Ultrasound is applied to the diagnosis of many different disease conditions: heart conditions, vascular health (e.g. to visualize plaque that may be associated with Stroke), liver and kidney diseases and a variety of high resolution shallow imaging applications – e.g. breast imaging for cancer diagnosis and musculoskeletal areas – wrists, shoulder muscles, etc. Our work encompasses: transducer design, microbubble-based drug delivery, 3D mouse heart imaging, ultrasound-based molecular imaging and ultrasound signal/image processing and quantification.
Therapeutic Applications of Microbubbles
In the past decade, the therapeutic applications of microbubbles have emerged, primarily motivated by the need of a suitable drug/gene delivery agent. Our efforts address clinical needs in the field of atherosclerosis – progressive narrowing of arteries (e.g. coronary and peripheral). Current methods use a drug eluting stent to deliver a fixed dose of a fixed drug to a limited region of a vessel wall. The drug serves to prevent in-stent restenosis – re-narrowing of the vessel following an initial procedure to treat the atherosclerosis. In our method, we use a modified intravascular ultrasound catheter that delivers drug-loaded microbubbles. We can then use the catheter to image the microbubbles. Separate transducers in the catheter can cause microbubbles to translate to the vessel wall and to break the microbubble thereby effecting drug delivery. We have obtained initial results demonstrating efficacy in small animals. Currently, we are developing new microfluidics-based approaches to form a stream of precisely controlled microbubbles that are optimized for drug delivery.

Microbubble Modeling
One-dimensional radial symmetric models are typically used for quantifying the microbubble’s behavior in response to acoustic insonation. However, this method has many limitations. We have developed a full non-linear 3D finite element analysis model for quantifying the microbubble dynamics. This model estimates the coupled 3D oscillatory-translational motion, the shell stress/strain, and the backscattered acoustic pressure.

Molecular Imaging
We have introduced a modified real-time approach for selectively imaging and guiding microbubbles in the context of identifying carotid arteries susceptible to stroke. A Singular Value Decomposition method is used to separate signals associated with bound microbubbles (i.e. the signature of a molecular marker (e.g. VCAM-1) being present) from unbound microbubbles that contain no information about the presence of molecular markers.

Mouse Heart Imaging
The mouse is the preferred species for cardiovascular research of both the genetic mechanisms that underpin cardiovascular disease and the evolution of anatomic and physiological responses to disease and therapy. One current method for non-invasive mouse imaging (MRI) has excellent image qualities but it has a number of significant drawbacks. We are researching an ultrasound method that provides accurate, low-cost, fast, and non-invasive quantification of cardiac left ventricular (LV) function in small animals. The spatial resolution is sufficient to enable calculation of important anatomic and physiologic parameters (chamber volumes, ejection fraction, etc.) Further, we take advantage of the superior temporal resolution to enable assessment of mouse LV perfusion using analysis of the time evolution of myocardial video intensity following a bolus contrast agent injection.

Bone Surface Imaging
A special-purpose compact 3D ultrasound imaging device has been developed that uses optimized image acquisition methods to form high resolution images of bone surfaces. Specular reflectors (e.g. bone) represent a significant challenge to conventional ultrasound imaging methods.

RECENT RESEARCH DEVELOPMENTS
• NIH grant to develop molecular imaging techniques with application to detecting risk for stroke.
• Prototyped fully functioning compact 3D bone surface imager.
• Developed new microfluidic devices with improved production rates for monodisperse (single size) microbubbles.

RECENT GRANTS
• NIH-Molecular Targeted, Focused, Ultrasound-Based Delivery of Antiproliferative Drugs
• NIH-High Resolution 3D Ultrasound Imaging and Quantification of Murine Cardiac Function