Molecular imaging to visualize cancer biomarkers

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Special Focus Session 3 (PHY): 9:40AM, RM 209

Dr. Yoon is leading Molecular Ultrasound Imaging and Delivery (MUID) laboratory. His long-term goal is to establish approaches for in vivo live imaging using ultrasound and molecular contrast agents while drugs and genes can be delivered by the same contrast agents for streamlined diagnosis and therapy. Having been trained at the nexus of ultrasound imaging, biology and molecular and cellular engineering, Dr. Yoon is uniquely positioned to successfully achieve his overarching goals by developing a vibrant research laboratory. He has strong track records on ultrasound imaging and ultrasound-based cellular engineering by developing novel techniques for tissue elastography, intravascular ultrasound (IVUS) imaging, ultrasound activatable chimeric antigen receptor (CAR) T cells for immunotherapy, acoustic-transfection for sustained intracellular delivery technique for stem cell engineering and immunotherapy, compressed-sensing based algorithm for super-resolution ultrasound imaging to improve image quality and acquisition time, and ultrasound molecular contrast agents using gas vesicles (GV).

Ultrasound imaging in cancer diagnosis has been a valuable tool to find cysts and solid tumors, image lymph nodes, and guide biopsies. The role of ultrasound has been limited to anatomical imaging because of relatively large size, limited functionalization, and fast diffusion of contrast agents. There is a significant unmet need for non-invasive and longitudinal imaging techniques that can analyze molecular changes in tumor microenvironment for accurate treatment decisions. To address these challenges, we develop approaches to use nanometer-sized gas vesicles (GV) as ultrasound contrast agents for easier extravasation into regions of interest to visualize cells expressing target proteins. GVs are gas-filled protein shells that can be easily isolated from host bacteria. In addition to passive delivery of GVs by enhanced permeability and retention effect, we use monoclonal antibody (mAb) as an active targeting approach. The uniqueness of our approach preserves the characteristics of individual components to allow us to achieve optimal biodistribution. We develop an approach to use eigen-images to efficiently track GV locations without registration using singular value decomposition.

The scientific premise of our study is based on cell-targeting ultrasound imaging assays to visualize human epidermal growth factor receptor 2 (HER2)+ and programmed death ligand 1 (PD-L1)+ cells targeted by ultrasound molecular contrast agents by site-specific conjugation in our group. In a human xenograft mouse cancer model, we demonstrated the accumulation of HER2 or PD-L1 targeting mAb conjugates imaged by eigen-image based approach combined with super-resolution ultrasound imaging for vessel visualization. Biodistribution and pharmacokinetics of developed conjugates indicate the efficient tumor targeting. All in all, our approach visualizes key biomarkers for cancer progression noninvasively. We will translate our approach to clinical trials.

References:

Development of ultrasound molecular contrast agents by site-specific conjugation of gas vesicles to antibodies by S Turner, A Bhattacharjee, L Diao, M Zhao, S Zhang, S Yoon, bioRxiv, 2025.07. 21.665993

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Multiplexed ultrasound imaging using spectral analysis on gas vesicles by S Kim, S Zhang, S Yoon, (2022) Advanced Healthcare Materials 11 (17), 2200568