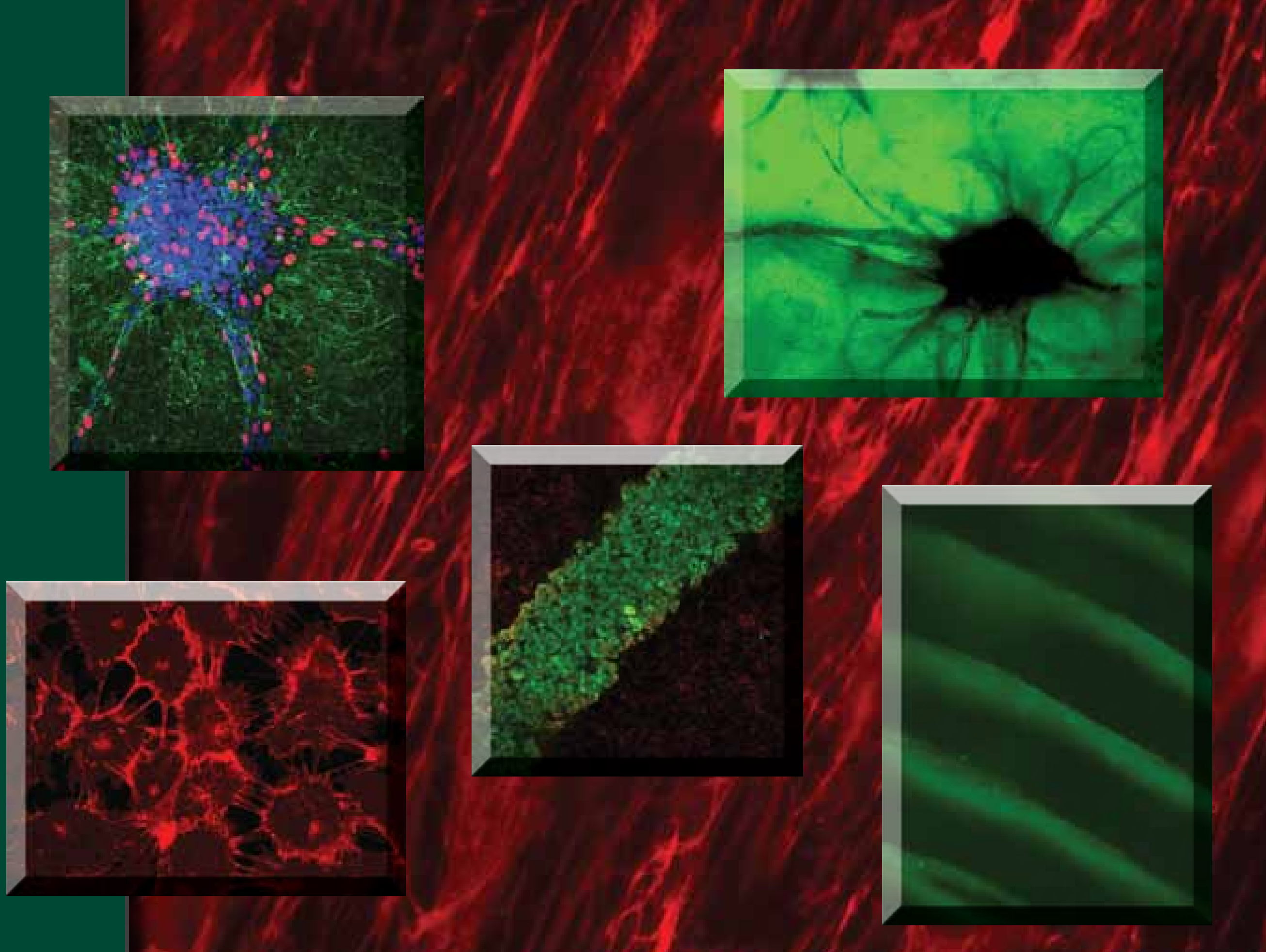
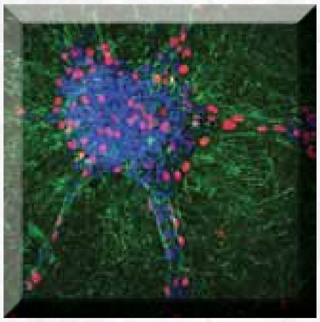


# Rochester Center for Biomedical Ultrasound 2009 Annual Report

# On the Cover

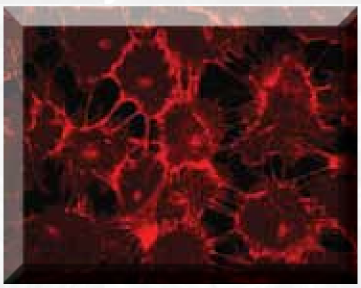
***RCBU investigators are advancing the use of ultrasound in tissue engineering and regenerative medicine. See related stories on 15, 17, 18, 20, 21, 24.***



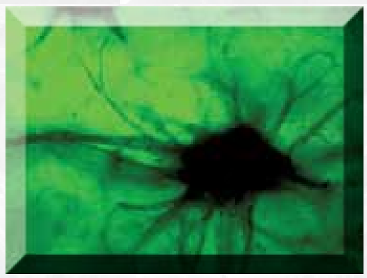
Immunofluorescence image captured by two-photon microscopy showing cell nuclei (blue), fibronectin (green), and actively proliferating cells (red) in a three-dimensional “tissue body” formed on native collagen gels.

Fibroblasts and bound fibronectin are spatially organized into distinct bands within collagen hydrogels using ultrasound standing wave fields.

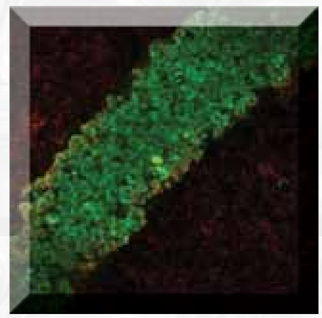
Immunofluorescence image of the extracellular matrix protein, fibronectin, after assembly into fine fibrillar strands by fibroblasts.



Human endothelial cells grown in tissue culture form cell-cell contacts containing the protein β-catenin that can be visualized using immunofluorescence microscopy.



Multiple capillary-like sprouts emerge to form a cluster of human umbilical vein endothelial cells organized in a three-dimensional hydrogel using ultrasound standing wave fields.



Second harmonic generation confocal microscopy was used to visualize collagen fibrils (red) and fibroblasts (green) that were spatially organized into multicellular bands using ultrasound standing wave fields.


## Rochester Center for Biomedical Ultrasound

***Director:*** **Diane Dalecki, PhD**
***Associate Director:*** **Deborah J. Rubens, MD**
***Executive Committee:*** **Diane Dalecki, PhD, Vikram S. Dogra, MD, Morton W. Miller, PhD, Kevin J. Parker, PhD, and Deborah J. Rubens, MD**
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***Dean of the Hajim School of Engineering and Applied Sciences:*** **Robert L. Clark, PhD**
***Editor and Designer:*** **Maria Randazzo**



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# Rochester Center for Biomedical Ultrasound
# 2009 Annual Report

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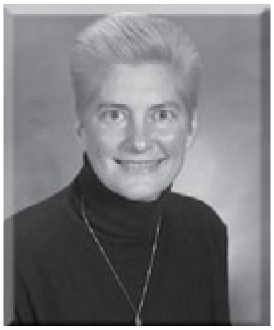
# FROM THE DIRECTORS

### Diane Dalecki, PhD, Director



Diane Dalecki

This year's annual report summarizes progress from RCBU laboratories across diverse topics in biomedical ultrasound imaging and therapy. The cover and related stories inside this report describe advances by RCBU members on novel applications of ultrasound for tissue engineering and regenerative medicine. The RCBU continues to advance the development of elastography techniques. Included within this report are highlights of innovations in sonoelastography and new techniques based on acoustic radiation force. This year also marked the naming of the UR Hajim School of Engineering and Applied Sciences.

The RCBU continues to play a prominent role in clinical and technological advances in the use of ultrasound for diagnostic imaging and therapy. Nonlinear imaging techniques, sonoelastography, and ultrasound contrast agents all have foundations from innovations within RCBU laboratories. Highlights of the Eighth International Conference on Ultrasonic Measurement and Imaging of Tissue Elasticity are reviewed in this report. Collaborative projects between RCBU clinicians, engineers, and scientists continue to advance novel diagnostic and therapeutic applications of ultrasound.

This annual report details research from RCBU members on many topics in biomedical ultrasound, including sonoelastography, acoustic radiation force imaging, ultrasound for tissue engineering, intravascular ultrasound, ultrasound therapies, acoustic cavitation, and bioeffects. The RCBU also provides a rich environment for education and training in biomedical ultrasound. This annual report highlights educational advances, as well as special awards and achievements by RCBU members and students. We welcome your comments on any of the enclosed reports.

### Deborah J. Rubens, MD, Associate Director

Deborah Rubens MD

The Imaging Sciences Ultrasound Department experienced more than 5% growth in exam and patient volumes in 2009; performing over 20,000 exams. The unit continued to expand its clinical coverage; adding more sonographer positions to manage the increased demand.

In the spring of 2009, GE's newest platform, the Logic E9, was installed; replacing the existing Logic9 units. The new machines provide enhanced image quality and improved workflow; allowing sonographers to merge real-time ultrasound with previously acquired CT, MR, or ultrasound images.

The University of Rochester Medical Center was represented by sonographers and physicians in education nationally and internationally. As faculty for Armed Forces Institute of Pathology, Washington DC, Dr. Rubens continued to teach courses on spleen, testis, scrotum, portal Doppler, and testicular Doppler. Drs. Bhatt, Dogra, Rubens, Strang, and Voci also participated as faculty at the Radiological Society of North America (RSNA), the American Institute of Ultrasound in Medicine (AIUM), the Society of Gastrointestinal Radiologists (SGR), and the Society of Uroradiology (SUR) Annual Meetings.

Dr. Rubens continued her research with the BME Department in collaboration with General Electric and Rensselaer Polytechnical Institute on the NIH funded grant, 3DProstate Cancer Imaging Based on "Crawling Wave" Excitation, to create and assess a novel 3D imaging scanner applied to prostate cancer. The Ultrasound Division is also co-investigator with Duke University, in assessing DVT in oncology patients. Dr. Charles Francis, URMC faculty and Dr. Gary Lyman, Duke University, are Principal Investigators on the study.

# ABOUT THE ROCHESTER CENTER FOR BIOMEDICAL ULTRASOUND

The Rochester Center for Biomedical Ultrasound (RCBU) was created at the University of Rochester to unite professionals in engineering, medical, and applied science communities at the University of Rochester, Rochester General Hospital, and the Rochester Institute of Technology. Since its founding in 1986, the RCBU has grown over the years to nearly 100 members, with several visiting scientists from locations around the country.

The Center provides a unique collaborative environment where researchers can join together to investigate the use of very high frequency sound waves in medical diagnoses and therapy.

The Center's mission encompasses research, education, and innovation.

## Research

- RCBU laboratories are advancing the use of ultrasound in diagnosis and discovering new therapeutic applications of ultrasound in medicine and biology.
- The Center fosters collaborative research between laboratories and investigators with expertise in engineering, clinical medicine, and the basic sciences.
- The RCBU provides an ideal forum to exchange information through formal Center meetings and monthly newsletters.
- Interactions of RCBU members with industry, governmental organizations, and foundations encourage mutually beneficial research programs.

## Education

- RCBU laboratories provide a rich environment for graduate training in biomedical ultrasound. Students have access to state-of-the-art research facilities to engage in leading-edge research in ultrasound.
- The UR offers graduate-level courses in biomedical ultrasound and closely related fields.
- RCBU laboratories offer opportunities for post-doctoral research in ultrasound and collaborations with other areas of biomedical imaging.
- Throughout its history, the RCBU has offered short courses in specialized topics in ultrasound that attract national and international experts.

## Innovation

- The RCBU maintains a long history of leadership and innovation in biomedical ultrasound.
- RCBU innovations have produced steady progress in new imaging modalities and therapeutic applications of ultrasound.
- RCBU members hold numerous patents in ultrasound and imaging. The UR ranks 9th in technology revenue income among all higher education institutions in the nation.

### *About the University of Rochester*

*The University of Rochester (www.rochester.edu) is one of the nation's leading private research universities. Located in Rochester, New York, the University's environment gives students exceptional opportunities for interdisciplinary study and close collaboration with faculty. Its College of Arts, Sciences, and Engineering is complemented by the Eastman School of Music, Simon School of Business, Warner School of Education, Laboratory for Laser Energetics, and Schools of Medicine and Nursing.*

***Collaborative Research, Education, and Innovation***

# Celebrating the Naming of the Edmund A. Hajim School of Engineering and Applied Sciences

In July 2009, the engineering school at the University of Rochester was officially named the Edmund A. Hajim School of Engineering and Applied Sciences. The naming recognizes alumnus Edmund Hajim's dedicated service and contributions to the University, including his $30 million gift commitment to the School of Engineering and Applied Sciences. Hajim earned his bachelor's degree in chemical engineering from the University of Rochester in 1958, has had a successful career as a senior executive for several Wall Street firms, has served for the past year as Chairman of the University's Board of Trustees, and has been a member of the Board since 1988.

"I have been proud to be associated with the University of Rochester for more than 50 years," Hajim said. "And I now consider myself lucky to be able to make a long-term contribution to its growth and the training of its students. This University will remain a leader in addressing the many challenges facing society, and I am honored to play a role in and be associated with that important legacy."

