Alavi-Bradley Symposium
September 19, 2024

Third Annual Alavi-Bradley Symposium on Molecular Imaging and Theranostics

SMC Campus Center
University of Maryland, Baltimore

September 19, 2024

Keynote Address:

Peter Choyke, MD, Chief Molecular Imaging Branch, National Cancer Institute, National Institutes of Health

Additional Speakers:

Dima Hammoud, MD, National Institutes of Health

Abbas Alavi, MD, MD (Hon), PhD (Hon), DSc (Hon.), University of Pennsylvania

Kristine Glunde, PhD, The Johns Hopkins University School of Medicine

Shun Kishimoto, MD, PhD, National Cancer Institute

James Bankson, PhD, The University of Texas MD Anderson Cancer Center

Graeme Woodworth, MD, University of Maryland School of Medicine

Miroslaw Janowski, MD, PhD, University of Maryland School of Medicine

Ryan Sochol, PhD, University of Maryland College Park

The symposium was organized by the Department of Diagnostic Radiology and Nuclear Medicine and made possible by a generous gift from Drs. Abass and Jane Alavi.

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Dear Colleagues:

On behalf of the Department of Diagnostic Radiology and Nuclear Medicine, we welcome you to the third annual Alavi-Bradley Symposium on Molecular Imaging and Theranostics at the University of Maryland School of Medicine (UMSOM). As in the past, this promises to be an exciting and enriching experience of learning, networking and sharing knowledge with each other on the topics of Molecular Imaging and Theranostics.

This outstanding symposium is made possible by a generous endowment from **Drs. Abass and Jane Alavi** to the Department of Diagnostic Radiology and Nuclear Medicine at the UMSOM to host this annual symposium.

For our third Alavi-Bradley Symposium on Molecular Imaging and Theranostics, our keynote speaker is **Peter Choyke,** from the National Cancer Institute. In addition, we have eight other outstanding speakers, including **Dima Hammoud** from NIH, **Kristine Glunde** from Johns Hopkins, **James Bankson** from the University of Texas MD Anderson Cancer Center, **Shun Kishimoto** from the National Cancer Institute, **Graeme Woodworth** from UMSOM, **Miroslaw Janowski** from UMSOM, and **Ryan Socho**l from UMCP. We are pleased to announce that **Dr. Abass Alavi** from the University of Pennsylvania will be presenting again this year.

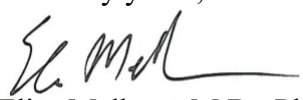
We received numerous abstract submissions and selected the five top abstracts for brief oral presentations. The other abstracts will be presented as posters that can be viewed throughout the day. Full texts of these abstracts can be accessed in the program.

Participants have registered from multiple institutions, including students, residents, research fellows, staff and faculty from various disciplines at all levels, who are interested in learning more about molecular imaging and theranostics.

This symposium is approved for **Continued Medical Education (CME).** The University of Maryland School of Medicine has designated this live activity for a maximum of **6.25** ***AMA PRA Category 1 Credits*** **™**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

We are grateful to our additional sponsors and for all those who contributed to the preparation of this symposium. We appreciate your interest and participation in this symposium, and we look forward to a stimulating day of learning and exchange of ideas.

Sincerely yours,



Elias Melhem, M.D., Ph.D. (Hon)
Professor and Former Dean John M. Dennis Chair of Diagnostic Radiology and Nuclear Medicine
and
The Alavi-Bradley Symposium Planning Committee:
Vikas Kundra, M.D., Ph.D. (Chair); Vasken Dilsizian, M.D.; Dheeraj Gandhi, MBBS; Dirk Mayer, Ph.D.; Piotr Walczak, M.D., Ph.D.

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AGENDA

8:00 AM	*Breakfast & Registration*	SMC Campus Center Ballroom Reception Area
8:40 – 8:50	*Introduction*	**Elias Melhem**, Professor and Former Chair, Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland Baltimore
8:50 – 9:00	*Opening Remarks*	**Arif Hussain**, Professor of Medicine and Co-Leader, Hormone Responsive Cancers Program, University of Maryland Greenebaum Comprehensive Cancer Center

Session One **Moderator: Vikas Kundra**

9:00 – 9:50	*Keynote Address* **Peter Choyke:** "Molecular Imaging of the Tumor Microenvironment: The Next Step in Oncologic Imaging"
9:50 – 10:00	*Questions*
10:00 – 10:25	**Dima Hammoud:** "Development of Structure and Metabolism-based Fungal-specific PET Tracers"
10:25 – 10:50	**Abbas Alavi:** "New Trends in PET Based Novel Imaging Techniques in Medicine"
10:50 – 11:00	*Round Table* Drs. Choyke, Hammoud, Alavi and Dilsizian
11:00 – 11:20	*Coffee Break and Networking*

