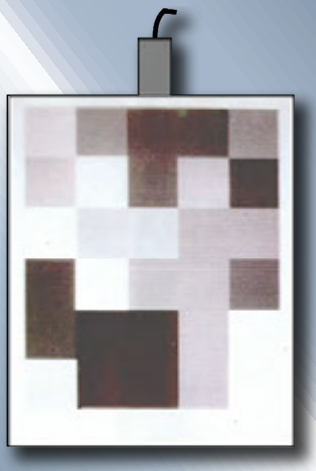

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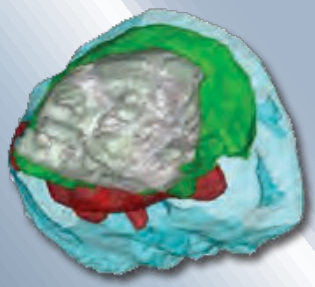
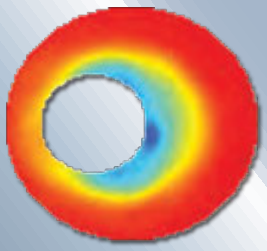
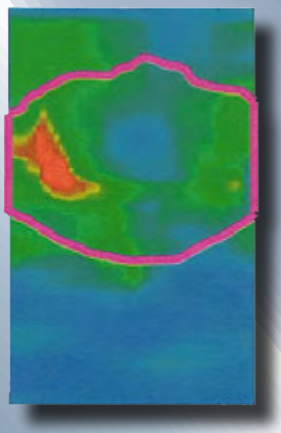
# Rochester Center for Biomedical Ultrasound







## 2010 Annual Report

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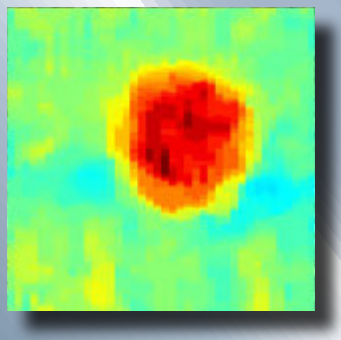

# On the cover

## *Images on the front cover recognize over 20 years of innovation in imaging the elastic properties of tissue at the Rochester Center for Biomedical Ultrasound.*

***A recent review article, titled "Imaging the elastic properties of tissue: The 20 year perspective'" by RCBU members Kevin J. Parker, Marvin M. Doyley, and Deborah J. Rubens, provides a comprehensive summary of the international evolution of the field of elastographic imaging from basic physics and engineering, through the development of major elastographic imaging approaches, to updates on clinical trials, and a look forward to the future of elastographic imaging (Phys. Med. Biol. 2011).***

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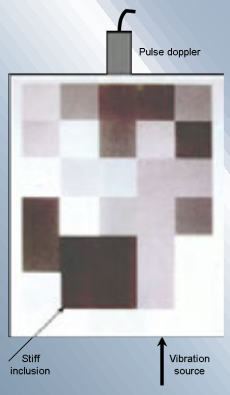
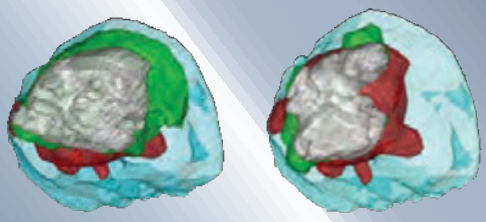
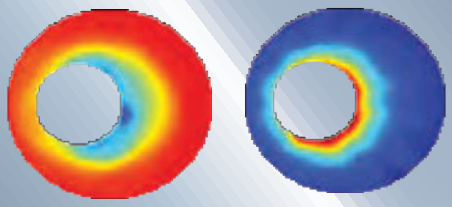



Schematic reconstruction of the first known image of the relative hardness of materials based on Doppler ultrasound signals. The image covers approximately 7 cm vertical x 5 cm horizontal. The figure was first published by Dr. Robert Lerner and Professor Kevin J. Parker in 1987. (Courtesy of Professor Kevin J. Parker)

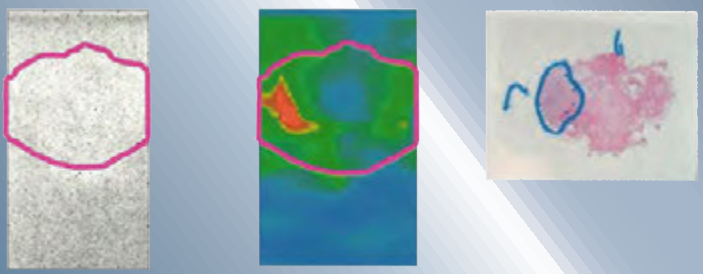
Comparison between sonoelastographic volumes and histology for ex-vivo (a) and in-vivo (b) data. In both cases the deficit found by sonoelastography is shown in green, the tumor outlined in histology is shown in red, and the intersection of sonoelastography and histology is shown in white. (Courtesy of Professor Benjamin Castaneda and Professor Kevin J. Parker)



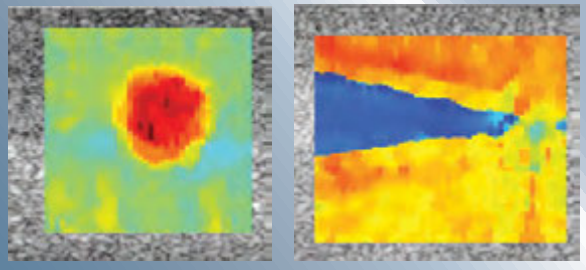
Radial (left) and circumferential (right) strain elastograms obtained from a heterogenous vessel phantom containing a soft plaque using a sparse array ultrasonic elastography imaging system. (Courtesy of Professor Marvin M. Doyley)



Corresponding B-mode (left), shear speed estimates from crawling waves (center), and histological (right) images of a cross-section close to the apex of a human prostate gland. The boundary of the gland is shown in pink. The shear speed image shows a region with elevated shear speed on the left side of the cross-section that corresponds to a cancerous region in the histological image. (Courtesy of Professor Benjamin Castaneda and Professor Kevin J. Parker)



Spatially Modulated Ultrasound Radiation Force (SMURF) imaging, invented by Professor Stephen McAleavey. Shear modulus images with SMURF imaging of (left) a stiff spherical inclusion in a soft background and (right) a soft conical inclusion within a stiff phantom. (Courtesy of Professor Stephen A. McAleavey)



2010

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***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**
***Provost:*** **Ralph W. Kuncl, MD, PhD**
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# FROM THE DIRECTORS

## Diane Dalecki, PhD, Director

This year's annual report summarizes progress from RCBU laboratories across diverse topics in biomedical ultrasound imaging and therapy. The illustrations on the cover of this report highlight 20 years of progress in imaging the elastic properties of tissue by laboratories at the RCBU. Early sonoelastography techniques originated at the RCBU, and today multiple RCBU laboratories continue to advance the development of various elasticity imaging techniques. Included within this report are highlights of innovations in sonoelastography, crawling waves, spatially modulated ultrasound radiation force imaging (SMURF), and new elasticity imaging techniques that employ intravascular ultrasound.

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 Ninth 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 elasticity imaging techniques, ultrasound technologies 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. Educational advances, as well as special awards and achievements by RCBU members and students, are summarized within this annual report. We welcome your comments on any of the enclosed reports.

## Deborah J. Rubens, MD, Associate Director

The Imaging Sciences Ultrasound Department experienced more than 15% growth in exam and patient volumes in 2010; performing examinations on 17,800 patients. The unit continued to expand its clinical coverage; adding more sonographer positions to manage the increased demand.

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. Internationally, Dr. Rubens lectured at Cambridge University in England and Dr. Dogra in Uganda and Guyana. Dr. Bhatt participated in the creation of the Maintenance of Certification examination for the American Board of Radiology, and Drs. Rubens, Bhatt, Voci and Dogra have all been ABR Ultrasound oral examiners.

Dr. Dogra, along with international colleagues, founded Medical Imaging Partnership, (MIP). MIP is a non-profit organization engaged in providing medical imaging equipment, training, and education in medical diagnostic imaging to developing countries around the world.

Dr. Rubens continued her research with the BME Department in collaboration with General Electric and Rensselaer Polytechnical Institute on the NIH funded grant, *3D Prostate Cancer Imaging Based on "Crawling Wave" Excitation*, to create and assess a novel 3D imaging scanner applied to prostate cancer. Investigations with elastography have expanded from the prostate to evaluation of thyroid cancer, with Dr. Jonathon Walsh of ENT, and to assessment of hepatic steatosis and fibrosis with Dr. Christopher Barry from the liver transplant program. 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. Dr. Mark Frampton, from Pulmonary Medicine, is beginning a clinical trial using ultrasound of the brachial artery to assess pulmonary response to environmental toxins. Clinical parameters for this trial will be assessed by the URMC ultrasound division.

# 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 is a leader 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 Hajim School of Engineering and Applied Sciences, 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***

# 2010 RESEARCH

Research laboratories of RCBU members are advancing the use of ultrasound for diagnosis and therapy. The pages that follow highlight research accomplishments in 2010. Selected publications and presentations of this year can be found on pages 27–29.

## Shear wave induced phase encoding (SWIPE)

**Stephen A. McAleavey, PhD and Vhabiv Kakkad**

Shear Wave Induced Phase Encoding (SWIPE) is a new ultrasonic imaging method under development in our laboratory. SWIPE generates images similar to conventional B-scan imaging, but uses a fundamentally different method to form the image. Conventional ultrasound imaging faces a resolution/depth of penetration tradeoff, wherein deep targets must be imaged at a lower frequency, and hence poorer resolution, than shallow targets. Preliminary results have shown that the lateral resolution obtained with SWIPE is not fixed by the ultrasound frequency used, allowing SWIPE to overcome the resolution/penetration tradeoff. We hypothesize that SWIPE has the potential to generate clinically useful images in situations where conventional methods are inadequate. Applications where low frequency ultrasound (0.5-2 MHz) is required for adequate penetration appear most likely to benefit from SWIPE, as B-scan lateral resolution is relatively poor due to the large ultrasound wavelengths involved (0.75-3 mm).

In the SWIPE method, low-frequency shear (transverse) waves are propagated through the object to be imaged (the "target"), such that the wave induces motion of ultrasound scatterers towards and away from the ultrasound transducer. This motion induces a phase shift of the echo associated with each scatterer. We have shown that, by propagating shear waves spanning a range of frequencies through the target and collecting ultrasound echo data at each shear wave frequency, the shear wave induced phase shift of the ultrasound echo signal may be used to reconstruct the lateral variation in target echogenicity at a given range. As in conventional ultrasound imaging, range is estimated from time-of-flight. SWIPE forms images of target echogenicity even with an entirely unfocused ultrasound transducer. The lateral resolution obtained with SWIPE is not fixed by ultrasound wavelength, but is limited only by shear wave frequency range and SNR considerations.

Undergraduate student Vhabiv "V" Kakkad has worked on laboratory experiments to demonstrate the feasibility of SWIPE. Using pulse-echo RF data acquired with a single element of a 6 MHz linear array, V has used SWIPE to reconstruct images of nylon monofilament targets, as well as hyperechoic inclusions in gelatin phantoms. Figure 1 is a representative example. Our work on this topic most recently appeared in IEEE UFFC in a paper titled "Ultrasonic backscatter imaging by shear-wave-induced echo phase encoding of target locations" in January 2011.

