L-dihydroxyphenylalanine ([F-18]FDOPA). Thus the goal of this project was to develop an immunoPET agent, using the anti-LAT1 monoclonal antibody, Sol131, labeled with Zr-89 for imaging the LAT 1 transporter expression. Initial studies were conducted in the human colorectal cancer cell line HCT 116, which has been reported to express the LAT 1 receptor. The anti-LAT 1 antibody, Sol 131, was conjugated with the chelator desferoxamine (DFO) and radiolabeled with Zr-89 and tracer uptake was investigated in vitro and in vivo. Tumor uptake was more pronounced at 5 days postinjection with Zr-89 labeled Sol 131, 4.47 %ID. In comparison to [F-18]FET, improved tumor to non-specific organ uptake was observed for the Zr-89 labeled Sol 131 with a tumor to blood ratios of 2.5 and 0.76 for [F-18]FET and Zr-89 labeled Sol 131 respectively.

The novel Zr-89 labeled anti-LAT1 antibody used in this study shows specific binding to the LAT-1 transporter and may be suitable for measuring expression levels non-invasively. To our knowledge, this study represents the first antibody-based imaging of amino acid transporters.
Hybrid or multimodality imaging is often applied in order to take advantage of the unique and complementary strengths of individual imaging modalities. This hybrid noninvasive imaging approach can provide critical information about anatomical structure in combination with physiological function or targeted molecular signals. While recent advances in software image fusion techniques and hybrid imaging systems have enabled efficient multimodal imaging, accessing the full potential of this technique requires development of new multimodal contrast agents that enhance the imaging process.

In this work, we report the development and evaluation of a hybrid dendrimer-based nanoprobe for both single photon emission computed tomography (SPECT) and X-ray computed tomography (CT) imaging that facilitates both high-sensitivity SPECT and high spatial resolution CT imaging. The co-localization of the nuclear and X-ray images offers the potential to facilitate image analysis and quantification including correction for SPECT attenuation and partial volume errors using the higher resolution anatomic information provided by the circulating CT contrast. This approach allows absolute quantification of intramyocardial blood volume and blood flow and may enable the ability to visualize active molecular targeting following clearance from the blood.

NOTES:
POSTER ABSTRACTS

Poster #1

In-line reference-delayed digital holography using a low-coherence light source

Amardeep S.G. Singh1, Tilman Schmoll1, Bahram Javidi2, Rainer A. Leitgeb1
1Center of Medical Physics and Biomedical Engineering, Medical University of Vienna, Währinger Gürtel 18-20, 4L, 1090, Vienna, Austria; 2Department of Electrical Engineering, University of Connecticut, Storrs, CT 06269-3157, USA

We present a novel holographic imaging approach with a low coherence light source that uses the reflex of the objective lens as reference illumination. This results in a simple setup and allows the principle to be applied to microscopy for aberration measurements with only small modifications of the setup. In addition, it opens the perspective of in-vivo ophthalmic imaging. We present first in-vitro experiments using a resolution test target to quantify the system performance. We demonstrate that we can achieve diffraction-limited resolution and show the possibility of aberration correction. We also present preliminary results on a scattering sample.

Poster #2

Static and quasi-static in-depth mapping of tissue elasticity using Full-Field Optical Coherence Tomography (FF-OCT)

Amir Nahas1,2, A. Claude Boccara1,2
1Institut Langevin, ESPCI, 10 rue Vauquelin 75005 Paris, France; 2LLTech, 6 place de la Madeleine 75008 Paris, France

Cells and tissues are characterized by their intrinsic mechanical properties. For example tissue stiffness has been used since the very beginning of medicine to diagnose pathologies through palpation. Moreover, the mechanical properties of cells are related to their structure and function so that changes in those properties can reflect the cellular healthy or pathological state. Adding this contrast to morphological biomedical images is a powerful help for diagnosis. In this study we try to add the elastographic contrast to the Full-Field OCT (FF-OCT) modality. FF-OCT is able to image biological tissues in-depth and in 3D with a micron resolution. By combining it with elastography, one should be able to recreate a “virtual palpation” at the micrometer scale.

Our custom FF-OCT setup includes an elastography system that creates various levels of compression on the sample. We present in this study two methods for retrieving the elasticity map, one static and one quasi-static. In the first static method we record a 3D image of the sample before and after compression, then we calculate the cross-correlation between the two stacks of images. Resolving the inverse problem we have access to the displacement and elastic modulus maps. The second quasi-static method is a novel method we have developed, in which we have direct access to the local displacement map without any cross-correlation calculation. The sample is submitted to periodical compression, and on the FF-OCT image allows us to retrieve the phase map directly related to the displacement. Those methods provide a relative value of the local elastic properties along the z axis.
**Poster #3**

**A simple method for cataract screening using a non-mydriatic digital fundus camera**

Ann Choi¹, Jessica Taibl¹,², Kelsey Martin², Bill Badie², Samir Sayegh²

¹University of Illinois Urbana-Champaign; ²The EYE Center, Champaign, IL

Cataracts are the number one cause of blindness and visual disability worldwide. They are typically age related but can be accelerated due to a variety of reasons including trauma, inflammation, diabetes and myopia. Detecting the presence of cataracts can help restore a patient’s vision but also hint at a patient’s diabetic state or other underlying pathologies.

We present a quick and simple method to determine the presence of a cataract that is usable by an observer with minimal training and no previous knowledge of cataract pathology or grading systems. The method is based on the comparison of a photo of the fundus obtained using a standardized setting of a digital non-mydriatic fundus camera, to that of a similar photo of a non-cataractous eye. Most previous approaches emphasized the direct imaging of the lens and the inference of a cataract grade based on a standardized scale, for example the Wilmer scale. These approaches may necessitate the modification of the camera or the addition of lenses and a degree of sophistication for the interpretation of the results.

We propose a method that allows a non-experienced grader, through the observation of the fundus image of a retina, to simply determine the presence of a cataract and the necessity to refer the patient. To do so, fundus photos obtained with a non-mydriatic camera were presented to an inexperienced observer that was briefly instructed on fundus imaging, nature of cataracts and their probable effect on the image of the retina. Preliminary results of pair testing indicate the method is very effective.

**Poster #4**

**Minimally invasive optical biopsy of biological tissues using Full-Field OCT with an endoscopic probe**

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Optical Coherence Tomography (OCT) has proven its interest for many biomedical fields thanks to its virtual slicing and 3D imaging capability. Full-Field OCT (FFOCT) is a particular approach that directly takes “en face” 2-D images with an isotropic resolution around 1µm. With such a high resolution FFOCT systems can produce images that are similar to that obtained with classical histology procedures and can thus be important tools for pathology. This is why we worked on combining the interest of an endoscopic setup with a needle probe with the performances of FFOCT. The principle of our endoscopic FFOCT setup is based on the coupling of two distinct interferometers under incoherent illumination: one is external to the probe, and one is placed at the distal end of the probe in contact with the tissue to image. The distal interferometer is common-path: interferences occur between the reference beam reflected at the tip of the probe and light backscattered by structures at each depth within the tissue. The advantage compared to scanning system is that it does not require any advanced miniaturized mechanical systems at the tip of the probe, which are likely to increase the diameter as well as the cost of the probe. Our simple design is well suited for in situ imaging. On a setup with a 150 mm long and 2 mm wide GRIN-based probe we achieve axial and lateral resolutions of 1.8 µm and 3.5 µm, and a sensitivity of -80dB. We present in vivo images on human skin up to depths around 200 µm revealing the different cell and tissue structures of each layer of the epidermis and the dermis. We also used the rigid probe inside a needle to penetrate inside the brain ex vivo. This approach could be used to guide needle-core biopsies.
**Poster #5**

Development and characterization of flavin-binding fluorescent proteins as a new class of oxygen-independent biological imaging probes

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In this work, we report the development and construction of a versatile palette of oxygen-independent fluorescent reporters with a potential to advance research in many fields including biomedical research for cancer diagnosis and metabolic engineering for the production of high value chemicals. Over the last few years, fluorescent reporter proteins have revolutionized our understanding of cellular bioprocesses by enabling live cell imaging with exquisite spatio-temporal resolution. Nearly all existing fluorescent proteins are based on the green fluorescent protein (GFP) and related analogs. However, GFP-family proteins strictly require molecular oxygen for maturation of fluorescence. This precludes their application to investigating biological processes in low-oxygen environments, which are frequently encountered in a broad range of biomedical and bioengineering applications such as bioremediation and fermentation platforms for the production of high value reduced biomolecules (e.g., biofuels), microbial pathogenesis, cancer metastasis and therapy. Consequently, there is a pressing need to develop and characterize fluorescent tools for probing anaerobic environments. Herein, we address these limitations by: 1) employing directed evolution to engineer brighter mutants of a wild type FbFP from *P. putida*, and 2) extensively characterizing key biochemical and photophysical properties of existing FbFPs. We successfully isolated two brighter mutants of the *P.putida* FbFP (mutants F37S and F37T) and explained the improved brightness in the mutants in terms of relieved quenching of the flavin chromophore and improved association between the protein and flavin. In the second part of our work, we estimated quantum yield, oligomeric state, fraction of fluorescent holoprotein in solution, intracellular stability, and denaturation/maturation kinetics of existing FbFPs. Furthermore, we investigated their potential as transcriptional reporters in *E.coli* by employing FbFP-tagged promoters to monitor gene expression under different conditions of growth. Based on our results, we identified the FbFP from *A.thaliana* as the most suitable FbFP for biological imaging.