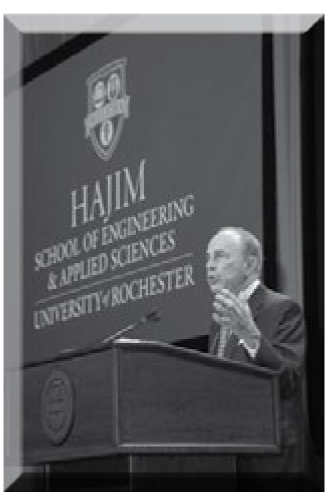
Celebrations of the naming occurred in October during Meliora weekend, the University of Rochester's official homecoming weekend. The events featured distinguished guest speakers Charles Vest, president of the U.S. National Academy of Engineering (NAE) and president emeritus of MIT, and Henry Petroski, member of the NAE and professor of civil engineering and history at Duke University, and author of more than a dozen books on engineering and design.

"I can think of no better time for the University to announce the naming of our engineering school than in its golden anniversary year, especially as we work to expand current programs and launch new ones so our students are prepared to meet the challenges of the 21st century," said Robert Clark, Dean of the Hajim School of Engineering and Applied Sciences. "Ed's contributions will make all of this possible, as well as provide increased financial support for students with need. This is a truly historic occasion for engineering at Rochester."


***Above:*** *Edmund A. Hajim and the Hajim family pose by the offical wall of the Edmund A. Hajim School of Engineering and Applied Sciences.*

*"I can think of no better time for the University to announce the naming of our engineering school than in its golden anniversary year, especially as we work to expand current programs and launch new ones so our students are prepared to meet the challenges of the 21st century."*

—Robert Clark, Dean of the Hajim School of Engineering and Applied Sciences.




***Left**: Edmund A. Hajim speaks at the dedication ceremony.*

***Above** (left to right): Charles Vest, president of the National Academy of Engineering, Edmund A. Hajim, and UR President Joel Seligman*

# RCBU FUNDING NEWS

*Above: Marvin Doyley, PhD*

**Marvin Doyley** was awarded an NIH grant titled "IVUS Detection of Rupture Prone Plaques." The project is devoted to developing ultrasonic methods to assess the functional and structural properties of life-threatening atherosclerotic plaques and the arterial wall (see related story on page 16). Dr. Doyley also received funding from the HSCCI/ DCFAR for the project "Elastographic Imaging of HIV Associated Brain Injury."

**Robert Waag** was awarded a grant from the NIH for the project titled "Ultrasound Imaging of Breast by use of a Hemispheric Array and Inverse Scattering." The objective of the project is to form high-resolution speckle-free quantitative ultrasound images throughout the volume of the breast in vivo by using a hemispheric transducer array for measurements and inverse scattering for image reconstruction.

**Maria Helguera** is a co-Principal Investigator on a new project supported by the NIH titled "NTHI Immunity in Young Children." This project focuses on using ultrasound in the detection and characterization of biofilms (see story on page 21).

**Sheryl Gracewski** received funding for summer research students through the UR Xerox Summer Research Program, and through an REU on her NSF grant titled "Dynamic Response of Constrained Bubbles to Acoustic Excitation."

**Ben Castañeda** received support from the Lindbergh Foundation for his project "Developing Computerized Screening for Early Detection of Tuberculosis in Peru." He also received funding for the project "Area Measurement of Cutaneous Leishmaniasis Wounds," from the Dirección Académica de Investigación of the Pontificia Universidad Catolica del Peru.

**Denise Hocking** and **Diane Dalecki** received funding from the NIH to support the summer research projects and career development of undergraduate and high school students. Research areas for student projects focus on effects of ultrasound on cells and protein conformation, and novel applications of acoustic radiation force.

**Maria Helguera, Diane Dalecki,** and **Denise Hocking** received NIH funding for collaborative investigations focused on developing novel ultrasound tissue characterization and imaging techniques for engineered tissues. This work is part of a larger project funded by the NIH to develop ultrasound-based technologies for the field of tissue engineering. Through this new collaborative project, Dr. Helguera will spend part of the academic year and summer as a Visiting Scientist in Dr. Dalecki's laboratory. (See related story on page 20).

*Above: Maria Helguera, PhD*

*Below: Denise Hocking, PhD*

*Above: Diane Dalecki, PhD*

**Amy Lerner, Ben Castañeda,** and Scott Seidman received funding from the National Collegiate Inventors and Innovators Alliance for their project titled "UR-PUCP: Collaborations for Healthcare in Developing Countries." This funding has established a new joint program between the University of Rochester and Pontificia Universidad Catolica del Peru that provides opportunities for students to work on biomedical engineering projects dedicated to enhancing health care in developing countries. (See related story on page 21.)

**Carlos Sevilla,** a graduate student in the Department of Biomedical Engineering, was awarded a prestigious NIH Ruth L. Kirschstein National Research Service Award Individual Pre-doctoral Fellowship. This three-year award will provide funding for his thesis research project titled, "Promoting Chronic Wound Healing with Ultrasound and Fibronectin." His thesis research is co-advised by Drs. Denise Hocking and Diane Dalecki.

**Maria Helguera** received funding from NYSTAR-CEIS Carestream Health, Inc. for a project titled "Development of a Novel 3-D Optical Molecular Imaging System Prototype." Dr. Helguera also received funding for a project titled "Registration and Normalization of Images" from the Museum of Fine Arts, Boston.

# 2009 RESEARCH

Research laboratories of RCBU members are advancing the use of ultrasound for diagnosis and treatment. The pages that follow highlight research accomplishments in 2009. Publications and presentations of this year can be found on pages 28–29.

## Minimization of bias due to high amplitude reflections in displacement estimation using partial echo normalization

**Manoj Menon, MS and Stephen McAleavey, PhD**

Pathological conditions and their treatments often result in a change in the mechanical properties of tissue. More recently, investigators have used elastographic techniques for applications such as the imaging of blood vessels. When there is significant acoustic impedance mismatch between objects of interest, strong reflections can occur at the interface. Windowed 1D cross-correlations based techniques are commonly employed for displacement estimation. The displacement estimate within a correlation window is assumed to be approximately the average of the displacements within that window. This assumption holds true when the speckle is homogeneous. When there is a local high-amplitude signal, it tends to dominate the displacement estimate, causing a bias towards the displacement that corresponds spatially to the high amplitude region of the echo. This bias results in a blurring of the displacement image in the vicinity of the reflective boundary.

In the McAleavey lab, graduate student Manoj Menon is working on a novel partial echo normalization technique to minimize amplitude-dependent blur without significant increases in the jitter magnitude. If echoes are fully normalized before displacement estimation, the blur is minimized, but SNR is augmented, resulting in a large increase in the jitter magnitude. Instead, normalization of the echo is weighted, such that larger values of an echo are reduced more than smaller values. Using this partial normalization technique, high-amplitude reflections are locally normalized without critically affecting the quality of the rest of the signal. It was found that by applying this algorithm, the ability to resolve bright boundaries in displacement images significantly improved for ultrasonic frequencies greater than 4 MHz, and correlation window lengths greater than 0.6 mm, with only slight increases in jitter.

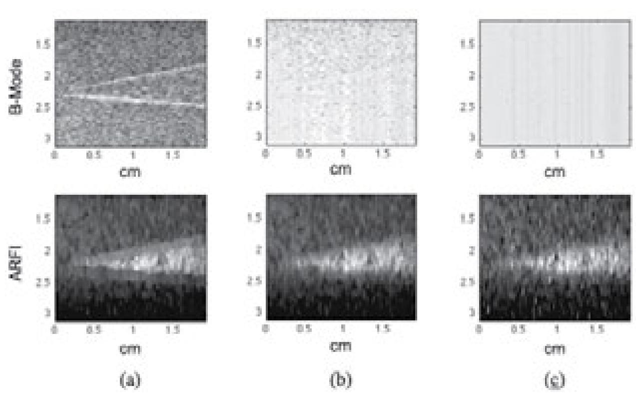



*Figure 1. B-mode and ARFI images using cross-correlation (a) without normalization, (b) partial normalization, and (c) full normalization. The center frequency is 5.33 MHz, the maximum displacement (white) is 2 μm, the correlation window length was 0.77 mm, and the tracking pulse length was 2 λ.*

## In vivo prostate cancer detection using sonoelastography: Preliminary results

**Benjamin Castañeda, PhD, Karin Westesson, Liwei An, MS, Shuang Wu, MS, Kenneth Hoyt, PhD, Jorge Yao, Laurie Baxter, John Strang, MD, Deborah Rubens, MD, Kevin Parker, PhD**

Previous work in ex vivo prostate glands showed that sonoelastography is a promising imaging technique for tumor detection. Recent work from our group evaluates the performance of sonoelastography for prostate cancer detection in vivo.

Eleven patients underwent a TRUS examination prior to their scheduled radical prostatectomy. External vibration was induced by a specially designed plate using 2 mechanical actuators, each driven by a low frequency harmonic signal between 70 and 110 Hz. Sonoelastographic volumes were acquired. Deficits in these volumes were identified by achieving a consensus of 3 observers. Each deficit was given a confidence measure representing the likelihood of being cancer from 1 to 5 (5 = highest confidence). After imaging, the gland was entirely step-sectioned using a whole-mount histology method. Cancer and BPH in the histological images were outlined by an expert pathologist. To assess detection performance, the sonoelastographic and histological volumes were divided in 12 regions and compared.

One case was discarded due to bad contact between the transducer and the gland. For the remaining cases, accuracy, sensitivity and specificity metrics are shown in Table 1 as a function of the confidence measure. Half of the false positive regions coincide with presence of BPH. Tumors with small diameter and little elasticity contrast are a source of false negatives. Boundary of internal structures, such as the urethra, caused artifacts which were not scored as cancer. The majority of the tumors were not visible in B-mode. Results show an improvement over B-mode but not yet sufficient to replace biopsy. A better performance can be achieved by increasing vibration frequency.

| Rank | Accuracy | Sensitivity | Specificity |
|---|---|---|---|
| >0 | 75.8% | 70.7% | 78.5% |
| >1 | 76.7% | 65.9% | 82.3% |
| >2 | 77.5% | 65.9% | 83.5% |
| >3 | 77.5% | 58.5% | 87.3% |
| >4 | 68.3% | 14.6% | 96.2% |

***Table 1.*** *Sonoelastography performance for prostate cancer detection.*

## Methods for generating crawling waves with radiation force from ultrasonic beam

**Zaegyoo Hah, PhD, Yong Thung Cho, PhD, Liwei An, MS, Christopher R. Hazard, Deborah J. Rubens, MD, John G. Strang, MD, Kevin J. Parker, PhD**

Crawling waves are formed by the interference pattern of two sinusoidal excitations with small frequency difference. These can be easily imaged using conventional color Doppler scanning and provide estimates of local elastic properties of tissues and lesions. The excitation source can be a mechanical vibrator or radiation force from a focused ultrasound beam.

Recent work from the Parker laboratory focuses on the methods to generate crawling waves with radiation force from ultrasonic beams. Two promising methods are spatiotemporal superposition and a multi-beam approach. In spatiotemporal superposition, measured displacement data are superposed to generate sinusoidal excitation corresponding to the frequency of firing. In the multi-beam approach, on the other hand, multiple beams are fired sequentially to form a wide beam with overall beam width close to half wavelength.

Crawling waves generated by both methods were investigated with FEM simulation and actual phantom experiments. The experiments were performed both with a pair of focused 5 MHz transducers and a commercial ultrasound array probe. For practical reasons, the excitations were in the range of 70-150 Hz frequency and duty cycle of less than 10%. The frequency difference between the sources was 0.1-0.5 Hz. The crawling wave data were analyzed to estimate the shear wave velocity of the medium. Both homogeneous media and a medium with an inclusion were investigated. The background medium was designed to have a shear velocity of 2-3 m/s while the inclusion had a higher velocity of 4-5 m/s.

It was confirmed that the crawling waves with displacements below 10 microns can be generated with radiation force induced by an ultrasound beam. Also the analysis of the data shows the validity of the methods in detecting the elastic properties of tissue.

## Resonance frequencies of bubbles in tubes

**Sheryl M. Gracewski, PhD**

The main goal of our research is to provide a comprehensive understanding of how a surrounding tube or channel affects the dynamic response of acoustically excited bubbles. Use of ultrasonically excited microbubbles within blood vessels has been proposed for a variety of clinical applications. Because forcing bubbles at resonance can increase the desired response in many applications (for example ultrasound assisted drug/ gene delivery or bubble assisted micromixing), recent efforts were focused on investigating the effect of bubble interactions and tube stiffness on a bubble's natural frequency. Coupled fluid-solid finite element models have been developed using the commercially available code COMSOL multiphysics. In addition, lumped parameter models were developed using energy methods to obtain approximate analytical expressions. Results of these models and experimental results for tubes with intermediate compliance values suggest that for a single bubble in a compliant tube, there are two main resonance frequencies. In addition, a system of two bubbles in a rigid tube has two natural frequencies. As the distance decreases between two bubbles of equal size centered about the midpoint of a tube, the higher frequency will increase dramatically, while the lower frequency is negligibly affected by the presence of the second bubble. During the summer of 2009, an REU recipient and a Xerox Engineering Fellow (awarded by the UR's Edmund A. Hajim School of Engineering and Applied Sciences Dean's Office) developed COMSOL models and experimental methods, respectively, for these investigations.

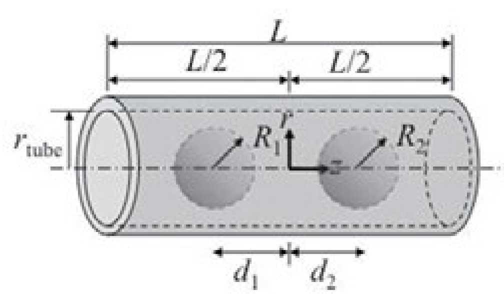



***Figure 1.*** Schematic of 2 bubbles inside a circular cylindrical tube immersed in a liquid. This is a model of interacting bubbles in a vessel, e.g. echo contrast agents in a capillary, excited by ultrasound.