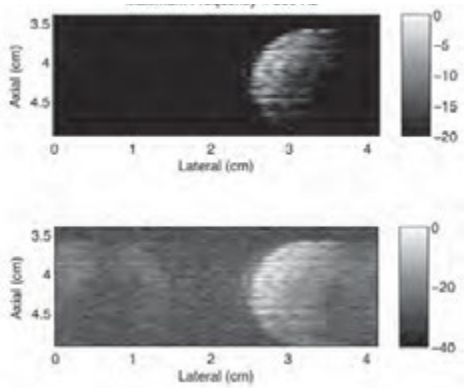



***Figure 1:*** *SWIPE image of a gelatin phantom containing a hyperechoic cylindrical inclusion, displayed with 20 dB (top) and 40 dB (bottom) dynamic range.*

## Cell patterning in engineered tissue using ultrasound standing wave fields

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

Controlling the spatial organization of cells within engineered tissue constructs is one of the major challenges facing the field of tissue engineering. The Dalecki and Hocking laboratories have developed an ultrasound standing wave field (USWF) technology to address this challenge. Acoustic radiation forces associated with USWF can actively move cells in suspension into multicellular bands that are perpendicular to the direction of sound propagation and that are spaced at half-wavelength intervals. To maintain

this USWF-induced banded distribution of cells after removal of the sound field, cells were suspended in an unpolymerized collagen type-I solution, and polymerization of the collagen solution into a gel was allowed to occur during USWF exposure. Using this technology, collagen-based engineered tissues with various spatial patterns of cells have been fabricated by our team. Figure 1 shows images of different types of cell patterns created within collagen constructs using our USWF technology. Low USWF temporal average intensities resulted in loosely clustered, planar cell bands throughout collagen gels (panel A). Increasing the temporal average intensity led to the formation of more densely packed cell bands localized to gel centers (panel B). The spacing between adjacent cell bands was controlled by altering the frequency of the USWF where an increase in the frequency resulted in decreased spacing between adjacent cell bands (panel C). In recent investigations, two acoustic sources situated perpendicular to each other were used to produce a grid pattern of cells within the collagen gel (panel D). In related work, the extracellular matrix protein fibronectin was co-localized to cell bands by binding fibronectin to the cell surface prior to USWF exposure. In this way, the spatial distribution of proteins, and other biologically active molecules, can be controlled using USWF technology. Taken together, our data demonstrate that USWF technology can be used to fabricate engineered tissue with several different spatial patterns of cells and cell-bound proteins.

As a further illustration of the versatility of our USWF technology for cell patterning, various mammalian cell types have been organized using this strategy. Myofibroblasts, a cell type important in the contraction of healing wounds, and endothelial cells, a cell type important in new blood vessel formation, were organized into banded patterns within collagen-based engineered tissue. In both cases, enhancements in cell function were observed following cell banding when compared to sham-exposed gels containing a homogeneous cell distribution. Aligning myofibroblasts into loosely aggregated planar cells bands enhanced cell contractility and cell-mediated extracellular collagen matrix remodeling. Organizing endothelial cells into tightly packed cell bands accelerated the formation and maturation of lumen-containing, capillary-like endothelial cell sprouts within the collagen gels (see related story on page 17). Therefore, not only is USWF technology a promising new strategy to control cell spatial distribution in engineered tissue, but USWF-patterning can stimulate key cell functions within engineered tissues.

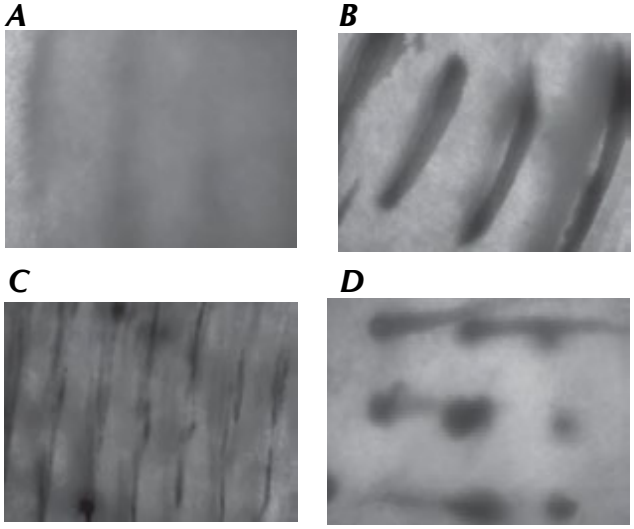



***Figure 1:*** *Various spatial patterns of cells within three-dimensional collagen-based engineered tissue created using USWF technology. Planar bands at 1 MHz (A & B), 2 MHz (C), and a grid produced by two perpendicular 1 MHz sources (D).*

## Dynamics of microbubbles in vessels

**Sheryl M. Gracewski, PhD, Neo Jang, MS**
**Aaron Zakrzewski, and Christina Rossi**

Motivated by various clinical applications of ultrasound contrast agents within blood vessels, the dynamic behavior of one, two, and three bubbles in a compliant tube were studied analytically, numerically, and experimentally. Because forcing bubbles at resonance can increase the desired response in many applications (e.g., ultrasound-assisted drug/gene delivery or bubble assisted micro-mixing), recent efforts of Professor Gracewski and Neo Jang, ME graduate student, were focused on investigating the effects of bubble interactions and tube stiffness on a bubble's natural frequency. A lumped parameter model for a five-degree-of-freedom system was developed, accounting for the compliance of the tube and coupled response of the two bubbles (see Figure 1 on next page). The results were compared to those produced by two different simulation methods: 1) an axisymmetric coupled boundary element and finite element code, and 2) finite element

models developed in COMSOL Multiphysics. Experimental results were obtained using a scaled model (see Figure 2). For the simplified case of two bubbles in a rigid tube, the lumped parameter model predicts two frequencies for in- and out-of-phase oscillations, in good agreement with both numerical simulation and experimental results. For two bubbles in a compliant tube, the lumped parameter model predicts four non-zero frequencies, each asymptotically converging to expected values in the rigid and compliant limits of the tube material. During the summer of 2010, Christina Rossi, an NSF REU recipient, and Aaron Zakrzewski, a UR/Xerox Undergraduate Fellow, completed the experiments and numerical simulations, respectively.

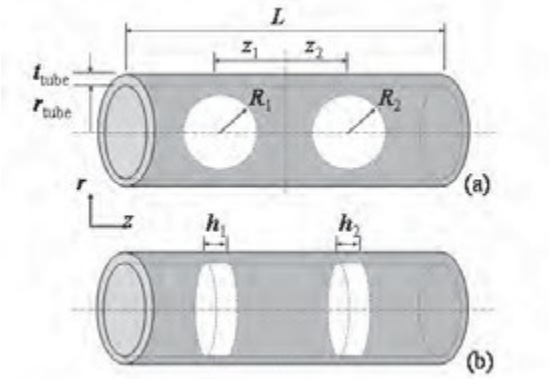



***Figure 1:*** *(a) Schematic diagram for two bubbles in a tube, showing bubble radii, $R_1$, $R_2$, bubble positions with respect to center of the tube, $z_1$, $z_2$, tube inner radius, $r_{tube}$, tube thickness, $t_{tube}$, and tube length, L. (b) Each spherical bubble is replaced with a cylindrical body of equal volume and radius equal to tube inner radius, so that the width of the $i^{th}$ cylindrical bubble is $h_i = \frac{4R_i^3}{3r_{tube}^2}$*

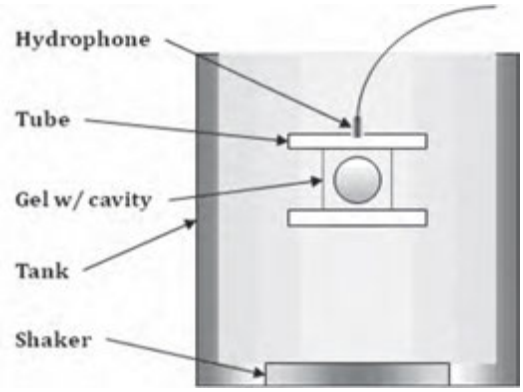



***Figure 2:*** *Schematic of the experimental exposure chamber showing one bubble inside a compliant tube immersed in water. The shaker was swept through a range of frequencies to excite the bubbles. A hydrophone, placed through a hole at the mid-span of the tube, was used to measure the pressure field around the bubble(s). The bubble resonance frequencies were identified by the peaks in the pressure versus frequency plot.*

## High-frequency ultrasound characterization of biofilms

**Maria Helguera, PhD, Karla Hatfield, Kunal Vaidya, and Michael Pichichero, MD**

Center member Maria Helguera and Dr. Michael Pichichero from the Rochester General Hospital Research Institute are investigating the use of ultrasound for biofilm characterization. The purpose of this project is to launch a systematic study to investigate the feasibility of high-frequency ultrasound as an in vivo biofilm imaging technology and therapeutic tool. The ultimate goal of this study is to develop a high frequency, pulse-echo ultrasound system to non-invasively image and characterize biofilms in children during nasopharyngeal (NP) colonization with potential otopathogens, and during acute ear infections (acute otitis media, AOM). This project focuses on biofilms grown in vitro on coverslips, and then on NP and middle ear epithelial cells, 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 over time, and differentiate between single-species and multiple-species biofilms. Preliminary experiments to test techniques have used non-typeable Haemophilus influenzae NTHi. Characteristic results at 50 MHz are shown for a single A-line (Figure 3). Currently, the Helguera lab is developing analysis methods that include quantitative evaluation of the integrated backscatter to estimate effective scatter size, and statistical analyses of the backscatter signal for quantitative characterization of the biofilms, such as differences in maturity and possible characteristic signatures depending on species present in the biofilm.

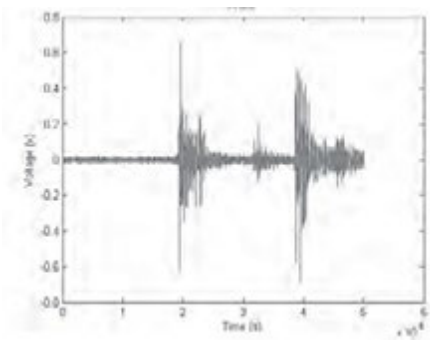


***Figure 3:*** *Representative A-line showing the backscatter of a biofilm, coverslip and bottom of dish where the biofilm was grown. The signal at 2–3.5 μs corresponds to backscatter from biofilm and coverslip.*

## A model-based approach to IVUS elastography using soft priors

**Michael Richards, PhD, and Marvin Doyley, PhD**

Cardiovascular disease, and in particular atherosclerosis, is the cause of approximately 1 in 3 deaths in the United States. The study of arterial plaque mechanics is essential to the detection and monitoring of vulnerable plaque. Intravascular ultrasound (IVUS) is a common diagnostic tool used in the monitoring of the disease and IVUS elastography (IVUSe) is a method in development for studying plaque mechanics. Mechanical properties, such as Young's modulus, can be estimated from IVUSe measured deformations by solving the linear elastic inverse problem. Current IVUSe inversion techniques use B-mode based segmentations and geometric parameter lumping to constrain the solution and improve the inherent ill-posedness of the inverse problem. The Doyley lab has developed a novel, soft prior based inverse reconstruction algorithm to quantify the Young's modulus of arterial tissue imaged with IVUS. This algorithm uses segmentation information in the reconstruction; however, it is imposed as a penalty rather than a constraint to allow for imperfect segmentations.

Studies were performed to characterize the accuracy of the inverse approach. Simulated US images were created of a finite-element modeled deforming material and the images were used to measure the deformation field. Figure 1(a) shows the Young's modulus distribution used to create the underlying deformation. Figures 1(b) and 1(c) show the soft-prior reconstructed Young's modulus found using no a priori segmentation and a 2-region segmentation, respectively. The plots below each modulus image show the modulus amplitude through the annulus shown in 1(a). In vitro studies were also performed using a tissue mimicking phantom and a commercially available IVUS scanner (Boston Scientific). Figure 2(a) shows an US image of a two-region arterial mimicking phantom and two Young's modulus reconstructions, one using no a priori segmentation information 2(b) and one using two regions as defined by manual segmentation of the US B-mode image 2(c). These results suggest that inclusion of segmentation information, even incomplete segmentations, improve the algorithm's ability to reconstruct accurate modulus distributions.

