Rochester Center for Biomedical Ultrasound

2011 Annual Report

RCBU laboratories are advancing biomedical ultrasound across many topics in diagnostic imaging, ultrasound therapy, and fundamental acoustics. See inside for highlights of RCBU research in 2011.

Rochester Center for Biomedical Ultrasound

Director: **Diane Dalecki, PhD**
Associate Director: **Deborah J. Rubens, MD**
Executive Committee: **Diane Dalecki, PhD, Vikram S. Dogra, MD, Morton W. Miller, PhD, Kevin J. Parker, PhD, and Deborah J. Rubens, MD**
Provost: **Ralph W. Kuncl, MD, PhD**
Senior Vice President and Robert L. and Mary L. Sproull Dean of the Faculty of Arts, Sciences, and Engineering: **Peter Lennie, PhD**
Dean of the School of Medicine and Dentistry: **Mark B. Taubman, MD**
Dean of the Hajim School of Engineering and Applied Sciences: **Robert L. Clark, PhD**
Editor and Designer: **Maria Randazzo**
Rochester Center for Biomedical Ultrasound, University of Rochester
311 Goergen Hall, PO Box 270168, Rochester, New York 14627
Phone: (585) 275-9542 ■ Email: rcbu@seas.rochester.edu
Web site: www.urmc.rochester.edu/rcbu

Rochester Center for Biomedical Ultrasound 2011 Annual Report

Table of Contents

FROM THE DIRECTORS

Diane Dalecki, PhD, Director

Diane Dalecki

This year's annual report summarizes progress from RCBU laboratories across diverse topics in biomedical ultrasound imaging and therapy. This year marked the tenth anniversary of the International Tissue Elasticity Conference. Over the years this conference has grown to become the premier conference for researchers in the field of elasticity imaging. The RCBU continues to advance new elastography techniques and included within this report are highlights of innovations by RCBU faculty and students in areas such as sonoelastography, crawling waves, intravascular ultrasound elasticity imaging, and radiation force imaging techniques.

On a more reflective note, this year the RCBU and the broader ultrasound community lost one of its most important pioneers, Wesley Nyborg. Wes was a Charter Member of the RCBU. His seminal theoretical and experimental work forms the foundation of our understanding of the biological effects of 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. This year a new patent in ultrasound imaging was issued to RCBU member Robert C. Waag. 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

Deborah Rubens MD

The Imaging Sciences Ultrasound Department continued its growth in exam and patient volumes in 2011, performing examinations on 24,800 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 the American Institute of Radiologic Pathology in 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, Drs. Rubens, Bhatt, Dogra, and Strang lectured at The Society for European Uroradiology in Dubrovnik, Croatia, and Drs. Rubens and Strang lectured at the Israeli Society for Ultrasound in Diagnostic Medicine in Haifa, Israel. Dr. Rubens also lectured at Cambridge University in England, and Dr. Dogra in Egypt and Turkey.

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. Dr. Barry with co-authors Parker, Hah, Rubens, Mills, Mooney, and Ryan, had their landmark paper, *Shear Wave Dispersion Measures Liver Steatosis*, accepted this year for publication in Ultrasound in Medicine and Biology. 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 conducting 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

2011 RESEARCH

Research laboratories of RCBU members are advancing the use of ultrasound for diagnosis and therapy. The pages that follow highlight research accomplishments in 2011. Selected publications and presentations of this year can be found on pages 27-29.

Crawling wave sonoelastography of benign and malignant thyroid nodules

J.M. Walsh, Brady Mills, BS, Deborah Rubens, MD, Kevin J. Parker, PhD, Liwei An, PhD, Morton Miller, PhD, Zaegoo Hah, PhD