**Poster #6**

Translation of magnetomotive optical coherence tomography toward applications in ultrasound for imaging SPIO labeled platelets

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Platelets play an important role in blood diseases and conditions including vascular damage, cardiovascular disease, hemostasis, inflammation, tumor metastasis, wound healing, and host defense. As such, the ability to image platelets may provide insight into clotting disorders and pre-occlusive thrombosis, etc. Furthermore, platelets are optimal platforms for contrast agents on the cellular level because they readily take up particles through innate immune mechanisms. We have chosen to label platelets with superparamagnetic iron oxide particles (SPIOs) so they may be used as magnetomotive contrast agents. Magnetomotive OCT has been used by Oldenburg et. al., to image SPIO platelets in *ex vivo* porcine arteries. We seek to translate these methods to magnetomotive ultrasound in an attempt to make the magnetomotive technique more practical for imaging large tissue volumes for the study of blood related diseases and conditions.
**Poster #7**

**White light Diffraction Phase Microscopy (wDPM)**

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Quantitative phase imaging (QPI) is an emerging field developing at an accelerated pace over the past several years. In QPI, we measure the optical path-length map associated with transparent specimens and translate those data into bio-medically relevant information. The main figures of merit in QPI are 1) acquisition rate, 2) transverse resolution, 3) temporal phase sensitivity, and 4) spatial phase sensitivity. Diffraction phase microscopy (DPM) is both off-axis and common-path such that it combines both the benefits of fast acquisition rates and high temporal sensitivity. These features allowed DPM to enable unprecedented biological studies, especially related to red blood cell membrane dynamics. However, due to the laser illumination DPM images suffer from speckles, which ultimately degrade the spatial phase sensitivity and the applicability to studying sub-cellular structures. Spatial light interference microscopy (SLIM) removed this obstacle by using white light illumination in a phased shifting geometry. However because of the phase shifting, SLIM requires the acquisition of 4 intensity images for each quantitative phase image and hence, relatively slower method. In this paper we present white light DPM (wDPM), which enables single shot images with high spatial and temporal sensitivity. Further a derivative method for phase calculation is also proposed which is simple and faster than conventional Hilbert or Fourier transform for phase calculation. Capability of the system will be presented by imaging of live red blood cells quantitatively and the growth of human cervical epithelial cell line, HeLa cells, (ATCC, CCL-2).

**Poster #8**

**14.1 T whole body MRI for detection of mesoangioblast stem cells in a murine model of Duchenne muscular distrophy**

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Noninvasive MRI approach to monitor transplanted stem cells in vivo is of great importance for potential therapeutic applications. An increase of magnetic field strength in MRI experiments benefits both sensitivity and spatial resolution for detection of labeled stem cells. Superparamagnetic Iron Oxide (SPIO) particles are MRI contrast agents that produce a relatively large susceptibility T2/T2* effect. However, as with all nanoparticle labeling techniques, local MRI contrast changes over time in an unpredictable way as cells migrate, divide or die and are scavenged by macrophages. As a best strategy, whole-body scans are required, followed by high-resolution scans of the specific areas where the cells were found. Patients with Duchenne muscular dystrophy are good candidates for stem cell therapy. In this study we developed a protocol for labeling stem cells with SPIO nanoparticles, injecting them into skeletal and cardiac muscle of mouse models for Duchenne muscular dystrophy, and tracking them in muscle tissue of live mice. Ultra-high magnetic field 14.1T MRI was used. Emphasis was placed on the development of an MRI coil with adjustable Field of View (FOV) which can be used for both whole body imaging as well as subsequent focusing on smaller, local regions where stem cells are present. We also used methods for labeling stem cells with a fluorescent dye to correlate, compare, and contrast results with MRI. We have shown that utilizing super high-field 14.1T MRI, developed protocol for labeling myogenic stem cells and specially designed FOV adjustable RF coil, it is possible to detect iron-oxide-labeled stem cells in vivo up to 2 weeks following injection and as few as 100 labeled cells up to 24 hours following injection.
Poster #9

Quantification of cilia-generated flow using OCT-based particle tracking and Shannon entropy

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Cilia are organelles that play an important role both in mucus clearance in the respiratory tract and in patterning of the left-right axis during development. It is well known that severe defects in ciliary function (i.e. primary ciliary dyskinesia, PCD) can lead to recurrent respiratory infections, and more recently, clinical genetic studies have also implicated ciliary genes in asthma. Current methods to quantify cilia function rely primarily on imaging of a single cilium but do not integrate the function of many coordinated cilia. Here we present two complementary methods for quantifying integrated ciliary function in *Xenopus tropicalis*, an important PCD model system that is characterized by expression of surface cilia during embryonic development. First, we use Optical Coherence Tomography (OCT) to image microspheres in a cilia-driven solution, and using particle tracking we calculate the velocity flow field generated by an embryo. Second, we use Shannon information entropy to quantify the mixing efficiency of blue dye, driven by the ciliated embryo in a custom-built microfluidic chip. We show that both approaches can be used to quantify integrated cilia function.

Poster #10

SERS engineered nanoparticles for highly sensitive chemical sensing

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Motivated by the development of early cancer diagnostics, we aim to design novel contrast agents for the sensing and imaging of cancerous tissues using surface enhanced Raman spectroscopy (SERS). Electromagnetic simulations of layered Mie theory indicate that nano-layered metal-dielectric probes (nano-LAMPs) potentially offer extremely high enhancement factors facilitating precise molecular species identification. Subsequently, we approach the chemical synthesis of gold-silica nano-LAMPs with strong consideration for electromagnetic enhancement. In this study we present bioconjugated engineered SERS nanoparticles targeting proteins such as E-cadherin. In combination with our work on nano-LAMPs we strive to provide a highly specific multiplexed targeting system for cancer diagnostics and imaging.
Poster #11

Exploiting the nonlinearity of upconverting nanoparticles for fluorescence diffuse imaging

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Currently fluorescence diffuse imaging and in particular fluorescence diffuse optical tomography (FDOT) suffers from a number of limitations. The presence of tissue autofluorescence degrades the signal and can cause severe artifacts in the reconstructions, and the diffusive nature of light in scattering tissues limits the obtainable spatial resolution. In this work, we show that the use of nonlinear upconverting nanoparticles leads to completely autofluorescence-free images, enabling FDOT reconstructions with superior qualities. In addition, since these nonlinear contrast agents require multiple photons to be absorbed before the emission of a fluorescent photon, we demonstrate that the resolution of FDOT can be significantly improved.

Poster #12

Dual beam Doppler optical coherence tomography at 1060nm

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Purpose: To image the blood flow dynamics quantitatively independent of the axial Doppler angle and to contrast the vasculature network of the retina with high penetration using a Dual Beam Doppler Swept Source OCT System at 1060nm.

Methods: Traditional Doppler OCT is highly sensitive to motion artifacts due to the dependence on the Doppler angle. This limits its reproducibility in clinical practice. To overcome this limitation, we use a bidirectional technique. Here, the volume is probed from two distinct illumination directions, allowing reconstruction of the true flow velocity. The principle was implemented with Swept Source OCT at 100,000 AScans/s. Furthermore, measurement at 1060nm shows better penetration below the RPE, so that choroidal flow can be effectively quantified. Simple flow contrast can be achieved by calculating intensity variance between successive B-scans. It offers the advantage to contrast the full range of flow present at the retina from small capillaries up to large vessels at the ONH.

Results: Circumpapillary and Line Doppler OCT scan series over time have been recorded. The angle independent quantitative flow dynamics have been extracted from specific vessel cross-sections of arteries and veins. The quantitative analysis profits from the intrinsic stability with respect to motion over time. The flow values fit well with previous findings. Furthermore we assessed choroidal flow quantitatively in selected vessel cross-section close to the optic nerve head. This marks an important step since the choroidal perfusion is believed to play an important role for retinal health and disease. Highly sensitive flow contrasting based on intensity variance has been performed on the parafoveal capillary network of the retina in a patch of 7x7°. Capillaries smaller than 10μm could be well visualized.

Conclusions: We introduce a large penetration bidirectional Doppler OCT system capable to perform quantitative imaging of retinal flow dynamics in the human retina. We demonstrated the advantage of 1060nm center wavelength to assess quantitatively the choroidal perfusion that plays a major role for various retinal diseases. The flow quantification and visualization may therefore lead ultimately to a better understanding and an enhanced early diagnosis of major retinal diseases.
**Poster #13**

**Non-invasive Raman imaging of human pancreatic tumor spheroids**

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It has been established that spheroids, 3D tumor models, are suitable for analysis of the tumor micro-environment. They accurately mimic tumor architecture and development. The self-organized aggregates of cells are known to have the features attributed to ‘multi-cellular resistance,’ characterized by an actively dividing outer layer, a quiescent intermediate area and a hypoxic core. Among different structural regions, hypoxic core is of the most interest due to decreased tissue penetration of chemotherapeutic agents. Thus, firm understanding of cellular behavior and drug diffusion patterns into the tumor core is essential and can contribute to the development of suitable cancer therapies.

We employ Raman micro-spectroscopy coupled with optical microscopy to characterize human pancreatic adenocarcinoma spheroids. This label-free technique offers the lateral sectioning of spheroids at different depths to get insights into the tumor layered structure without superfluous labels. Utilizing this technique in synergy with multivariate method of analysis, such as the Vertex Component Analysis (VCA), allows us to reconstruct the biochemical images of studied biological system. Apart from establishing biochemical signatures of the tumor micro-environment, nano-particle penetration and subsequent drug dissociation patterns can be easily monitored using nano-scale imaging.