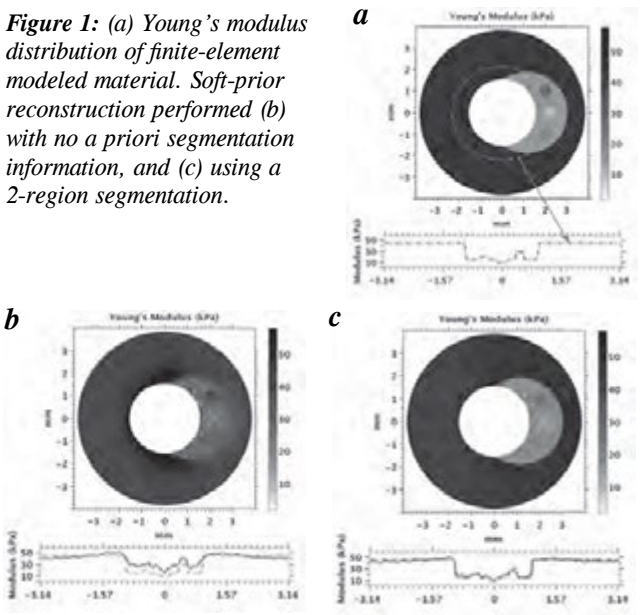



***Figure 1:*** *(a) Young's modulus distribution of finite-element modeled material. Soft-prior reconstruction performed (b) with no a priori segmentation information, and (c) using a 2-region segmentation.*

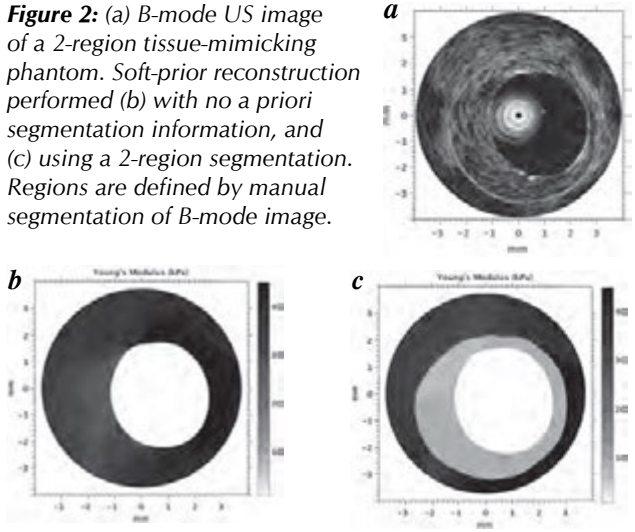



***Figure 2:*** *(a) B-mode US image of a 2-region tissue-mimicking phantom. Soft-prior reconstruction performed (b) with no a priori segmentation information, and (c) using a 2-region segmentation. Regions are defined by manual segmentation of B-mode image.*

## Improving crawling wave detection of prostate cancer

**Liwei An, PhD, Zaegyoo Hah, PhD, Yong Thung Cho, PhD, Bradley Mills, S Mao, L Baxter, L Kushner, J Yao, Deborah J. Rubens, MD, John Strang, MD, Kevin J. Parker, PhD**

The crawling wave (CrW) technique for local tissue shear velocity estimation was recently introduced into the sonoelastographic field. The Parker lab has applied this technique to depict the elastic properties of biological tissues including radiofrequency ablated hepatic lesions in vitro, human skeletal muscle in vitro, and excised human prostate. A recent study was undertaken to establish a protocol based on CrW sonoelastography to detect prostate cancer.

In this study, the whole prostate gland

was obtained after radical prostatectomy and embedded in a 10.5% gelatin mold. Two vibration sources were positioned at each side of the mold with an ultrasound transducer scanning from the top of the cross-section under observation. The gland was imaged at three positions (apex, mid-gland and base) at three vibration frequencies (100, 120 and 140 Hz) with a small frequency offset between the sources. The average shear velocity estimation over three frequencies was obtained by globally selecting and averaging the highest 90% of the data ranked by correlation coefficient. The tumor regions were then segmented using a semi-automatic region-growing segmentation technique. The sites for the three cross-sections were marked, and the corresponding histological slices were obtained, which provided the ground truth of cancer distribution.

Results indicated the ability of the shear velocity estimator to distinguish prostate cancer from normal tissue and that the approach based on CrW sonoelastography can be adapted to detect prostate cancer. The segmentation of the cancerous region was in approximately the same position as the outline of the tumor on the histological slice. The shear wave velocities of cancerous and non-cancerous tissues were 3.71 $\pm$ 0.20 m/s and 2.38 $\pm$ 0.24 m/s, respectively. The elastic contrast was 1.56, similar to the ratio found in prostate cancer by mechanical testing.

## Enhanced detection by statistical modeling of targets

**Michael Sealander, MS and Stephen McAleavey, PhD**

In clinical ultrasound, many pathologically relevant reflective targets are spread in range causing multiple reflections. These reflections can have significantly degrading effects on target detection. When the resolution of these reflections is less diagnostically relevant than accurately learning the presence or absence of the target itself, the range-spread nature can be incorporated into the signal processing algorithms enhancing the probability of detection. We have derived optimum receivers, the form of which is familiar to the radar literature, based on statistical models of targets and the surrounding speckle suitable to an ultrasound framework and continue to investigate the detection/resolution tradeoffs involved.

In addition to range-extended targets, interrogation signals can undergo additional distortion traditionally unaccounted for while propagating, including from inhomogeneous media, multipath returns, frequency dependent attenuation, and nonlinear propagation effects. Such effects represent formidable obstacles in the adoption of coded waveforms, widely used for decades in radar/sonar environments to improve both resolution and detection performance. We have developed a signal coding scheme using waveforms suitable to a clinical ultrasound machine that is self-adaptive to these distortions that could significantly enhance system

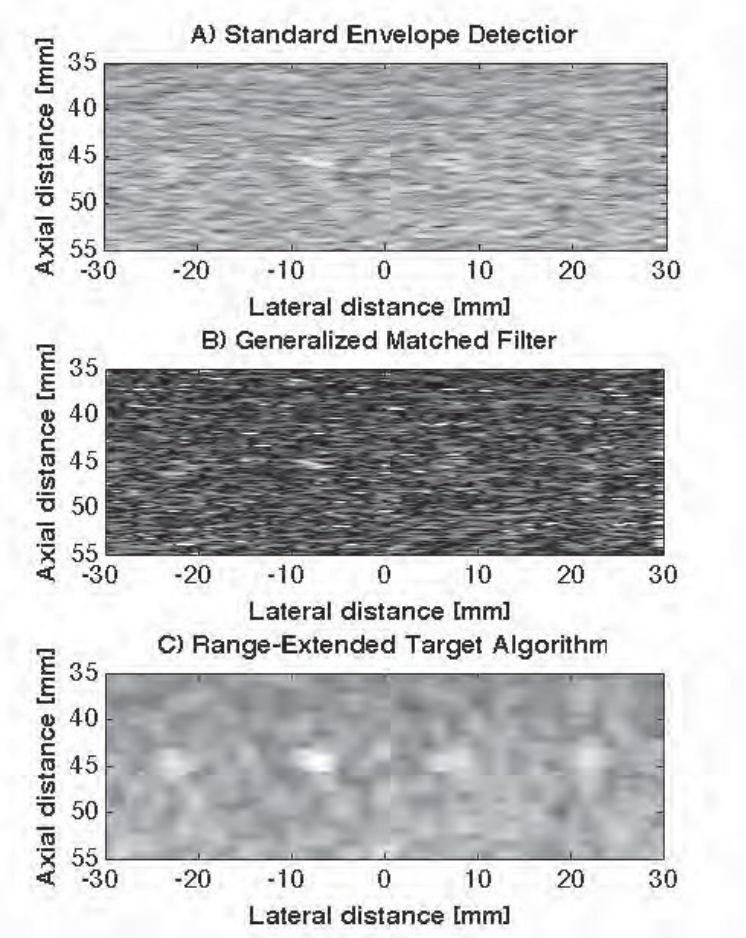



***Figure 1:*** *Three images of the same phantom simulated using Field II. The phantom contains four 2-mm radius range-extended targets containing small-amplitude reflectors relative to the speckle background: A) uses standard envelope detection, B) uses a generalized matched filter, and C) uses an algorithm matched to range-extended targets of the same size.*

## 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 our facility at Red Creek Drive. The total number of examinations was 12,780, including 10,619 obstetric, and 2,261 gynecological scans. Invasive procedures included 213 amniocenteses for karyotype or lung maturity, 109 chorionic villus samplings, and 135 sonohysterograms and 25 other procedures including OR guidance for minor gynecological procedures, intracardiac KCL injections or cyst aspirations. Interpretation of ultrasound examinations at FF Thompson Hospital are continued utilizing a combination of telemedicine and onsite service. 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. Examples of ongoing research projects are provided below.

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

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

The aim of this project is to investigate the impact of pelvic floor muscle contraction on the labor and delivery outcomes. The 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 are included in the study. Three dimensional ultrasound volume data sets are obtained 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 peripartum urinary and fecal dysfunction rates.

### Evaluation of the presence of a subchorionic hematoma on first trimester ultrasound and midtrimester transvaginal cervical length: A retrospective cohort

**Erin M Lemcke-Berno RDMS, MPH and David Hackney MD**

Both first trimester intrauterine events and a decreased second trimester cervical length have been associated with an increased risk of subsequent spontaneous preterm birth. However, potential associations between the two have not yet been previously explored. The objective of this study was to determine if first trimester subchorionic hematomas (SCHs) or self-reported vaginal bleeding was associated with a subsequent decrease cervical length at 16-20 weeks. Retrospective cohort of all patients with both a second trimester transvaginal cervical length and first trimester ultrasound at the University of Rochester ultrasound department over a six-month period during which screening cervical lengths were obtained in all patients undergoing anatomic surveys. Cervical lengths were compared in subjects with or without a SCH and/or clinical vaginal bleeding and adjusted for potential confounders. 353 ethnically diverse subjects fulfilled the inclusion criteria, of whom 40 had a first trimester SCH, 53 reported an episode of first trimester vaginal bleeding and 18 had both. There were no significant differences in cervical length for subjects with or without a SCH ($p = 0.42$), clinical bleeding ($p = 0.23$) or both ($p = 0.38$). Linear regression did not identify any statistically significant associations between intrauterine bleeding and cervical length when adjusted for confounders.

Analyses did not validate our hypotheses. There were no significant associations between the presence of a first trimester subchorionic hematoma and second trimester cervical shortening, or with bleeding of any type and cervical length. Thus, the two preterm birth risk factors appear to be independent of one another, and the increased risk of preterm delivery associated with early bleeding is not mediated through cervical shortening.

## Bioeffects of underwater acoustic impulses

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

Underwater impulsive sound fields are employed in the ocean for both commercial and military applications. Sponsored by the U.S. Naval Submarine Medical Research Laboratory (NSMRL), the Dalecki lab investigated the effects of low frequency, underwater acoustic impulses on biological systems. For these investigations, underwater acoustic impulses were produced with an air gun source system (Figure 1). 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 were used to generate underwater acoustic impulses for our bioeffects investigations.

Through a collaborative project, the Dalecki lab and Hydroacoustics, Inc. (HAI) investigated 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 the 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, the response of lung to acoustic impulses with peak acoustic pressure amplitudes ranging from ~0-110 kPa was investigated. It was 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 collaborated with the laboratory of John Olschowka, Ph.D. (Neurobiology and Anatomy) to study the effects of underwater acoustic impulse fields on the mammalian brain and spinal cord. The results of this work are relevant to establishing safety guidelines for swimmers and divers exposed to underwater sound fields.