The purpose of this study was to determine if Crawling Wave (CrW) Elastography, a novel sonoelastography technique, can be utilized to provide quantitative measurements of thyroid tissue shear velocity (a measure of tissue stiffness) and distinguish between benign and malignant thyroid nodules. Fresh thyroid specimens (N = 21) with 44 regions of interest were imaged over a 9-month period at a single institution. CrW sonoelastography was performed and shear velocity (SV) estimations with contrast to noise ratios (CNR) were calculated. Histologic diagnosis was correlated with SV and CNR values. The SV and CNR of Papillary Thyroid Carcinoma (PTC) (N = 11, CNR = 4.04, SV = 2.39 m/s) was significantly higher than benign nodules (N = 22, CNR = -0.988, SV = 1.90 m/s) (for CNR pp = 0.003, [95% CI 0.199 - 0.801]). CNR values have a sensitivity and specificity of 100% and 90.9%, respectively, for differentiating PTC from benign nodules. Additionally, SV has a sensitivity and specificity of 81.8% and 68.2%, respectively. Insufficient samples were obtained for SV and CNR comparison of other histologic types. In conclusion, crawling wave sonoelastography can provide quantitative estimations of shear velocity (SV) depicting the elastic properties of thyroid nodules. The SV with CNR can differentiate between benign thyroid nodules and papillary thyroid carcinoma. However, prospective in-vivo studies are needed to verify the accuracy and utility of CrW elastography.

Shear Wave Induced Phase Encoding (SWIPE)

Stephen McAleavey, PhD

We have recently demonstrated a technique, Shear Wave Induced Phase Encoding (SWIPE), that allows B-scan-like images of tissue echogenicity to be formed without using a focused aperture. Briefly, this method uses multifrequency (< 2 kHz) shear wave propagation perpendicular to the direction of ultrasound propagation to apply a variety of deformations to the target to be imaged. These deformations shift the phase of the received ultrasound echo. By proper demodulation of the phase shift of the ultrasound signal, the lateral position of the echo source may be determined. The axial (range) component of position is determined through time of flight as in conventional ultrasound. In SWIPE imaging, lateral resolution is determined by the range of shear wave frequencies used to interrogate the target, rather than the focal properties of the aperture. Lateral focusing provided by an extended aperture serves to determine the illuminated region of the tissue.

Our previous experimental results demonstrated the ability of SWIPE to achieve lateral resolution independent of aperture focusing. However, the point spread function (PSF) showed higher sidelobe levels than anticipated. The increased sidelobe levels were found to be due to deviations from a linear dependence of target motion phase on shear wave frequency.

The model developed assumes the presence of a plane, z-polarized, $+x$-going harmonic shear wave, which is conveniently described analytically. Unfortunately, waves generated by finite sources are more complex to describe, and do not lend themselves to compact analytical expressions. A further complication exists when the excitation is at the surface of the elastic body. Surface or Rayleigh waves are generated in addition to shear waves. The speed of the Rayleigh wave is ~ 0.96 that of the shear wave in an incompressible medium, and its amplitude is dominant near the surface, falling exponentially with depth into the medium. The interaction of Rayleigh and shear waves, and their varying relative amplitude at a given excitation frequency, result in a non-linear dependence on

the phase of the displacement in response to a harmonic excitation as a function of frequency. This non-linear dependence violates the assumptions made in the SWIPE model, resulting in distortion of the image.

To better understand the effects of source geometry on SWIPE image quality, finite-element simulation was used to calculate the total wave motion due to the application of surface and sub-surface forces in a 2D axi-symmetric model. Two sinusoidal driving forces were simulated: a surface load applied over a 5 mm diameter region centered atop the cylinder, modeling the displacement applied in our experimental apparatus by an electromagnetic shaker, and an internal, Gaussian distributed load, designed to mimic the forcing that would be applied by an acoustic radiation force source.

The phase of the z component of displacement in response to the two sources was calculated for a source frequency of 0.1-1 kHz. The lateral component of the point spread function (PSF) was calculated from the measured phase response, with Hamming windowing used to avoid sidelobes due to the otherwise abrupt truncation of the k-space data. The excess width of the PSF at the -6 dB and -30 dB levels was computed on the same mesh.

The effect of non-linear phase dependence is readily apparent in the simulated PSFs, shown in Figure 1. At all points except directly under the excitation source, the PSFs resulting from surface excition are significantly wider than the ideal response. In contrast, the more nearly linear phase response associated with the internal source results in near-ideal PSFs. The non-linear dependence of phase on frequency and the resulting distortion of the SWIPE PSFs associated with surface excitation of shear and surface waves seen in the finite element simulations shows good qualitative agreement to previous experimental observations.