**Poster #14**

**Neural imaging in songbirds using fiber optic fluorescence microscopy**

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The song control system of male songbirds is a valuable model for studying the developmental acquisition and generation of complex learned vocal motor sequences, two processes that are fundamental to human speech and language. An understanding of how the complex sounds of songbirds are generated by the identified neurons in the song control system may illuminate mechanisms specific to the production of complex learned communicative signals (e.g., speech, language), as well as more general principles of motor control. We propose to utilize optogenetic approaches as an ideal suite of tools to study the contribution of a prominent brain nucleus (HVC) to song motor control. We will develop a wide-field fluorescence microscope with aberration correction and genetically encoded reporters of neural activity for in vivo imaging in freely behaving birds, specifically in zebra finches. We have used a LED illumination, a fiber bundle for transmission of fluorescence excitation and emission light, a ~2× GRIN lens, and a CCD for image acquisition. The system has 2 µm resolution, 375 µm field of view, 200 µm working distance, and 1 mm outer diameter. As an initial characterization of this setup, we imaged injected dye boluses at depths similar to HVC depth in fixed brain tissue using a simple handheld fiber optic microscope. The imaging results were confirmed using a Lucid Vivascope confocal microscope. Long-term imaging of the activity of these neurons in juvenile birds during singing may lead us to a better understanding of the central motor codes for song and the central mechanism by which auditory experience modifies song motor commands to enable vocal learning and imitation.
Poster #15

Engineering a multiplex biosensor for the quantification of angiogenic biomarkers in mammalian cells

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Antibody-conjugated quantum dots (QDots) offer great potential for multiplex bioimaging due to their wide excitation spectra and narrow emission spectra. In particular, the use of multicolor QDots in immunohistochemistry is considered one of the most promising applications. Despite this potential, biomedical applications of QDots-based immunohistochemistry have achieved only limited success thus far. The present study aims to engineer a microfluidic biosensor to quantitatively measure levels of angiogenic biomarkers in mammalian cells and apply this data to the development of better therapies for angiogenesis-related diseases. Precise monitoring of the vascular microenvironment is key to determining the mechanisms governing angiogenic regulators and identifying how cellular signaling correlates to macroscopic modulation, inhibition and promotion of blood vessel formation. This research will help to unravel these complexities by developing a nano-scale biosensor using quantum dot technology. The investigation proposed here is at the forefront of developing the tools necessary to study blood vessel growth and regulation under healthy and disease states.

Poster #16

Nanoparticle dynamics in non-Newtonian aqueous dispersions

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Understanding the dynamics of nanoparticles in non-Newtonian media is required to optimize their design for wide-ranging applications in the oil industry for exploration of hydrocarbons through nanoparticle enabled imaging, improved oil recovery through profile and conformance control, and change in wettability through interfacial interactions of nanoparticles, as well as in biomedical engineering in drug delivery including cancer therapies and tissue engineering and nano-enabled nutrient transport. In this work, two micro-rheology techniques namely particle tracking and differential dynamic microscopy are validated against bulk rheology for Newtonian fluids. Results show that viscosity of Newtonian fluids measured by particle tracking and DDM micro-rheology using 400 nm polystyrene nanoparticles is in excellent agreement with bulk viscosity measurements. In addition, the dynamics of nanoparticles in a non-Newtonian polymer solution are investigated. While the DDM and particle tracking micro-rheology based viscosity of such a non-Newtonian polymer solution are in excellent agreement, these values are not consistent with the bulk zero shear viscosity. Interestingly, the micro-rheology based viscosity corresponds to a bulk viscosity at a shear rate intermediate between that corresponding to the longest relaxation time of the polymer and that corresponding to the segmental relaxation time.
Poster #17

High-speed data acquisition, processing, and display for real-time computed imaging using optical coherence tomography

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Optical coherence tomography (OCT) is an imaging technique capable of providing high-resolution label-free images of tissue microstructure. However, as the transverse resolution approaches the cellular scale two major obstacles are encountered: a reduction in the depth-of-field and an increase in optical beam aberrations. We have developed novel computed imaging techniques to address these issues. These techniques include interferometric synthetic aperture microscopy (ISAM) which achieves depth-independent resolution, and computational adaptive optics (CAO) which corrects for optical system aberrations. These computed imaging techniques are likely to significantly improve the imaging performance and image data quality for many types of OCT systems. To fully realize our novel OCT algorithms for real-time diagnostic applications, a high-speed imaging scheme was implemented. Our spectral-domain and swept-source OCT systems acquire data at axial scan rates of 120 kHz and 92 kHz, respectively. In addition to standard OCT processing, real-time volumetric ISAM was achieved using a dual-GPU implementation. Processed data was displayed directly from the GPU. This high-speed imaging strategy allows for real-time implementation of more advanced computational techniques which provide improved and more diagnostically useful image quality. Novel applications of this work include primary care retinal imaging and in vivo tumor detection.

Poster #18

Automatic processing of intravascular optical coherence tomography images

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Background: Intravascular Optical Coherence Tomography (IV-OCT) is an imaging modality recently introduced into clinical practice. Due to its very high axial (~15μm) and lateral (20-40μm) resolution it allows for in-vivo evaluation of atherosclerotic disease, stent strut analysis and to assess coronary artery events in general. The major drawback of the current OCT methodology is that the analysis of these images requires a heavy amount of – currently manual – post processing. Images are analyzed by a time consuming manual procedure based on the interpretation of qualitative image features. Our aim is the development of novel methods for an automatic and robust analysis of IV-OCT images.

Methods and Results: We first proposed an algorithm for fully-automated stent analysis. After a preprocessing step including automatic removal of the imaging catheter and guide-wire artifact, vessel wall and stent struts are automatically segmented through analysis of individual A-lines. The algorithm was validated against manual assessment of 108 IV-OCT images randomly extracted from 9 coronary arteries visualized in-vivo. As such, we demonstrated that it enables a fully-automated assessment of stent apposition and coverage. For a detailed assessment of novel stent platforms, many clinical research projects make use of IV-OCT to study stent healing at different time points after PCI (e.g. baseline, 6, 9 and 12 months follow-up). As datasets are currently matched manually, we proposed an algorithm for the automatic registration of IV-OCT data of a given vessel through time. The method makes use of the metallic stent framework as a landmark for a 3D rigid registration procedure. Validation was obtained by the use of vessel phantoms and on 6 in-vivo datasets. This algorithm allows for a fully-automated procedure for registration of OCT datasets.

Conclusion: Methods for the automatic analysis of IV-OCT datasets have been developed and validated. This will be important for a better integration of this imaging modality into cardiovascular research and clinical practice.
Poster #19

Handheld optical imaging technology for primary care medicine

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We demonstrate a system that integrates a high resolution optical imaging technique with the functionality of standard otoscope/ophthalmoscope instruments. In addition to conventional video of tissue surface features, cross-sectional OCT images of eye, ear, skin, and oral tissues provide quantitative data for diagnostic decision and patient monitoring. The combined functionality is implemented with a handheld probe using a MEMS-based scanner and interchangeable tips to permit high-resolution real-time imaging of multiple tissue sites. Initial studies are focused on middle ear infections and diabetic retinopathy.

Poster #20

Single molecule study of the CUG repeat-MBNL1 interaction and its inhibition by small molecules

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Effective drug discovery and optimization can be aided dramatically by a mechanistic description of the targeted biomolecular recognition event. This requires techniques capable of deconvoluting multiple steps to build a thermodynamic and kinetic platform to dissect the features of the system that can be targeted most efficiently. Herein, we report a single-molecule approach that uses total internal reflection fluorescence microscopy (TIRFM) to study the binding of the alternative splicing regulator MBNL1 by a model CUG triplet repeat and the effect of small molecules on the kinetics and affinity of this interaction. CUG repeats are believed to be toxic and the causative agent of myotonic dystrophy type 1 by sequestering MBNL1. Using the TIRFM approach, the rate constants and affinities were measured directly for each interaction. Unexpectedly, MBNL1 is able to bind the CUG repeat-inhibitor complex indicating that the inhibition is not a simple competitive process. This finding provides insight into the design of more effective inhibitors of the CUG repeat-MBNL1 interaction. In this study, a simple ligand previously known to be highly selective for CUG repeats was used as the basis for synthesis of a new dimeric ligand that binds (CUG)4 100-fold more tightly and is more effective in destabilizing the MBNL1·(CUG)4 complex. In addition to its utility to guide inhibitor design, the single-molecule method and the analysis framework we developed should be generalizable to the study of a broad range of biomolecular interactions.
**Poster #21**

**Patterning of functional neovessels with ‘living’ microvascular stamp**

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In the past, extensive efforts have been made to control the growth direction and the spacing of neovessels because of their critical roles in homeostasis, pathogenesis and regeneration of tissue. However, no success has been achieved to regulate the physiologically relevant micro-scale spacing between functional neovessels through which blood flows, and this has been a grand challenge for tissue engineers and biomedical scientists for many years. Here, we present a study of a ‘living’ microvascular stamp that releases multiple angiogenic factors and subsequently creates neovessels with the same pattern as that engraved in the stamp. The stamp consists of live cells that secrete angiogenic factors, an engineered hydrogel matrix that promotes cellular expression of angiogenic factors, and a three-dimensional (3D) geometry that localizes the angiogenic factors within the pattern. When the stamp was implanted on a target tissue, it created the desired pattern of neovessels based on 3D geometry of the stamp, allowing the control of the density and spacing of blood vessels. Analytical modeling and numerical simulations validated the experimental observations that the desired blood vessel patterns were formed under specific physical 3D designs of the stamp. Thus, controlling the ‘bottoms-up’ emerging behavior of the neovessel formation via ‘directed top-down’ cues using the living microvascular stamp is a major step forward to better understand vascular biology and also improve quality of a variety of clinical treatments necessitating the neovascularization.

**Poster #22**

**Asynchronous vs. synchronous co-registered fluorescein angiography and optical coherence tomography in macular disease: intersections and collisions**

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Macular edema and exudative macular degeneration may result in accumulation of fluid in and around the macula. Fluorescein Angiography (FA) remains the gold standard to evaluate macular fluid accumulation and leakage while optical coherence tomography (OCT) is establishing a prominent role in its semi-quantitative analysis. Indeed while the dynamic aspect of blood flow in the retina is still better described by FA, OCT allows for cross-sectioning of the macula and retina and the ability to characterize the presence of fluid and determine its location, distribution and volume. The synergistic use of FA and OCT provides more relevant information than using either modality alone. However, there is no standard methodology to co-register the images following acquisition on often disparate imaging devices. Recently new technologies have provided the ability to simultaneously capture FA and OCT images, allowing a cross-section to be taken at the exact point of interest. This study compares patients who have had separate FA and OCT on the same day to patients who have had simultaneous FA/OCT. We establish that the combined imaging protocol is easier on the patient, easier and faster for the technician to obtain, and ultimately and most importantly more helpful in guiding the physician to a diagnosis and treatment.
Active repolarization of light through turbid media

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Multiple light scattering plays a decremental role in virtually all aspects of light transfer within or through highly scattering media. This also applies directly to the vectorial properties of light where the polarization state of the incident beam is scrambled and the delivery of light with specific polarization state is impossible. Here, we demonstrate, for the first time to our knowledge, that an intense focus of light with arbitrary state of polarization can be transferred through highly scattering media by shaping the wavefront of the impinging beam.