Session Two **Moderator: Dirk Mayer**

11:20 – 11:45	**Kristine Glunde**: "MALDI Imaging to Discover and Map Reprogrammed Molecular Pathways in Cancer Progression"
11:45 – 12:10	**Shun Kishimoto:** "Improved Tumor Blood Flow Enhances the Abscopal Effect: Preclinical Assessment in Mice Treated with Combined Radiation and PD-1 Blockade Therapy"
12:10 – 12:35	**James Bankson:** "Imaging Tumor Metabolism with Hyperpolarized Pyruvate"
12:35 – 12:45	*Round Table* Drs. Glunde, Bankson, Kishimoto and Mayer
12:45 – 1:45	*Lunch and Poster Presentations*

Session Three **Moderator: Dheeraj Gandhi**

1:45 – 2:10	**Graeme Woodworth:** "Focused Ultrasound-enhanced Neurosurgery: Opening the Window of Opportunity for Treating Residual, Infiltrating Gliomas"
2:10 – 2:35	**Miroslaw Janowski:** "Guideomics"
2:35 – 3:00	**Ryan Sochol:** "3D Micro/Nanoprinted Soft Robots: From Super Mario Bros. to Minimaly Invasive Surgery"

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3:00 – 3:10 *Round Table* Drs. Woodworth, Janowski, Sochol and Gandhi

3:10 – 3:30 *Coffee break*

Awards Session (Talks from submitted Abstracts) Moderator: Piotr Walczak

3:30 – 3:35 **Bonghwan Chon** (UMB): "Intraperitoneal Ovarian Cancer Imaging Enhanced by BrCy112: Dual-Mode-Dual-Gd Contrast Agents in Near-Infrared Imaging"

3:35 – 3:40 **David Gulisashvili** (UMB): "Enhancing Treatment of Diffuse Intrinsic Pontine Glioma: Synergistic Effect of Focused Ultrasound and Anti-CD47 Immunotherapy"

3:40 – 3:45 **Behnaz Ghaemi** (JHU): "Label-Free Imaging of Cancer Stem Cells and Glioblastoma Grading Using Mannose-weighted CEST MR"

3:45 – 3:50 **Zinia Mohanta** (JHU): "Advanced MRI Monitoring of Gene Expression: Evaluating rAAV-Delivered SuperCESTide for Liver Imaging"

3:50 – 3:55 **Guanda Qiao** (UMB): "Osmotic Blood-Brain Barrier Opening 2.0"

3:55 – 4:00 **Divya Nambiar** (NCI): "Isolation and Characterization of Anti-BSG Nanobody to Target Hepatocellular Carcinoma"

4:00 – 4:05 *Presentation of Awards*

Panel Discussion

4:05 – 4:35 *Panel discussion on the topic voted by the participants (~5 proposed topics) & Future Directions: All speakers & Dr. Dilsizian*

4:35 – 4:40 *Closing Remarks* **Elias Melhem**

4:40 – 4:45 *Closing Remarks* **Vikas Kundra**

End

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SPEAKERS

Keynote Speaker: Peter Choyke, MD

Chief, Molecular Imaging Branch, National Cancer Institute, National Institutes of Health

Dr. Peter Choyke is a Senior Investigator and Chief of the Molecular Imaging Branch (MIB) of the National Cancer Institute. The MIB develops targeted molecular imaging agents for preclinical and clinical translational research in prostate cancer, multiple myeloma, bladder cancer, osteosarcoma, neuroendocrine cancer and hepatocellular carcinoma. The MIB is also developing targeted radionuclide therapies based on alpha and beta emitters. The MIB also manages the Artificial Intelligence Resource, that develops customized AI algorithms to assist basic, preclinical and clinical research. The MIB also houses a physics group focused on developing the next generation of PET scanners.

Title: *"Molecular Imaging of the Tumor Microenvironment: The Next Step in Oncologic Imaging"*

Abstract

There is currently much excitement about new theranostic radiopharmaceuticals that target tumor antigens. There has been less focus on targets in the tumor microenvironment. The tumor microenvironment (TME) is important because it is where immune responses to tumors develop and also can provide structural support to cancers. An example of a TME-directed agent is Fibroblast Activation Protein (FAP) that targets activated fibroblasts. PET agents based on FAP are finding broad application in tumors

characterized by fibrosis such as pancreatic and biliary cancers. CXCR4 is a cytokine receptor that has also been proposed for cancer imaging, especially hematopoetic tumors such as myeloma and lymphoma. Several other agents that are earlier in the pipeline will be discussed including an agent targeting T-regulatory cells. Such agents can not only be used for diagnosis but also have potential for therapy as will be illustrated. Imaging the TME is challenging because the number of receptors is lower and in many cases may not be amenable to theranostic probes but it has already shown promise for the next generation of PET agents.