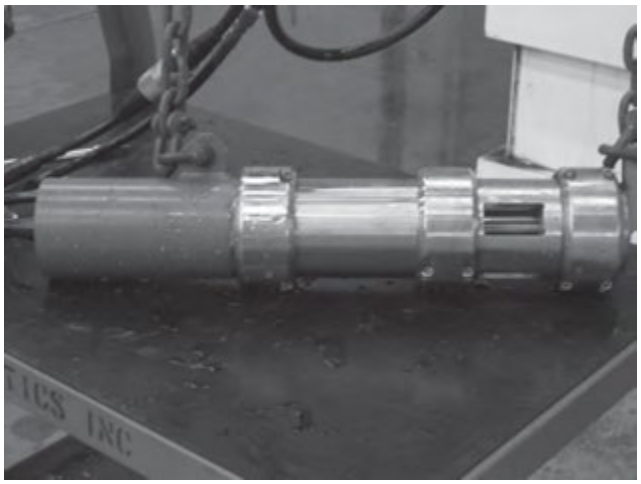


***Figure 1:*** *Air gun source used for investigations of bioeffects of underwater acoustic impulses.*

## Synthesis and analysis of crawling waves generated from radiation force

**Zaegyoo Hah, PhD, Christopher R. Hazard, PhD, Deborah J. Rubens, MD, Kevin J. Parker, PhD**

Conventional crawling waves (CR waves) are formed by the interference pattern of two continuous sinusoidal excitations with small frequency differences. Advantages of CR waves are ease of imaging using conventional color Doppler scanning and well-posed estimation of local elastic properties of tissues and lesions. However, with radiation force from the ultrasound beam acting as the excitation source, the resulting vibration will be more pulsatile in time and space. Recent work in Professor Kevin Parker's lab has applied a synthesis scheme to create the sinusoidal interference and, therefore, CR waves over a range of frequencies.

A GE Logiq 9 ultrasound system was modified to collect the data required to generate the synthetic acoustic radiation crawling wave displacement time histories. A special research scan sequence format was developed. Complex baseband demodulated data (IQ) were stored for offline processing. The sampling rate of the IQ data was 10 MHz. The duty cycle of the overall

scan sequence was maintained at less than 0.5% to avoid thermal limits of the components. IQ data were processed to extract displacements. The displacements were further processed to generate CR waves. One such frame is shown in Figure 1. Two types of phantoms were made and scanned with the modified Logiq 9 system: a gelatin phantom with an inclusion, and a fatty phantom with 30-50% oil. The displacement data for each of the phantoms were used to generate CR waves and further analyzed to estimate local shear speed. It was confirmed that CR waves with displacements below 10 microns can be generated with radiation force induced by an ultrasound beam. The study demonstrated the methods to generate CR waves with radiation force from ultrasonic beams and showed results of CR waves synthesized from the measurement of phantoms.

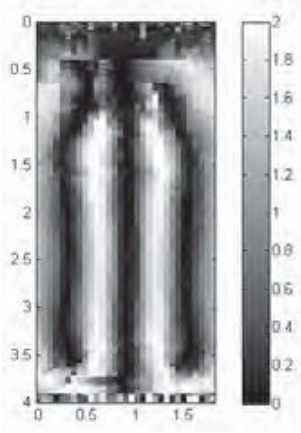



***Figure 1:*** *A frame of CR wave synthesized from left and right displacement data.*

## Effects of ultrasound on microvessel tone

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

A collaborative project between the laboratories of 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. Vasodilation is the predominant microvascular response to tissue injury and provides nutritive blood flow to injured cells.

Reports in the literature indicate that vasodilation can occur in response to ultrasound. However, the mechanism underlyling this phenomenon is currently unknown. Our guiding hypothesis is that ultrasound can noninvasively control the structure of the extracellular matrix resulting in localized vasodilation. In recent work, Drs. Sarelius and Hocking demonstrated dynamic roles for the extracellular matrix protein, fibronectin, in regulating vascular tone in an intact animal. Using intravital microscopy, they have shown that extracellular matrix fibronectin fibrils function in vivo as mechanotransduction elements that couple skeletal muscle contraction with local vasodilation. Specifically, 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. Their studies point to the possibility that in the body, tensile forces from actively contracting skeletal muscle extend extracellular matrix fibronectin fibrils and "open" matricryptic III-1 sites to modulate blood flow.

Ongoing studies by the team of investigators are using intravital microscopy of the murine cremaster muscle to study the effects of ultrasound exposure on microvessel tone in vivo. Ultrasound sources have been specially designed to integrate with intravital microscopy instrumentation. Initial studies are performed at 1 MHz. A series of investigations aim to characterize and optimize the use of ultrasound fields to noninvasively regulate arteriolar tone. Related studies are investigating the role of the interaction of ultrasound and the extracellular matrix protein fibronectin.

## Image registration software

**Maria Helguera, PhD, Karl G. Baum, PhD, and Patrick Ravines, PhD**

The Helguera Lab, in collaboration with Karl Baum of 4Q Imaging and Patrick Ravines of the George Eastman House International Museum of Photography, is developing new approaches to image registration. This project aims to develop techniques to visually document, and generate a baseline or benchmark of condition, of the daguerreotypes of Southworth and Hawes at the George Eastman House International Museum of Photography & Film. Various imaging modalities such as high-resolution scans using modified flat-bed scanners, and full frame digital cameras with special lighting arrangements for high dynamic range (HDR), ultra-violet A (UVA) fluorescence, and axial specular imaging have been developed and refined to capture the fine surface features of daguerreotypes. The accumulation of a wide range of visual information of daguerreotypes from the various imaging modalities led to the development of an open source image registration program for multimodality image comparison. The affine transform registration algorithm is based on user-defined point pairs between two images that are used to describe the displacements between them. After correcting for image shearing, rotation, scaling and translation the images can be compared side-by-side or layered on top of each other. The Helguera Lab is applying these image registration techniques to the analyses of images in other fields of study, including tissue engineering and medical imaging. The software is freely available and can be downloaded from this address: http://www.cis.rit.edu/research/biomedical/projects/daguerreotypes.html

## Ultrasound thin film polymer characterization

**Maria Helguera, PhD, Todd Fernández, MS, and Benjamin Varela, PhD**

Advances in materials science have led to significantly improved novel materials, often with useful and advanced engineering properties. One specific category of these materials is known as polymer-layered systems. These materials contain repeating layers of thin film polymers that form a single thicker polymer matrix. By tailoring the specific materials, individual layer thicknesses, and number of layers, it is possible to specifically tune the properties for a specific application. This leads to new challenges in analyzing the different combinations, yet provides an almost limitless array of polymer combinations that are adjustable to application-specific properties for a large number of purposes. The Helguera lab is currently developing a method for experimentally determining the viscoelastic properties of thin film polymers and periodic layered thin film polymer stacks using ultrasound, as well as developing a model of ultrasonic propagation in thin multilayered polymers.

## Ultrasound characterization of three-dimensional engineered tissues

**Nicholas Berry, BS, Karla Mercado, MS, Sally Z. Child, MS, Maria Helguera, PhD, Denise C. Hocking, PhD, and Diane Dalecki, PhD**

This collaborative project among RCBU members focuses on developing novel, ultrasound tissue characterization techniques for engineered tissues. The overarching goal is to develop high frequency ultrasound-based, tissue characterization techniques to monitor non-invasively the biological and structural properties of cells and extracellular matrix proteins within three-dimensional engineered tissues. A series of experiments this year investigated three focused transducers operating at 5-, 15-, and 30-MHz. The spatial and spectral beam characteristics of the acoustic sources were determined experimentally. Three-dimensional engineered tissues were fabricated by suspending varying concentrations of normal human dermal neonatal fibroblasts in collagen. Studies investigated different interrogating frequencies and cell concentration. An example image at 15 MHz is shown in Figure 1 (next page). Analyses of backscatter coefficient and echo statistics were employed to quantify differences in cell concentrations. High frequency ultrasound was also employed to monitor cell migration within collagen gels and the extent of collagen gel contraction. Results indicate that high frequency ultrasound is an advantageous technology for quantitatively characterizing and monitoring engineered tissues because it offers non-invasive, non-destructive, and real-time imaging capabilities.

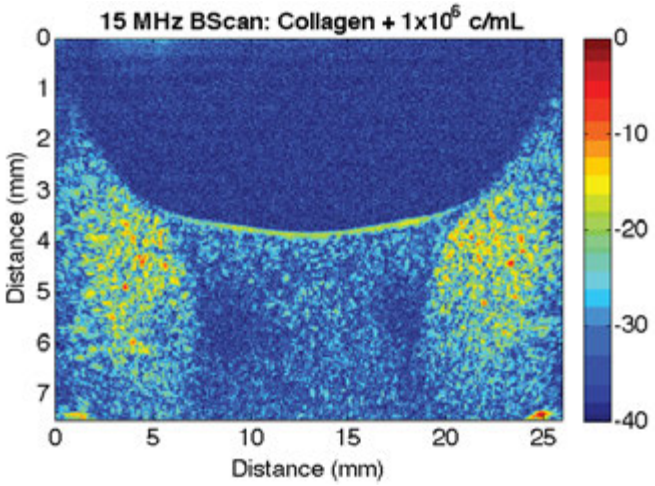



***Figure 1:*** *High frequency (15 MHz) ultrasound image of a three-dimensional engineered tissue. Cell migration to the periphery of the sample is evident.*

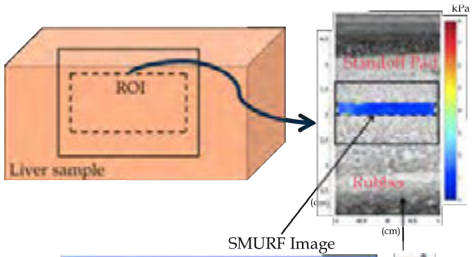



***Figure 2a:*** *Image of the SMURF set-up.*

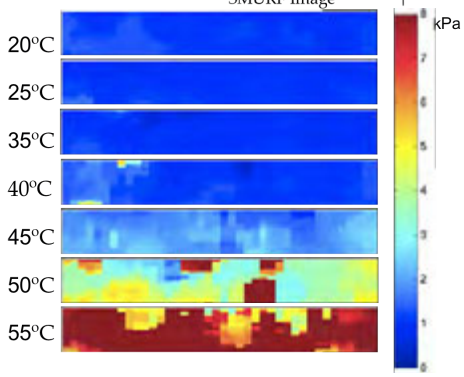



***Figure 2b:*** *SMURF images of a porcine liver sample at different temperature points during the experiment.*

## Measurement of thermally-induced variation in liver shear modulus

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

The process of tissue necrosis and coagulation as a result of thermal ablation is characterized by changes in the stiffness of the tissue. These changes are not discernible in a B-mode image, thus making standard ultrasound images inadequate for monitoring ablation processes. Spatially modulated ultrasound radiation force (SMURF) imaging is an elastographic technique that determines the shear modulus of a material by using acoustic radiation force impulses to generate shear waves of a known distance apart, and using motion-tracking techniques to measure the arrival time difference of the induced shear waves, allowing estimation of shear wave velocity. In a recent study from the McAleavey lab (Figure 2), fresh porcine liver samples were submerged in 0.9% saline and thermally ablated in a water bath from 10-70°C, while monitoring the progressive stiffening using SMURF. Thermal lesions were also induced in excised samples of porcine liver using a 2-cm RF ablation electrode. The samples were ablated for 52 minutes with an average power of 5W while monitoring the changes in stiffness using SMURF. The results show that SMURF imaging is effective in determining the shear modulus in liver tissue and in monitoring changes in the tissue stiffness. This study also indicated that between approximately 45-75°C there is a rapid increase in the rate of stiffening as a function of temperature.