These results suggest that further development of SWIPE is best suited to applications where acoustic radiation force or other means can be employed to generate shear waves sufficiently distant from boundaries to avoid surface wave generation. The simulation results make clear that the previously observed distortion is due in large part to the mechanical response of the elastic target. The use of an internal source was found to very closely approximate the PSF quality expected for an ideal plane source. Future work will investigate the use of acoustic radiation force to realize this shear wave source.

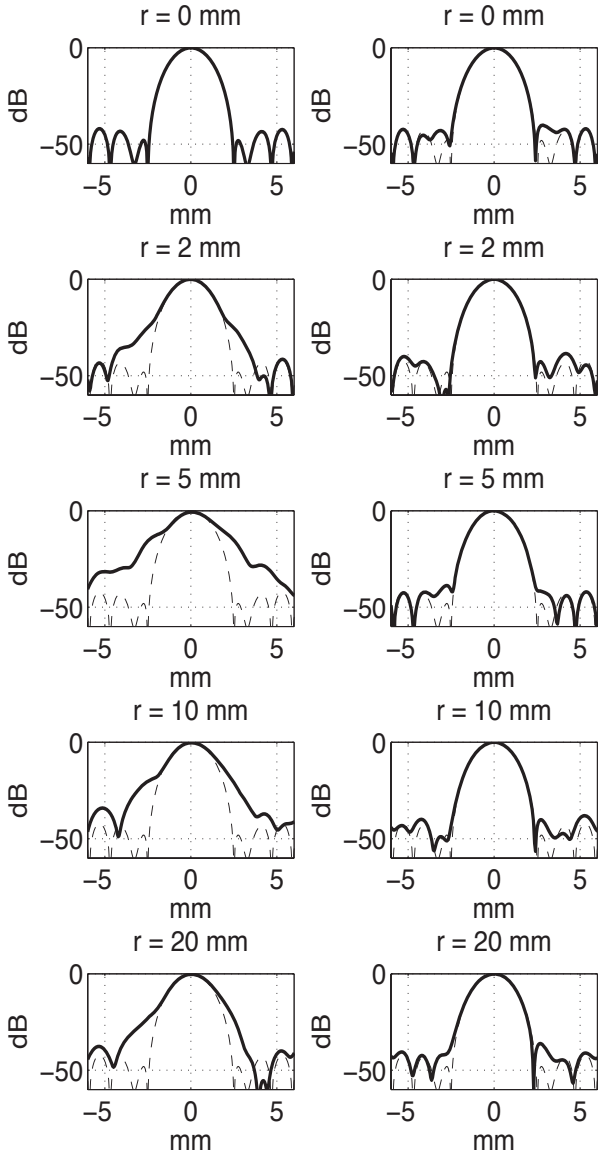


Figure 1. *Lateral point spread funtion profiles. The PSFs associated with the surface source are on the left, the internal source on the right. The dahsed lines indicate the PSF for the shear wave frequency used.*

Investigating the impact of spatial priors on the performance of model-based IVUS elastography

Michael Richards, PhD, Marvin Doyley, PhD

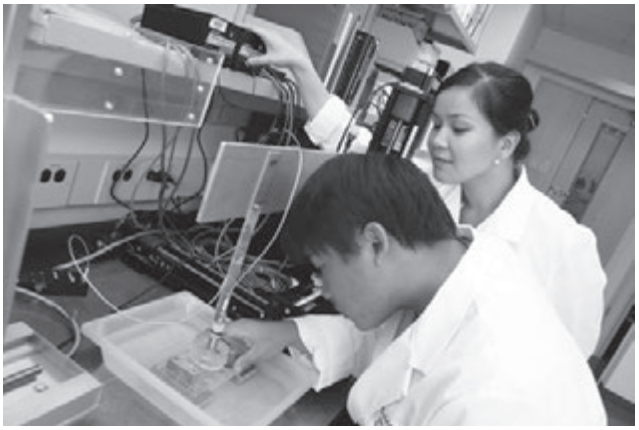
Recent work by RCBU members Mike Richards and Marvin Doyley developed methods that provide pre-requisite information for computing circumferential stress in modulus elastograms recovered from vascular tissue. This information could help cardiologists detect life-threatening plaques and predict their propensity to rupture.