Learning Objectives:

1. To understand the potential role of tumor microenvironment PET agents for cancer diagnostics.
2. To understand the role of such emerging agents as Fibroblast Activating Protein PET and CXCR4 PET in oncologic imaging.
3. To understand potential new agents, still in preclinical development, that target the tumor microenvironment that may impact the future of oncologic imaging.

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Dima Hammoud, MD

Senior Investigator, Radiology and Imaging Sciences, Intramural Research Program, NIH

Dr. Dima A. Hammoud is a tenured Senior Investigator in Radiology and Imaging Sciences (NIH-CC) at the Intramural Research Program at NIH. Her research interests include the development of preclinical, translational and clinical molecular imaging tracers to improve the understanding of the pathophysiology of infection and provide reliable imaging biomarkers of infectious diseases. Current research in her laboratory focuses on the development and validation of novel fungal-specific imaging biomarkers in animal models of infection using non-invasive molecular imaging techniques, mainly positron emission tomography (PET), which can then be translated to human applications. Another interest of the lab is utilizing PET imaging to better understand the pathophysiology of HIV in the brain and periphery and to identify HIV reservoirs.

Dr. Hammoud is board-certified in diagnostic imaging and has completed fellowships in neuroradiology and PET imaging. She is a practicing neuroradiologist at the NIH-CC. Currently, she serves as deputy director of the Center for Infectious Disease Imaging (CIDI), a joint initiative between the NIH-CC and NIAID, Chair of the "Imaging of Infections" (IOI) interest group at the World Molecular Imaging Society (WMIS), Chair of the animal care and use committee (ACUC) at the NIH-CC, a committee member of the intramural PET Steering Committee at NIH and since 2021, as a member of the scientific program committee of the World Molecular imaging Congress (WMIC).

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Title: "*Development of Structure and Metabolism-based fungal-specific PET Tracers*"

Abstract

Invasive fungal diseases, caused by pathogens such as *Aspergillus fumigatus*, are common life-threatening infections in immunocompromised patients. Often, effective treatment is hampered by delays in timely and specific diagnosis. Fungal-specific molecular imaging tracers can potentially provide non-invasive *in vivo* readouts of deep-seated fungal pathologies allowing for early diagnosis and the ability to assess treatment response longitudinally. In this presentation, advances in developing and validating fungal-specific positron emission tomography (PET) ligands which capitalize on the unique sugar metabolism of fungi will be discussed. Another approach of targeting fungal-specific cell wall components with radiolabeled antibodies and antibody fragments will also be reviewed. The presentation will conclude with a discussion of future potential molecular imaging applications in the field.

Learning Objectives:

1. Appreciate the increasing threat posed by fungal infections to human health
2. Understand the challenges associated with developing fungal-specific imaging tracers
3. Review different approaches for targeting fungal infections using metabolism and structural characteristics of fungi

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Abass Alavi, MD, MD (Hon), PhD (Hon), DSc (Hon.)

Professor of Radiology and Associate Director at the **Institute on Aging at the University of Pennsylvania Perelman School of Medicine**.

Dr. Alavi is recognized as a pioneer in molecular and nuclear imaging, having contributed to the development of positron emission tomography (PET), in particular utilizing the radiotracer ^{18}F fluorodeoxyglucose (FDG) in PET imaging, and later using ^{18}F-FDG-PET in conjunction with computed tomography (CT) and magnetic resonance imaging (MRI) to understand many diseases.

Working under the guidance of Dr. David Kuhl, Dr. Alavi and colleagues were pioneers in performing modern tomographic imaging by utilizing single gamma emitting radionuclides-- single photon emission computer tomography (SPECT).

In 1973, Drs. Alavi, Kuhl and Reivich devised the concept of labeling deoxyglucose with positron-emitting fluroide (^{18}F), which led to the development of FDG, the first clinically approved radiopharmaceutical for PET imaging that is still widely used today.

In August 1976, Dr. Alavi was part of the team, with mentor Dr. Kuhl, that performed the first human PET studies of the brain and whole body using ^{18}F-FDG. [1] He also was among the first to utilize iodine-123 in the diagnosis of thyroid cancer, meta-iodobenzylguanidine in the assessment of pheochromocytoma, radiolabled white blood cells in the evaluation of infection, and technetium 99m in the detection of gastrointestinal bleeds. Dr. Alavi, along with his wife, Dr. Jane Alavi, a specialist in hematology and oncology at the University of Pennsylvania, pioneered the use of ^{18}F-FDG PET for the demonstration of recurrent brain tumors.[1]

Dr. Alavi received his medical degree from University of Tehran School of Medicine in 1964. He did his post-graduate training in Internal Medicine at Albert Einstein Medical Center in Philadelphia, a second year residency in medicine at Veterans Administration Hospital in Philadelphia, a fellowship in hematology (1969-1970) at the Hospital of the University of

Pennsylvania, one year of radiology at Beth Israel Hospital in Boston, and a fellowship in nuclear medicine (1971-1973) at the Hospital of the University of Pennsylvania. He has served on the faculty at Penn since then, and directed the Nuclear Medicine training program and led the Division of Nuclear Medicine for many years. Many of his trainees are now leaders in Nuclear Medicine in the U.S., India, and South America.