Development of multimodal microspheres for targeted PET and Cerenkov luminescence imaging of cancer

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Cerenkov radiation is a phenomenon that occurs when a charged particle travels faster than the phase velocity of light in a dielectric medium. Recently, it has been demonstrated that positron-emitting radionuclides used for PET imaging can generate measurable light due to this phenomenon. This discovery has led to the development of a new molecular imaging modality, known as Cerenkov Luminescence (CL) Imaging. The purpose of our studies is to characterize Cerenkov radiation emitted from selected PET radioisotopes and to develop targeted multimodal microspheres for optical and nuclear imaging of cancer.

We have so far conducted a number of CL characterization studies, including examining the effect of the refractive index of the medium on signal intensity and an \textit{ex vivo} subcutaneous injection of the radioisotope (\textsuperscript{18}F-FDG) into the chicken tissue. Results show that CL is intensified in media with higher index. However, CL was not observed in the \textit{ex vivo} study due to attenuation of visible wavelengths by the tissues. To overcome the limitation, a red-shift fluorescent agent was introduced and CL was utilized as the excitation source. Another characterization study was then performed using both test tubes and the mouse tissue. Initial results illustrate radiation-induced fluorescence to have slightly higher optical signals and less tissue attenuation of visible wavelengths than CL alone.

Preliminary results demonstrate CL as a promising analytical signal source for optical imaging. Utilizing this principle, radiolabeled targeted microspheres, which contains a higher index oil core to facilitate higher CL emission, will be developed for combined \textit{in vivo} PET and CL imaging.
Silicon pillar arrays as photonic crystal biosensors

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Arrays of silicon pillars are one example of a class of materials known as photonic crystals, that is to say, that due to their crystalline symmetry in the x-y plane only certain electro-magnetic modes are permitted to propagate throughout this plane. These photonic band gap (PBG) properties are extremely sensitive to changes, either refractive or geometric; consequentially such a device may be used as a sensor. Here we show preliminary work exploring the potential sensitivity of a device consisting of an array of silicon pillars used to detect the adsorption of proteins in liquid. Due to the scale invariance of PBG devices we are able to calculate over the entire range of possible configurations of silicon pillars on a square lattice. We calculate that the peak sensitivity in terms of change of band gap position to be of the order of 0.2nm of wavelength for every nm of protein adsorbed. While the results presented here are preliminary they suggest a relatively simple device could prove an effective biosensor, especially when one considers the small sample volume and enormous surface to volume ratios inside such a device.

Imaging, hyperthermia, and controlled drug delivery: multi-functional carbon/iron oxide microspheres synthesized via ultrasonic spray pyrolysis

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Combining multiple diagnostic and therapeutic tools into one biomedical material allows a safer, one time use of the material. One such example is a drug delivery material that releases its cargo upon heating. With the addition of nanomagnets which can undergo RF heating, release can be controlled safely from outside the body. The addition of the nanomagnets also allows their use as both hyperthermia agents and imaging contrast agents. Here, we have used ultrasonic spray pyrolysis to create nanomagnet-containing, porous carbon microspheres in a one-step reaction using simple and cheap precursors (sucrose, sodium salts, and iron salts). The sodium salts create an easily removable and reusable template \textit{in situ} during the pyrolysis of the sucrose (the carbon precursor) which also evolves gas, further defining the pore structure. The iron salts create iron oxide nanomagnets within the carbon spheres during the reaction, unlike other techniques which require premade iron oxide nanoparticles. These materials show promise as possible multi-functional biomedical materials which could be used for controlled drug delivery, hyperthermia, and imaging.
Poster #27

Developments in damage detection and imaging for bridge components

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Recent developments in imaging with mechanical waves and vibration applied to reinforced concrete bridge elements are presented. Contactless sensors are employed to collect seismic, vibrational and ultrasonic data, which allow for rapid, efficient and consistent data collection over a large volume of material. These data are then used to build up images that enable internal damage detection and characterization. In this paper, two such imaging applications are discussed: concrete bridge deck scanning using seismically generated waves and vibrational responses, and internal reconstruction of reinforced concrete columns using ultrasonic tomography. The first application aims to locate and characterize shallow delamination defects within concrete bridge decks. A practical seismic testing configuration is described, and imaging results for a range of bridge deck samples are shown. In those images, the locations of damage are accurately identified. The second application aims to locate and characterize internal damage in concrete bridge columns. The testing concept is described, and preliminary imaging results from concrete samples show ability to locate internal defects. The results demonstrate that seismic and ultrasonic imaging provides ability to evaluate unseen material defects within concrete structures, and promises to improve capability for infrastructure assessment efforts.

Poster #28

The 3dsvm plugin for pattern analysis and real-time fMRI

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3dsvm (http://lacontelab.org/3dsvm.html) is a command line program and plugin for AFNI [1] built around SVM-Light [2]. 3dsvm performs support vector machine (SVM) analysis on fMRI data [3]. Its capabilities include SVM-based regression, multiclass classification, and the use of non-linear kernels. For real-time fMRI (rtfMRI) experiments [4,5], we have integrated SVM-based analysis of fMRI data and neurofeedback with AFNI’s real-time framework. 3dsvm requires access to the scanner’s imaging data (through network file sharing or direct TCP/IP communication). During testing, 3dsvm can transmit the results to a stimulus presentation computer for neurofeedback. Since 3dsvm is open source, other sites can inspect the source code, build custom capabilities for their own experiments, and even contribute to ongoing development efforts.

References:
**Poster #29**

**Magnetomotive contrast in optical coherence tomography for detecting early-stage atherosclerosis using targeted microspheres**

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In this work, we show that molecularly-sensitive contrast can be generated in OCT using targeted multifunctional magnetic microspheres. These microspheres were engineered to target the $\alpha_v\beta_3$ integrin for the localization of atherosclerotic lesions in excised aortas from a rabbit animal model. The aortas were extracted and placed in a flow chamber, which mimicked the physiological blood flow conditions in the living rabbit. Magnetic microspheres were perfused through the aorta inside the flow chamber and catheter-based OCT imaging, magnetomotive optical coherence tomography (MM-OCT), fluorescence confocal, and bright field microscopy were performed on the ex vivo aorta specimens for localizing the microspheres. Results showed successful targeting of the functionalized microspheres to early atherosclerotic lesions, and good co-registration of MM-OCT signal with confocal microscopy.

**Poster #30**

**MRI for speech analysis**

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This work explores magnetic resonance imaging’s potential to provide insights into brain-articulator relationships during speech production. Data were collected at the University of Illinois Urbana-Champaign using a novel multi-shot, field-corrected, dynamic spiral FLASH MRI sequence. Images of the mouth and speech sounds were recorded simultaneously. SVM classification analysis was implemented using 3dsvm in AFNI. In an extension of earlier work, the SVM was trained to distinguish each of the four spoken words from each of the others. We used CCA to examine the multivariate relationships between the audio recording of speech (a time x frequency matrix) and the MRI data (a time x space dataset). A cross-validated accuracy of 96% was obtained using the SVM classification, demonstrating the utility of our recently developed MR sequence, and that such measurements capture important information about the corresponding speech signal. Applications and extensions of this work include extracting more refined behavioral descriptions for combined structural and functional studies and monitoring speech as a tool for speech therapy and diagnosis.

References:
**Poster #31**

**Performance of a reference-laser free spectrometer**

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Fourier transform infrared (FT-IR) spectroscopy is a widely-used technique for examining the chemical constituents of a sample. Modern FT-IR spectrometers are typically based on an interferometer design that allows the simultaneous measurement of absorption at multiple wavelengths when the interferogram is deconstructed using a Fourier transform. In commercial instruments, a reference laser accurately encodes the position of the moving mirror. However, this laser creates an additional upkeep cost as they need to be replaced every few years. Here, we have built a reference-laser free FT-IR spectrometer and characterized its performance by measuring SU-8 polymer thickness on a Barium Fluoride slide. Errors in measuring stage position over time results in stretching and shifting of the interferogram along the retardation axis. We have demonstrated the absence of a reference laser results in a 2% stretch in the interferogram which proportionally affects the measured polymer thickness. The variation of this measurement, as determined by two standard deviations, increased by 6.3-fold from to 0.3% to 2%. These results summarize the degree in which a reference-laser free approach can be used to approximate spectroscopic data.

**Poster #32**

**A phase-sensitive optical coherence tomography (OCT) based optical electrode for non-contact neural recording**

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Nerve activity in a biological neural network is mostly characterized by generation and propagation of impulses through the nerves. These impulses, known as action potentials, are generated when the nerves are excited by a stimulus either as an external input or as a means of internal communication between nerves. This project is aimed to develop an optical imaging based minimally invasive technique for neural recording. Existing technologies largely limit the analysis of neuronal processing to a single or small cluster of neurons using different varieties of electrodes or the introduction of exogenous contrast agents and most of these techniques are invasive in some ways. Recent developments in spectral domain optical coherence tomography (SD-OCT) technique enable us to detect very small transient structural changes in biological tissues by using differential phase measurements.