## Backscatter imaging by shear wave induced phase encoding

**Stephen McAleavey, PhD**

Typical ultrasound backscatter medical imaging systems (e.g. B-scan) use geometric focusing to form ultrasound beams. The frequency, size and apodization of the aperture determine the beam pattern and lateral resolution. Deviations in assumed sound speed (c = 1540 m/s typically) of the media between the transducer and target can degrade the ideal beam pattern. Often, as in medical imaging, the target to be imaged can support shear waves in addition to the longitudinal waves used for ultrasound imaging. The shear wave speed is much lower than the longitudinal wave speed, and shear wave motion in the target can be tracked ultrasonically.

We have proposed a novel method to form an image of the ultrasonic echogenicity of the target under the assumption of uniform shear modulus, using traveling shear waves to obtain lateral resolution, rather than a focused aperture. We show that the lateral resolution of this method is independent of the aperture size. Rather, the range of shear wave wavelengths that can be induced and tracked determine lateral resolution.

We have simulated this image formation process, as well as performed in vitro tests on tissue mimicking phantoms. To simulate the technique, point targets subject to plane shear wave vibration in a uniform, lossless elastic medium (G = 5 kPa) were modeled using Field II (Jensen). A single element transducer, comparable to a single element of a 6 MHz array (0.2 mm wide), was modeled as the source and receiver. Shear wave propagation was modeled as a plane wave from 50-1500 Hz and scatterers were translated according to the shear wave equation. Echoes were calculated at shear wave phases of -90, 0, 90 and 180 degrees. Both point targets (wires) and a diffuse, hyperechoic lesion were simulated.

A gelatin block phantom containing nylon monofilament "wire" targets was imaged using the setup depicted schematically in Figure 1. The blocks were 10x4x6.5 cm in size, composed of 7.5% gelatin by weight, with a shear modulus of ~5 kPa. Lengths of nylon monofilament (0.13 mm diameter) were embedded in the gelatin block parallel to the y-axis, arranged along the diagonal of a 2.5-mm (0.1") square grid. The shear modulus of the phantom was determined by unconfined compression.

Pulse-echo RF data were acquired using a single element of a 7-MHz linear array (Aloka) driven by a pulser-receiver. A digital oscilloscope was used to record the echo signals. Echo averaging was used to improve SNR and the effective resolution of the oscilloscope. For each vibration frequency, 1024 echoes were obtained, 256 for each (0°, 90°, 180°, 270°) phase.

Simulated and experimental images of point targets using this technique are shown in Figure 2. The lateral profile of the point targets demonstrates the correct position of the wires. A Hamming window was applied to the simulated echo data along the frequency axis to reduce ringing artifacts in the image reconstruction. Simulated lesion with the proposed method is shown in Figure 3. A presentation of this method was made at the 2009 IEEE Ultrasonics Symposium in Rome, Italy, with the title "Image Reconstruction from Shear Wave Modulated Ultrasound Echo Data."

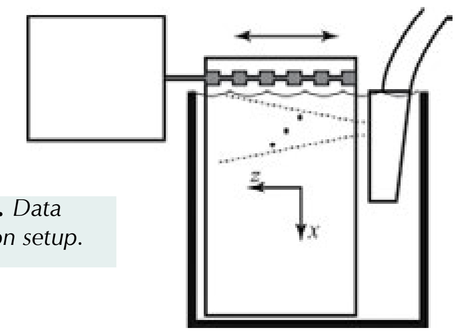



***Figure 1.*** *Data acquisition setup.*

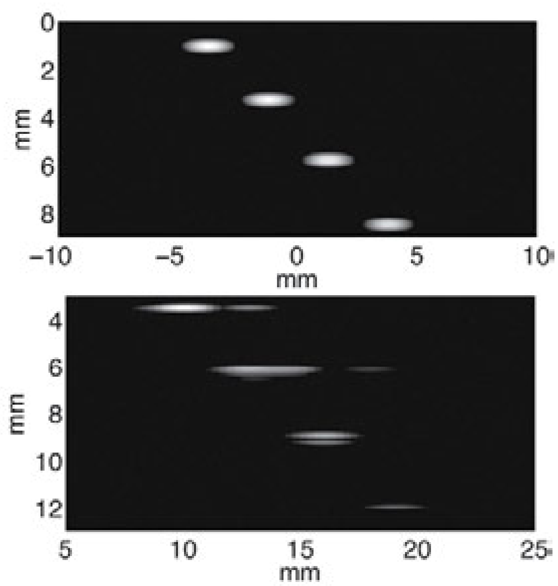



***Figure 2.*** *Simulated (top) and experimentally acquired (bottom) images of wire targets in an elastic gel using the proposed method.*

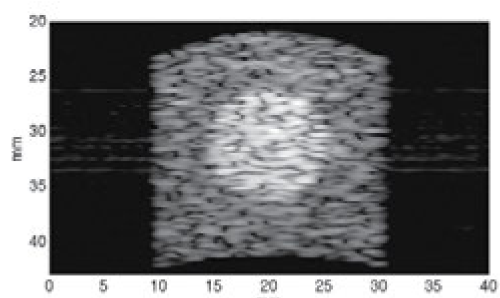



***Figure 3.*** *Simulated +12 dB hyperechoic lesion in elastic medium with the proposed method. The displayed dynamic range is 40 dB.*

## ARFI imaging of small phantom and tissue lesions

**Manoj Menon, MS and Stephen McAleavey, PhD**

In an investigation of the resolution of acoustic radiation force impulse (ARFI) imaging, Manoj Menon, a graduate student in the McAleavey lab, imaged objects of physiologically relevant size and stiffness. Cross-sections of a stiff cone in a compliant background were imaged to illustrate the resolution capability of the ARFI imaging system given a phantom with clinically relevant geometry and elastic contrast. A gelatin phantom was fabricated with a compliant background material ($\mu$ ~1.4 kPa), and a stiffer cylinder and cone ($\mu$ ~ 2.7 kPa). The phantom was first imaged on its side with the profile of the cone in the imaging plane. The phantom was rotated 90 degrees, so that the imaging plane imaged the cone transaxially. Cross-sectional ARFI images were acquired at cone diameters of 2.5 mm, 1 mm, and 0.5 mm.

For tissue imaging, a fresh porcine liver was submerged in room-temperature 0.9% saline solution and ablated. A section was removed from the liver, and a 0.14 mm nichrome resistance wire was threaded through the specimen while submerged in saline. Both ends of the wire were attached to a DC power supply. A Siemens VF7-3 linear array transducer was fixed above the sample for real-time B-mode imaging. A 1.5 A current using a voltage of 0.3 V was used until the region around the wire started to visibly change in brightness (presumably due to boiling). The time required for this local brightening was 6.5 min and 4 min for the larger (d ~ 2.1 mm) and smaller (d ~ 0.5 mm) cylindrical lesions, respectively. ARFI images were captured and the tissue was subsequently dissected. For both cross-sections of the stiff phantom conical inclusion and tissue ablation lesions, when the diameter of the stiff region was less than 1 mm, the brightness contrast decreased, suggesting that 1 mm was close to the ARFI resolution limit.

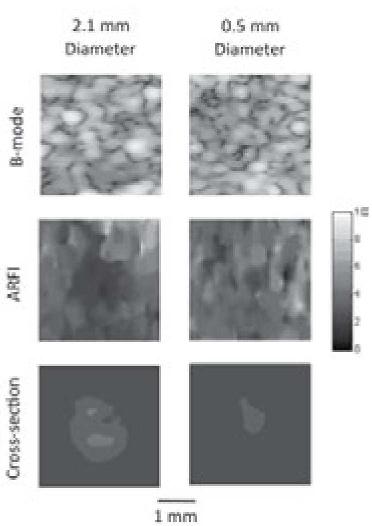



***Figure 1.*** *Images of ablation lesions with diameters of 2.1 and 0.5 mm. The center frequency was 4.2 MHz, the tracking pulse length was 0.7 mm, and the correlation window length was 0.8 mm. The displacement contrast between the background and the lesion was 1.89 and 1.62 for diameters of 2.1 mm and 0.5 mm respectively. The displacements are given in microns at 0.40 ms after the pushing pulse.*

## Bioeffects of underwater impulses

**Diane Dalecki, PhD, Sally Z. Child, MS, Carol H. Raeman, AAS, and Sheryl M. Gracewski, PhD**

Sponsored by the U.S. Naval Submarine Medical Research Laboratory (NSMRL), the Dalecki lab is investigating the effects of low frequency, underwater acoustic impulses on biological systems. Underwater impulsive sound fields are employed in the ocean for both commercial and military applications. For the investigations, underwater acoustic impulses are produced with an air gun source system.

To generate and test the bioeffects of these impulsive acoustic fields, the Dalecki lab has an active collaboration with a Rochester-based company, Hydroacoustics, Inc. (HAI). HAI manufactures and supports unique low frequency, continuous wave and impulsive underwater sound sources. The HAI facility, located a short distance from the UR, includes 12,000 square feet of laboratory space dedicated to acoustic research and testing of underwater sound sources. Air gun technology, water tanks, and measurement facilities at HAI are used to generate underwater acoustic impulses for our bioeffects investigations.

The Dalecki lab and Hydroacoustics, Inc. (HAI) are working together to investigate the effects of underwater acoustic impulses on mammalian systems. Robert De La Croix, Vice President of Engineering at HAI, has been a key collaborator in adapting the HAI exposure apparatus for the Dalecki team's biological experiments. The team completed a series of investigations to characterize the acoustic impulse fields generated by various air gun systems in the water tanks available at the HAI facility. Professor Sheryl Gracewski and her students used finite element modeling techniques to simulate the acoustic fields under the specific geometries relevant to our experimental field measurements. The Dalecki lab completed a series of experimental investigations on the effects of underwater acoustic impulses on murine lung in vivo. Using a 10 cubic inch air gun system, they investigated the response of lung to acoustic impulses with peak acoustic pressure amplitudes ranging from ~0 - 110 kPa. They found that murine lung hemorrhage could be produced following exposure to five underwater acoustic impulses with pressure amplitudes equal to or greater than ~50 kPa. The Dalecki lab also collaborates with the laboratory of John Olschowka, Ph.D. (UR Neurobiology and Anatomy) to study the effects of underwater acoustic impulse fields on the mammalian brain and spinal cord. Ongoing studies continue to characterize the response of lung and neural tissues to these underwater acoustic impulse fields. The results of this work are relevant to establishing safety guidelines for swimmers and divers exposed to underwater sound fields.

## Comparison between 1D and 1.5 D arrays for the formation of spatially modulated ultrasound radiation force beams

**Etana Elegbe, MS and Stephen McAleavey, PhD**

Spatially Modulated Ultrasound Radiation Force (SMURF) imaging is an elastography technique based on estimating the shear modulus of an elastic material. SMURF determines shear modulus through measurement of the frequency of shear waves of known wavelength propagating in a medium of unknown modulus. The shear modulus is then computed using the relationship $G = (\lambda f)^2 \rho$. The spatial frequency k of the force variation is equal to the desired spatial frequency of the shear wave, that is, $k = 2\pi/\lambda$. Because the acoustic radiation force used to create the shear waves is proportional to intensity, generation of this spatially varying force is a matter of determining how to generate an equivalently varying ultrasound intensity field.

Presented in this study is the Focal Fraunhofer method, which is one of the techniques that can be used to create the desired beam intensity pattern within a region of interest. To create a push that results in discernible displacements while minimizing tissue heating in the near field, we investigate the use of both a linear and a multi-row 1.5D array. A 1.5D array allows for more aggressive focusing in the elevation direction and thus a greater intensity in the region of interest. The efficacy of both configurations is analyzed based on the ability to generate beams of the desired well-defined spatial wavelength at various focal depths, the ability to localize the pushing beam to the region of interest, and the ability to maximize the depth-of-field.

The quality of our shear modulus estimate is greatly affected by the ability to create a pushing beam with a well-defined spatial frequency that is constant over the lateral distance of interest, as well as its axial extent (i.e. a forcing function with a constant, known $\lambda$). The intensity of this beam will remain constant with distance from the transducer face over the region of interest. One apodization technique that approximates this desired beam configuration is the Focal Fraunhofer method. The Focal Fraunhofer method relies on the fact that lateral pressure distribution within the focal zone is determined by the Fourier transform of the transducer's apodization. In theory, the ideal aperture apodization function would consist of two impulses since the Fourier transform of two impulse functions is a cosine function in the far field (we set the focus here) and represents the ideal intensity pattern. In reality, however, it is not feasible to create a perfect impulse function with a finite aperture; instead two narrow Gaussian beam profiles are simulated using a group of transducer elements, and result in a sinusoidal beam pattern with a Gaussian envelope that limits its spatial extent in the lateral direction. The spatial frequency of the pressure distribution will be determined by the distance between the two near-impulses and the widths of the Gaussian beams used in creating them. The energy at the focus will be determined by the pressure amplitude at the transducer as well as the number of elements being turned on to create the field. The attenuation of the material under study, also greatly affects the resulting energy at the region of interest. It is very important that the generated energy is used efficiently and that dissipation into areas outside the ROI is minimized. 1.5D arrays are thus desirable because they allow more control in terms of focusing in the elevation direction as well as the lateral direction. The ultrasound fields are simulated in MATLAB with FIELD II. The linear array transducer is comprised of a single row of 96 elements. The 1.5D array has 7 x 96 elements. Both transducers have a center frequency of 5.33 MHz, a mechanical focus at 3.75 cm and a 100-cycle pushing beam.

