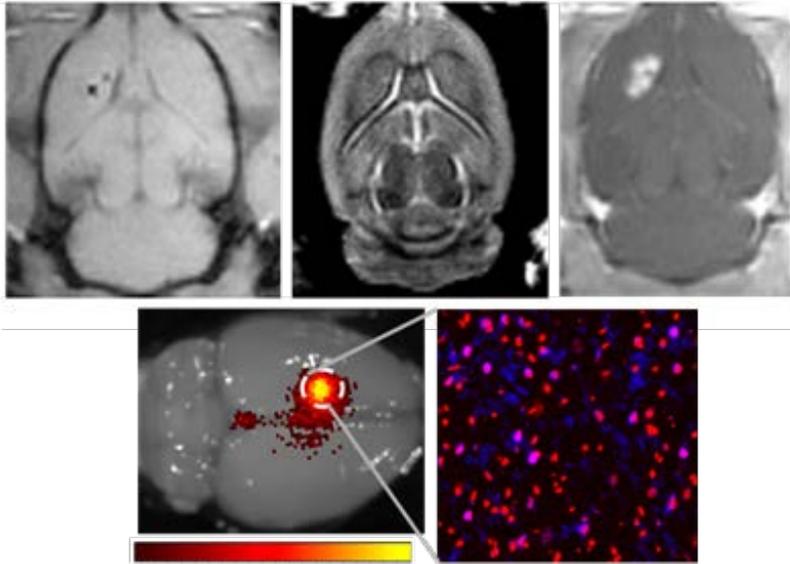


## Price Lab: Image Guided Nanoparticle Delivery & Microvascular Biomechanics



Our research group investigates a novel combination of nanoparticles, microbubbles and focused ultrasound – a combination we believe could effectively treat and possibly cure diseases of the central nervous system, including brain tumors, dementia and Parkinson’s disease. Besides surmounting the daunting technical challenges of delivering drugs across the brain blood barrier, the envisioned treatments will use smaller doses of drugs and deliver them at higher concentrations than current therapies. For patients, this could mean less systemic toxicity, fewer side effects and more effective therapy.

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“Developing MR image-guided methods to non-invasively deliver nanoparticles across the blood-brain barrier for the treatment of brain tumors and Parkinson’s disease”



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### Ultrasound Targeted Delivery of Nanoparticle Drug and Gene Carriers

The targeted delivery of intravascularly injected genes and drugs to specific regions within body remains a significant challenge in the treatment of many pathologies. To address this problem, we are developing ultrasound-activated drug delivery systems that are comprised of various combinations of tissue-penetrating therapeutic (i.e. drug- or gene-bearing) nanoparticles and contrast agent microbubbles. As these agents pass through an ultrasound-targeted region, the microbubble components oscillate and induce microvessel permeabilization which then facilitates the deposition of the nanoparticles in the tissue. In pre-clinical studies, we are using these ultrasound-activated drug delivery systems for restoring blood flow to ischemic tissue via growth factor delivery and therapeutic arteriogenesis, for treating of brain tumors via enhanced chemotherapeutic drug deposition, and for treating Parkinson's disease by delivering nanoparticles housing genes for neurotrophic factors.

### Regulation of Vascular Structure by Hemodynamic Forces

The chronic occlusion of a major artery, such as occurs during peripheral arterial disease in humans, leads to enhanced shear stress and structural remodeling (arteriogenesis) in collateral arteries that bypass the occlusion. Meanwhile, ischemic tissues downstream of the occlusion experience new blood vessel growth via angiogenesis. Our laboratory is focusing on understanding the molecular signaling pathways that regulate collateral arteriogenesis in response to changes in shear stress magnitude and direction. Ongoing studies have shown that shear stress reversal, which is experienced by a small subset of collateral artery segments, leads to the paradoxical activation of inflammation - and quiescence-associated molecular signaling pathways in endothelial cells. In turn, these pathways synergize to elicit amplified arteriogenesis, an outcome that may be used for the improved design of revascularization therapies. An emerging area of interest for the lab entails developing approaches for treating peripheral arterial disease that consider both arteriogenesis and angiogenesis as necessary for successful clinical outcomes.

### RECENT RESEARCH DEVELOPMENTS

- Identified epigenetic regulators of shear stress-mediated artery growth through analysis of collateral artery endothelium exposed to reversed flow conditions.
- First demonstration of image-guided brain transfection via the delivery of brain-penetrating non-viral gene nanoparticles with focused ultrasound.

### RECENT GRANTS

- NIH R01 – Brain Tumor-Penetrating Nanoparticle Delivery with MR-Guided Focused Ultrasound
- NIH R01 – MRI-Guided Delivery of miRNA-Bearing Nanoparticles to Glioblastoma with Focused Ultrasound
- NIH R01 – Immunotherapeutic Nanoparticle Delivery to Melanoma with Focused Ultrasound
- Focused Ultrasound Foundation - Minimally-Invasive Therapy for Parkinson's Disease Achieved by Focused Ultrasound-Targeted Delivery of Non-Viral Gene Nanocarriers

#### SEAS Research Information

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