Dr. Alavi's over 1,600 journal articles have been cited over 79,000 times according to Google Scholar and he has received numerous awards, including the Georg Charles de Hevesy Nuclear Pioneer Award in 2004 and the Benedict Cassen Prize for Research in Nuclear Medicine of Society of Nuclear Medicine and Molecular Imaging (SNMMI) in 2012. He also holds honorary degrees from several universities, including the University of Southern Denmark and the University of Bologna.

[1] Høilund-Carlsen PF. Abass Alavi: A giant in Nuclear Medicine turns 80 and is still going strong! Hell J Nucl Med. 2018 Jan-Apr;21(1):85-87.

Title: *"New Trends in PET Based Novel Imaging Techniques in Medicine"*

Abstract

The introduction of molecular imaging techniques with combined PET-CT-MRI has had a major impact on the day-to-day practice of medicine as well as the implementation of meaningful research over the past few decades. While FDG-PET imaging has led the way in demonstrating the importance of molecular imaging to the medical community, many other radiotracers have been employed in various settings that have further enhanced the unparalleled contribution of this technology in medicine. Several areas will be highlighted during this presentation with emphasis on skeletal metastasis, atherosclerosis, osteoporosis, and finally, advances in theranostics. The importance of cancer metastasis to red marrow and its implications for early diagnosis and effective treatment of various malignancies will be described. While FDG has been very important for detecting the spread of cancer to the red marrow, newer tracers that target specific malignancies will be

a focus of this presentation. It will be further emphasized that bone scans with conventional SPECT tracers or Sodium Fluoride (NaF) have limited roles to play in detecting skeletal spread of malignancies.

The rapidly evolving impact of PET to detect and quantify atherosclerotic plaques will also be described during this presentation. While FDG appears to be a very successful tracer for detecting inflammation in the plaques, its role is limited because of the significant uptake of this compound in the myocardium. Therefore, the role of NaF to target molecular calcification in the coronary and carotid arteries, as well as other major vessels, will be emphasized. The existing data heavily supports the importance of detection of molecular calcification in this serious and potentially fatal disease. Based on the data that has been generated, NaF-PET scanning appears to be very successful and even superior to the existing imaging techniques.

Finally, the rapid evolution of theranostics as a major domain for PET imaging will be described during the final segment of this presentation. The use of diagnostic tracers that target certain cancers including prostate and neuroendocrine tumors has paved the way for therapeutic applications of radiolabeled compounds. This new field built on PET-based imaging technology will have a major impact on the future developments of effective interventions. Based on what has been accomplished by PET-related molecular imaging techniques, there is great potential for its revolutionary impact on the daily practice of medicine.

Learning Objective:

- This presentation is intended to introduce the extraordinary capabilities that are provided by Positron Emission Tomography (PET) and have made a major impact on research and the day-to-day practice of medicine.

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Kristine Glunde, PhD

Professor of Radiology, Oncology and Biological Chemistry, Founding Director, Applied Imaging Mass Spectrometry (AIMS) Core, The Johns Hopkins University School of Medicine

Dr. Glunde is Professor of Radiology, Oncology and Biological Chemistry at The Johns Hopkins University School of Medicine, and the founding Director of the Applied Imaging Mass Spectrometry (AIMS) Core. Her research program focuses on cancer biology and molecular imaging of cancer. Her lab combines cancer biology approaches with multi-scale molecular imaging to investigate and visualize molecular events that drive cancer growth, invasion, and metastasis. Her lab also develops novel applications which integrate mass spectrometry imaging with optical microscopy technologies. Molecular imaging technologies used in Dr. Glunde's lab span magnetic resonance imaging, mass spectrometry imaging, and fluorescence imaging.

Title: "*MALDI Imaging to Discover and Map Reprogrammed Molecular Pathways in Cancer Progression*"

Abstract

Reprogramming of metabolic pathways is a hallmark of cancer, enabling cancer cells to rapidly proliferate, invade, and metastasize. My lab team is investigating such altered key metabolic pathways in breast cancer, including their specific roles in migration, invasion, and metastasis. An integral part of our methodological approach is matrix-assisted laser desorption/ionization (MALDI) imaging, as it allows us to spatially map a plethora of different biomolecules in primary tumors and corresponding metastases. This presentation will highlight our recent progress in discovering key metabolic pathways in N-

glycosylation, creatine metabolism, and phospholipid reprogramming which significantly contribute to cancer progression and metastasis. This lecture will also briefly discuss our recently developed RaMALDI and FluoMALDI applications, which are streamlined, integrated, multimodal imaging workflows of Raman and fluorescence microscopy with MALDI imaging.