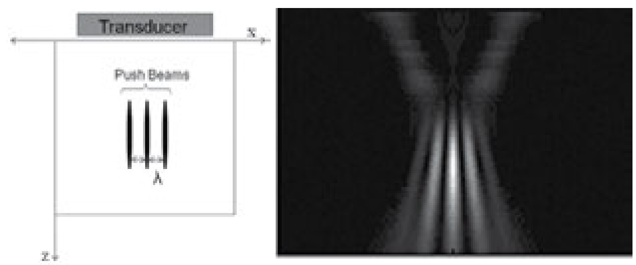



***Figure 1.*** *The ideal pushing pulse pattern (left). The simulation of the pushing pulse using the Focal Fraunhofer technique (right).*

## Developing synthetic data sets for medical imaging

**Maria Helguera, PhD**

Creating software models of the human anatomy and imaging systems, and modeling the medical physics of the imaging acquisition process, can provide a means to generate realistic synthetic data sets. In many cases synthetic data sets can be used, reducing the time and cost of collecting real images, and making data sets available to institutions without clinical imaging systems. Students in the Helguera lab have been investigating and implementing tools for creating these synthetic data sets. Existing software packages such as SimSET, GATE, and SIMRI are being leveraged and modified as necessary to enable the generation of large quantities of high-resolution data. Efforts have included grid implementations, and most recently a porting of SIMRI for the IBM Blue Gene super computer systems. What resulted is perhaps the first tool for generating high-resolution, three-dimensional magnetic resonance images.

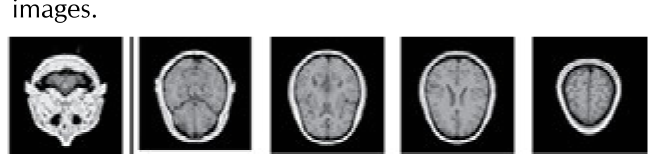


***Figure 2.*** *Five slices from a simulated image acquisition of the Montreal Brain Phantom.*

## Obstetrics & Gynecology Ultrasound Unit

**Tulin Ozcan, MD**

The UR OB/GYN Ultrasound Unit provided clinical service at multiple sites including Strong Memorial Hospital, Highland Hospital, Rochester General Hospital, FF Thompson Hospital and the facilities at Red Creek Drive and West Ridge Road. The total number of examinations was 14,645, including 12,381 obstetric, and 2,264 gynecological scans. Invasive procedures included 315 amniocenteses, 107 chorionic villus samplings, and 146 sonohysterograms and 24 other procedures including OR guidance for minor gynecological procedures, intracardiac KCL injections or cyst aspirations. Intepretation of ultrasound examinations at FF Thompson Hospital are continued utilizing a combination of telemedicine and onsite service and a total number of 1,879 examinations were read. The Unit also continued to provide ultrasound and consulting services to Rochester General Hospital OB/GYN Department. Additional equipment has been obtained to improve the quality of 2D and to increase the utilization of 3D and 4D scanning in both obstetrics and gynecology including high end scanners.

## Impact of pelvic floor musculature on peripartum outcomes: A prospective study

**Tulin Ozcan, MD, Veruna Raizada, MD, Buschbaum G**

In this study, our specific aim is to investigate the impact of pelvic floor muscle contraction on the labor and delivery outcomes. Our hypothesis is that primiparous women who are able to increase the size of their pelvic floor hiatus with maximal valsalva are more likely to have a successful normal vaginal delivery and less likely to have pelvic floor muscle avulsions and peripartum urinary and fecal dysfunctions.

Term primiparous patients admitted for early labor who are candidates for vaginal delivery or admitted for induction of labor will be included. We will obtain three dimensional ultrasound volume data sets of the pelvic floor muscle at rest, squeeze and valsalva using a transperineal probe before active labor and 6 weeks postpartum. The pelvic floor muscle hiatus dimensions which include dynamic pelvic floor muscle hiatal length and area with various maneuvers will be compared for mode of delivery, perineal tear, pelvic muscle avulsion, and  and peripartum urinary and fecal dysfunction rates.

## The effect of vaginal progesterone in patients with active preterm labor

**Tulin Ozcan, MD, Danielle Durie, MD, David Hackney, MD**

The objective of this project is to assess the efficacy of vaginal progesterone on the rate of spontaneous preterm delivery in women with active preterm labor. The following hypotheses will be tested: 1) The use of daily vaginal progesterone gel in patients with active preterm labor will prolong the interval from preterm labor episode to delivery and decrease the rate of preterm delivery and improve perinatal outcomes. 2) The use of vaginal progesterone gel will reduce the amount of cervical shortening and levels of pro-imflammatory cytokines following an episode of preterm labor. 3) Preterm labor associated with decidual hemorrhage may be refractory to progesterone effects.

## Tumor pathology report in 3D dynamic image format

**Benjamin Castañeda, PhD, Daniel Hosey, John Strang, MD, Deborah Rubens, MD, Kevin J. Parker, PhD, Jorge Yao, PhD, Zhenhong Qu**

Tumor pathology reports are a critical component in the clinical management of cancer patients. Currently, pathology reports of malignant neoplasm remain in text format with the occasional presence of selected 2D still images. Images are considered the most comprehensive and intuitive form of information for morphological abnormalities. In this work, we propose a 3D image pathology reporting module using prostate as a model that allows direct and visual assessment of several critical tumor attributes such as size, volume, shape, location, extent and margin status.

Intact prostate glands with carcinoma were received after radical prostatectomy. A landmark device, which consisted of two sets of four (3 mm diameter) mating metal prongs, was inserted into the specimen through the apex and base to provide fiducial markers for 3D reconstruction. Subsequently, a whole-mount protocol was followed and complete serial sections were mounted and stained by routine H&E for microscopic evaluation. The carcinoma was outlined in the slides. Image segmentation techniques were used to extract the contours of the gland and the tumor. These contours were interpolated to create a 3D model that was dynamically visualized using a web interface. Figure 1 illustrates the implemented web interface showing a 3D model of the prostate gland (light gray) and the carcinoma (dark gray). Users can access this interface to view a colored 3D model of a tumor from several angles to reveal the tumor size, shape and location in the specimen. This reporting method allows for a more comprehensive appreciation and assessment of several critical cancer attributes. Furthermore, this 3D reporting methodology can be applied to other organ systems (such as liver) and used to validate radiology imaging modalities.

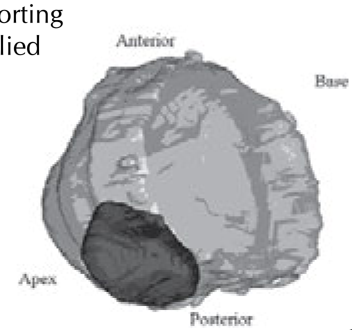



***Figure 1.*** *3D model of the prostate gland (light gray) with a carcinoma (dark gray).*

## Investigations of resolution of acoustic radiation force impulse (ARFI) imaging

**Manoj Menon, MS and Stephen McAleavey, PhD**

Imaging the mechanical properties of small tissue structures and pathological boundaries can aid in the characterization of a variety of conditions, such as atherosclerotic vessels, cancerous tumors, and ablation lesions. Acoustic Radiation Force Impulse (ARFI) imaging measures the mechanical response of tissue to a local acoustic radiation force using a standard diagnostic ultrasound scanner. The measurement of the spatial resolution limit of a number of elastographic techniques have been previously simulated.

In this study, Manoj Menon, a graduate student in the McAleavey lab, developed and implemented an experimental method to measure spatial resolution of an ARFI imaging system using a phantom composed of a compliant cylinder in a stiff background material. Due to the dynamic nature of the ARFI displacements, resolution was estimated as a function of time after excitation. Due to jitter artifacts and underlying spatial variation of the acoustic radiation force, a curve-fitting algorithm was applied to extract the step function and therefore the point spread function of the imaging system. To study the relatively simple dependence of axial resolution on window length and pulse length, a 1D echo simulation was developed. In order to study the more complicated mechanically dynamic beam dependent effects, a 3D FE/FIELD II based simulation was created. These measurements were compared to experimental results. The investigators found axial resolution to depend on the order of the tracking pulse length and the correlation window length. The lateral resolution was found to coincide with the tracking beam width. The resolution was found to depend on the time after the pushing pulse. When the frequency was 4.2 MHz, the bandwidth was 0.5, and the window length was 1 mm, the axial resolution was estimated to be 1 mm. With a lateral beam-width of 1 mm, the lateral resolution was also found to be approximately 1 mm. Simulation and experimental results showed agreement.

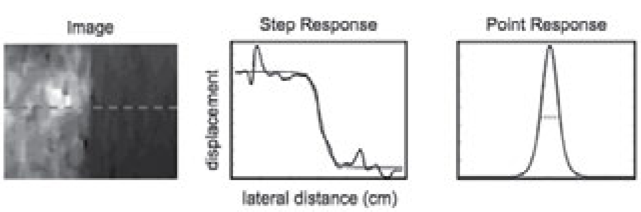



***Figure 1.*** *Nonlinear least squares fit, full-width half maximum resolution estimation using an ARFI image of a step phantom.*

## Spatially modulated ultrasound radiation force (SMURF) imaging

**Stephen A. McAleavey, PhD**

Changes in tissue stiffness have long been associated with disease and motivate both manual palpation and newer elastography techniques. While palpation and non-quantitative elastography can reveal local stiffness contrast, they do not provide definite values for overall or global stiffness. Quantification of tissue stiffness is needed to reveal diffuse disease, e.g. liver fibrosis. Indeed, there is strong evidence that quantification of tissue stiffness can replace hazardous biopsy methods, which necessarily sample a tiny fraction of an organ, with overall indicators of tissue stiffness. Spatially Modulated Ultrasound Radiation Force (SMURF) imaging has the potential to provide this information quickly, non-invasively and safely.

SMURF imaging uses the acoustic radiation force of a pulsed ultrasound beam, with a carefully controlled lateral variation in intensity, to generate a shear wave of known initial wavelength ($\lambda$). The frequency ($f$) of this wave, which depends solely on its point of generation and not the surrounding environment, is then measured to determine the shear modulus ($G$) of the tissue using the relationship $G = (\lambda f)^2 \rho$, where $\rho$ is the tissue density ($\sim 10^3$ kg/m$^3$). The frequency is estimated from tissue motion tracked ultrasonically using the same transducer that generated the radiation force beam. The pulsed nature of the shear waves avoids interference from standing waves inherent in continuous wave methods, while the use of acoustic radiation force to generate the shear wave at the point of interest eliminates difficulties in propagating a shear wave from the body surface to the region of interest, i.e. attenuation, refraction, and slip boundaries between tissues. Our ability to control the lateral ultrasound beam attenuation allows the tissue to be probed at a variety of (shear wave) frequencies, allowing viscoelastic properties of the tissue to be characterized. Our preliminary in vitro studies have shown that SMURF imaging is capable of providing rapid estimates of shear modulus in good agreement with values obtained through standard mechanical testing methods.

In our research, a Siemens Antares scanner is used for pulse generation and echo acquisition. The scanner allows acquisition of beamformed RF echo data sampled at 40 MHz and digitized with 16-bit resolution. Additional software allows modified transmit and receive beamforming sequences to be implemented on the scanner. SMURF sequences have been implemented for VF10-5 and VF7-3 linear arrays, operating at 6.7 and 4.2 MHz, respectively. Displacement estimates are generated from the RF echo data using normalized cross-correlation and a parabolic fitting to estimate displacement with sub-sample resolution.

Sequences for imaging, wherein the pushing and tracking beams are "walked" across the array, as in ordinary B-mode imaging, have been implemented. A tracking pulse is transmitted at one scan line location. The echo, dynamically focused and apodized, is collected to generate a reference A-line. Two pushing pulses are then transmitted in rapid succession. The focus of each beam is at the same depth but translated laterally by a specified distance Δx. A series of tracking pulses is transmitted and echoes collected along the same scan line as the reference echo. Correlation processing of the resulting echo signals allows the time between the induced shear wave peaks to be estimated. Example SMURF images of liver tissue during RF ablation are shown below.

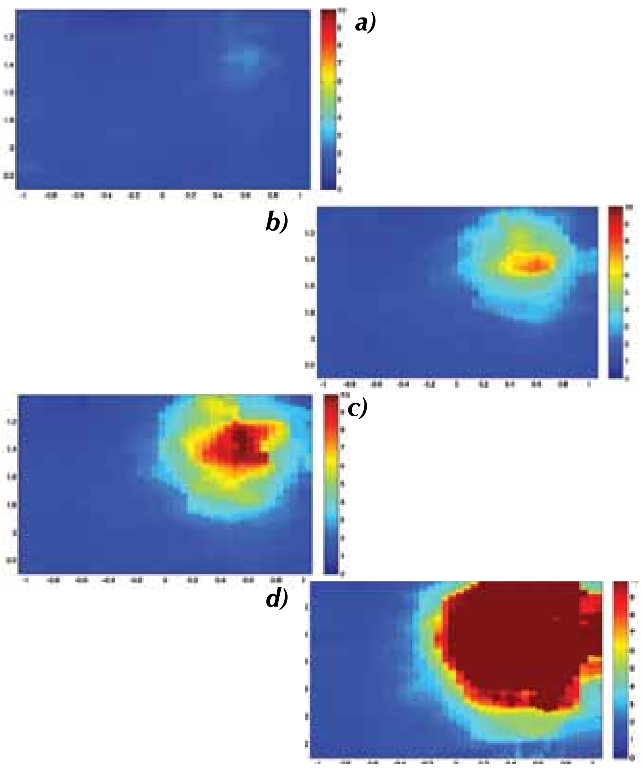



***Figure 1.*** *SMURF images formed during RF liver ablation ex vivo at times of a) 8, b) 24, c) 32, and d) 52 minutes.*

## Ultrasound standing wave fields promote capillary network formation in engineered tissue constructs

**Kelley A. Garvin, MS, Denise C. Hocking, PhD, Diane Dalecki, PhD**

The Dalecki and Hocking laboratories are actively developing ultrasound technologies for the fabrication of three-dimensional engineered tissues. One recent project is gathering exciting evidence that ultrasound can play a role in the creation of vascularized tissue constructs for the field of tissue engineering.