The modulus recovery process is an ill-posed problem; therefore, additional information is needed to provide useful elastograms. In this work, prior geometrical information was used to impose hard or soft constraints on the reconstruction process. Simulation and phantom studies were conducted to evaluate and compare modulus elastograms computed with soft and hard constraints versus those computed without any prior information. The results revealed that the contrast-to-noise ratio of modulus elastograms achieved using the soft prior and hard prior reconstruction methods exceeded those computed without any prior information. Also, the soft prior and hard prior reconstruction methods could tolerate up to 8% measurement noise, and the performance of soft and hard prior modulus elastograms degraded when incomplete spatial priors were employed. This work demonstrates that including spatial priors in the reconstruction process should improve the performance of model-based elastography, and the soft prior approach should enhance the robustness of the reconstruction process to errors in the geometrical information.

High frequency ultrasound characterization of engineered tissues

Karla Mercado, MS, Maria Helguera, PhD, Stephen McAleavey, PhD, Denise C. Hocking, PhD, Diane Dalecki, PhD

Advances in the fabrication of engineered tissues require quantitative techniques to characterize the tissues' structural, biological, and mechanical properties. Histology and direct mechanical tests are current standard techniques to assess the properties of engineered tissues; however, these techniques are often destructive and lack the ability for monitoring dynamic changes in tissue properties over time. The overarching goal of this collaborative project among RCBU members is to develop novel, high frequency ultrasound technologies for nondestructive characterization of the structural, biological, and mechanical properties of three-dimensional engineered tissues. This project focuses on developing quantitative ultrasound and elastographic techniques to assess tissue properties during fabrication and post-implantation, in order to facilitate the fabrication of fully-functional engineered tissues. Quantitative ultrasound techniques, including analyses of the backscatter spectrum and echo statistics, are being tested to estimate the structural and biological properties in engineered tissues, such as cell concentration, spatial organization of cells, cell proliferation, and cell migration. In addition, the mechanical properties of engineered tissues can be estimated by the acoustic radiation force-based techniques such as Spatially Modulated Ultrasound Radiation Force (SMURF) imaging. High frequency ultrasound is used to attempt to improve the spatial resolution of quantitative parametric images and stiffness maps that are representative of engineered tissue properties. In recent work, analyses of the frequency-dependent backscatter coefficient are used to detect relative differences in the concentration of fibronectin-null mouse embryonic fibroblasts in 3-D agarose-based tissue constructs. The successful completion of this project will provide researchers and clinicians with ultrasound-based imaging and quantitative techniques for nondestructive assessment of engineered tissues.



BME graduate students Nicholas Berry (left) and Karla Mercado (right)

Estimating axial and lateral strain using a synthetic aperture elastographic imaging system

Sangamithra Korukonda, MS, Marvin Doyley, PhD

Model-based elastography is an emerging technique with clinical applications in imaging vascular tissues, guiding minimally invasive therapies and diagnosing breast and prostate cancers. Its usage is limited because ultrasound can measure only the axial component of displacement with high precision. The goal of recent work in the laboratory of Professor Marvin Doyley was to assess the effect of lateral sampling frequency, lateral beam-width and the number of active transmission elements on the quality of axial and lateral strain elastograms. Elastographic

imaging was performed on gelatin-based phantoms with a modified commercial ultrasound scanner. Three groups of radio-frequency (RF) echo frames were reconstructed from fully synthetic aperture data. In the first group, all 128 transmission elements (corresponding to a lateral beamwidth of 0.22 mm at the center of the field of view) were used to reconstruct RF echo frames with A-line densities that varied from 6.4 lines/mm to 51.2 lines/mm. In the second group, the size of the aperture was varied to produce RF echo frames with lateral beamwidths ranging from 0.22 mm to 0.43 mm and a fixed A-line density of 25.6 lines/mm. In the third group, sparse arrays with varying number of active transmission elements (from 2 to 128) were used to reconstruct RF echo frames, whose A-line density and lateral beamwidth were fixed to 25.6 lines/mm and 0.22 mm, respectively. Applying a two-dimensional displacement estimator to the pre- and post-deformed RF echo frames produced displacement elastograms. Axial and lateral strain elastograms were computed from displacement elastograms with a least squares strain estimator. The quality of axial and lateral strain elastograms improved with increasing applied strain and A-line density but decreased with increasing lateral beamwidth and deteriorated as the number of active transmission elements in the sparse arrays were reduced. This work demonstrated that the variance incurred when estimating the lateral component of displacement was reduced considerably when elastography was performed with a synthetic aperture ultrasound imaging system. Satisfactory axial and lateral strain elastograms were produced using a sparse array with as few as 16 active transmission elements.