Learning Objectives:

1. Understand the basics of MALDI mass spectrometry imaging
2. Describe the molecular classes that can be mapped from tissue with MALDI imaging
3. List key steps in sample preparation for different analyte classes

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Shun Kishimoto, MD, PhD

Staff Scientist, Urologic Oncology Branch, Center for Cancer Research, Center for Cancer Metablolism, National Cancer Institute

Dr. Shun Kishimoto is a distinguished cancer researcher with an M.D. and Ph.D. from Kyoto University Medical School and a Master's in clinical research from Duke University. He began his career at the Radiation Biology Branch of the National Cancer Institute (NCI), where he made significant discoveries about photoimmunotherapy and its effects on cancer cells. His research expanded to include tumor physiology and metabolism, leading to the identification of crucial imaging biomarkers for immune checkpoint blockade therapy.

Currently, he works as a staff scientist in the Urologic Oncology Branch at the CCR Center for Cancer Metabolism. His work focuses on preclinical in vivo imaging studies and clinical research on metabolic profiling of cancer, aiming to develop advanced diagnostic and therapeutic strategies. Dr. Kishimoto's career is dedicated to translating research into effective cancer treatments.

Title: *"Improved Tumor Blood Flow Enhances the Abscopal Effect: Preclinical Assessment in Mice Treated with Combined Radiation and PD-1 Blockade Therapy"*

Abstract

The abscopal effect, a phenomenon where localized radiation therapy (RT) leads to regression of non-irradiated metastatic lesions, is rarely observed when RT is used alone due to the immunosuppressive tumor microenvironment (TME). This study investigates the enhancement of the abscopal effect through the combination of RT and PD-1 blockade therapy, focusing on the role of tumor blood flow. Using MC38 colon adenocarcinoma and

B16.F10 melanoma mouse models, we assessed the efficacy of combined therapy and identified imaging biomarkers that correlate with the abscopal effect. Enhanced blood perfusion in primary tumors, achieved through brief carbogen exposure, significantly increased the abscopal effect. Imaging techniques such as EPRI, DCE-MRI, and 13C DNP MRI provided non-invasive monitoring of metabolic and functional changes in the TME. Our findings suggest that higher blood perfusion in the primary tumor prior to treatment enhances the induction of the abscopal effect, offering a potential predictive biomarker and therapeutic strategy for metastatic tumors.

Learning Objectives:

1. Understanding Cancer Cell Biology and Metabolism:
    - Gain in-depth knowledge of cancer cell biology, focusing on the mechanisms of tumor growth, survival, and metastasis.
    - Study the metabolic alterations in cancer cells and their implications for cancer progression and treatment.
2. Developing and Identifying Imaging Biomarkers:
    - Identify and validate imaging biomarkers for assessing the efficacy of cancer treatments, particularly immune checkpoint blockade therapy.
    - Utilize imaging biomarkers to monitor treatment responses and predict patient outcomes.
3. Translating Research into Clinical Practice:
    - Focus on the translation of basic and preclinical research findings into practical diagnostic and therapeutic strategies.

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James Bankson, PhD

Professor, Department of Imaging Physics, The University of Texas MD Anderson Cancer Center

Dr. Bankson is a Professor in the Department of Imaging Physics at The University of Texas MD Anderson Cancer Center in Houston, Texas. He leads the Magnetic Resonance Engineering Laboratory and currently serves as Section Chief for Imaging Physics Research, Deputy Director of MD Anderson's Small Animal Imaging Facility (SAIF) and Director of SAIF MR Services. Jim received undergraduate and graduate training in the Department of Electrical Engineering at Texas A&M University, where his research focused on MRI from the engineering perspective, including the development of new coil arrays and image reconstruction algorithms. His research interests focus on the development of new imaging strategies that improve our ability to assess disease, treatment, and response to therapy, including quantitative imaging strategies such as dynamic contrast-enhanced MRI, cell tracking, and imaging of hyperpolarized imaging agents. Dr. Bankson enjoys close collaboration with physician/scientists, radiologists, oncologists, and basic cancer researchers to advance imaging sciences advances alongside the study of novel therapeutic approaches to improve the next generation of clinical care. He has coauthored more than 110 peer-reviewed publications describing technical developments and the use of novel imaging strategies in preclinical and translational cancer research. He is a member of the Institute for Electrical and Electronics Engineers (IEEE), the International Society for Magnetic Resonance in Medicine (ISMRM), and the World Molecular Imaging Congress (WMIC), and has been recognized as a Distinguished Investigator by the Academy for Radiology and Biomedical Imaging Research.