## Self-assembled microtissues as a model system to assess ultrasound-induced conformational changes in extracellular matrix proteins

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

Wound healing is a tightly regulated process that requires the coordination of temporal and spatial signals from cells and extracellular matrix proteins, such as fibronectin, to restore tissue integrity. Disruptions in the healing process can lead to non-healing chronic wounds that can impair quality of life or result in death. It has been suggested that the observed defects in chronic wound healing are due to impaired extracellular matrix reorganization. The Hocking and Dalecki laboratories are investigating whether mechanical forces associated with ultrasound are capable of triggering conformational changes in extracellular matrix proteins that in turn promote chronic-wound healing. The research team has developed a model of self-assembled microtissues by combining compliant, polymerized collagen substrates with the cell-mediated assembly of fibronectin matrix fibrils. Fibronectin matrix assembly induced cell proliferation and the formation of three-dimensional (3D) cellular structures on polymerized collagen. Cells assembled into cellular structures with tall ($\sim 50\ \mu$m) dome-like central cores surrounded by cells that extended onto the collagen substrate. Dome-like central cores contained non-proliferating cells that associated with a pericellular form of fibronectin matrix. In contrast,

cellular extensions at the base of the tissue body contained proliferating cells and a fibrillar form of fibronectin matrix characterized by rope-like fibronectin-collagen bundles that extended onto the underlying substrate. Figure 1 is an immunofluorescence image captured using two-photon microscopy showing fibronectin (white) and collagen (blue) in 3D microtissues. Ongoing studies in the Hocking and Dalecki labs are using 3D self-assembled microtissues as a model system to test whether ultrasound can modify cellular behaviors by altering the conformation of the extracellular matrix.

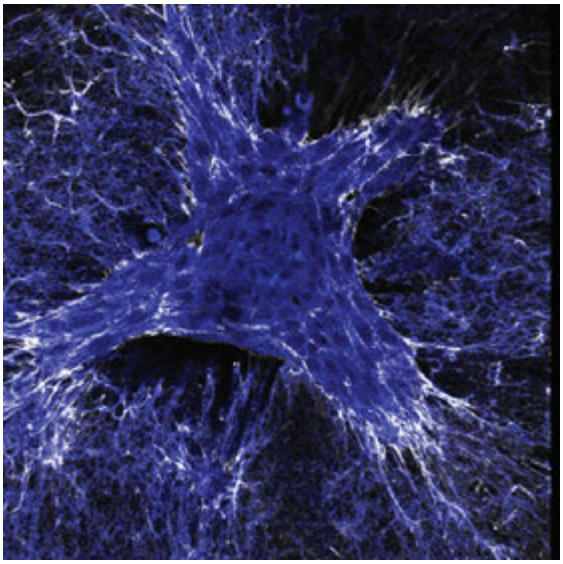


***Figure 1:*** *Immunfluorescence image captured using two-photon microscopy showing the spatial organization of fibronectin (white) and collagen (blue) within three-dimensional microtissues.*

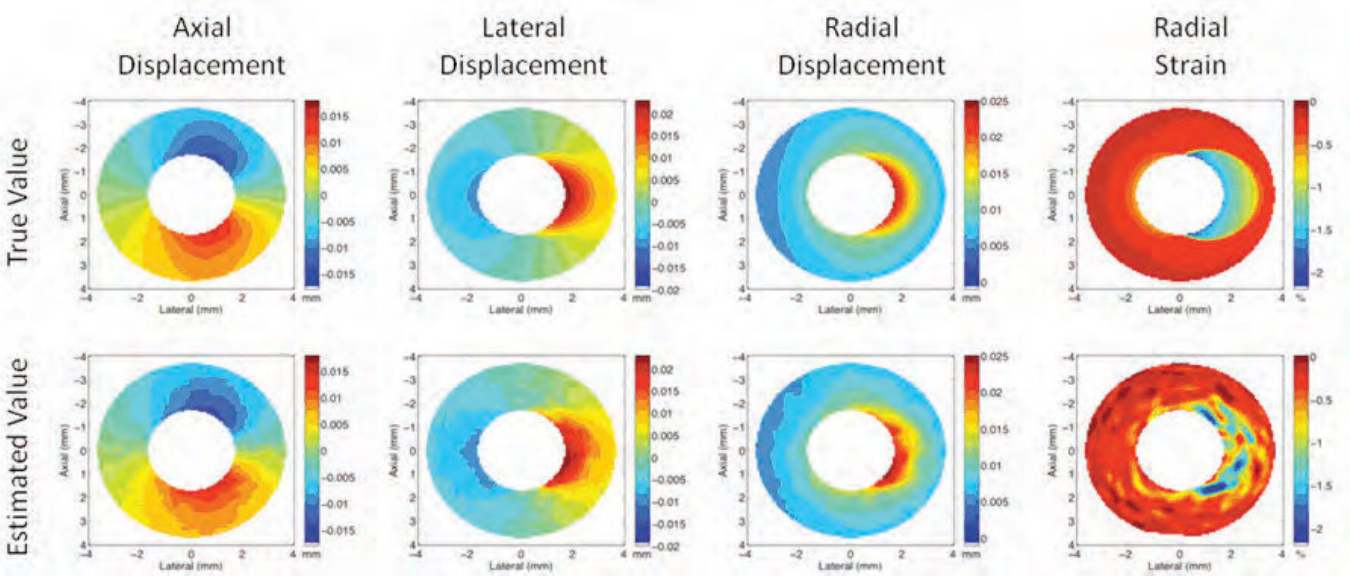
## Displacement estimation of the carotid artery using synthetic aperture imaging

**Sanghamithra Korukonda, MS, and Marvin M. Doyley, PhD**

Plaques can be classified as being either stable or unstable based on their mechanical properties. The Doyley lab is working to develop ultrasound elastography to provide relative estimates of shear modulus within the carotid artery based on strain elastograms. Recent studies assessed the utility of synthetic aperture (SA) method for elastographic imaging of the carotid artery. A mechanical model of a cross-section of a carotid artery (outer and inner radii of 4 mm and 1.5 mm, respectively) containing a soft plaque was constructed. The simulated artery contained three regions, as illustrated in Figure 1 (at right): a normal vessel wall, a lipid pool and a thin fibrous cap. A Young's modulus value of 100 kPa, 25 kPa, and 125 kPa was assigned to the normal vessel wall, the lipid pool and the fibrous cap, respectively. Additionally, all regions were assumed to be nearly incompressible (i.e., Poisson's ratio of 0.495 for all regions). The internal tissue displacements were computed by solving the forward elasticity problem using a commercially available finite element code, Abacus/CAETM, with an intraluminal pressure difference of 5 mmHg. Synthetic aperture scans were generated with a 128 element linear array (center frequency 5 MHz and sampled at 40 MHz) simulated using Field II. SA images were reconstructed by numerically adding coherent wave fronts at each location within the image. The internal tissue displacements were estimated by performing cross-correlation analysis on the simulated radiofrequency (RF) echo frames obtained at different intraluminal pressures. To assess the performance of the proposed method under realistic experimental conditions, experiments were conducted on elastographically homogeneous and inhomogeneous gelatin-based vessel phantoms. All echo imaging was performed using a SONIX RP ultrasonic imaging system (Ultrasonix, Richmond, BC, Canada) that was equipped with L14–5/38 128 element linear transducer array, and the vessel was pressurized using a simple water column system. It was apparent from the simulation results (Figure 2, next page) that cross-correlation analysis of synthetic aperture data provided good estimates of both the axial and lateral displacements within the simulated carotid artery. Over a 3x reduction in the RMS error was obtained when compared to lateral estimates obtained from conventional linear array simulation data. Similar observations were made in experimental studies with synthetic aperture data. Synthetic aperture imaging is a promising technique to produce high-resolution elastograms of the carotid. As the carotid is a surface vessel, it does not suffer from the depth of penetration and low SNR issues that SA imaging is susceptible to. As part of future work, the Doyley lab will implement this acquisition in real time without incurring motion artifacts.

***Figure 1:*** *Stiffness model of the carotid artery with a soft plaque.*

***Figure 2:*** *Results obtained from simulation of imaging a carotid artery model with Synthetic Aperture Imaging. The simulated vessel has a soft plaque with a hard fibrous cap. The top row shows the actual values for axial, lateral and radial displacement, followed by true radial strain values. The bottom row displays the corresponding estimated values that compare favorably with the true values.*

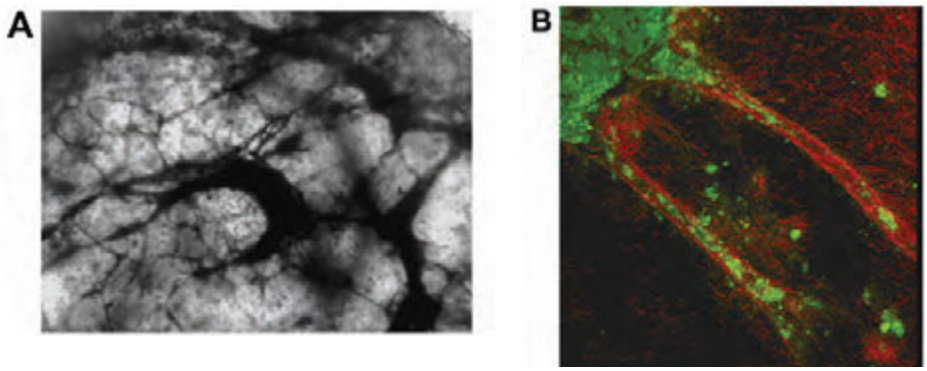



## Using ultrasound standing wave fields to vascularize three-dimensional engineered tissue

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

One of the major obstacles preventing tissue engineers from growing replacement tissues and organs in the laboratory is the need to create a vascular system within the tissue to maintain cell viability and function. The Dalecki and Hocking laboratories have developed ultrasound standing wave field (USWF) technology as a novel strategy to rapidly vascularize engineered tissues. Using acoustic radiation forces associated with USWF, endothelial cells were organized into multicellular planar bands within three-dimensional collagen-based engineered tissue (see related story on pages 6-7). Endothelial cells are the cells that line the lumen of all blood vessels and are the primary cell type involved in new capillary formation. Following USWF-induced cell organization, the formation and maturation of capillary-like sprouts was monitored over time within the collagen gels and compared to sham-exposed constructs which were characterized by a homogeneous cell distribution. USWF exposure accelerated the formation of endothelial cell sprouts where multiple sprouts were observed only 1 day after ultrasound exposure. In contrast, sham constructs did not contain endothelial cells sprouts until day 4. The maturation of endothelial cell sprouts in USWF-exposed collagen gels also occurred more rapidly than in sham gels. By day 6, sprouts in USWF-exposed constructs had elongated and formed interconnections with other sprouts and neighboring cell banded areas indicating the formation of anastomosing networks within these gels. In contrast, sprouts in sham constructs failed to elongate to the same extent as USWF-exposed sprouts and only some interconnections between sprouts were observed by day six. Ten days following USWF exposure, anastomosing networks were comprised of thick, vascular structures found throughout the entire volume of the three-dimensional collagen gel (Figure 1). Any endothelial cell networks found in sham-exposed collagen gels at day 10 were

***Figure 1:*** *(A) USWF exposure results in the rapid formation of extensive vascular networks (dark stain) within collagen-based engineered tissue. (B) Second harmonic generation microscopic image showing endothelial cell sprouts emerging from a cell banded area (green) into the surrounding collagen matrix (red).*



concentrated to the gel periphery and were absent from gel centers indicating an uneven distribution of network formation within these constructs. Histological analyses confirmed the presence of lumen within the multicellular endothelial cell sprouts found in USWF-exposed collagen gels. Interestingly, the original USWF-induced cell bands become lined by elongated endothelial cells as early as day 4, indicating the formation of large lumen areas with smaller, branching capillary-like structures emerging from them. This vascular-tree like network formation was absent in sham constructs. Taken together, these data demonstrate that USWF exposure results in the rapid and extensive vascularization of collagen-based engineered tissue. Minimizing the time to tissue vascularization, and ultimately blood perfusion, maximizes the likelihood for cell survival. Therefore, our novel application of USWF technology provides a promising new strategy to vascularize engineered tissue for the field of tissue engineering.