Measuring dispersion of a biological medium with crawling waves synthesized from ultrasonic radiation force

Zaegoo Hah, PhD, Brady Mills, BS, Christopher Hazard, MD, Kevin J. Parker, PhD, Deborah Rubens, MD

Crawling waves can be generated with the radiation force from ultrasonic beams. Crawling waves generated can be analyzed to provide local shear speed and elasticity. Although most crawling wave experiments have used mechanical sources, recent studies showed that radiation force from ultrasonic beams can generate crawling waves as well. Since crawling waves from radiation force can be synthesized at arbitrary frequencies, they can be used to measure the change of shear speed as a function of frequency. Recent research from the laboratory of Professor Kevin Parker aims to measure the dispersion of biological samples by using synthesized crawling waves from radiation force.

A GE LOGIQ 9 system has been modified for acoustic radiation crawling wave experiments. A specially designed sequence produces push/scan pulses to obtain displacement data at points inside the region of interest. Scanned biological phantoms include gelatin-oil phantoms (10%–50% oil and 10%–20% gelatin), veal livers, and human livers embedded in a gelatin background. IQ data are averaged over several runs to minimize the background noise. Cross-correlation of IQ data sets provides displacement data sets that are further processed to generate crawling waves at different frequencies, nominally 80 to 450 Hz.

Local speed estimations are performed on synthesized crawling waves over a frequency range of 85 to 400 Hz for each of the phantoms to produce the mean and SD of the shear speed inside the medium at different frequencies. Two parameters are derived for further analysis: shear speed at the median frequency and the dispersion slope over an interval of 100 Hz. Veal liver, for example, showed about 1.6 to 2.1 m/s of shear speed with a dispersion slope of 0.2 to 0.85 m/s per 100 Hz. The results were compared with the composition of the samples, and fat was identified as increasing the dispersion. In conclusion, synthesized crawling waves from radiation force can be used to measure the dispersion of biological samples, which indicates the composition of the biomaterials.

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 oor 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 rst trimester ultrasound and midtrimester transvaginal cervical length: A retrospective cohort

Erin M Lemcke-Berno RDMS, MPH, 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.

Effect of imaging parameters on estimates of shear modulus using a single tracking location ARFI method

Etana Elegbe, MS, Stephen McAleavey, PhD

Ultrasound elastography is of increasing clinical significance because it provides a relatively low cost method for producing image contrast that is associated with disease and distinct from conventional modalities (X-ray, US, MRI). Acoustic radiation force elastography methods are particularly attractive because of the ability to directly interrogate the tissue at the region of interest. In addition, the propagation of the induced shear waves in soft tissue, generally occurs on a time scale that is long enough to allow for adequate motion tracking without the need for elaborate hardware. On the other hand, the generated shear waves are rather quickly attenuated, and, in the case of dispersive media, distorted. Consequently, the algorithm and choice of imaging parameters can affect the ability to accurately and precisely determine the true velocity of the induced shear waves.

In the past, we developed a Single-Track-Location (STL) ARFI method and have identified speckle noise as a significant source of measurement variance in shear wave velocity estimation methods that rely on ultrasonic tracking of tissue motion at two or more locations (the Multiple-track-location methods). The STL ARFI algorithm determines the shear velocity of a material by pushing in two locations a known distance apart and determining the difference in arrival time of the induced shear waves. We have shown success in measuring the shear wave velocity and shear modulus of both mildly dispersive materials (such as tissue mimicking phantoms) as well as dispersive materials (such as excised porcine tissue). We have also successfully monitored heat-induced changes (water and rf-ablations) in excised porcine liver tissue over time.

More recently, we have been investigating the effect of processes that result in the distortion of the shear waves, SNR of the displacement data, and sampling errors. Specifically, we have been investigating the effect of the distance between the pushing locations, the distance from the pushing location to the tracking location, the ratio of the width of the push beam to that of the track beam, the frequency of the push beam and the displacement SNR. We have been able to identify the appropriate imaging parameters to select during different conditions. This is significant because selecting the appropriate imaging parameters can improve the precision of our estimates, which ultimately enhances elastographic image quality.