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Title: *"Imaging Tumor Metabolism with Hyperpolarized Pyruvate"*

Abstract

Altered metabolism is a hallmark of cancer, and changes in metabolic activity can provide important insight into tumor aggressiveness and response to therapy. Many cancers have high levels of glucose consumption and lactate production, even under normoxic conditions, a phenotype referred to as aerobic glycolysis or the "Warburg Effect." Metabolic MRI using hyperpolarized (HP) [1-^{13}C]-pyruvate to probe aerobic glycolysis provides a promising new diagnostic platform for assessing tumor metabolism, and the potential for this technology to provide new and earlier insight into response to therapy in the clinical setting is currently under evaluation. HP pyruvate is administered via bolus injection and crosses multiple biological barriers prior to interaction with intracellular enzymes that mediate chemical conversion of HP pyruvate into lactate. Imaging and quantification of pyruvate metabolism is challenging because the signal is nonstationary, nonrenewable, attenuated by spin-lattice relaxation (the half-life of the spin label is less than 45s), and consumed by excitation pulses that are necessary for imaging.

Several semi-quantitative and quantitative metrics have been proposed to summarize the conversion of pyruvate into lactate. The area-under-the-curve (AUC) of the dynamic lactate signal, normalized to the AUC of the pyruvate signal, is straightforward to calculate but may be sensitive to acquisition parameters and to physiological characteristics that are peripherally related to metabolism. Pharmacokinetic (PK) models of varying complexity can be used to more specifically assess the apparent rate constant for conversion of pyruvate into lactate, but complex models seeking to capture physiological characteristics that affect signal evolution are computationally expensive and prone to higher variations.

In this presentation, we will review these approaches to quantification of HP MRI signal evolution and describe a relationship between PK model parameters and the lactate-to-pyruvate AUC ratio that may further aid interpretation. We will apply these metrics to pilot data obtained at baseline and after 8 days of induction chemotherapy in a patient with

anaplastic thyroid cancer (ATC) and in test-retest scans carried out approximately 40 minutes apart in a patient with oropharyngeal squamous cell carcinoma. These datasets demonstrate promising reproducibility and sensitivity for visualizing heterogeneous metabolism and early metabolic changes in response to treatment.

Learning Objectives:

1. Recognize the difference between traditional magnetic resonance imaging and methods that are used for visualizing hyperpolarized imaging agents
2. Identify the metabolic pathway that is illuminated by hyperpolarized [1-13C]-pyruvate and the importance of this pathway in oncology
3. Compare and contrast methods for quantification of tumor metabolism from dynamic imaging of HP [1-13C]-pyruvate and its metabolites.

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Graeme Woodworth, MD, FACS

Professor and Chair, Department of Neurosurgery, University of Maryland School of Medicine, Director, Brain Tumor Program, Director, Translational Therapeutics Research Group

Graeme Woodworth, MD, FACS isProfessor and Chair of the Department of Neurosurgery at the University of Maryland School of Medicine. He also serves as the Director of the Brain Tumor Program and the Translational Therapeutics Research Group in the Greenebaum Comprehensive Cancer Center at the University of Maryland. Dr. Woodworth completed medical school and neurosurgical residency training at Johns Hopkins. He also completed fellowships in cancer nanomedicine at Johns Hopkins and cranial endoscopy at Cornell. His clinical subspecialty areas of interest are Neurosurgical Oncology and Skull base and Stereotactic surgery. Dr. Woodworth's research focuses on developing new therapeutic strategies to improve the treatments and outcomes for patients with malignant brain tumors. These efforts include (1) leveraging the diverse interstitial effects of transcranial focused ultrasound and hyperthermia, (2) developing advanced nano-therapeutics to improve treatment efficacy, and (3) expanding the suite of patient-derived and genetically engineered models of human brain tumors to improve predictive therapeutic testing. A core component of the research has been centered on the concept of using the operating room as a portal for discovery and opportunity to improve our understanding of and therapeutic delivery to brain tumors. Dr. Woodworth's team is leading the first-in-human clinical trials of focused ultrasound (FUS) mediated blood brain barrier opening in the United States. Dr. Woodworth leads the Maryland Focused Ultrasound Program with multi-disciplinary partners from Bioengineering, Radiology, Neurology, and Neurobiology Departments.

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Title: *"Focused Ultrasound-enhanced Neurosurgery: Opening the Window of Opportunity for Treating Residual, Infiltrating Gliomas"*

Abstract

The blood-brain barrier (BBB) is a critical obstacle to effectively delivering many therapeutic agents into the brain. For patients with primary brain tumors, specifically infiltrating gliomas, the inability to effectively treat the invasive tumor cells beyond the primary mass due to limited BBB penetrance of therapeutics contributes to disease recurrence. Even after the most successful surgery, invasive tumor cells lead to recurrence and patient death. As surgical advances enable safer and greater degrees of tumor removal, even from sensitive brain regions, new therapeutic tools, and approaches designed to address the residual invasive disease will become increasingly valuable. Transcranial microbubble-enhanced focused ultrasound (MB-FUS) offers the opportunity to address this limitation by enabling spatially localized and contoured, temporary, repeatable, and safe opening of the BBB in the regions of glioma infiltration. This presentation will discuss previous and ongoing clinical trials with MB-FUS for gliomas, and examine future studies linking MB-FUS optimization, confirmation of drug delivery, and the biology of therapeutic responses.