In our experiments, we use the lateral eye of horseshoe crabs (*Limulus polyphemus*) to stimulate them with light and then detect the activity in its optic nerve by using our SD-OCT system. We have developed our own OCT imaging system (both hardware and software) in the lab and completed some preliminary imaging and electrophysiology experiments. Our preliminary results from phase measurements of glass slide have shown that our system has the enough sensitivity to detect any small thickness change as small as 0.8nm. In addition to that, the system uses the line scan camera that can acquire depth profiles at a rate of 144 kHz and that gives us the temporal resolution of 6.9μs, which is sufficient to detect rapid neural activity. Preliminary experiments indicate that this system has both the spatial and temporal resolution to detect action potential induced rapid structural changes and as a result, to monitor neural activity in real time manner. Future work involves improving the phase measurement accuracy and sensitivity of the developed system so that it can reliably monitor nerve activity in different controlled conditions. We believe that this ongoing study may serve as the basic ground work for future experiments and will hopefully have an overall significant impact on functional neuroimaging.
Poster #33

Benefits of using multi-modal retinal imaging to guide the diagnosis and treatment of challenging cases in ophthalmology

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Purpose: To show how using multi-modal imaging can provide more useful information in guiding the diagnosis and treatment of challenging cases. A 76 year old male presented with subretinal hemorrhage OD that was determined to be secondary to wet AMD. He was treated successfully with anti-VEGF Bevacizumab (Avastin), but OD retinal hemorrhaging reoccurred a year later when he was diagnosed with myelodysplastic syndrome and refractory anemia with excess blasts.

Methods: Serial Optical Coherence Tomography (OCT), Fluorescein Angiography (FA), Indocyanine Green Angiography (ICG), color, red-free, and autofluorescent fundoscopic images were obtained and the patient was treated with monthly intravitreal injections of Avastin®.

Results: Initially, FA and fundoscopic images revealed OD subretinal hemorrhaging and drusen OU. Visual acuity was 20/200 OD and 20/30 OS. After five months of Avastin treatment, imaging revealed resolution of hemorrhaging, and visual acuity improved to 20/40 OD. Less than a year later, a reoccurrence of OD retinal hemorrhaging was observed that was consistent with a leukemia-like syndrome. Continued treatment with Avastin® stabilized visual acuity at 20/40 OD.

Conclusion: Through the use of multi-modal imaging, we were able to clearly track the progression of this patient's retinal hemorrhaging and achieve success in his treatment. Retinal hemorrhaging can occur for a variety of reasons, and the use of multi-modal imaging can serve to guide the diagnosis and treatment in such challenging cases.

Poster #34

Transmission Raman tomography for determining the position and size of targets buried in light scattering media

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The use of Raman spectroscopy to provide label-free chemical contrast of analytes buried below light scattering media has a wide variety of biomedical related applications ranging from disease diagnosis to monitoring drug delivery. Developing and validating methods for obtaining the size, shape, and position of buried targets is a first step towards realizing this potential. In this research, we present experimental results and theoretical considerations from a series of transmission Raman tomography measurements on targets (Teflon spheres) buried inside of Intralipid-based tissue phantoms along with the resulting two-dimensional image reconstructions. Measurements were collected with a fiber-based Raman instrument using varying source-detector collection angles. We compare two forward-modeling methods, radiative transport calculation (NIRFAST, an open-source diffuse optical tomography modeling package)[1] and Monte Carlo simulation (written in-house), for the modeling of light fluence throughout the phantom. Reconstruction of the size and position of buried targets can be employed without the use of spatial priors via an iterative modified-Tikhonov minimization algorithm, and these results are validated against computed tomography (CT) images. We present the differences between the two forward algorithms and highlight the important advantages and disadvantages of each approach.

**Poster #35**

**Analysis of two-photon fluorescence from a mouse model of ovarian cancer**

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The goal was to analyze multiphoton microscopy images of ex vivo mouse ovaries, and determine whether significant differences existed between features extracted from these images. Ovaries were harvested from four groups of 7 month old mice; control mice, mice given VCD to induce ovarian failure via follicular atresia, those given the carcinogen DMBA via intrabursal injection, and those given both DMBA and VCD. Two photon excited fluorescence images of the ovaries displayed bright punctate fluorescence, possibly from the fluorophore lipofuscin. Subsequent histology was used as a gold standard for diagnosis. Ovaries categorized into five groups: normal, DMBA effect, tubular adenoma, tubular adenoma with dysplasia, and carcinoma. I wrote a MATLAB routine that analyzed the size, intensity and number of particles (punctate fluorescence) for each ovary. Using the student’s t-test, I found that there was a statistically significant difference in the size of particles between normal ovaries and those with tubular adenoma and tubular adenoma with dysplasia, as well as a significant difference in the number of particles between normal ovaries versus those with carcinoma.

**Poster #36**

**Chemical imaging for histopathology: an emerging route for molecular and structural analysis of tissues**

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Mid-Infrared (IR) spectroscopic imaging is an emerging approach to derive chemical images from tissues based on their inherent biochemistry. Histological diagnosis is the gold standard for evaluating the presence and severity of most diseases. Current histopathological techniques use panel of special stains and immunohistochemistry (IHC) to assess tissue architecture, determine cell types present and to classify disease. Here, we report on the evaluation of an automated means to accurate histological recognition using IR spectroscopic imaging. This method does not need dyes or probes and dispenses with human input but relies on computational approaches to provide decisions. Recent advances in IR spectroscopic imaging for tissue histopathology with a focus on breast cancer diagnosis will be presented. IR imaging coupled with computational approaches has the potential be a powerful adjunct to current histopathological procedures, with the ability to take a single unstained tissue section and give decisions on the cell types present and to provide novel chemical information to the pathologist in a useful format.
Measurement of single erythrocyte morphology and hemoglobin concentration

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It has recently been demonstrated that quantitative phase imaging (QPI) is capable of providing detailed morphological analysis as well as several novel clinically relevant parameters for red blood cells. However, since the optical phase shift through a red blood cell is a function of both thickness and refractive index, a priori knowledge of the hemoglobin concentration has so far been necessary for QPI techniques. This limits the reliability, accuracy and scope of single cell analysis using such technologies. By combining the quantitative phase information measured using a Spatial Light Interference Microscope with bright field absorption measurements it is possible to quantitatively determine single cell hemoglobin concentration, oxygenation state and cell morphology. It is shown that it is possible to use QPI in combination with absorption measurements as a label free smear analysis technique that provides more information than current automated analyzers. Such an instrument may be deployed as a standalone blood smear analyzer in a clinical setting without relying on external measurements of hemoglobin concentrations as in previous blood screening QPI instruments. The additional set of parameters measured may offer the ability for earlier diagnosis and could lead to the automated detection of conditions that currently require manual smear analysis.

Synthesis of magnetically active Au-Fe₃O₄ nanoclusters for magnetomotive imaging

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Our research goal is to develop Au@Fe₃O₄ nanoparticles (NPs) for magnetomotive imaging in viscoelastic materials (e.g., collagen). To attain good magnetomotive response in hydrogels and other viscoelastic materials, we require a high content of Fe₃O₄ and minimal Au as a plasmon-resonant shell layer. The main objective of this project is to synthesize Au@Fe₃O₄ NP's with high moment-to-mass ratio, with characterization by TEM, XRD, and optical (microscopic) imaging using magnetomotive conditions. Successful products will be used as optical nanoprobes suspended in hydrogels, to evaluate the matrix's viscoelastic properties based on the probe's magnetomotive responses.
Poster #39

Doppler-based lateral motion tracking for optical coherence tomography

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Non-uniform lateral scanning of the probe beam in optical coherence tomography produces imaging artifacts and leads to a morphologically inaccurate representation of the sample. Here, we demonstrate a solution to this problem which is based on the Doppler shift carried by the complex-valued depth-resolved scattering amplitude. Furthermore, we demonstrate the feasibility of Doppler flow velocity measurements in underlying flow channels while laterally scanning the imaging probe over large surfaces with arbitrary and varying velocity. Finally, we performed centimeters-long hand-held B-mode imaging of skin in-vivo.

Poster #40

Evolutionary algorithms for localized plasmon resonances engineering

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Localized plasmonic resonances in metal nanoparticles [1] are of great importance for various applications [2, 3]; however no general method for spectral location of resonances was hitherto presented. We propose and demonstrate on-demand engineering of the plasmonic resonances using an algorithm based on small shape perturbations of an arbitrary initial particle. Resonances at specific spectral locations and even co-location of several resonances are shown. Perturbations to a particle's geometry cause shifts of its resonances, which are tracked by numerical method based on the solution of the Fredholm integral equation. We proved analytically that the proposed algorithm is capable of moving the resonances towards the demands. Specifically, at least two arbitrary resonances may be moved simultaneously till they reach their destinations. To emphasize, any single resonance (dipole, quadrupole, etc) also may be shifted as required. A series of particles with resonances over entire visible and NIR spectrum were produced by our algorithm and transmission spectrum was verified by FDTD. More detailed information may be found in [4].

References:
Poster #41

Imaging technology for investigating the developing embryonic heart

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The avian and mammalian heart begins as a straight tube and then it loops and undergoes septation to form a four-chambered heart in a process called cardiac looping. Abnormalities that occur during cardiac looping can result in congenital heart disease. The mechanisms driving cardiac looping are not well understood due to the lack of adequate imaging technology. Direct observation of the looping heart is difficult due to the size of the heart (<2mm) and small rapid events that influence heart development. Optical Coherence Tomography (OCT) has the spatial and temporal resolution to monitor embryos during cardiac looping and provide us with structural and functional information in the embryonic heart.