The field of tissue engineering is working toward the in vitro development of fully functional tissues and organs for the repair or replacement of diseased or injured tissues and organs. Currently, a primary challenge in creating large, three-dimensional organs is maintaining cell viability throughout the tissue. Large organs cannot rely on passive diffusion of oxygen and nutrients but instead, require a vascular system to deliver these essential components to all areas of the tissue. Therefore, the engineering of large, three-dimensional functional tissues and organs requires the development of a vascular network throughout the tissue.

We have applied an ultrasound standing wave field to a suspension of endothelial cells in unpolymerized type-I collagen. Endothelial cells are the cells that comprise the inner wall of blood vessels. Acoustic radiation forces developed in the ultrasound standing wave field resulted in the formation of planar "bands" of cells separated by cell-free regions (see related story "Using acoustic radiation forces to spatially organize cells in three-dimensional engineered tissue", page 18, Figure 2). By allowing the collagen solution to polymerize during ultrasound exposure, this banded pattern of cells was maintained within a three-dimensional collagen gel after removal of the sound field. One day after ultrasound standing wave field exposure, endothelial cell sprouts, or the precursors to capillary blood vessels, were found emerging from the cell banded areas. The length of these structures was ~100 $\mu$m. In contrast, sham-exposed samples were characterized by randomly distributed cells with round morphology. Over the course of ten days, the endothelial cell sprouts in ultrasound standing wave field exposed samples progressed into longer, tube-like, branching networks that extended throughout the collagen gel (Figure 2). Less extensive networks containing shorter tube-like structures were found in sham-exposed samples but were confined to the gel periphery. These results provide promising evidence that ultrasound standing wave fields can be used to create a vascular network throughout three-dimensional engineered tissue and could serve as a novel technological advancement for the field of tissue engineering.

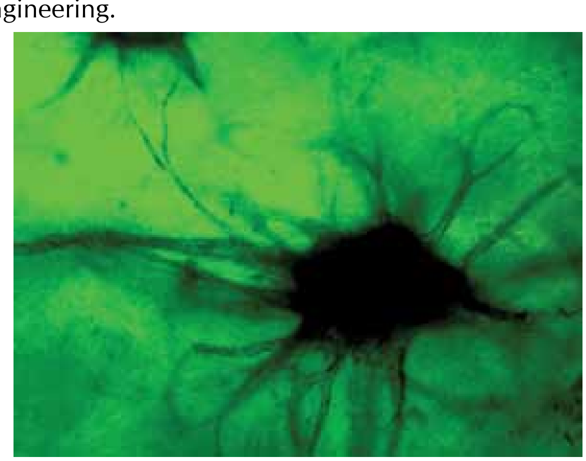


***Figure 2.*** *Day 10-Extensive tubular networks develop in ultrasound standing wave field-exposed collagen gels.*

## Imaging of atherosclerotic plaque mechanics with intravascular ultrasound elastography and inverse modeling

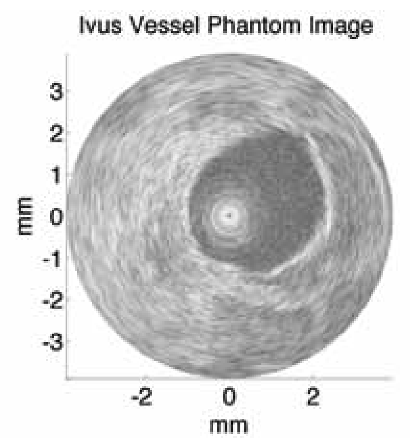
**Michael S. Richards, PhD, Shayin Jing, MS, and Marvin M. Doyley, PhD**

Complications from cardiovascular disease occur primarily from fatty plaques inside an artery that rupture, and cause clots that disrupt blood flow. The study of arterial plaque mechanics can aid in monitoring atherosclerosis and the detection of vulnerable plaques or the likelihood of their rupture. The aim of work in the laboratory of Professor Marvin Doyley is to measure and image the mechanical behavior of plaques using a clinically available Intravascular Ultrasound System (IVUS).

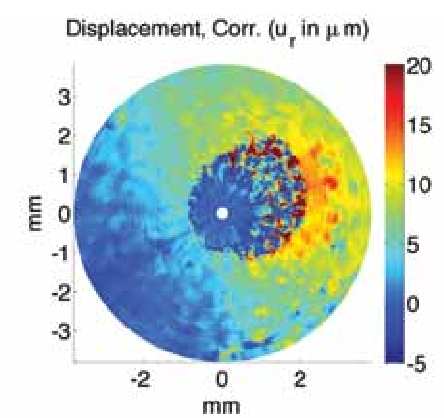
Two-dimensional IVUS images are acquired of an artery, with a plaque in cross-section, perpendicular to the blood flow as the internal blood pressure is causing the plaque and vessel to deform. Figure (a) shows an IVUS image of a vessel and plaque mimicking phantom undergoing deformation due to an internal pressure. The IVUS images are then used to measure the relative displacements of the deforming tissue. The radial (axial) displacement measurements are calculated using standard cross correlation, block-matching techniques (i.e. speckle tracking) (Figure b). Alternatively, the displacements may be calculated using novel image registration based algorithms, which may lead to a higher order of accuracy in the radial direction as well as the circumferential (lateral) measurements (Figure c and Figure d).

*Members of the Doyley lab.*

Typically, the displacements measured from these algorithms are used to create radial strain images, which are correlated to the relative stiffness of the tissue. However, the Doyley group uses finite element models of the tissue and simulations under physiologic conditions to more accurately investigate the material properties and stresses seen throughout the imaged region. A schematic of an example finite element mesh and material distribution is shown in Figure (e). Finally, the displacements measured from the IVUS images and the finite element model are used in novel inverse algorithms that predict the mechanical property distribution and values which would result in a displacement field that ideally matches the measured field.




(a)

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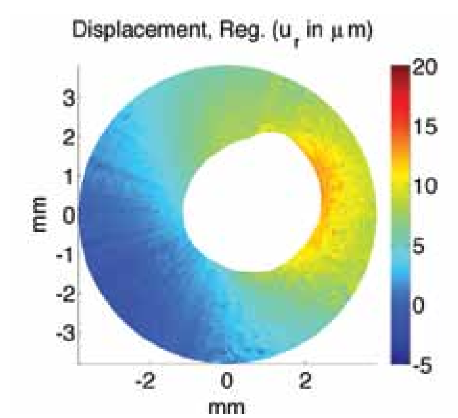


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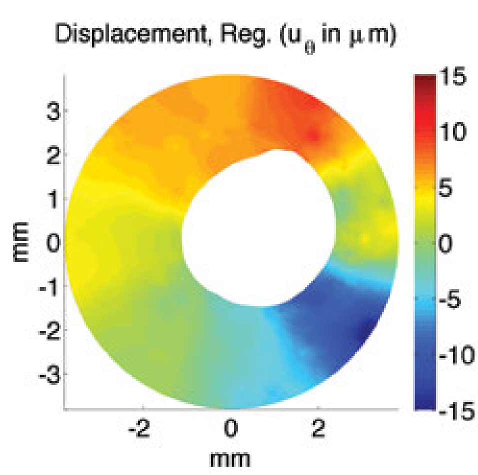


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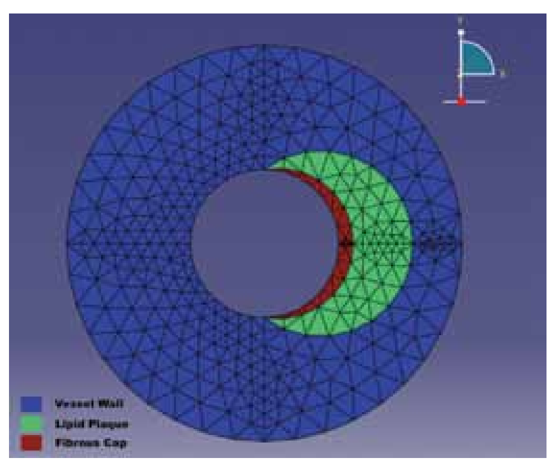



(e)

## Tissue body formation as an in vitro model of impaired wound healing

**Carlos Sevilla, MS, Diane Dalecki, PhD, Denise C. Hocking, PhD**

Chronic cutaneous wounds are characterized by decreased fibroblast proliferation and the loss of the extracellular matrix protein, fibronectin. The Hocking and Dalecki laboratories are performing investigations to determine the biological and acoustic mechanisms by which therapeutic ultrasound enhances healing of chronic cutaneous wounds. To do so, the team has developed an in vitro model of wound tissue in which mouse embryonic myofibroblasts are seeded onto thick gels of native collagen. In the absence of the extracellular matrix protein, fibronectin, cells do not spread or proliferate. In contrast, the formation of a fibronectin matrix by cells stimulates behaviors essential to wound healing, including cell migration, and cell proliferation, and in turn, leads to the formation of large, three-dimensional, multicellular structures, termed tissue bodies. Cell proliferation and tissue body formation are dependent on the concentrations of both fibronectin and collagen. Figure 1 is an immunofluorescence image captured using two-photon microscopy showing cell nuclei (blue), fibronectin (green), and actively proliferating cells (red) in a three-dimensional tissue body formed on native collagen gels. Ongoing studies in the Hocking and Dalecki labs are using this novel tissue body model to test a series of hypotheses aimed at understanding the biological and physical mechanisms underlying the effects of ultrasound on wound healing.

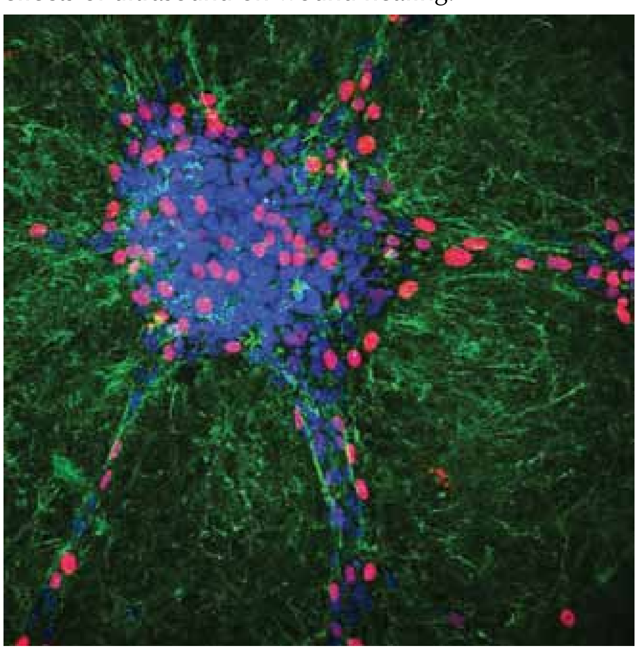


***Figure 1.*** *Immunofluorescence image captured by two-photon microscopy showing cell nuclei (blue), fibronectin (green), and actively proliferating cells (red) in a three-dimensional "tissue body" formed on native collagen gels.*

## Evaluation of crawling wave estimator bias on elastic contrast quantification

**Liwei An, MS, Deborah J. Rubens, MD, John G. Strang, MD, Yong Thung Cho, PhD, Zaegyoo Hah, PhD, Bradley Mills, Kevin J. Parker, PhD**

An estimation of local elastic modulus based on the crawling wave (CrW) technique has been applied to imaging biological tissues including radiofrequency ablated hepatic lesions in vitro, human skeletal muscle in vitro, and excised human prostate. The objective of a recent study from our group was to quantify the elastic contrast for heterogeneous elastic phantoms and to evaluate frequency dependence, bias, and spatial resolution of lesion detection based on CrW sonoelastography. We focus on parameters of particular interest in prostate cancer detection.

Heterogeneous elastic phantoms were prepared by embedding stiff spherical inclusions (11% gelatin) with diameter of 2, 1 and 0.6 cm in otherwise soft homogeneous backgrounds (6% gelatin) separately. Two vibration sources were positioned at each side of the phantom with the ultrasound transducer scanning from the top of the cross-section to be observed. CrWs at 70, 100, 120, 140, 200 and 300 Hz were acquired by offsetting a small frequency difference between two sources. Independent reference measurements were obtained in homogeneous specimens. The elastic contrast of the lesions, $E_{lesion}/E_{background}$, was 1.52, similar to the ratio found in prostate cancer.

The CrW movies were first normalized to compensate for the gain difference at different depth levels of the image. A sinusoidal curve fitting over one cycle of crawling waves was then applied to improve the SNR. A 2-D local shear velocity estimator was employed with the CrW phase pre-conditioned to a favorable range of the estimator. A mean estimation over frequencies was obtained by globally selecting and averaging 90% qualified data points. Finally, the shear velocity information from both the hard region and the soft region was extracted from the estimation map and was compared against the reference values obtained from homogeneous phantoms.

The averaged shear velocity estimation for each phantom is shown in Figure 1 (next page). The 2 cm inclusion phantom gives the highest contrast of hard and soft regions at 1.29 averaged over frequency, followed by the 1 cm case at 1.27 and the 6 mm case at 1.14. The estimations followed an upward tendency with frequency increase due to the higher resolution of CrW at higher frequencies. Better contrast was acquired for inclusions with larger size. The effect of under-estimation and loss of contrast, which is caused by noise and the spatial support of the estimator, was revealed.

In this study, contrast details were demonstrated for phantoms with stiff inclusions of different sizes. The experiment showed the ability of the shear velocity estimator to distinguish the lesion from the background. Lesions similar in elastic contrast to prostate cancer that are 6 mm in diameter or larger are resolvable at frequencies above 100 Hz, using our current system and methods.