Learning Objectives:

1. Review the current progress in focused ultrasound-mediated blood brain barrier opening for infiltrating gliomas
2. Understand the results from the completed clinical trial using focused ultrasound to enhance gliomas resections
3. Explore opportunities to leverage this clinical paradigm to investigate drug-device combinations for residual and infiltrating gliomas

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Miroslaw Janowski, MD, PhD

Professor, Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine

Dr. Janowski, a distinguished neurosurgeon, embarked on his professional journey at the Medical University of Warsaw in Poland where he completed his residency in neurosurgery in 2009. His passion for advancing medical science led him to the Department of Radiology at Johns Hopkins University in 2011 where he assumed the role of a postdoctoral fellow. During this tenure, he focused on groundbreaking preclinical research in image-guided neurointerventions.

Dr. Janowski's ascent through the academic ranks was remarkable. From his initial position as a postdoctoral fellow, he steadily progressed to Associate Professor by 2016. His expertise and dedication caught the attention of the University of Maryland, Baltimore, which recruited him in 2019, and he was promoted to full professor in 2023. He was pivotal in establishing the Program in Image Guided Neurointerventions (PIGN). PIGN serves as a vibrant hub at the intersection of molecular imaging, biotechnology, and precision medicine.

As a continuously funded investigator by the National Institutes of Health (NIH) since 2012, Dr. Janowski has made significant contributions to the field. He co-founded the Society for Image-Guided Neurointerventions (SIGN) and successfully organized four SIGN conferences across three continents. Additionally, Dr. Janowski holds several patents and boasts an impressive portfolio of over 130 peer-reviewed publications.

His commitment to translational research in image-guided neurointerventions and innovative biological drug delivery methods—such as antibodies, nanoparticles, viruses, and targeted cell therapies—continues to shape the future of precision medicine for brain diseases. His pioneering concept, "Guideomics," applies the omics concept to image guidance, promising transformative advancements in brain health.

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Title: *"Guideomics"*

Abstract

The therapeutic efficacy of central nervous system disorders lags behind that of peripheral diseases. This is mainly driven by advances in biological drugs, which, due to their size, are particularly challenging to deliver effectively to the brain because of the blood-brain barrier (BBB). Therefore, there is a huge effort to shuttle biological drugs to the brain, including osmotic BBB opening (OBBBO), microbubble-assisted focused ultrasound (MB-FUS), and transcytosis. However, every procedure potentiates uncertainty on the drug penetration into the brain, which leads to variability of outcomes and difficulty in achieving statistical significance necessary for approval by regulatory agencies and reimbursement. Moreover, BBB and potentially glymph seem very effective in clearing therapeutic agents from the brain. Current blind and imprecise state-of-the-art biological drug delivery to the brain is akin to the pre-MRI era of poor brain diagnostics. Therefore, it is appealing to routinely label therapeutic agents to understand their brain penetration and subsequent clearance via image guidance. Additionally, initial data suggests that this concept could extend beyond the brain to other body parts. Hence, coining the term 'Guideomics' to encompass all aspects of guided drug delivery aims to elevate its recognition within precision medicine, placing it on par with other 'omics.' The long-term goal of Guideomics includes replacing current weight- or surface-based dosing with imaging-based titration to optimize drug accumulation in the target area.

Learning Objectives:

1. To understand the potential benefits of imaging to understand the dynamic process of therapeutic agent uptake and clearance from the brain.
2. To demonstrate the value of imaging in guiding the process of osmotic blood-brain barrier opening (OBBBO).
3. To discuss the potential for a paradigm shift from drug dosing per body weight to dosing guided by quantitative measurement of drug accumulation in the brain.

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Ryan D. Sochol, PhD

Associate Professor, Department of Mechanical Engineering, Affiliate Faculty, Fischell Department of Bioengineering, Executive Committee Member, Maryland Robotics Center, Fischell Institute Fellow, Robert E. Fischell Institute for Biomedical Devices, Affiliate Faculty, Institute for Systems Research, A. James Clark School of Engineering, University of Maryland, College Park