## Method for minimizing the effect of catheter eccentricity & intravascular ultrasound elastography

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

Each year, over 750,000 Americans experience an acute coronary syndrome or sudden cardiac death when a life-threatening atherosclerotic plaque ruptures in the later stages of coronary atherosclerosis. To determine the propensity of atherosclerotic plaque rupture, the Doyley lab is developing ultrasound techniques to measure the mechanical properties of atherosclerotic plaque. One method that intravascular ultrasound (IVUS) elastography visualizes the radial strain is by performing cross-correlation analysis on radio frequency (RF) echo frames obtained at different intraluminal pressures. Although radial strain correlates well with the intrinsic tissue, artifacts will occur when the vessel and catheter coordinate systems are misaligned. The goal of recent work in the Doyley lab was to develop a mapping method for reducing the effect of catheter eccentricity. In this work, the catheter eccentricity problem was modeled as a simple translation between two polar coordinate systems. Note that by knowing the radial and circumferential displacement, a closed form expression can be derived that can be used to map the displacement fields measured in one coordinate system (i.e., the catheter) to the other coordinate system (i.e., the vessel coordinate system). To demonstrate the algorithm, simulation studies were conducted with the displacement field obtained from different eccentric locations. Figure 1 shows radial strain elastograms obtained when the catheter was at different locations in an elastically homogeneous vessel, before and after coordinate systems were realigned. Strain artifacts are apparent in the elastograms computed in the catheter coordinate system, which was minimized by mapping the displacement field to the vessel coordinate system before computing radial strain. Figure 2 shows radial strain elastograms obtained for different IVUS catheter locations in an elastically inhomogeneous vessel model. Again, artifacts incurred when radial strain was computed in the catheter coordinate system; however, this problem was circumvented by computing strain in the vessel coordinate system. The method can reduce artifacts incurred from catheter eccentricity by mapping radial displacements measured in the catheter coordinate system to the vessel coordinate system using knowledge of radial and circumferential displacement obtained from a non-rigid image registration method.

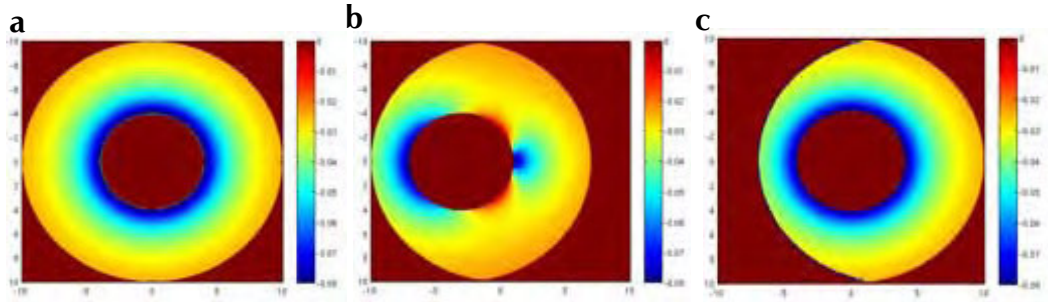



***Figure 1:*** *(a) Radial strain of an elastically homogeneous vessel observed from the vessel coordinate system. (b) Strain elastogram calculated from measured displacement field with catheter 3 mm off center. (c) Strain elastogram calculated from correct displacement field.*

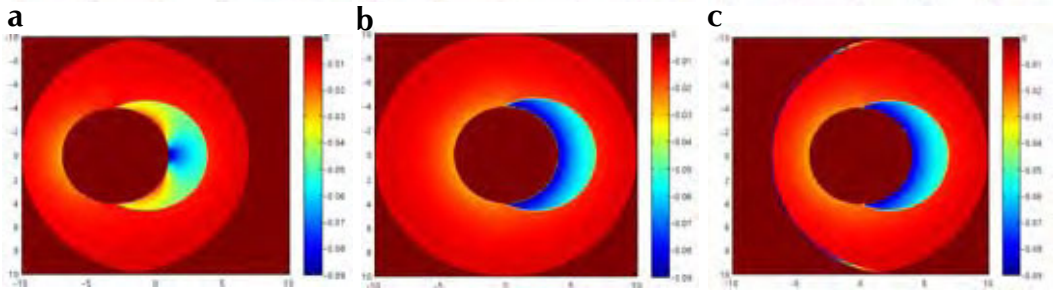



***Figure 2:*** *(a) Radial strain of an elastically inhomogeneous vessel with respect to the vessel center. (b) Strain elastogram calculated from measured displacement field with catheter 3 mm off center. (c) Strain elastogram calculated from correct displacement field.*

## Visualizing atherosclerotic plaques using ultrasound contrast agents and IVUS

**Marvin M. Doyley, PhD, Himanshu Shekar MS, John Allen, PhD, and Joshua Rychak, PhD**

Acute coronary syndromes may occur when life-threatening atherosclerotic plaques rupture in the later stages of advance cardiovascular disease. Coronary angiography is currently the gold standard for assessing the severity of coronary disease; however, its efficacy is questionable. The Doyley laboratory has developed a prototype intravascular ultrasound (IVUS) system to assess the functional properties (i.e., inflammation or angiogenesis or both) of atherosclerotic plaques and the arterial wall. In recent work, flow studies were conducted to assess the nonlinear acoustic behavior of a novel perflourocarbon ultrasound contrast agent, Targestar, at high-transmit frequencies (30 and 40 MHz). Pulsatile flow studies were conducted with vessel phantoms. The subharmonic responses of targeted and non-targeted contrast agents were measured. The fundamental and subharmonic signals were compared in absolute and relative terms using paired t-tests. Subharmonic imaging IVUS improved the visualization of the plaque relative to the main vessel, and the subharmonic behavior of the bubbles compared favorable to theoretical expectations.

## Interactions of underwater sound fields and mammalian lung

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

Underwater sound over a broad frequency range can be produced from a variety of sources including sonar systems and underwater blasts. 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 have supported recent projects in this area. 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. We have investigated the response of murine lung to underwater sound exposure for frequencies spanning ~100 Hz to 1000 kHz. Using several different acoustic systems we have developed the capability to generate acoustic fields at frequencies of 100 Hz to 10 MHz within the laboratory setting. All systems are designed to easily accommodate exposure of small lab animals to the sound fields in vivo. Sheryl Gracewski has developed both analytical and computational models to predict the acoustic fields within the exposure chambers of our experimental acoustic systems.

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. A series of experiments were performed to determine the roles of exposure timing parameters on sound-induced lung damage for exposure at the lung resonance frequency. Through several experimental tests, we have demonstrated that sound-induced lung hemorrhage can occur for exposure durations as short as 1 s. 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.

# RCBU FUNDING NEWS

**Robert Waag** was awarded a grant from the NIH for the project titled "Estimation and Correction of Ultrasound Beam Aberration Caused by Breast." The objective of the project is to form significantly improved ultrasonic images throughout the volume of the breast by using adaptive focusing that compensates for tissue aberration.

**Maria Helguera** received funding for her project titled "High-Frequency Ultrasound Characterization of Biofilms". The purpose of this project is to systematically investigate the feasibility of high-frequency ultrasound as an in vivo biofilm imaging technology and therapeutic tool. Dr. Helguera also received a CFC Center for Imaging Science Innovative Research Grant to support an undergraduate research student on a related project.

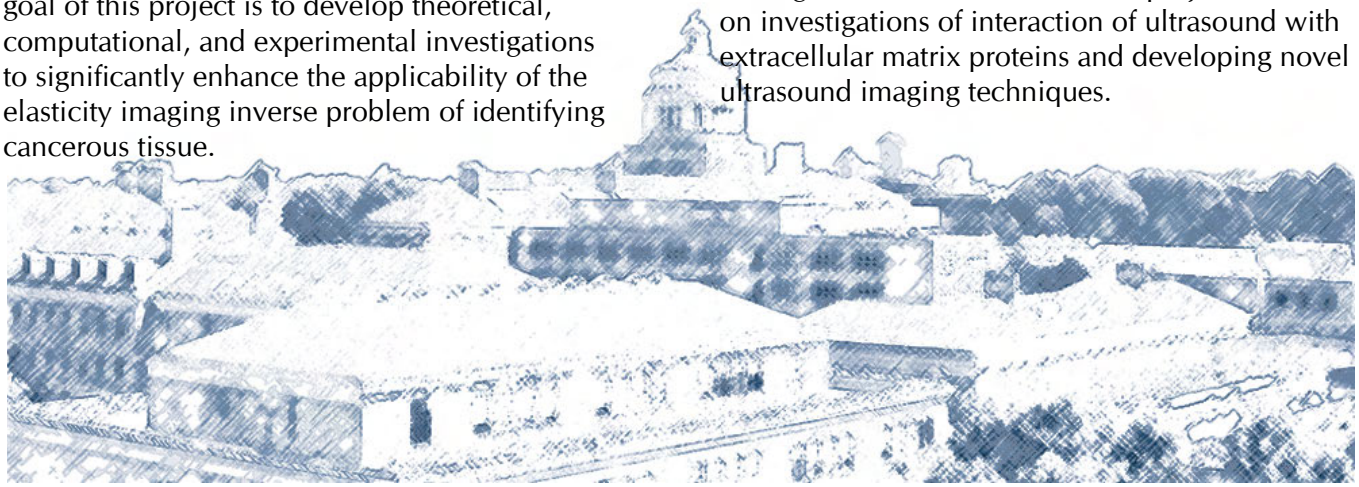
**Maria Helguera** received funding for her project titled "Adaptive Methods, Noise Removal and Preconditioning for Elasticity Imaging Inverse Problem" funded by the RIT Vice-President of Research Faculty Accelerating Funds. The goal of this project is to develop theoretical, computational, and experimental investigations to significantly enhance the applicability of the elasticity imaging inverse problem of identifying cancerous tissue.

## University of Rochester/Xerox Undergraduate Research Fellows Program

Several RCBU faculty members received funding from the UR/Xerox Undergraduate Research Fellows Program. The program provides support for engineering undergraduates to participate in research during the summer preceding their senior year, and continuing as independent research projects through the senior year. The 2010 UR/Xerox Undergraduate Research Fellows included: Aaron Zakrzewski (ME) mentored by **Sheryl Gracewski**, Jasmine Carvalho (BME) mentored by **Diane Dalecki**, Steven Archer (BME) mentored by **Marvin Doyley**, and Eric Lam (BME) mentored by **Rick Waugh**. Selection of UR/Xerox Undergraduate Fellows is highly competitive and provides a unique and distinguishing research experience.

**Sheryl Gracewski** received funding for a summer research intern through an REU on her NSF grant titled "Dynamic Response of Constrained Bubbles to Acoustic Excitation."

**Denise Hocking** and **Diane Dalecki** received funding from the NIH to support the summer research projects and career development of two undergraduate students. Research projects focused on investigations of interaction of ultrasound with extracellular matrix proteins and developing novel ultrasound imaging techniques.



# RCBU AWARDS

## Engineer of the Year Award

**Kevin J. Parker, Ph.D.** was named the 2009 Engineer of the Year by the Rochester Engineering Society (RES) during its annual Gala held in April 2010. The award recognizes Dr. Parker's impact on both the global medical imaging field and the Rochester engineering community. Dr. Parker, dean emeritus of the University of Rochester (UR) School of Engineering and Applied Sciences and past director of the RCBU, is currently the William F. May professor of engineering in the UR Department of Electrical and Computer Engineering with a secondary appointment in BME. In addition to serving as Dean, he operated his own medical imaging business and continued to teach actively. Dr. Parker's innovations in sonoelastography and Blue Noise Mask technologies have revolutionized medical imaging fields. With nearly 30 years of affiliation with the UR, Dr. Parker has garnered prestigious awards and recognition for his research in biomedical ultrasound, mentored numerous graduate students, and holds many patents in the area of medical imaging. His leadership and vision helped to spearhead the development of the UR Department of Biomedical Engineering.