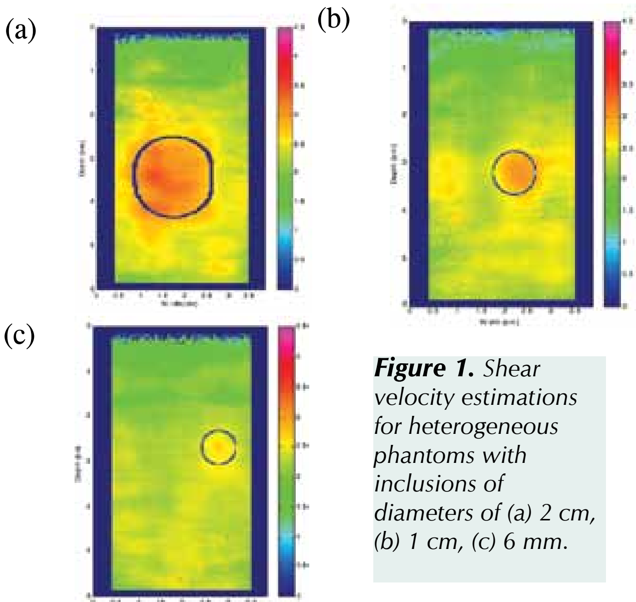



***Figure 1.*** *Shear velocity estimations for heterogeneous phantoms with inclusions of diameters of (a) 2 cm, (b) 1 cm, (c) 6 mm.*

## Using ultrasound to spatially organize cells in engineered tissues

**Kelley A. Garvin, MS, Denise C. Hocking, PhD, Diane Dalecki, PhD**

The application of an ultrasound standing wave field to a suspension of cells can result in the radiation force-mediated movement of cells into bands that are perpendicular to the direction of sound propagation and that are spaced at half-wavelength intervals. The Dalecki and Hocking laboratories have utilized this principle to develop an ultrasound standing wave field technology for the fabrication of three-dimensional collagen-based tissue constructs with a controlled spatial distribution of cells.

In an ultrasound standing wave field, a primary acoustic radiation force is generated along the direction of sound propagation and is largely responsible for cell movement within the field. To maintain the banded cellular distribution following removal of the sound field, we have suspended cells in unpolymerized type-I collagen and have allowed the collagen to polymerize around the cell-banded pattern during ultrasound standing wave field exposure. The magnitude of the primary acoustic radiation force has a second order dependence on the ultrasound standing wave field peak pressure amplitude. To determine pressure amplitudes that induce cell banding within our system, cells in unpolymerized collagen solutions were exposed to an ultrasound standing wave field at various peak pressure amplitudes, and the collagen was allowed to polymerize during the sound exposure. Gels were then examined for the presence or absence of cell bands. As shown in Figure 2 (below), bands of cells were formed in samples exposed to 0.1 MPa and above using a 1 MHz source. This is in contrast to a homogeneous cell distribution observed in sham-exposed samples and samples exposed to pressure amplitudes less than 0.1 MPa.

Cells embedded in a collagen gel can attach to and reorganize surrounding collagen fibers. Since results indicate that different ultrasound standing wave field pressure amplitudes lead to various patterns of banded cells, we hypothesized that different cell banded patterns would result in different collagen matrix organizations. To test this hypothesis, we used a collagen gel contraction assay as a measure of cell-mediated collagen reorganization. Cell-embedded collagen gels were fabricated using a range of ultrasound standing wave field pressure amplitudes. One hour after exposure, collagen gel diameters were measured and were compared to the original gel diameter to calculate percent contraction. Results indicate that ultrasound standing wave field-induced cell organization leads to a biphasic effect on cell-mediated collagen gel contraction. We found no difference in collagen gel contraction between sham-exposed samples and samples exposed to 0.02 or 0.05 MPa, where cells remain in a homogeneous distribution. However, a significant 1.5-fold increase in collagen gel contraction was found at 0.1 MPa, the threshold for cell banding, where cells first become aligned into planar bands. As pressure amplitude of the ultrasound standing wave field is increased above 0.1 MPa, collagen gel contraction levels start to decrease. These findings suggest that different ultrasound standing wave field cell banded patterns result in different collagen matrix organizations. Since the organization of the extracellular matrix plays a role in determining the mechanical properties of tissue, this technology has applications to controlling the mechanical properties of tissue constructs for the field of tissue engineering.

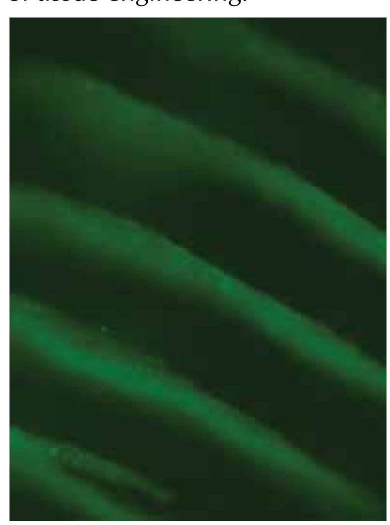


***Figure 2.*** *Fibroblasts and bound fibronectin are spatially organized into distinct bands within collagen hydrogels using ultrasound standing wave fields.*

## Interactions of underwater sound fields and mammalian lung

**Diane Dalecki, PhD, Sheryl Gracewski, PhD, Sally Z. Child, MS, Carol H. Raeman, AAS**

Underwater sound fields are used for numerous commercial and military applications, including imaging, oil exploration, mapping the ocean floor, and harbor surveillance. The Dalecki lab continues to investigate the interaction of underwater sound fields with biological tissues. The U.S. Navy and the Naval Submarine Medical Research Laboratory (NSMRL) in Groton, CT support our projects in this area. Underwater sound over a broad frequency range can be produced from a variety of sources including sonar systems and underwater blasts. An understanding of the interaction of underwater sound fields with biological systems is necessary to develop safe exposure guidelines for humans, marine mammals, and fish exposed to these acoustic fields. Tissues containing gas are particularly sensitive to underwater sound exposure. Over the years, our laboratory has been working to quantify the thresholds for sound-induced damage to tissues containing gas and identify the physical mechanisms for tissue damage.

The air-filled lung is particularly sensitive to underwater sound exposure. When the intact, air-filled lung is exposed to sound at frequencies where the wavelength is much greater than the radius of the lung, we have demonstrated that the whole lung oscillates radially in response to exposure to this spatially uniform sound field. Using both an acoustic scattering technique and a pulse-echo ranging technique, we have shown that the response of the lung is maximized for exposure at the resonance frequency of the lung. At the resonance frequency of the lung, the threshold for damage to the lung and surrounding tissues is lowest. In the adult mouse, the resonance frequency of the lung is ~325 Hz and the threshold for lung damage at the resonance frequency is ~2 kPa. Mammalian lung can also be damaged by exposure to low frequency sound above resonance frequency. Using an open tube exposure system, our lab determined the thresholds for murine lung hemorrhage from exposure to continuous wave underwater sound at frequencies ranging from ~2.5–1000 kHz. The equation $P_{thresh} = 0.01f^{0.64}$, where $P_{thresh}$ is the threshold pressure in MPa and f is the acoustic exposure frequency in kHz, represents a best-fit to our experimental lung threshold data over the 2.5–1000 kHz range.

Recent investigations focused on the response of lung to sound exposure at and near lung resonance frequency, and the response of lung to underwater impulses (see related story on page 11). Further studies in our lab continue to characterize the response of lung to continuous wave sound exposures of short duration over a broad frequency range.

## Bioeffects of ultrasound contrast agents

**Diane Dalecki, PhD, Carol H. Raeman, AAS, Sally Z. Child, MS**

A long-standing area of research in our laboratory is ultrasound contrast agents. Ultrasound contrast agents currently enhance the capabilities of diagnostic imaging and are also providing new avenues for therapeutic applications of ultrasound. Efforts in our laboratory focus on developing an understanding of the physical and biological mechanisms of interaction of acoustic fields with tissues containing microbubble contrast agents. Microbubble contrast agents can increase the likelihood of bioeffects of ultrasound associated with acoustic cavitation. Ongoing work from our lab continues to investigate ultrasound-induced bioeffects of microbubble contrast agents in the cardiovascular system. Recent work from our lab has demonstrated that the presence of ultrasound contrast agents lowers the threshold for ultrasound-induced premature cardiac contractions, and capillary rupture in various organs and tissues. Current collaborations with Sheryl Gracewski provide unique capabilities to computationally simulate the response of a microbubble to sound exposure within a confining blood vessel (see story on page 9). Experimental measurements within our lab will be used to validate the simulation results and obtain additional insights into the nonlinear bubble dynamics that can occur within blood vessels.

## Ultrasound materials characterization of geopolymeric materials

**Maria Helguera, PhD**

This project is a collaboration between Center Member Maria Helguera and Dr. Benjamin Varela (Mechanical Engineering, RIT). Current methods of determining the elastic modulus and Poisson’s ratio for geopolymeric materials are limited by the destructive nature of compressive strength and bending testing analysis techniques. Since these tests are not repeatable, there is no means of evaluating whether measured properties are a result of the actual materials or the effect of possible mechanical defects. This study applies a relationship between the speed of sound through a material and its elastic properties to determine the elastic modulus and Poisson’s ratio of geopolymeric samples. In addition to these elastic properties, the density, percent pore volume, average pore diameter and standard deviation of pore diameter were also evaluated. These material characteristics were determined as a relationship to the Si:Al ratio of sodium activated metakaolin based geopolymers with Si:Al ranging from 1.49 to 6.4. It was found that lower Si:Al values were consistently around 8.5 GPa in samples above 3.1 Si:Al ratio. The Poisson’s ratio for each sample decreased proportionally to the Si:Al ratio with a maximum of 0.22 and a minimum of 0.05.

# New Collaborations—New Directions

Innovations in biomedical ultrasound require the collaborative expertise of basic scientists, engineers, physicians, and clinicians. The RCBU provides an ideal forum to stimulate such cross-disciplinary research. Below are highlights of new, multidisciplinary research collaborations that have been forged by RCBU members.

## Using ultrasound to characterize engineered tissues

**Diane Dalecki, PhD, Maria Helguera, PhD, Denise C. Hocking, PhD**

A new collaboration, funded by the NIH, brings together the expertise of Professor Maria Helguera (Center for Imaging Sciences, RIT), Professor Diane Dalecki (BME, UR), and Professor Denise Hocking (Pharmacology & Physiology, UR). The collaborative effort focuses on developing novel, ultrasound tissue characterization techniques for engineered tissues. This work is part of a larger project, led by Drs. Hocking and Dalecki and funded by the NIH, that aims to develop ultrasound-based technologies for the field of tissue engineering.

Dr. Helguera's laboratory is devoted to advancing multimodal imaging and materials characterization techniques. Over the years, she has developed a suite of nondestructive, ultrasound-based materials characterization techniques for non-biological materials, such as polymers, ceramics, and layered materials. Through this new collaborative effort, the novel approaches that Dr. Helguera has developed and implemented for ultrasound characterization of non-biological materials will be translated to characterize the biological properties of engineered tissues. We propose to extend and apply high frequency ultrasound-based, tissue characterization techniques to monitor non-invasively biological and structural properties of cells and extracellular matrix proteins within three-dimensional engineered tissues. NIH support for the next two years will allow Dr. Helguera to spend the fall semesters and part of her summers devoted full-time to the research project as a Visiting Scientist in the Dalecki lab at the UR BME department.

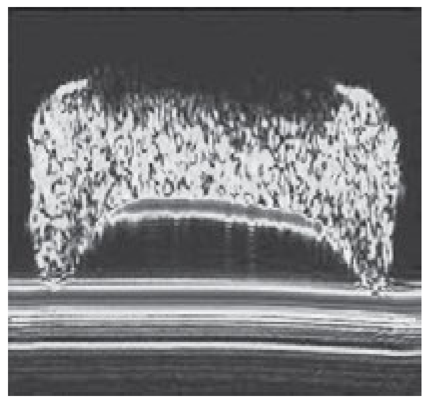


***Figure 1.*** *High-frequency ultrasound image of a three-dimensional engineered tissue.*

***Figure 2.*** *UR BME student Nicholas Berry performing imaging experiments with engineered tissues.*

## Studying biofilms with ultrasound

**Maria Helguera, PhD and Michael Pichichero, MD**

Center member Maria Helguera has established a new collaboration with Dr. Michael Pichichero, Director of the Rochester General Hospital Research Institute at Rochester General Hospital. The goal of the project is to determine if an innovative imaging technology can be developed to identify and subsequently destroy biofilms in medical devices. Intravascular and peritoneal catheter-related infections are a major cause of morbidity in hospitalized patients and considerably increase medical costs. Detection and disruption of microbial biofilms growing in medical devices is critical since bacteria become recalcitrant to antibiotic therapy. In this study, biofilms will be analyzed using high-frequency pulse-echo ultrasound to determine the feasibility of detecting and characterizing parameters such as biofilm thickness, viscosity, density, macrostructure and microstructure. These parameters are needed to understand image properties and design an efficient non-invasive protocol to identify, map the progression of the biofilm over time, predict the likelihood of catheter-related bacteremia, and disrupt these films.

## The University of Rochester/Pontificia Universidad Catolica del Peru Collaboration

**Amy Lerner, PhD, Benjamin Castañeda, PhD, and Scott Seidman, PhD**

The National Collegiate Inventors and Innovators Alliance (NCIIA) is funding *Collaborations for Healthcare in Developing Countries,* spearheaded by RCBU members Amy Lerner and Benjamin Castañeda. The international program between universities provides opportunities for students to work on biomedical engineering projects dedicated to enhancing health care in developing countries.

The goal of the program is to:

- Target urgent health needs established by the Peruvian Ministry of Health;
- Supplement the number of global-health related design teams in UR BME Senior Design course;
- Provide more realistic and innovative design experiences for PUCP students; and
- Build an infrastructure for collaborative experiences between international engineering students and healthcare providers.