BME graduate student Etana Elegbe

Prostate cancer detection using 3-dimensional vibration sonoelastography: Ex vivo and in vivo results

Benjamin Castaneda, PhD, K. Westesson, Liwei An, PhD, Jorge Yao, M.D., L. Baxter, Jean Joseph, MD, Kevin Hoyt, PhD, John Strang, MD, Deborah Rubens, MD, Kevin J. Parker, PhD

Vibration sonoelastography (VS) is an elasticity imaging technique that has shown promise for cancer detection in ex vivo prostate glands. A recent study from the Parker lab compared VS performance in prostate cancer detection between ex vivo and in vivo experiments. Eleven patients underwent VS examination prior to their scheduled radical prostatectomy. Vibration was induced by a specially designed plate with 2 mechanical actuators driven by a low-frequency harmonic signal (70–140 Hz). In vivo ultrasound (US) and VS volume data were acquired using a GE LOGIQ 9. After surgery, the same prostate gland was received and embedded in a gelatin mold. External low-frequency vibration (combination of 105, 140, 175, and 210 Hz) was applied by a mechanical piston. Ex vivo US and VS volume data were acquired. After imaging, the entire gland was step sectioned using a whole-mount histologic method. A pathology volume was reconstructed and registered to the US and elastographic volumes. To assess detection performance, cancer and benign prostatic hyperplasia (BPH) findings from the in vivo and ex vivo volumes were compared in size and

position to 3D pathology.

Ten cases were analyzed (1 case was discarded due to poor contact between the gland and transducer).Tumors detected with VS showed good agreement in size with findings in histology. When only tumors >4 mm in diameter (as measured on histology) were considered for analysis, in vivo VS showed 83% accuracy, 91% sensitivity, and 81% specificity, whereas ex vivo VS showed 82% accuracy, 75% sensitivity, and 84% specificity. This study evaluated the entire prostate, by fusing volumes from in vivo and ex vivo VS experiments to histology, permitting quantification and localization of tumors. Both experiments presented similar performance in cancer detection (>80% accuracy for tumors >4 mm in diameter). These results are an improvement over gray scale US but not yet sufficient to replace biopsy.

High-frequency ultrasound characterization of bio lms

Maria Helguera, PhD

RCBU member Maria Helguera is investigating the use of ultrasound for biofilm characterization. This project is in collaboration with Dr. Michael Pichichero of Rochester General Hospital Research Institute and Dr. Robert Osgood of Biomedical Sciences at RIT. The study employs biofilms grown in vitro on silastic substrates to determine the feasibility of detecting and characterizing parameters such as biofilm thickness, backscatter coefficient, integrated backscatter, shift of center frequency and reduction of bandwidth. These parameters are needed to understand image properties and design an efficient non-invasive protocol to identify biofilms, map their progression over time, and differentiate between single-species and multiple-species biofilms.

A single element focused transducer (F number 1.5) was fully characterized and used to study the acoustic properties of biofilms. The transducer had a center frequency of 15 MHz and a 50 percent -3dB/echo bandwidth. Three independent batches of Non-typeable Haemophilus influenzae, NTHi, harvested from the middle ear fluid of a case of AOM were studied over a period of one week. Each batch was probed over three phases during the entire span of the study. The three phases were named 'Early', 'Middle', and 'Old' corresponding to samples that are 1-3 days old, 3-5 days old and 5-7 days old, respectively. Changes in these parameters due to maturation are shown in Table 1. One sample was allowed to continue maturation and was imaged using a Matec Micro Electronics PSS-18 acoustic scanning system fitted with a 130 MHz focused immersion transducer housed in the Center for Integrated Manufacturing Studies at RIT (Figure 1). Maturity of the biofilm over the time span of the study was corroborated with increase in biofilm thickness and IBC values, shift in center frequency and narrowing of the bandwidth. Future investigations will involve studying different strains subject to a similar experimental protocol. Newer and more sophisticated quality metrics will be developed and used to evaluate changes in the biofilm over time. We expect to be able to identify unique signatures that will help us distinguish one strain from another. The changes observed in the acoustic signals from the three batches can be used as a benchmark to compare to different strains in isolation and in combination with epithelial cells. The experiment described above demonstrates the efficacy of high frequency ultrasound as a diagnostic tool in testing properties of biological materials.