Ryan D. Sochol, PhD is an Associate Professor of Mechanical Engineering within the A. James Clark School of Engineering at the University of Maryland, College Park. Prof. Sochol received his B.S. in Mechanical Engineering from Northwestern University in 2006, and both his M.S. and Ph.D. in Mechanical Engineering from the University of California, Berkeley, in 2009 and 2011, respectively, with Doctoral Minors in Bioengineering and Public Health. Prior to joining the faculty at UMD, Prof. Sochol served two primary academic roles: (*i*) as an NIH Postdoctoral Trainee within the Harvard-MIT Division of Health Sciences & Technology, Harvard Medical School, and Brigham & Women's Hospital, and (*ii*) as the Director of the Micro Mechanical Methods for Biology (M^3B) Laboratory Program within the Berkeley Sensor & Actuator Center at UC Berkeley. Prof. Sochol also served as a Visiting Postdoctoral Fellow at the University of Tokyo. In 2019, Prof. Sochol was elected Co-President of the Mid-Atlantic Micro/Nano Alliance. His group received *IEEE MEMS Outstanding Student Paper Awards* in both 2019 and 2021, the *Springer Nature Best Paper Award (Runner-Up)* in 2022, and both the *Microsystems & Nanoengineering/ Springer Nature Outstanding Paper Award* and the *Micromachines – MDPI Outstanding Poster Award* in 2024. Prof. Sochol received the *NSF CAREER Award* in 2020 and the *Early Career Award* from the IOP Journal of Micromechanics and Microengineering in 2021, and was honored

as an inaugural *Rising Star* by the journal, Advanced Materials Technologies, in 2023, and will be honored as an ASME Rising Star in November 2024.

Title: *"3D Micro/Nanoprinted Soft Robots: From Super Mario Bros. to Minimally Invasive Surgery"*

Abstract

Over the past decade, the field of "soft robotics" has established itself as uniquely suited for applications that would be difficult or impossible to realize using traditional, rigid-bodied robots. The reliance on compliant materials that are often actuated by fluidic (*e.g.*, hydraulic or pneumatic) means presents a number of inherent benefits for soft robots, particularly in terms of safety for human-robot interactions and adaptability for manipulating complex and/or delicate objects—characteristics that are advantageous for biomedical applications. Despite this potential, progress has been impeded by broad challenges associated with manufacturing such systems at smaller length scales. In this lecture, Prof. Ryan D. Sochol will discuss how his *Bioinspired Advanced Manufacturing (BAM) Laboratory* is leveraging the capabilities of two alternative types of additive manufacturing (or "three-dimensional (3D) printing") technologies to address these barriers. Specifically, Prof. Sochol will describe his lab's recent strategies for using the inkjet (material jetting) 3D microprinting technique, "PolyJet 3D Printing," to engineer soft robotic systems that comprise integrated fluidic circuitry—including a soft robotic "hand" that plays Nintendo—and the 3D nanoprinting approach, "Two-Photon Direct Laser Writing," to enable new classes of soft robotic surgical tools.

Learning Objectives:

1. To understand the unique advantages of soft robotics, particularly in terms of safety and adaptability, compared to traditional rigid-bodied robots.
2. To explore the application of advanced additive manufacturing techniques, such as PolyJet 3D Printing and Two-Photon Direct Laser Writing, in overcoming the challenges of creating soft robotic systems at smaller scales.

3. To examine recent innovations in soft robotics for biomedical applications, including the development of integrated fluidic circuitry and soft robotic surgical tools.

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1. Label-free imaging of cancer stem cells and glioblastoma grading using mannose-weighted CEST MR

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2. Impact of isoflurane anesthesia on brain metabolism in mice: calibration and validation with EEG

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3. In vivo metabolic sensing of hyperpolarized [1-13C]-pyruvate in mice using a recyclable perfluorinated iridium signal amplification by reversible exchange catalyst

Dr. Jessica Ettedgui,*[a] Dr. Kazutoshi Yamamoto,[b] Prof. Dr. Eduard Y. Chekmenev,[c] Prof. Dr. Boyd M. Goodson,[d] Dr. Murali C. Krishna,[b] Dr. Rolf E. Swenson[a]

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Divya Nambiar, BS[1], Thomas J. Esparza, BS[2], Woonghee Lee, PhD[1], Joon-Yong Chung, PhD[1], Julia Sheehan-Klenk, BA[1], Peter L. Choyke, MD[1], Freddy E. Escorcia, MD, PhD[1]

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Shylah Healy1,2, Jinghui Wang2 , Miroslaw Janowski2, Piotr Walczak2, Yajie Liang2

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Bonghwan Chon, PhD1, Mukesh P. Yadav, PhD1, William Ghann, PhD 2, Jamal Uddin, PhD 2,Bahman Anvari, PhD3 and Vikas Kundra, MD, PhD1,4*

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Jinghui Wang, Miroslaw Janowski, Piotr Walczak and Yajie Liang

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Lukasz Kalkowski, PhD1; Guanda Qiao, MD, PhD1; Yajie Liang, PhD1; Miroslaw Janowski, MD, PhD1,2; Piotr Walczak, MD, PhD1

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Dawei Gao, Colleen Russel, Miki Walczak, Jinghui Wang, Miroslaw Janowski, Piotr Walczak, Yajie Liang

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