Poster #42

The development of a Shp2 activator in live cells

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Src Homology 2 (SH2) Domain-containing Protein Tyrosine Phosphatase 2 (Shp2) is a ubiquitous tyrosine kinase playing crucial roles in various cellular processes. Its mutation can cause different diseases, such as noonan syndrome and leukemia. It has been revealed that the enzymatic activity of Shp2 is the central target of abnormal regulation during these disease developments. While Shp2 has been well studied on its activation mechanism, there is a lack of method to directly activate it in live cells to provide a tool for the investigation of Shp2 activity in regulating cellular functions. In this work, we generated a Shp2 activator based on a hetero-dimerization system, which enables the elevation of Shp2 activity with a fast fashion in live cells. It can serve as a fast trigger to specifically induce shp2 activation. This tool should enable us to visualize and investigate the role of Shp2 activity in regulating cellular functions with high spatiotemporal resolutions in live cells.
Chemically gated motion of gyromagnetic nanostars using neurotransmitters

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The gyromagnetic (GM) activity of gold nanostars (NSTs) with magnetic cores can be controlled by a supramolecular brake-and-release system, using cucurbituril[8] (CB[8]) and neuroactive compounds such as dopamine. NSTs functionalized with methyl viologen (MV) were tethered onto gold substrates coated with 2-naphthol (Np)-terminated polymers in the presence of CB[8], and imaged by darkfield microscopy with gyromagnetic modulation in polarized NIR scattering. Increasing the CB[8] concentration resulted in "handcuffed" NSTs and loss of mechanical motion, based on the decay in signal strength related to gyromagnetic activity. The handcuffed NSTs were able to resume their rotational freedom by introducing neurotransmitters such as dopamine or serotonin as competitive inhibitors of CB[8] tethering. The chemically gated behavior of NSTs represents a form of chemionic control over nanoscale motion.

Design of high resolution FT-IR spectroscopic imaging instruments for cancer detection

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Fourier transform infrared (FT-IR) spectroscopic imaging provides simultaneous chemically and spatially resolved information. Recent work has demonstrated that this spatially resolved chemical information from mid-infrared wavelengths can be utilized for automated determinations of pathologic state of biological specimens, like prostate or breast cancer tissue. Here, we present an optical model for propagation of light through an FT-IR spectroscopic imaging system and use this model to improve the design of existing imaging systems. We modify an existing FT-IR spectroscopic imaging system to obtain significantly higher resolution and higher image quality while simultaneously retaining chemical contrast. The model and design are validated by comparing experimental data to simulations on a standard USAF 1951 bar target. Furthermore, we obtain high quality prostate and tissue imaging data using the new design. Fine details in tissue morphology which were previously inaccessible from FT-IR spectroscopic imaging have now become available as a consequence of the improved design. We demonstrate that it is possible to identify previously obscured tissue types by performing histological classification based on bio-chemically derived spectral features.
**Poster #45**

**Dispersion-relation Fluorescence Spectroscopy (DFS)**

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Due to its ability to study specifically labeled structures, fluorescence microscopy is the most widely used technique to study live cell dynamics and function. *Fluorescence correlation spectroscopy* is an established method for studying molecular transport and diffusion coefficients at a fixed spatial scale. We propose a new approach, dispersion-relation fluorescence spectroscopy (DFS), to study the transport dynamics over a broad range of spatial and temporal scales. The molecules of interest are labeled with a fluorophore whose motion gives rise to spontaneous fluorescence intensity fluctuations that can be further analyzed to quantify the governing molecular mass transport dynamics. These data are characterized by the effective dispersion relation in the form of a power law, $\omega(q) \sim q^\alpha$, which describe the relaxation rate of fluorescence intensity fluctuations. This approach applies equally well to both discrete and continuous mass distributions to quantitatively map spatially the heterogeneous dynamics of the concentration field of the cargos at submicron resolution without the need for tracking individual components. These data are characterized by the effective dispersion relation. We report on experiments demonstrating that DFS can distinguish diffusive from advection motion in a model system, where we obtain quantitatively accurate values of both diffusivities and advection velocities. Due to its spatially-resolved information, DFS can distinguish between directed and diffusive transport in living cells. Our data indicate that the fluorescently labeled actin cytoskeleton exhibits active transport motion along a direction parallel to the fibers and diffusive on the perpendicular direction.

**Poster #46**

**Magnetic resonance techniques for mapping of brain temperature during thermal treatments**

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Induced cerebral hypothermia, or brain cooling, can provide protection against various neurological insults, including stroke and traumatic brain injury. The development of effective cooling strategies requires techniques for measuring how the temperature map of the brain changes during the cooling treatment. Magnetic Resonance Thermometry (MRT) is well-suited for this application because it is non-invasive and safe. One common method of performing MRT measurements makes use of the fact that the resonant frequency of water is temperature-dependent, changing approximately 1 Hz for every degree Celsius. However, these measurements are complicated by the fact that the magnetic field drift can also cause the resonant frequency of water to change. Here we incorporate measurements of field drift into our MRT measurements, thereby allowing us to accurately measure temperature changes over long time scales. Our method makes use of the fact that the resonant frequency of brain metabolites is insensitive to temperature. The method employs a combination of spectroscopic imaging and gradient echo scans to obtain high-resolution temperature maps that are independent of drift in the magnetic field.
Poster #47

Intraoperative evaluation of tumor margins and lymph nodes in breast cancer surgery with three-dimensional optical coherence tomography

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We present the development and translational use of three-dimensional optical coherence tomography (3D-OCT) as an intraoperative high-resolution imaging technique for real-time assessment of breast tumor margins and sentinel lymph nodes. Present histological techniques require tissue to be resected and processed in the pathology lab for analysis. Our portable OCT system allows cellular-level information to be determined in the operating room, providing critical diagnostic information when it is most needed.

OCT is capable of providing high-resolution label-free images of intact tissue microstructure based on intrinsic optical scattering properties with 5-10 µm resolution and 1-2 mm penetration depth. As a result, OCT is able to visualize tumor margins on the micron scale to depths consistent with histopathological evaluations. In a feasibility study, positive and close tumor margins were identified intraoperatively with a sensitivity of 100% and a specificity of 82%. OCT is also capable of differentiating normal, reactive, and metastatic lymph nodes based on microstructural scattering changes. Preliminary results of a current ongoing study demonstrate that OCT is capable of differentiating normal and metastatic lymph nodes intraoperatively with a sensitivity of 100% and a specificity of 60%.

Poster #48

Corneal and retinal pathologies: MEMS-based handheld OCT scanner vs. commercial OCT system

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A handheld MEMS-based scanner for fast 3-D OCT imaging with co-registered video-based imaging is presented. Designed to be multifunctional with interchangeable tips for tissue site specific imaging it can easily access both the cornea and the retina through interchangeable optics and a user-friendly interface. We evaluate its exclusive performance in the area of ophthalmology and present results relating to eye imaging both in the anterior and posterior segments in comparison to those obtained by commercial Fourier domain OCT systems.

We present cases of diabetic macular edema, posterior uveitis, neovascular membranes in macular degeneration and vitreomacular traction and epiretinal membranes both prior to and following surgical intervention. In the anterior segment we also present corneal imaging prior to and following LASIK surgery. A particular strength of the system is in macular conditions and central corneal pathology and its portability offers unique potential in the area of telemedicine and intraoperative decision making in particular in vitreomacular surgery.
Image quality assessment in ultrasonic imaging systems

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A diagnostic imaging system can be viewed as a communication channel that transfers (task) information from the target object to the observer of the image. Accordingly, the image-assessment method for diagnostic imaging, should objectively quantify the performance of the system in serving the given task. In this work, we focus on objective assessment of sonographic quality using information theoretic approach which was first described by Wagner and Smith. They derived the ideal observer for the B-mode image for binary decisions regarding the detection of low-contrast tasks. In a recent work, Nguyen et al. [1], extended the ideal-observer framework for discrimination tasks in ultrasonic images. They introduce the Kullback-Leibler divergence, J to define visual task information which they argue can be a better performance metric as the test statistic slightly deviates from normal distribution which is the case for sonographic images. Through J they derive a relationship for ideal observer detectability in acquisition stage which can be factorized into task and instrument properties. This factorization is analogous to the factorization of detectability index in radiographic images. In this work, we try to analyze the effectiveness of this factorization in predicting the performances of the envelope detected image.

References:

Poster #50

The PalmGrip utensil holder

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In the United States, people who suffer from arthritis currently number 50 million. This includes osteo and rheumatoid arthritis as well as other rheumatic diseases. The Center for Disease Control estimates that this number will increase to 67 million by 2030. An opportunity for collaboration and innovation arose at the University of Illinois at Urbana-Champaign in the spring of 2012. Brainstorming, concept generation and ideation was done by one of the authors, a graduate student and designer. Utilizing the facilities at the Beckman Institute for Advanced Science and Technology the designer was able to create a device to assist those with arthritis in becoming more independent. This process included the initial ideation, casting and scanning hands with the Steinbichler Comet L3D scanner into Geomagic Studio software and final model rendering completed in Solidworks and printed using a ZCorp Spectrum z510 model 3 dimensional printer. This paper will elaborate upon the process and discuss what did and did not work as well as the results of the modeling.
A label-free spectroscopic signature associated with hormone sensitivity in 3D co-culture models of breast cancer

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Treatment of estrogen-receptor positive breast cancers relies on endocrine therapies; however, up to 30\% of patients become resistant to this treatment. It is beneficial to identify patients who will remain sensitive to endocrine therapy using markers inherent in tissue at the time of diagnosis. Using a three-dimensional (3D) co-culture, we developed a method to determine the chemical signature of hormone sensitivity based on Fourier Transform Infrared (FT-IR) spectroscopic imaging, a highly sensitive label-free method that can detect chemical changes in tissue samples.

We used a 3D co-culture model comprised of MCF7 breast cancer cells and MCF7 Tam-resistant cells grown as spheroids on Matrigel™ and different densities of human mammary fibroblasts (HMFs) embedded within collagen gels. Upon treatment with 17β-estradiol (E2) or tamoxifen (Tam), samples were paraffin embedded for imaging and, in parallel, RNA was isolated to determine hormone sensitivity. Based on the application of FT-IR, we identified a novel spectroscopic signature that can distinguish between hormone-responsive and non-responsive tumor cell lines. Although there is already considerable insight into molecular signatures of endocrine response in cell culture and in vivo models of breast cancer, FT-IR spectroscopic imaging provides a label-free and global chemical signature that could be used in addition to immunohistochemical analysis of the initial biopsy as a way to predict endocrine sensitivity.