Students travel between universities and are currently working on projects such as early detection of diabetic neuropathy, improved medical lighting, bedsore prevention, and automated tuberculosis processing techniques.

## Effects of ultrasound on microvessel tone

**Ingrid Sarelius, PhD, Denise Hocking, PhD, Diane Dalecki, PhD, Carol Raeman, AAS, and Patricia Titus, MS**

Vasodilation is a predominant microvascular response to tissue injury and provides nutritive blood flow to injured cells. A collaboration between Ingrid Sarelius (Pharmacology & Physiology, UR), Diane Dalecki (BME, UR), and Denise Hocking (Pharmacology & Physiology, UR) focuses on using ultrasound to noninvasively regulate arteriolar tone and increase blood flow to tissues. The guiding hypothesis is that ultrasound can noninvasively control the structure of the extracellular matrix resulting in localized vasodilation. Drs. Sarelius and Hocking recently demonstrated an important role for the extracellular matrix protein, fibronectin, in regulating vascular tone in an intact animal. Using intravital microscopy, they showed that extracellular matrix fibronectin fibrils function in vivo as mechanotransduction elements that couple skeletal muscle contraction with local vasodilation. Their data indicate that in the body, tensile forces from actively contracting skeletal muscle transiently expose a matricryptic site in fibronectin that triggers a nitric oxide-dependent increase in arteriolar diameter, providing the first evidence that extracellular fibronectin fibrils play a dynamic role in regulating arteriolar tone in vivo. Ongoing studies by the team of investigators aim to characterize and optimize the use of ultrasound fields to regulate arteriolar tone, and investigate whether the interaction of ultrasound and the extracellular matrix protein fibronectin mediates vasodilation in response to ultrasound.

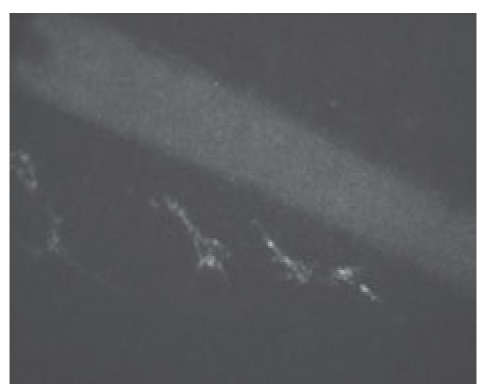


***Figure 1.*** *Intravital confocal microscopy shows that fluorescently-labeled fibronectin is rapidly taken up from the blood and assembled into fibrils within the connective tissue surrounding blood vessels.*

# TISSUE ELASTICITY CONFERENCE HIGHLIGHTS

**The Eighth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity** was held in Vlissingen, Zeeland, The Netherlands from September 14–17, 2009. Co-organized by Kevin Parker (RCBU past director), the annual conference provides an international forum for the advancement of knowledge and methods for the measurement and imaging of elastic properties of tissues with ultrasound.

RCBU members Marvin Doyley, Michael Richards, Sanghamithra Korukonda, Liwei An, Stephen McAleavey, and Ben Castañeda attended the conference and presented seven abstracts.

The University of Rochester's Dr. Kevin Parker, a cofounder of the conference, said, "The conference in Holland marks the eighth annual meeting on imaging the elastic properties of tissues, sponsored since inception by the RCBU and by the University of Texas, Houston by Professor Ophir. The field continues to grow in techniques, equipment, research results, and clinical trials, as evidenced by the full four-day schedule of the conference along with the global scope of participants."

In addition to posters, exhibits and abstract presentations, two tutorials were presented: *Elasticity Imaging: To Boldly Measure What No One Has Sheared Before* by Dr. Sinkus of the Laboratories Ondes at Acoustique in Paris, and *Elasticity Imaging Systems: How Do They Work and Where Are We Headed?* by Dr. Hall of the University of Wisconsin-Madison.

The Conference is conducted under the joint auspices of the University of Rochester Center for Biomedical Ultrasound and the Ultrasonics Laboratory in the Department of Diagnostic and Interventional Imaging at the University of Texas Health Science Center at Houston.

Next year's conference will be held at The Cliff Lodge Snowbird Ski and Summer Resort in Utah, USA from Saturday, October 16 through Tuesday, October 19, 2010. Please visit www.ElasticityConference.org for more information.

**The conference had 17 sessions, including:**

- *Clinical and Animal Applications – I*
- *Forward and Inverse Problems*
- *Methods for Imaging Elastic Tissue Properties – I*
- *Instrumentation*
- *Cardiovascular Elasticity*
- *Signal and Image Processing*
- *Mechanical Properties of Tissues*
- *Methods for Imaging Elastic Tissue Properties – II*
- *Clinical and Animal Applications – II*
- *Methods for Imaging Elastic Tissue Properties – III*
- *Clinical and Animal Applications – III*
- *Mechanical Properties of Tissues – II*
- *Signal and Image Processing – II*
- *Methods for Imaging Elastic Tissue Properties – IV*
- *Oral Presentations of Finalists for Student Awards Session*
- *Poster Session – Live Oral Summaries*
- *Tutorials*

# INNOVATION

The RCBU is continually advancing novel concepts in ultrasound technology. Recent news, and some of the patents that originated at the RCBU are summarized below. For more information, contact the University of Rochester Technology Transfer office at (585) 275-3998 or http://www.urmc.rochester.edu/technology-transfer/.

## U.S. Patents

- ***Real Time Visualization of Shear Wave Propagation in Soft Materials with Sonoelastography***
  U.S. Patent No. 7,444,875 issued to **Zhe Wu** and **Kevin J. Parker** on November 4, 2008
- ***Finite Amplitude Distortion-Based Inhomogeneous Pulse Echo Ultrasonic Imaging***
  U.S. Patent No. 7,104,956 issued to **Ted Christopher** on September 12, 2006
- ***System for Model-Based Compression of Speckle Images***
  U.S. Patent No. 5,734,754 issued to **Kevin J. Parker** on March 31, 1998
- ***Blue Noise Mask***
  U.S. Patent Nos. 5,111,310 (1992); 5,477,305 (1995); 5,708,518 (1998); 5,543, 941 (1996); and 5,726,772 (1998) issued to **Kevin J. Parker** and Theophano Mitsa
- ***Thin-Film Phantoms and Phantom Systems***
  U.S. Patent No. 5,756,875 issued to **Daniel B. Phillips** and **Kevin J. Parke**r on May 26, 1998
- ***System and Method for 4D Reconstruction and Visualization***
  U.S. Patent No. 6,169,817 issued to **Kevin J. Parke**r, Saara Totterman, and Jose Tamez-Pena on January 2, 2001
- ***The Acoustic Filter***
  U.S. Patent No. 5,334,136 issued to **Karl Schwarz, Richard Meltzer**, and Charles Church on August 2, 1994
- ***Multiple Function Infant Monitor***
  U.S. Patent No. 5,479, 932 issued to Joseph Higgins, **E. Carr Everbach**, **Kevin J. Parker** on January 2, 1996
- ***Apparatus for Bone Surface-Based Registration***
  U.S. Patent No. 6,106,464 issued to WA Bass, RL Galloway, Jr., CR Maurer, Jr, and RJ Maciunas on August 22, 2000
- ***Sonoelasticity Imaging Estimators***
  U.S. Patent No. 5,086,775, issued to **Ron Huang, Robert Lerner, and Kevin Parker** on February 11, 1992
- ***Butterfly Search Technique***
  U.S. Patent No. 5,419, 331 issued to S. Kaisar Alam and **Kevin J. Parke**r on May 30, 1995
- ***Smart Endotracheal Tube***
  U.S. Patent No. 5,785,051 issued to **Jack Mottley** and Randy Lipscher on July 29, 1998

## University of Rochester a Leader in Technology Commercialization

The University of Rochester is again rated as one of the best educational institutions in the nation for patent licensing revenue, according to the Association for University Technology Managers. The AUTM U.S. Licensing Activity Survey is an annual report of the technology transfer activity of top universities, research institutions, and teaching hospitals across the nation.

In 2008, the UR received over $72 million in royalty revenue for its patented technologies, ranking it ninth in the nation. For eight years in a row, the UR has ranked in the top ten among U.S. universities. The technological advances by members of the Rochester Center for Biomedical Ultrasound continue to contribute to the UR's success.

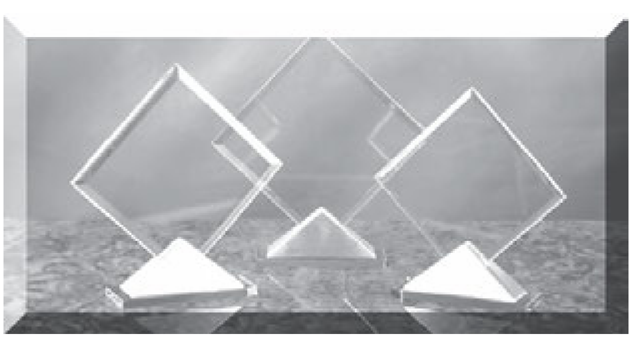
The University of Rochester Office of Technology Transfer protects the scientific and intellectual advances developed at the UR, and engages in activities to transfer these technologies into the private sector where they can benefit society. For more information, visit the University of Rochester Technology Transfer office at http://www.urmc.rochester.edu/ technology-transfer/.

# RCBU Awards

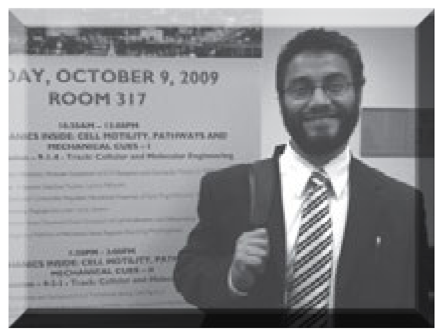
**Kelley Garvin,** a graduate student in the UR Department of Biomedical Engineering, won a Best Student Paper Competition at the 157th Meeting of the Acoustical Society of America held in Portland, OR. Her paper, titled "Ultrasound standing wave fields control the spatial distribution of cells and protein in three-dimensional engineered tissue," was recognized as the best student paper in the Biomedical Ultrasound/Bioresponse to Vibration Technical Section. She is developing technologies using ultrasound standing wave fields for the fabrication of engineered tissues with desired tissue characteristics. Her thesis research is co-advised by Dr. Dalecki and Dr. Hocking.

**Diane Dalecki,** associate professor of biomedical engineering and director of the RCBU, was elected a Fellow of the Acoustical Society of America. She was recognized by the society for her "contributions to the bioeffects of sound and ultrasound."

**Benjamin Castañeda** received *Premio a la Investigación PUCP 2009*, a research award from the Pontificia Universidad Catolica del Peru, for his publication *Prostate cancer detection using crawling wave sonoelastography*.



The University of Vermont hosted a special symposium in celebration of RCBU member **Dr. Wesley Nyborg's** fiftieth year in the Department of Physics, honoring his pioneering work in the field of physical acoustics and biomedical ultrasound. The Symposium consisted of a morning session of invited papers and an afternoon session of contributed papers related to Dr. Nyborg's research interests. The celebration continued with an evening banquet. Dr. Nyborg has been an honorary member of the RCBU since its inception in 1986. "The RCBU joins ultrasound researchers around the world in honoring Wes and his achievements over the years. His pioneering research has been an inspiration to many," said Diane Dalecki, Director of RCBU.




**Carlos Sevilla** was awarded a prestigious NIH Ruth L. Kirschstein National Research Service Award Individual Pre-doctoral Fellowship. This three-year award will provide funding for Carlos' thesis research project, titled "Promoting Chronic Wound Healing with Ultrasound and Fibronectin." Carlos is a graduate student in the Department of Biomedical Engineering and his thesis research is co-advised by Dr. Denise Hocking and Dr. Diane Dalecki. Carlos is investigating the ability of ultrasound to produce conformational changes in the extracellular matrix which, in turn, stimulate cellular processes important for accelerating wound repair.

**Richard Waugh,** Chair of the BME Department and RCBU member, was elected president of the Biomedical Engineering Society (BMES). The election announcement was made at the BMES annual meeting held in Pittsburgh, Pennsylvania in October.

# RCBU MEMBERS

## RCBU Remembers Edward L. Titlebaum

The RCBU lost a valued member when **Edward L. Titlebaum,** a Professor in the University of Rochester's Department of Electrical and Computer Engineering and a pioneer in mathematical communications theory and its application to radar and sonar, passed away at age 72.

Edwin Carstensen, Professor Emeritus and Founding Director of the RCBU, said, "Ed was a charter member of the RCBU. His work tended to the animal bioacoustics side of biomedical ultrasound. He made many contributions to the understanding of bat and dolphin sonar. Bats use a remarkably effective kind of frequency modulation to gain information that has value in the design of physical ultrasound detection and imaging systems. His work on dolphins for the Navy extended over many years. His interest in medical applications of communication theory extended up until his death."

After completing undergraduate studies in Electrical Engineering at Northeastern University and the Massachusetts Institute of Technology, Titlebaum attended Cornell University and earned his doctorate in Electrical Engineering in 1965. He joined the faculty of the Department of Electrical Engineering at the University of Rochester in 1964.

Titlebaum's scientific and academic career spanned five decades. His mathematical work in radar and sonar systems led to many widely employed improvements in naval sonar systems. He also explored echolocation in bats and whales and applied his insights from studying these naturally occurring sonars to improving man-made sonar systems. Among his other numerous contributions were the development of more precise electrocardiogram analysis methods and creating new music analysis and synthesis techniques. He had a lifelong passion for computers and computing, which led to his assuming the position of Vice Provost for Computing at the University of Rochester in 1996, a position that he held for several years before returning to research and teaching full-time.