***(Left to right) UR BME professor Greg Gdowski, Kevin J. Parker, and Rochester Engineering Society President Wendy Smith.***

**Diane Dalecki** was honored as the Professor of the Year for Engineering by the University of Rochester Students' Association for excellence in undergraduate teaching in April, 2010.

**Kelley Garvin,** a graduate student in the UR Department of Biomedical Engineering, won the Best Student Paper Competition at the 159th Meeting of the Acoustical Society of America held in Baltimore, Maryland in April, 2010. Her invited paper, *Ultrasound standing wave fields induce endothelial cell sprouting within three-dimensional engineered tissues,* was recognized as the Best Student Paper in the Biomedical Ultrasound/Bioresponse to Vibration Technical Section. Her thesis research is co-advised by Dr. Dalecki and Dr. Hocking.

**Kevin Parker,** Dean Emeritus of the School of Engineering & Applied Sciences at the University of Rochester and past director of the Rochester Center for Biomedical Ultrasound (RCBU), was elected a Fellow of the American Institute for Medical & Biological Engineering (AIMBE).

**Nicholas Berry** (UR BME class of 2010) was awarded the Professors' Choice Award for Undergraduate Research in Engineering at the UR Undergraduate Research Expo for his poster, *High Frequency Pulse-Echo Ultrasound for Three-Dimensional Engineered Tissue Characterization.* His coauthors were Diane Dalecki, Maria Helguera, and Denise Hocking.

**Denise Hocking** (Pharmacology & Physiology) was recognized with the University Dean's Award for Meritorious Service in Ph.D. Defenses. She was one of four faculty members so honored for their commitment to graduate education.

# TISSUE ELASTICITY CONFERENCE HIGHLIGHTS

**The Ninth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity** was held in Snowbird, Utah from October 16-19, 2010. Co-organized by Kevin Parker (RCBU past Director), the annual conference provided an international forum for the advancement of knowledge and methods for the measurement and imaging of elastic properties of tissues with ultrasound.

RCBU members Kevin Parker, Michael Richards, Sanghamithra Korukonda, and Shayin Jing attended the conference and presented seven abstracts. Michael Richards was thanked for his enthusiastic co-leadership of the formal poster presentation sessions.

Due to popular demand, the conference again offered a tutorial series. This year, Dr. Tim Salcudean from the University of British Columbia, Vancouver, presented a tutorial on *Prostate Elastography and Its Applications*. Dr. Guy Cloutier from the University of Montréal Hospital Research Center, Montréal, Québec, presented *Non-Invasive Vascular Ultrasound Elastography: A Review of Challenges of Potentially High Impact Clinical Imaging Methods*.

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 in Arlington, Texas from Wednesday, October 12 through Saturday, October 15, 2011 and marks the Conference's tenth anniversary. Please visit www.ElasticityConference.org for more information.

***Above (left to right): RCBU members Michael Richards, Shayin Jing, and Sanghamithra Korukonda.***

***Below: Photo of the beautiful surroundings the Conference participants enjoyed in Snowbird, Utah.***

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

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

# 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 Offices of Technology Transfer 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 is a Leader in Technology Commercialization

The University of Rochester has a long-standing tradition of being at the forefront of innovation and scientific research. In the 2010 fiscal year, the University received a record $460.6 million in research funding. The UR Offices of Technology Transfer received over 120 invention disclosures, including several novel diagnostic and therapeutic uses of ultrasound. The University was granted 19 new U.S. patents, 20 foreign patents, and successfully completed 21 licensing agreements. To propel some of these UR technologies forward on the path of commercialization, the University has instituted a new Technology Development Fund to accelerate translation of scientific and engineering research into commercial opportunities.

The UR is consistently rated as one of the best educational institutions in the nation for patent licensing and revenue, according to the Association for University Technology Managers (AUTM). 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 2010, UR royalty revenue exceeded $40.5 million. The technological advances of members of the Rochester Center for Biomedical Ultrasound continue to contribute to the UR's success.

The University of Rochester Offices of Technology Transfer play an important role in facilitating the transfer of University research results and innovative ideas to the commercial marketplace. For more information, and to view the 2010 UR Technology Commercialization Annual Report, visit the University of Rochester Office of Technology Transfer at http://www.urmc.rochester.edu/technology-transfer/.

# RCBU MEMBER NEWS

## Sally Child Celebrates 45 Years with the University of Rochester

In April, 2010, **Sally Child** was honored for her 45 years of employment at the University of Rochester. Sally began working at the UR in June 1965 in the Department of Electrical Engineering. She was first hired as a technician in **Professor Edwin Carstensen's** laboratory where she worked for over 30 years. In recent years, Sally has been an important member of **Professor Diane Dalecki's** lab in the Department of Biomedical Engineering. Currently, Sally is a Senior Technical Associate, an author of over 70 publications, and a recognized expert in biomedical ultrasound. Sally has been a member of the Rochester Center for Biomedical Ultrasound since its founding.

***At the April 2010 University of Rochester Staff Recognition Dinner, from left to right: Chairman Emeritus of the Board of Trustees, G. Robert Witmer, Jr.; SEAS benefactor Edmund A. Hajim; RCBU member Sally Child; and University of Rochester President Joel Seligman***

**Stephen McAleavey** (BME) was promoted to Associate Professor with tenure in the Department of Biomedical Engineering, with a secondary appointment in the Department of Electrical and Computer Engineering.

**Marvin Doyley** (ECE) was re-appointed to the International Advisory Board of the journal Physics in Medicine and Biology. Professor Doyley was also appointed the Conference Chair for the 2011 SPIE Medical Imaging Conference: Ultrasound Imaging, Tomography, and Topography Section.

## Medical Imaging Partnership

RCBU member **Dr. Vikram Dogra,** along with colleagues from Rochester, the United States, and around the world, including Chile, China, Egypt, El Salvador, Guatemala, India, Israel, Italy, Singapore, South Korea, Tunisia, United Kingdom, and Uganda, founded an ultrasound outreach organization, Medical Imaging Partnership (MIP). MIP is a non-profit organization that provides ultrasound imaging equipment, training, and education in medical diagnostic imaging to developing countries around the globe. In 2010, MIP donated an ultrasound machine to Mengo Hospital in Kampala, Uganda and also to Haiti, in collaboration with H.O.P.E. Haiti. In both locations, the machine was accompanied by a clinician who held training and educational sessions for the local medical providers. For more information on MIP, please visit http://medicalimagingpartnership.org/index.cfm.

## Peru/Rochester Collaboration

In a collaboration between the University of Rochester (UR) BME Department and the Pontificia Universidad Catolica del Peru (PUCP) EE Department in Lima, teams of engineering students were formed within the context of Senior Design programs of both schools to address global health problems in Lima. The innovative program was jointly led by RCBU members **Amy Lerner** and **Benjamin Castaneda**, along with Scott Seidman of the UR BME department. The goals were to enhance exposure to global health issues in UR curriculum and to increase entrepreneurial and customer-based aspects of design at PUCP. During a first visit to Lima, teams of students and faculty toured medical sites to identify projects, including medical lighting; a bed to promote postural pulmonary drainage; a device to identify risk of diabetic foot ulcers; a pressure-sensing mattress; and a system for medical aspiration. Design reviews by stakeholders and a workshop on medical device marketing took place through videoconferencing during a US visit by some Peruvian participants and in person during a second visit to Lima. All teams produced prototypes at various stages of completion, and all established proof of concept.

# RCBU 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 imaging and therapy.

## Summer Acoustics Course

Each year, Professor **David Blackstock** spends the summer at the UR and teaches a course in acoustics. This year, Professor Blackstock provided UR students with a unique educational opportunity by teaching a course in Nonlinear Acoustics. Graduate students with various interests in acoustics and ultrasound attended the course. "We are very fortunate to have Dr. Blackstock visit the UR each summer. Dr. Blackstock is a long-standing member of the RCBU. Over the years, his expertise in acoustics has been very valuable to students' education and research projects at the RCBU," said **Diane Dalecki**, RCBU Director.

***Summer Acoustics Class:*** *Back row (left to right): Roland Cheng, Etana Elegbe, Himansu Shekhar, Dr. David Blackstock, Vaibhav Kakkad, Nick Berry; Front row: Karla Mercado, Carlos Sevilla, Kelley Garvin. Not pictured: Xing Sun*

## Forbes Entrepreneurial Competition

BME Senior Design teams won all four awards at the 2010 annual Forbes Entrepreneurial Competition. Business plans were based on projects completed as part of the BME Senior Design class offered by **Amy Lerner** and Scott Seidman. RCBU Student Member, **Nicholas Berry**, was a member of the team that won First Place for their design of an improved arm-brace for rehabilitation of traumatic brain injury patients.

## Training Completed

- **Jing Jin** received her PhD degree in Electrical and Computer Engineering from the University of Rochester in April 2010. Her PhD dissertation, *Image Reconstruction Based on Estimated Scattering Object Characteristics,* was supervised by Professor Robert Waag.
- **Manoj Menon** received his PhD degree in Biomedical Engineering from the University of Rochester in July 2010. His PhD dissertation, *Resolution Estimation and Bias Reduction in Acoustic Radiation Force Impulse Imaging,* was supervised by Professor Stephen McAleavey. He is currently working as a Senior Systems Engineer at Siemens Medical Solutions, Ultrasound Division, located in Issaquah, WA.
- **Liwei An** received her PhD degree in Electrical and Computer Engineering from the University of Rochester in October 2010. Her PhD dissertation, *Analysis of Crawling Waves and Estimation of Tissue Elasticity,* was supervised by Professor Kevin Parker. She is now working for KLA-Tencor Corporation in San Jose, CA.

## New BME Program at the Rochester Institute of Technology

RCBU member **Dan Phillips, Ph.D.** was selected to guide the newly formed biomedical engineering program at the Rochester Institute of Technology (RIT). The new RIT BME B.S. degree is a five-year program. Areas of concentration include biomedical device and system design, biomedical signal processing, physiological modeling dynamics and control, and biomaterials. The inaugural class of about 40 students will graduate in 2015. "Our goal is to provide rigorous training in quantitative and analytical engineering skills while making students aware of the highly variable nature of biological systems," said Dr. Phillips. Dr. Phillips is a long-time member of the RCBU. He received his Ph.D. in Electrical Engineering from the University of Rochester where he studied with **Professor Kevin Parker**.

# 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 or www.rochester.edu for more information.

# SELECTED 2010 PUBLICATIONS


**Bhatt S,** Jafri SZ, Wasserman N, **Dogra VS.** Imaging of non-neoplastic intratesticular masses. Diagn Interv Radiol. 17:1305-3825; 2010.

**Doyley MM,** Perreard I, Patterson AJ, Weaver JB, Paulsen KM. The performance of steady-state harmonic magnetic resonance elastography when applied to viscoelastic materials. Med Phys. 37:3970-9; 2010.

Gaborski TR, **Sealander MN**, Ehrenberg M, **Waugh RE,** McGrath JL. Image correlation microscopy for uniform illumination. J Microsc. 237:39-50; 2010.

**Garvin KA, Hocking DC, Dalecki D.** Controlling the spatial organization of cells and extracellular matrix proteins in engineered tissues using ultrasound standing wave fields. Ultrasound Med Biol. 36:1919-32; 2010.

Grace D, Eggers P, Glantz JC, **Ozcan T**. Mitral valve-tricuspid valve distance as sonographic marker of trisomy-21. Ultrasound Obstetrics Gynecology 35: 172-177; 2010.

**Hah Z,** Hazard C, **Cho YT**, **Rubens D, Parker K.** Crawling waves from radiation force excitation. Ultrason Imaging 32:177-89; 2010.

**Hesford AJ,** Astheimer JP, Greengard LF, **Waag RC.** A mesh-free approach to acoustic scattering from multiple spheres nested inside a large sphere by using diagonal translation operators. J Acoust Soc Am. 127:850-61; 2010.

**Hesford AJ, Waag RC.** The fast multipole method and Fourier convolution for the solution of acoustic scattering on regular volumetric grids. J Comput Phys. 229:8199-8210; 2010.

