West Virginia University
BENJAMIN M. STATLER COLLEGE OF ENGINEERING AND MINERAL RESOURCES

MATERIALS SCIENCE AND ENGINEERING (MS&E) SEMINAR SERIES

Friday October 2, 2020 at 3:00 pm via Zoom
https://wvu.qualtrics.com/jfe/form/SV_80QQi6E8CUXmzwF

"Tumor and blood cell tracking in breast cancer"

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Abstract: Mammography is currently the gold standard method for breast cancer screening, but it misses 20% of cancers present and results in 50% of women being falsely diagnosed with breast cancer over 10 years of annual screening. Magnetic resonance imaging (MRI) detects more breast cancers than mammography; however, false positive diagnoses can also remain high with MRI due to the nonspecific and passive nature of the contrast agent. We aim to develop a tumor-targeted, pH-sensitive nanoparticle MRI contrast agent that can enhance diagnostic accuracy and reduce false positives for high risk women during breast cancer screening. Manganese oxide (MnO) nanoparticles can serve as robust pH-sensitive contrast agents for MRI due to Mn^{2+} release at low pH, which generates a ~30 fold change in T_1 relaxivity. We will discuss strategies to control nanoparticle size, composition, and Mn^{2+} dissolution rates to improve MRI signal generated from pH-responsive MnO nanoparticles.

Patients with metastatic breast cancer have a poor prognosis, with a 25% survival rate at 5 years. In addition, breast cancer patients have a 3 to 4 times increased risk of developing venous thromboembolism (VTE) compared to healthy subjects. VTE results in shorter survival and greater tumor recurrence. Neutrophil extracellular traps (NETs) have been identified as a common link to thrombosis, vascular injury, circulating tumor cell capture and metastasis. NETs are released from activated neutrophils and include their DNA, histones, and granular content. Activated platelets and soluble tumor mediators are known to cause NET release; however, the role of tumor-derived extracellular vesicles (EVs, small cell fragments) in promoting NETosis is unknown. We have utilized state-of-the-art spinning disk confocal microscopy of the lung microvasculature in live mice to evaluate in real-time if tumor EVs cause neutrophil-platelet aggregation and NET formation. We hypothesize that tumor EVs activate platelets to adhere to neutrophils in lungs to cause NET release and begin metastatic colonization through increased thrombosis and trapping of circulating tumor cells.

Biography: Dr. Margaret Bennewitz received her BS degree in Bioengineering from the University of Pittsburgh in 2007 and her PhD from Yale University in Biomedical Engineering in 2012. At Yale, she specialized in MRI cell tracking and contrast agent development for the diagnosis of glioblastoma multiforme. After completing her doctorate, Dr. Bennewitz accepted a postdoctoral fellowship in the M+Visión Program, a collaborative venture between the Massachusetts Institute of Technology and hospitals and laboratories in Madrid, Spain. Unlike a traditional post doctorate, this program searched globally for scholars who would define their own translational imaging projects centered around clinically relevant unmet needs. One of her projects involved the early detection of ovarian cancer using optical imaging. To diversify her imaging skills, Dr. Bennewitz subsequently accepted a second postdoctoral fellowship in the Vascular Medicine Institute at the University of Pittsburgh-School of Medicine. There, she created a setup to perform multiphoton imaging of the blood vessels in the lungs of live mice with sickle cell disease. Dr. Bennewitz used this technique to study the cellular and molecular mechanism of vascular blockage (vaso-occlusion) in the lungs. Dr. Bennewitz joined the faculty at West Virginia University as an Assistant Professor in the Department of Chemical and Biomedical Engineering in August 2017. Her lab specializes in the development of new MRI contrast agents for early breast cancer detection and the use of *in vitro* and *in vivo* fluorescence imaging techniques to elucidate the role of the tumor microenvironment in promoting breast cancer metastasis to the lungs.

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