Table 1. *Change in properties as biofilm matures.*

	Batch 1			Batch 2			Batch 3		
	Early	Mid	Old	Early	Mid	Old	Early	Mid	Old
Fo (MHz)	14.3	13.43	10.9	14.04	12.82	11.9	14.08	13.92	13.01
BW (MHz)	4.19	3.89	3.58	3.21	2.38	2.14	3.86	3.22	2.85
IBC (mm^{-1})	16.3	1.71	1.74	3.25	7.25	15.15	9.055	0.91	3.24
Thickness (μm)	n/a	119.8	219.43	10	80.2	88.06	18.2	45.25	65.56

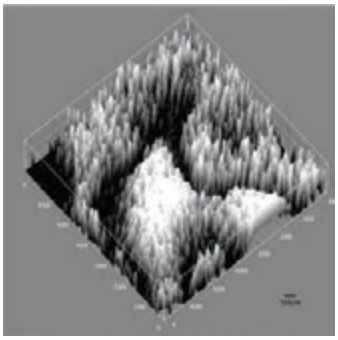


Figure 1. *130 MHz C-scan of a 19-day old biofilm. Scanned area is 4 mm^2.*

Investigating cavitation in vivo

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

A long-standing area of collaborative research between Professor Sheryl Gracewski and Professor Diane Dalecki centers on understanding acoustic cavitation in vivo. The work has direct relevance to the response of contrast agents to ultrasound exposure. Ultrasound contrast agents are suspensions of gas-filled microbubbles.

Ultrasound contrast agents currently enhance the capabilities of diagnostic imaging and are also providing new avenues for therapeutic applications of ultrasound. Research efforts focus on developing an understanding of the physical and biological mechanisms of interaction of acoustic fields with tissues containing microbubble contrast agents.

Microbubble contrast agents can increase the likelihood of bioeffects of ultrasound associated with acoustic cavitation. Ongoing work from the Dalecki lab continues to investigate ultrasound-induced bioeffects of microbubble contrast agents in biological systems. Previous work has demonstrated that the presence of ultrasound contrast agents lowers the threshold for ultrasound-induced premature cardiac contractions, and capillary rupture in various organs and tissues. Results of a series of mechanistic investigations are consistent with the hypothesis that acoustic cavitation is the mechanism for the production of these bioeffects of ultrasound and microbubble contrast agents. Sheryl Gracewski and her laboratory are developing unique capabilities to computationally simulate the response of microbubbles to sound exposure within a confining blood vessel. In recent work, the dynamics of microbubbles in vessels were modeled using a lumped parameter model for a five-degree-of-freedom system, accounting for the compliance of the tube and the coupled response of two microbubbles. Two different simulation approaches are also employed: 1) an axisymmetric coupled boundary element and finite element code, and 2) finite element models developed in COMSOL Multiphysics. Ongoing work in the Gracewski lab continues the development of more sophisticated computational models of bubble dynamics. Experimental measurements and observations within the Dalecki lab are used to validate the simulation results from the Gracewski lab in order to obtain new insights into the nonlinear bubble dynamics that can occur within blood vessels.

Using crawling wave sonoelastography for the measurement of intrahepatic fat content

Brady Mills, BS, Christopher Barry, MD, Zaegoo Hah, PhD, Deborah Rubens, MD, Kevin J. Parker, PhD

Hepatic steatosis affects 31% of the U.S. population and as much as 67% of those who are obese. Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver dysfunction in Western countries and can progress to end stage liver disease as a result of non-alcoholic steatohepatitis (NASH). Current understanding of the pathophysiological progression from NAFLD to NASH is incomplete. The gold standard for measuring intrahepatic fat content is liver biopsy followed by histologic analysis. This procedure can increase patient risk and discomfort, be logistically cumbersome and subject to interpretive errors upon analysis. The ability to effectively measure hepatic fat content is essential for both evaluating livers for transplant and diagnosing all stages of NAFLD.