He remained an active member of the department until his passing. He was primary advisor to numerous doctoral students and a highly regarded instructor in the classroom.

**Michael Richards, PhD** joined the University of Rochester Electrical and Computer Engineering Department as a post-doctoral fellow working in the lab of Marvin Doyley. His research is focused on developing and testing an advanced intravascular ultrasound for the diagnosis of atherosclerosis.

**Carol Raeman**, Technical Associate working in the laboratory of Professor Diane Dalecki in the Department of Biomedical Engineering, marked a milestone anniversary of 20 years of employment at the University of Rochester. Throughout her career at the UR, Carol has contributed significantly to our understanding of many topics in biomedical ultrasound.

**Vikram Dogra** was invited to work with Radiology Resident trainees at the Hacettepe University in Ankara, Turkey during his six-month sabbatical.

**Maria Helguera** began an appointment as a Visiting Scientist in the Department of Biomedical Engineering at the University of Rochester. This position facilitates her collaborations with Denise Hocking and Diane Dalecki on projects to develop ultrasound imaging and tissue characterization techniques for engineered tissues.

*Above: Rochester Institute of Technology's Center for Imaging Science*

# EDUCATION

The RCBU provides a rich environment for education and training in biomedical ultrasound. Students have access to state-of-the-art research facilities to engage in leading-edge research in ultrasound. Students can pursue advanced degrees in various engineering and basic science departments. The UR offers graduate-level courses in biomedical ultrasound and closely related fields. RCBU laboratories offer exciting opportunities for post-doctoral research in ultrasound and collaborations with other areas of biomedical ultrasound imaging and therapy.

## Training Completed

- **Karl Baum** completed his post-doctoral training in the laboratory of Maria Helguera PhD, at the Rochester Institute of Technology. Karl is now employed at 4Q Imaging in Rochester NY.

- **David Duncan** received his PhD degree in Electrical and Computer Engineering from the University of Rochester in May 2009. His PhD dissertation, titled, "The Use of Focused Beams with Unique Biomedical Ultrasonic Imaging Systems" was supervised by Robert C. Waag, PhD.

- **Benjamin Castañeda Aphan** received his PhD degree in Electrical and Computer Engineering from the University of Rochester in May 2009. His PhD dissertation, titled, "Extracting Information from Sonoelastographic Images" was supervised by Kevin J. Parker, PhD and Deborah Rubens, MD. Dr. Castañeda accepted a faculty position in the Department of Electrical Engineering at the Pontificia Universidad Catolica del Peru (PUCP) and was also appointed as the director of a newly created Medical Imaging Research Laboratory. In that capacity, he heads PUCP's new master's degree program in Signal and Digital Image Processing.

- **Stephanie Shubert** completed her MS in Imaging Sciences from the Rochester Institute of Technology. Her master's research titled, "Effect of Anisotropy on the High-frequency Ultrasound Backscatter of Simulated Nerve Fiber", was supervised by Maria Helguera, PhD.

## BME Senior Design Students Develop Ultrasound Needle Guidance System

At the University of Rochester, senior biomedical engineering students have the opportunity to help real-life customers solve bioengineering problems through a two-semester BME Senior Design course. Center member **Amy Lerner, PhD,** has developed and taught this nationally-recognized senior design course for many years. Student design teams work with their customer, under the supervision of a biomedical engineering professor and produce working prototypes at the end of their senior year.

In 2009, seniors Aaron Gelinne, Bo Wang, Andrew Bochenko, and Tony Broyld became interested in a problem presented by RCBU member **Paul Bigeleisen, MD,** from the URMC Anesthesiology Department, who described the need for a system to stabilize an ultrasound probe when inserting a needle into tissue. Working through the year, the student design team developed a system to address the clinical need for a more accurate and efficient system for needle guidance used in conjunction with ultrasound imaging. By stabilizing the patient, needle, and ultrasound probe, the system improves the efficiency of ultrasound-assisted procedures, such as the placement of local anesthesia or a catheter.

According to Dr. Bigeleisen, "Our design team created a very practical and useful needle guide for ultrasound guided procedures. In preliminary studies, it significantly shortened the time necessary to perform a vascular puncture on a phantom. It is a major improvement on anything available on the market at the present time."

# EDUCATION

### Biomedical Ultrasound (BME 251/451)

Presents the physical basis for the use of high-frequency sound in medicine. Topics include acoustic properties of tissue, sound propagation (both linear and nonlinear) in tissues, interaction of ultrasound with gas bodies (acoustic cavitation and contrast agents), thermal and non-thermal biological effects, ultrasonography, dosimetry, hyperthermia, and lithotripsy.

### Advanced Biomedical Ultrasound (BME 453)

Investigates the imaging techniques applied in state-of-the-art ultrasound imaging and their theoretical bases. Topics include linear acoustic systems, spatial impulse responses, the k-space formulation, methods of acoustic field calculation, dynamic focusing and apodization, scattering, the statistics of acoustic speckle, speckle correlation, compounding techniques, phase aberration correction, velocity estimation, and flow imaging.

### Medical Imaging–Theory and Implementation (ECE 452)

Provides an introduction to the principles of X-ray, CT, PET, MRI, and ultrasound imaging. The emphasis is on providing linear models of each modality, which allows linear systems and Fourier transform techniques to be applied to analysis problems.

### Fundamentals of Acoustical Waves (ECE 432)

Introduces acoustical waves. Topics include acoustic wave equation; plane, spherical, and cylindrical wave propagation; reflection and transmission at boundaries; normal modes; absorption and dispersion; radiation from points, spheres, cylinders, pistons, and arrays; diffraction; and nonlinear acoustics.

### MR Imaging: From Spins to Brains (BME 513)

Introduces the physics of magnetic resonance (MR) imaging and reviews its application to medical imaging. Provides a comprehensive background of the MR imaging technique and its application to medical or research issues. Discusses how the MR technique takes advantage of physiological principles and tissue structure to provide diagnostic images for clinicians and researchers. Introduces functional brain imaging and related issues in data analysis.

### Biosolid Mechanics (BME 483)

This course examines the application of engineering mechanics to biological tissues, including bone, soft tissue, cell membranes, and muscle. Other topics include realistic modeling of biological structures, including musculoskeletal joints and tissues, investigations of the responses of biological tissues to mechanical factors, and experimental methods and material models.

### Elasticity (ME449)

Presents an analysis of stress and strain, equilibrium, compatibility, elastic stress-strain relations, and material symmetries. Additional topics include torsion and bending of bars, plane stress and plane strain, stress functions, applications to half-plane and half-space problems, wedges, notches, and 3D problems via potentials.

### Nonlinear Finite Element Analysis (BME 487)

Examines the theory and application of nonlinear finite element analysis in solid and biosolid mechanics. Topics include generalization of FE concepts, review of solid mechanics, nonlinear incremental analysis, displacement-based FE formulation for large displacements and large strains, nonlinear constitutive relations, incompressibility and contact conditions, rubber-like materials, biomechanical materials, and solution methods.

### Biomedical Optics (BME 492)

Introduces the major diagnostic methods in biomedical optics. The course emphasizes spectroscopy (absorption, fluorescence, Raman, elastic scattering), photon migration techniques (steady-state and time-resolved), and high-resolution subsurface imaging (confocal, multi-photon, optical coherence tomography). Essential methods of multivariate data analysis are taught in the context of spectroscopy.

### Physiological Control Systems (BME 428)

Focuses on the application of control theory to physiological systems. Presents modern control theory in the context of physiological systems that use feedback mechanisms. Begins with an overview of linear systems analysis, including Laplace transforms and transfer functions. Discusses the response dynamics of open- and closed-loop systems such as the regulation of cardiac output and level of glucose, stability analysis, and identification of physiological control systems.

### Models and Simulations of Biomedical Systems (BME 267/467)

Introduction to analytical modeling and computational simulations of systems. Examples will include cardiovascular, respiratory, muscle, neural and population models. Analytical models for several physiological systems will be studied, and simulations will be written in Matlab.

All courses are not offered each semester. See the University of Rochester Undergraduate and Graduate Bulletins for more information.

## 2009 PUBLICATIONS

**Duncan DP,** Astheimer JP, **Waag RC.** Scattering calculation and image reconstruction using elevation-focused beams. J Acoust Soc Am. 125: 3101-19; 2009.

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Grace D, Thornburg LL, Grey A, **Ozcan T, Pressman EK.** Training for percutaneous umbilical blood sampling during Maternal Fetal Medicine fellowship in the United States. Prenat Diagn. 29: 790-3; 2009.

Hovinga KR, **Lerner AL.** Anatomic variations between Japanese and Caucasian populations in the healthy young adult knee joint. J. Orthop Res. 27: 1191-6; 2009.

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**Rao NA,** Lai D, **Bhatt S,** Arnold SC, Chinni B, **Dogra VS.** Acoustic lens characterization for ultrasound and photoacoustic C-scan imaging modalities. Conf Proc IEEE Eng Med Biol Soc. 2177-80; 2009.

Thornburg LL, Christensen N, Laroia N, **Pressman EK.** Prenatal diagnosis of total arhinia associated with normal chromosomal analysis: A case report. J. Reprod Med. 54: 579-82; 2009.

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Tretheway D, Gebhardt JG, **Dogra VS,** Schiffhauer LM. Metastatic versus primary oncocytic papillary adenocarcinoma of the endometrium: A report of a case and review of the literature. Int J. Gynecol Pathol. 28: 256-61; 2009.

Turgut AT, Odev K, Kabaalioglu A, **Bhatt S, Dogra VS**. Multitechnique evaluation of renal hydatid disease. Am J. Roentgenol. 192: 462-7; 2009.

## 2009 PRESENTATIONS

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Antos L, Heneka P, Luquette B, McGee B, Nguyen D, Phipps A, **Phillips D, Helguera M.** Development of a novel 3-D optical molecular system incorporating structured illumination technology. Proceedings of the 2009 IEEE/IS&T Western New York Image Processing Workshop, 2009.

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**Dalecki D, Child S, Raeman C.** Lung hemorrhage produced by exposure to underwater acoustic impulses. Presented at the 157th Meeting of the Acoustical Society of America, Portland, OR, May 2009.

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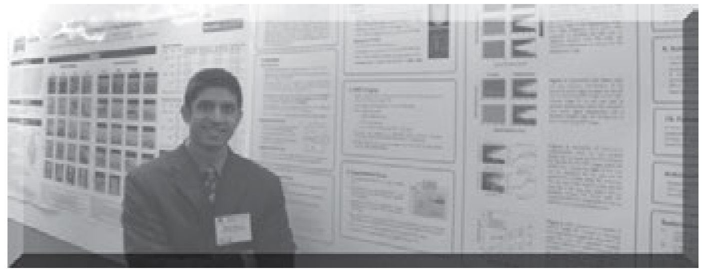

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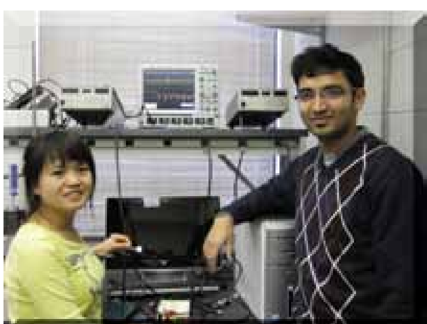
# Graduate Training Opportunities in Biomedical Ultrasound at the RCBU

**The Rochester Center for Biomedical Ultrasound (RCBU)** provides exciting opportunities for graduate and post-graduate research and training in the field of biomedical ultrasound. Research at the RCBU spans a wide range of topics in diagnostic imaging and therapeutic applications of ultrasound. With access to RCBU laboratories at the University of Rochester's River Campus, Hajim School of Engineering and Applied Sciences, UR Medical Center, and Rochester Institute of Technology, students can tailor their own interdisciplinary training experiences. Students can pursue advanced degrees (M.S. and Ph.D.) through various departments of engineering and basic science with a research focus in biomedical ultrasound.

A wide range of relevant course offerings complements the rich research environment. Students tailor their formal coursework individually to complement their research focus and meet requirements of their home department.

The Ultrasound Journal Club is attended by an interdisciplinary group of students and faculty interested in biomedical applications of ultrasound.

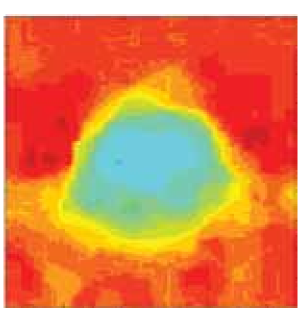


The RCBU has a long history of innovation in biomedical ultrasound. Research of student members of the RCBU has led to numerous patents in ultrasound imaging and therapy.

Students have access to state-of-the-art research facilities to engage in leading-edge research in ultrasound. Core facilities in the new Goergen Hall include an ultrasound teaching laboratory, imaging and bioinstrumentation equipment, cell and tissue culture facilities, biomedical microscopy equipment, and mechanical testing apparatus.

## Research Areas and Graduate Training Opportunities

RCBU laboratories are advancing the use of ultrasound in diagnosis and discovering new therapeutic applications of ultrasound, including:



- Diagnostic imaging
- Sonoelastography and elasticity imaging
- 3D and 4D ultrasound imaging
- Acoustic radiation force imaging
- Harmonic imaging
- Nonlinear acoustics
- Novel therapeutic applications
- Biological effects of ultrasound fields
- Tissue characterization
- Ultrasound technologies in cell & tissue engineering
- Acoustic scattering and wave propagation in tissue
- Ultrasound contrast agents
- Acoustic cavitation
- High frequency imaging
- Lithotripsy
- Multi-modal imaging techniques
- Doppler ultrasound
- High intensity focused ultrasound (HIFU) techniques

**For additional information please see www.urmc.rochester.edu/rcbu**

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