Fluorescence-enhancement based Dynamic staining: applications for vegetative bacterial and bacterial-spore detection

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Despite numerous advances in medical technology and treatments, the reliability and the expediency of detection and identification of infectious bacterial agents still remains challenging. In many instances, slow diagnoses of bacterial agents leads to opportunistic infections that frequently results in patient fatalities. We hypothesized that the kinetics of responses to staining fluorophores contains a wealth of information about the identity of the stained bacterial species, i.e., information related to the composition of the cell wall and membrane in vegetative cells, and the exosporium and coat proteins in bacterial endospores. Recently, we demonstrated for the first time that the kinetics of emission enhancement, caused by cell uptake of fluorophores, provides statistically significant discernibility between closely related bacterial species, such as different Bacilli. Concurrently, the kinetics of staining has a minimum or no concentration dependence. Furthermore, using kinetic signatures, rather than steady-state DC-intensity signal, decreases the susceptibility to the exact environmental conditions and to the sample preparation.

In order to ensure consistent differentiation between bacterial endospores via the staining kinetics, we explored two complementary fluorescent cationic dyes: a cyanine dye, 3,3’diethylthiacyanine (THIA); and an amyloid staining dye, thioflavain T (ThT). The dynamic staining of vegetative bacterial cells and endospores with THIA and ThT provided discernibility not only between different species, but also between certain strains of the same species. These findings suggested that for each species, the dynamic staining with 3 to 5 different dyes will provide “fingerprint” characteristics for their identification. Therefore, the staining dynamics provides venues for bacterial assays with considerable specificity that complements in an unprecedented manner their speed and simplicity.
More IMPATIENT: a gridding-accelerated Toeplitz-based strategy for non-Cartesian high-resolution 3D MRI on GPU

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Improvements to the Illinois Massively Parallel Acceleration Toolkit for Image reconstruction with ENhanced Throughput in MRI (IMPATIENT MRI) package enable a variety of advanced image acquisitions and reconstruction techniques to be used. The improved IMPATIENT implements a faster Toeplitz-based iterative image reconstruction method, whose computation time is further reduced by an optimally tuned, GPU-accelerated gridding implementation. The Toeplitz code running on a NVIDIA Tesla C1060 can reduce an 18 hour image reconstruction problem to 5 minutes when using field inhomogeneity correction and SENSE with 4 receiver coils. These improvements will enable advances in 3D non-Cartesian sequences, such as cones and stacks of spirals, by allowing them to incorporate more information into the image reconstruction process. To demonstrate the capabilities of the software package, a high resolution 3D diffusion imaging acquisition using multiple receiver coils and long data readouts that necessitate magnetic field correction are performed. The resulting images show significantly improved image quality compared with images that do not use field correction. Additionally, the software provides significant speedups over the previous IMPATIENT toolkit, with larger speedups for large image sizes. The speedup for large image sizes are important as advances are made to achieve higher resolution images.

High-frame-rate multislice speech imaging with sparse sampling of $(k, t)$-space

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Dynamic MRI is a potentially powerful tool for real-time visualization of vocal tract shaping, providing contrast from soft tissue structures while being free from the risks of ionizing radiation. However, low imaging speed hampers its ability to investigate spatiotemporal dynamics. We incorporate parallel imaging methods, sparse sampling techniques based on the partial separability (PS) model [1], and compressed sensing [2] to accelerate imaging speed. Dynamic speech imaging with high spatiotemporal resolution is achieved, reaching speeds of 100 frames per second (fps) for a single mid-sagittal slice or 25 fps for 4 slices. In addition to integrating the PS model, we have developed a composite data acquisition scheme where $k, t$ -space is highly undersampled in a way that two data sets are acquired: a navigator data set with high temporal resolution and an imaging data set with high spatial resolution. Reconstructions of /za/-/na/-/za/ sounds had a matrix size of $128 \times 128 \times 4$, a spatial resolution of $2.2 \text{ mm} \times 2.2 \text{ mm} \times 8.0 \text{ mm}$ and a frame rate of $\sim 25 \text{ fps}$ for the whole stack of 4 slices. By visualizing a third dimension, tongue grooving can be seen in the /za/ sound versus the /na/ sound.

References:
Poster #55

Distinct mechanisms regulating calcium signals at the plasma membrane and endoplasmic reticulum in response to mechanical stimulation

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Mechanical environment plays a pivotal role in regulating stem cell commitment and functions. However, it remains unclear on how mechanical stimuli are transmitted into biochemical signals in stem cells. In this study, we investigated the molecular and biophysical mechanisms by which mechanical forces regulate Ca²⁺ signaling in human mesenchymal stem cells (hMSCs), integrating genetically encoded Ca²⁺ biosensor based on fluorescence resonance energy transfer (FRET) and optical laser tweezers. Laser-tweezer-traction of the cell membrane induces intracellular Ca²⁺ oscillations caused by Ca²⁺ release from endoplasmic reticulum (ER) in the absence of extracellular Ca²⁺. These force-induced Ca²⁺ oscillations produced by ER Ca²⁺ release are mediated not only by the mechanical support of cytoskeleton and actomyosin contractility, but also by mechanosensitive Ca²⁺ channels on the plasma membrane, specifically TRPM7. When the ER Ca²⁺ release is inhibited and the extracellular Ca²⁺ level is restored, laser-tweezer-traction of the cell can induce the intracellular Ca²⁺ increase, which is mediated by the cytoskeletal structure but not actomyosin contractility. Taken together, our results indicate that active actomyosin contractility regulated by MLCK and myosin II is essential for the force transmission into the deep intracellular organelles but dispensable for the mechanical regulation of plasma membrane channels.

Poster #56

Phase derivative microscopy for label-free imaging of dynamic biological structures

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Laplace and gradient field microscopy use a spatial light modulation in the Fourier plane of a microscope image to measure the intensity of field derivatives which is valuable in studying the dynamics of biological samples.
Poster #57

Novel light sources for stimulated Raman scattering (SRS) spectroscopy
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Widespread adaptation of SRS and other nonlinear-optical spectroscopy techniques is hampered by the high cost and complexity of the required pulsed laser light sources. To address this problem we are optimizing a new type of pulsed laser light source called a fiber optical parametric oscillator (FOPO). We report an analysis of three different output coupling schemes: dichroic mirrors, variable beam splitter, and polarization beam splitter. We conclude that using the polarization beam splitter set to 40% output coupling optimizes the output power for our application. Work in progress includes refinement of a spatial beam overlap and development of a time-synchronized lock-in measurement system.

Poster #58

Implantable perfusion and oxygenation sensor for monitoring liver transplants
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Around 2,000 people die every year on the waitlist for liver transplants in the US alone. This clear organ shortage lead doctors to use “extended criteria organs” that are associated with higher complications rate. Most graft failures are linked to insufficient tissue perfusion and 55% of these failures take place in the first two weeks after transplant. Our group is developing an implantable perfusion and oxygenation sensor based on Near Infrared Spectroscopy (NIRS) to monitor transplants in that critical period. Unlike current technology that mostly measures perfusion, arterial oxygen saturation or venous oxygen saturation separately; our sensor measures all three signals simultaneously giving the doctors valuable data on when and how to intervene to prevent graft failure. In this work, we report the results of our latest in vivo porcine studies. We were able to measure venous and arterial oxygen saturation changes in the intervals 50-92% and 60-100% respectively with a prediction error as low as 1.15%.
**Poster #59**

**Computationally cost-effective three-dimensional Fourier-transform second-harmonic generation imaging of collagen-based tissues**

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Collagen fibers in biological tissues are effective media for second-harmonic generation (SHG) because of their non-centrosymmetric structure. Therefore, SHG microscopy can generate high contrast images of collagen-based tissues without the need of staining. In addition, due to the fact that SHG is confined to a sub-femtoliter volume, SHG microscopy is capable of 3D imaging. To fully utilize the 3D-imaging capability of SHG microscopy, we propose three dimensional Fourier transform-second-harmonic generation (3DFT-SHG) imaging. Similar to our FT-SHG imaging, where we extract quantitative information, such as preferred orientation and spacing between fibers through Fourier analysis, 3DFT-SHG extends the quantification to 3D. Previous studies utilizing FT-SHG has already shown great promise in assessing changes in collagen fiber organization for injured horse tendons and in exploring age-related structural changes in porcine cortical bones. We, therefore, strongly believe that 3DFT-SHG will be particularly useful for studying biological tissues such as bone, cartilage, and skin, where collagen fibers are organized in 3D. Our analyses on known test objects showed accuracy up to 0.25 degrees. For a 512 x 512 x 96 test object, the average runtime is approximately 1.5 minutes on a regular desktop computer. Moreover, an example application is provided to quantify 3D collagen fiber orientation in porcine sclera.

**Poster #60**

**Joint inhomogeneity estimation for water-fat separation with multi-peak fat modeling**

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Key to the success of phase-sensitive water-fat separation lies in robust estimation of field inhomogeneities, which remains difficult in many clinically important imaging scenarios. The difficulty often arises when the spectral field-of-view is not sufficient to accommodate field inhomogeneities, causing spectral aliasing. Extensive research efforts have been directed to robust field map estimation by imposing spatial field map smoothness [1-3] and/or deriving a priori likelihood of water and fat existence [4]. This work describes a novel field map estimation technique that systematically incorporates field map smoothness and a priori likelihood of field map values via belief propagation (BP) algorithm, which perform joint estimation of field inhomogeneities across 2D image grid.