Loberant N, **Bhatt S**, McLennan GT, **Dogra VS.** Striated appearance of the testes. Ultrasound Q. 26:37-44; 2010.

**Menon M, Langdon J, McAleavey S.** Minimization of displacement estimation bias due to high amplitude-reflections using envelope-weighted normalization. Ultrasonic Imaging 32; 65-80; 2010.

**Parker KJ, Doyley MM, Rubens DJ**. Imaging the elastic properties of tissues: The 20 year perspective. Physics in Medicine and Biology 56:R1-R29; 2010.

Perreard IM, Pattison AJ, **Doyley MM**, McGarry D J, Barani Z, Van Houten EE, Weaver J B, Paulsen KJ. Effects of frequency and direction dependent elastic materials on linearly elastic MRE image reconstructions. Physics in Medicine and Biology 55:6801-6815; 2010.

**Pressman EK, Thornburg LL,** Glantz JC, Earhart A, Wall PD, Ashraf M, Pryhuber GS, **Woods JR Jr**. Inflammatory cytokines and antioxidants in midtrimester amniotic fluid: Correlation with pregnancy outcome. Am J Obstet Gynecol. 204:155. e1-7; 2010.

Reynolds DG, Takahata M, **Lerner AL,** O'Keefe RJ, Schwarz EM, Awad HA. Teriparatide therapy enhances devitalized femoral allograft osseointegration and biomechanics in a murine model. Bone 48:562-70; 2010.

Salahura G, **Tillett JC**, Metlay LA, **Waag RC**. Large-scale propagation of ultrasound in a 3-D breast model based on high-resolution MRI data. IEEE Trans Biomed Eng. 57:1273-84; 2010.

Thornburg LL**,** Grace D, Gray AL, Glantz JC, **Pressman EK.** Placement of laminaria tents does not improve time to delivery in patients undergoing second trimester labor induction with misoprostol. J Matern Fetal Neonatal Med. 23:928-31; 2010.

Thornburg LL, Smith-Hartmann SA, Pegoli W, Eggers P, **Ozcan T.** Prenatal presentation of inginoscrotal hernia. Journal of Diagnostic Medical Sonography 26:299-302; 2010.

**Tillett JC**, Astheimer JP, **Waag RC.** A model of distributed phase aberration for deblurring phase estimated from scattering. IEEE Trans Ultrason Ferroelectr Freq Control 57:214-28; 2010.

Tsai L, Ho M, **Pressman EK**, Thornburg LL. Rates of completion of 'soft marker' aneuploidy screening in obese gravidas. Prenatal Diagnosis 30: 821-826; 2010.

Tsai LJ, Ho M, **Pressman EK, Thornburg LL.** Ultrasound screening for fetal aneuploidy using soft markers in the overweight and obese gravida. Prenatal Diagnosis 30:821-6; 2010.

Yanoso-Scholl L, Jacobson JA, Bradica G, **Lerner AL,** O'Keefe RJ, Schwarz EM, Zuscik MJ, Awad HA. Evaluation of dense polylactic acid/beta-tricalcium phosphate scaffolds for bone tissue engineering. J Biomed Mater Res A. 95:717-26; 2010.

# SELECTED 2010 PRESENTATIONS

**An L, Hah Z, Cho Y,** Mills B, Mao S, Baxter L, Kushner L , Yao J, **Joseph J, Rubens DJ, Strang J, Parker KJ**. Improving crawling wave detection of prostate cancer: Preliminary in vitro results. Presented at the Ninth Annual International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, UT, October 2010.

**An L, Rubens DJ, Strang J, Cho YT, Hah Z,** Mills B, **Parker K.** Evaluation of crawling wave estimator bias on elastic contrast quantification. Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

Antos L, Heneka P, Luquette B, McGee B, Nguyen D, Phipps A., **Phillips D, Helguera M**. A 3D fluorescence imaging system incorporating structured illumination technology. Presented at SPIE BiOS, January 2010.

**Berry N, Helguera M, Hocking DC, Dalecki D.** High frequency ultrasound characterization of three-dimensional engineered tissues. Presented at the Meeting of the Biomedical Engineering Society, Austin, TX, October 2010.

**Bhatt S.** Ultrasonography of the parathyroid glands. Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

**Blackstock DT.** Mack Breazeale and E. A. Hiedemann's group at Michigan State University. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

**Castaneda B, Rubens D J, Parker K J.** Clinical applications of sonoelastography. Presented at the Pan American Health Care Exchanges Conference, Lima, Peru, March 2010.

**Cho YT, Hah Z, An L,** Hazard CR, **Rubens DJ, Strang J, Parker KJ**. Theoretical investigation of strategies for generating crawling waves using focused beams. Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

Dhillon G, **Bhatt S**, Sidhu R, **Dogra V**. Striated appearance of the testes: What does it mean? Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

Eslami R, Huntzicker S, **Doyley MM**. Magnetic resonance elastography for HIV-associated brain injury. Presented at the 14th National Center for AIDS Research Conference, University of California, Los Angeles, CA, November 2010.

**Doyley MM.** Ultrasound elastography. Presented at the Image-Guided Spectroscopy Symposium & Workshop, Dartmouth College, Dartmouth, NH, July 2010.

**Doyley MM, Shekhar H,** Allen JS, Rychak J. Visualizing the functional properties of life-threatening atherosclerotic plaques using targeted ultrasound contrast agent and intravascular ultrasound. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

**Elegbe E, McAleavey S.** Measurement of thermally-induced variation in liver shear modulus. Presented at the Ultrasonic Imaging and Tissue Characterization Symposium, May 2010.

**Elegbe E, McAleavey S.** Spatially modulated ultrasound radiation force imaging of thermally-induced variation in liver shear modulus. Presented at the SPIE Medical Imaging Conference, San Diego, CA, February 2010.

Forsberg F, Lobel BE, de Muinck ED, **Doyley MM.** Visualizing atherosclerotic plaque neovasculature using subharmonic intravascular ultrasound: A feasibility study. Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

**Garvin K, Hocking DC, Dalecki D.** Ultrasound-based cell patterning for the vascularization of three-dimensional engineered tissue. Presented at the Meeting of the Biomedical Engineering Society, Austin, TX, October 2010.

**Garvin KA, Hocking DC, Dalecki D**. Ultrasound standing wave fields induce endothelial cell sprouting within three-dimensional engineered tissue. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

# SELECTED 2010 PRESENTATIONS

Ginat DT, **Voci S, Rubens DJ.** Society of radiologists in ultrasound guidelines for fine-needle aspiration of thyroid nodules: Can false-negative rates be reduced? Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

**Hah Z, Cho YT, An L,** Hazard CR, **Rubens DJ, Strang J, Parker K.** Methods for generating crawling waves with radiation force from ultrasonic beams. Presented at the AIUM Annual Convention, San Diego, CA, March 2010.

**Hah Z,** Hazard CR, **Rubens DJ, Parker KJ.** Synthesis and analysis of crawling waves generated from radiation force. Presented at the Ninth Annual International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, UT, October 2010.

**Hesford AJ**, Astheimer JP, **Waag RC**. A generalized formulation for scattering from arbitrary distributions of homogeneous cylinders or spheres. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

**Jang N,** Zakrzewski A, Jensen C, Halm R, **Gracewski SM**. Dynamic response of bubbles within a compliant tube. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

**Jing S, Richards MS, Doyley MM.** Method for minimizing the effect of catheter eccentricity in intravascular ultrasound elastography. Presented at the Ninth Annual International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, UT, October 2010.

**Korukonda S, Doyley MM.** Displacement estimation of the carotid artery using synthetic aperture imaging. Presented at the Ninth Annual International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, UT, October 2010.

**Lerner AL**, Seidman SH, **Castaneda B**, Carrera W. Collaboration for healthcare in developing countries. Presented at the Meeting of the Biomedical Engineering Society, Austin, TX, October 2010.

Lin K, Thomas A, McLaughlin JR, Hazard CR, Thomenius K, **Hah Z, Parker KJ, Rubens DJ.** New combination of ARC data: Imaging shear moduli and matching phantom recovery frequency dependence to viscoelastic model. Presented at the Ninth Annual International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, UT, October 2010.

**Parker K J.** Imaging the biomechanical properties of tissues–The 20-year perspective. Presented at the American Society of Mechanical Engineers International Mechanical Engineering Congress, Vancouver, Canada, November 2010.

**Parker K J.** Medical uses of cold plasmas. Presented at the U.S. Army Telemedicine and Advanced Technology Research Center Product Line Review, Ft. Detrick, MD, September 2010.

**Richards MS, Jing S, Doyley MM.** Visualization of atherosclerotic plaque mechanical properties using model based intravascular ultrasound elastography. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

Roy DC, **Hocking DC.** Engineered matrix mimetics support assembly of a growth-promoting fibronectin matrix. Presented at the Meeting of the Biomedical Engineering Society, Austin, TX, October 2010.

**Sevilla C, Hocking DC, Dalecki D.** Fibronectin matrix conformation defines regions of cell proliferation and stress fiber formation. Presented at the Meeting of the Biomedical Engineering Society, Austin, TX, October 2010.

**Tillett JC,** Salahura G, Metlay LA, **Waag RC**. Three-dimensional calculation of ultrasound propagation through a breast model. Presented at the Joint 159th Meeting of the Acoustical Society of America and Noise-Con 2010, Baltimore, MD, April 2010.

Welch S, Cox N, Baum KG, Ravines P, **Helguera, M**. Registration and normalization of images. Presented at the Third International Workshop on Image Processing in Art Investigations at the Museum of Modern Art, New York, NY, October 2010.

# Rochester Center for Biomedical Ultrasound Members

## University of Rochester/ Strong Memorial Hospital

**Anesthesiology**
- Paul Bigeleisen, MD
- Janine Shapiro, MD
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- Jacek Wojtczak, MD

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- Nicholas Berry, BS
- Sally Child, MS
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- Himanshu Shekhar, MS
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- Charles Francis, MD

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- Robert Lerner, MD, PhD

## Rochester Institute of Technology

**Center for Imaging Sciences**
- Maria Helguera, PhD
- Navalgund Rao, PhD

**Electrical Engineering**
- Daniel Phillips, PhD

## Visiting Scientists

- David Blackstock, PhD
  University of Texas at Austin
- E. Carr Everbach, PhD
  Swarthmore College
- Wesley Nyborg, PhD
  University of Vermont
- Zhe Wu, PhD
  General Electric Healthcare

## Honorary Member

- Floyd Dunn, PhD
  University of Illinois

# Graduate Training Opportunities in Biomedical Ultrasound at the RCBU

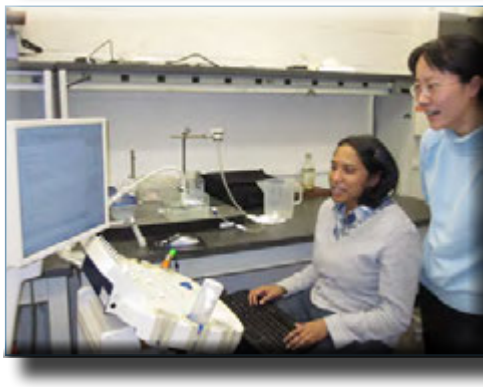
**The Rochester Center for Biomedical Ultrasound (RCBU)** provides exciting opportunities for graduate and post-graduate research and training in the field of biomedical ultrasound. Research at the RCBU spans a wide range of topics in diagnostic imaging and therapeutic applications of ultrasound. With 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.

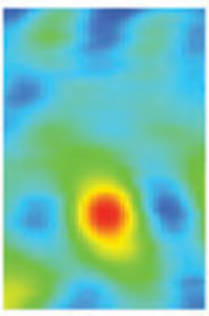
The RCBU has a long history of innovation in biomedical ultrasound. Research of student members of the RCBU has led to numerous patents in ultrasound imaging and therapy.

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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