References:
Integrated multimodal optical microscopy for structural and functional imaging of engineered and natural skin

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Engineered skin grafting is a promising treatment option for skin loss. Desired skin substitutes should be able to restore the multiple roles and functions performed by natural skin, including mechanical integrity, photoprotection, immuno-surveillance, water resistance, and temperature regulation. While these functions are fulfilled by a complex interplay of a variety of cells in the extracellular matrix, a better understanding of these processes within a multi-layered skin construct is paramount to the successful development of desired skin substitutes. A powerful noninvasive imaging tool that has cellular spatial resolution and functional imaging capability would be indispensable. In this work, we developed an integrated optical microscope, which incorporates multiple imaging modalities, including multi-photon excitation fluorescence (MPM), second harmonic generation (SHG), optical coherence microscopy (OCM), and fluorescence lifetime imaging (FLIM). This imaging platform enables us to obtain high-resolution, real-time, spatially co-registered images which carry structural, molecular, and functional information of living tissues under investigation. These imaging functions are realized based on the complementary information provided by different modalities, i.e., scattering information from OCM, molecular information from MPM, and cellular metabolism from FLIM. Bi-layer (dermis and epidermis) engineered skin tissues were investigated in this study. Detailed structure and morphology from cells at different layers, including keratinocytes, collagen, and fibroblast were readily observed with OCM and MPM. In particular, different morphology and metabolic states of keratinocyte from different epidermal layers were visualized, which demonstrates the complex, multi-step cornification process of keratinocytes. Apoptosis and necrosis processes of keratinocytes were investigated in real time with the combination of FLIM and OCM, which renders both cellular level change in metabolism and light scattering at the same time. The knowledge of cellular dynamics in developing engineered skin and following in vivo grafting that can be obtained with this integrated microscope platform will guide us to refine the control and culturing conditions necessary to obtain a more robust and physiologically-relevant engineered skin substitute.

Multimodal nonlinear optical histopathology of breast cancer by pulse-shaping of a fiber supercontinuum

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Cancer diagnosis by conventional histopathology is often time-consuming and subjective. Modern nonlinear optical microscopy presents a fast, label-free and more quantitative approach to visualize molecular contents in biological tissues. In this work, a rat mammary tumor model is investigated by multimodal nonlinear optical imaging and compared with normal mammary samples. Two-photon fluorescence (TPF), second harmonic generation (SHG), and third-harmonic generation (THG) microscopy are performed by amplitude and phase shaping of a single fiber supercontinuum (SC) light source spanning from 900-1160 nm. Multi-dimensional optical signals are analyzed in order to differentiate tissue types and to identify optical and molecular biomarkers in breast cancer development. Multimodal nonlinear optical histopathology provides an alternative method to visualize tissue samples. The single-beam and pulse-shaping setup greatly simplifies the complex multiple-laser system for multimodal imaging and also improves the efficiency of generation of nonlinear optical signals. The method can potentially be developed as a cancer-screening tool and can bring new insight in cancer research by correlating the optical data with genomic and proteomic data.
Poster #63

Investigating mechanoenvironment change in tumor growth using multimodal contrast agents

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The tumor microenvironment is mechanically modified during cancer progression. Imaging of tumor mechanical environment will provide new information for early cancer diagnosis. The goal of this study is to understand more clearly the contrast mechanisms of elasticity images in terms of molecular and cellular activities that drive cancer. Two imaging modalities (ultrasound and OCT) and several imaging techniques were implemented and compared. Magnetic nanoparticles could be the best in vivo contrast agents in monitoring cancer progress.

Poster #64

Si nanoparticles and PANI-Si capsules imaging and behavior analysis

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Recently synthesized water-soluble dispersion of nanocapsules with a polyaniline shell and a luminescent ultrasmall Si nanoparticles core with diameters of about 50-400 nm seem to enable a wide range of biosensing/imaging applications. The multiplicity of luminescent nanoparticles enclosed in the core allows high sensitivity sensing hence provides a highly amplified and reproducible signal for luminescence-based imaging. This shows potential capability of light detection from single capsules using the fluorescence microscope. We report the brightness analysis of PANI-Si single capsules in comparison to pure Si nanoparticles using standard fluorescence microscope.
Multimodality imaging of breast cancer experimental lung metastasis

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Objectives: Metastatic breast cancer (MBC) is incurable. The clinical standard to assess tumor microvesSEL density (MVD), a prognostic marker in MBC, is CD105 staining. The goal of the study is to develop a PET/near-infrared fluorescent (NIRF) probe for imaging of CD105 expression in MBC, and other applications such as intraoperative guidance.

Methods: TRC105, an anti-CD105 mAb, was labeled with a NIRF dye and 89Zr to yield 89Zr-Df-TRC105-800CW. Luciferase-transfected 4T1 breast cancer cells were injected intravenously into female BALB/c mice to establish a lung MBC model. Bioluminescence imaging (BLI) was used to monitor the tumor burden. In vivo/ex vivo studies were done to investigate 89Zr-Df-TRC105-800CW in the MBC model. Cetuximab was used as a control.

Results: PET imaging revealed that 4T1 lung tumor uptake of the tracer was 8.7 ± 1.4, 10.9 ± 0.5, and 9.7 ± 1.1 %ID/g at 4, 24, and 48 h post-injection (n = 4). Biodistribution studies, blocking, control studies with cetuximab, ex vivo BLI/PET/NIRF imaging, and histology all confirmed CD105 specificity of the tracer. NIRF imaging-guided removal of 4T1 tumors in a subcutaneous model was also straightforward.

Conclusions: We report the first PET/NIRF imaging of CD105 expression in a MBC model. Broad clinical potential of the tracer was shown in many tumor types, which enabled early detection of metastases and provided intraoperative guidance for tumor removal.

Phototoxic effect of zinc sulphophthalocyanine photosensitizer on human colon (DLD-1) and lung (A549) carcinoma cells in vitro

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Background: Cancer is amongst the most challenging diseases regarding treatment. According to the World Health Organization (WHO) cancer is the most devastating disease worldwide and 83.2 million people will die by 2015. Photodynamic therapy (PDT) is a minimally invasive therapeutic modality for different cancers, it comprises of three components viz. light (usually in the red or near-infrared spectrum), photosensitizer (PS; light absorbing compound) and molecular oxygen to induce cell death. The PS localizes in tumour cells which are then irradiated with an appropriate wavelength, resulting in tumour destruction.

Objective: To determine the phototoxic pattern of Zinc sulphophthalocyanine (ZnPc) PS alone in DLD-1 and A549 cells and the extent of PDT using different concentrations of PS.

Methods: Cells were divided into PS only (control) and PDT (light and PS). DLD-1 and A549 cells were grown in DMEM/F12 and RPMI 1640 media respectively and cultivated for 4 h. ZnPc at different concentrations [0, 5, 10, 20 and 40 μM] was added thereafter and incubated for 24 h. PDT cells were irradiated at a wavelength of 680 nm with 5 J/cm² and incubated for a further 24 h. Cellular morphology was determined by light microscopy and biochemical changes by Trypan Blue (cellular viability), adenosine triphosphate (ATP) and lactate dehydrogenase (LDH).

Results: Morphologically, cells looked irregular and detached after PDT, Trypan Blue and ATP decreased in a dose-dependent manner in PDT cells, while LDH decreased with an increase in PS except in 40 μM PDT cells.

Conclusion: In the absence of light, ZnPc has insignificant toxicity and PDT at 20 μM appeared optimum in killing both colon and lung cancer cells.
Poster #67

Inflammatory response of injured fibroblasts after low intensity laser irradiation at a wavelength 830 nm

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Photostimulation is a non-invasive treatment that utilizes low intensity laser irradiation to provide healing or stimulate appropriate cellular functions. Diabetes mellitus is a chronic disease preceded by diabetic ulcers which are chronic due to deteriorated healing process. Hypoxia, decreased fibroblast proliferation and impaired growth factors are amongst root factors that contribute to impaired healing.

Materials and Methods: Commercially available human skin fibroblasts (WS-1) were used. Study consisted of four groups viz. Normal, normal wounded, diabetic wounded and hypoxic cells, each with a non-irradiated control. Wound was simulated by creating central scratch using pipette, diabetic state was obtained by growing cells continuously in media that contained glucose to a final concentration of 22.56 mM, and for hypoxic insult cells were incubated in an anaerobic jar (0% O₂ and 20% CO₂) for 4 h at 37 °C. Cells were then irradiated with 5 J/cm² and incubated for 1 or 24 h. Morphological changes were observed by light microscope; ELISA and flow cytometry were used to determine IL-1β, IL-6 and TNF-α as inflammatory markers; and caspase 3/7 for apoptosis. Results: After 24 h incubation wounded area appeared decreased and hypoxic cells had regained normal morphologic features when irradiated, TNF-α and IL-1β had decreased in irradiated samples, whereas IL-6 was increased. Caspase 3/7 had decreased in irradiated samples at both 1 and 24 h. Conclusion: This study has demonstrated the beneficial effects of low intensity laser therapy since the results showed significantly reduced inflammatory response in vitro and hastened wound healing particularly in diabetic and hypoxic insults.

Poster #68

Gradient field microscopy

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Gradient field microscopy (GFM) is a high intrinsic contrast microscopy technique that increases the contrast of the image of a transparent sample by measuring the derivative of the optical field. It is built as an outside module for a conventional bright field microscope by adding two lenses and a spatial light modulator (SLM) starting from the image formed by the microscope. The amplitude change applied after the first lens provides the first-order derivative of the field at the image that is formed after the second lens, simply by following the Fourier transform properties.

GFM preserves the spirit of regular differential interference contrast (DIC) microscopy by providing the first-order derivative of the field and high sensitivity at the edges, along with providing some advantageous features, such as no directional artifact, using birefringent materials, and fast acquisition speed. Therefore, with all these advantages and high contrast, GFM can be used for a very wide range of biological specimens, from the single cell level (i.e. red blood cells), to the non-invasive tissue imaging.
Thank you very much for attending the Imaging at Illinois Conference. We would like to express our personal appreciation to all of the faculty, staff, students, and volunteers who helped make this workshop a success. We share your enthusiasm and anticipation for Imaging at Illinois. Please visit our website for more information:

http://www.imaging.beckman.illinois.edu/

We would like to hear your comments. Please contact us:

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