The objective of recent work in the Parker laboratory is to demonstrate the correlation between hepatic steatosis and shear speed frequency dependence (dispersion) of viscoelastic liver tissue. A non-invasive technique using crawling waves (CrWs) to measure both the stiffness and fat content of liver samples is employed.

Excised mouse and human liver specimens were examined using CrW sonoelastography. Phantoms were prepared by embedding the samples in a porcine gelatin background (8–11%). Two vibration sources were positioned at each side of the phantom with the ultrasound transducer scanning from the top. CrWs were driven at frequencies ranging from 100-300 Hz by offsetting a small frequency difference between two sources. CrW data was de-noised and sinusoidal curve fitting was applied to a similar ROI in each frame to determine the relative wavelength. Wavelengths were then used to calculate respective shear velocities at each frequency for a given sample. The rate of increase in shear velocity over a frequency band was collected to reveal the dispersion of each specimen.

In ob/ob genetically obese mice (n = 10), the mean dispersion slope was 0.15 +/-0.015 cm/sec per 100 Hz, compared to lean ob/- littermates (n = 10) at 0.075 +/-0.02 cm/sec per 100 Hz. Histologic analysis using H&E and oil red O staining confirms steatosis up to 65% in ob/ob animals and 0% to < 5% in ob/- animals. Additionally, human liver scans from patients over a range of steatosis and fibrosis suggests this method can discriminate degrees of steatosis (e.g., minimal < 20%, moderate 20–40%, and severe > 40%) as well as fibrosis.

CrW sonoelastography is potentially a non-

invasive, cost effective and efficient technique for grading not only the stiffness but also the fat content of liver tissue. This method has promise as a safe and effective way to assess liver health in both the realm of liver transplant patients as well as the general population.

Ultrasound standing wave fields pattern cells and affect vascular network formation in engineered tissues

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

Advances in the field of tissue engineering hold great promise in saving the lives of the hundreds of thousands of patients currently awaiting organ transplantation. In the Dalecki and Hocking laboratories, ultrasound-based technologies for the fabrication of engineered tissue are actively being developed to aid in the advancement of this field. These technologies are aimed at overcoming two of the major challenges hindering progress in the field of tissue engineering – reconstructing complex tissue organization in a laboratory setting, and forming a vascular system within engineered tissue to maintain cell viability and function of large, three-dimensional tissue constructs. We have developed a novel ultrasound standing wave field (USWF)-based technology to spatially pattern cells and extracellular matrix proteins within three-dimensional, collagen-based engineered tissue and have utilized this technology to accelerate the formation of extensive vascular networks throughout the three-dimensional volume of tissue constructs.

Acoustic radiation forces associated with the development of an USWF can actively direct cells in suspension into multicellular planar bands that are perpendicular to the direction of sound propagation and that are spaced at half-wavelength intervals. To maintain the USWF-induced spatial pattern of cells after removal of the sound field, cells were suspended in an unpolymerized type-I collagen solution, and the solution was allowed to polymerize into a gel during USWF exposure. By varying the magnitude of the acoustic radiation force experienced by the cells, as well as utilizing different acoustic frequencies, various spatial patterns of multicellular planar bands were created within three-dimensional collagen gels using our USWF technology (Figure 1, next page). The USWF-induced patterns produced within the gels ranged from homogeneously distributed cells to loosely aggregated bands of cells to more densely packed cell bands as the radiation force magnitude increased (Figure 1, panel A). As such, cell band density was controlled by varying the radiation force magnitude of the USWF. Spacing between adjacent cell bands was controlled by utilizing a different frequency USWF (Figure 1, panel B). Additionally, 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 organization of proteins, and other biologically active molecules, can be controlled using our USWF technology. Taken together, these data indicate that our USWF technology has the ability to create complex spatial patterns of cells and proteins within engineered tissue constructs, and therefore, holds promise in aiding the field of tissue engineering in reconstructing tissues with complex organization in a laboratory setting.

In previous work, we utilized our USWF technology to demonstrate that USWF-induced patterning of endothelial cells (the cells that line the inner wall of blood vessels) into multicellular planar bands led to the rapid and extensive vascularization of the three-dimensional collagen gel. To further investigate whether the initial USWF-induced pattern of cells affects vascular network formation or morphology, collagen gels with various spatial patterns of endothelial cells were created using our USWF technology and both the rate of formation and morphology of vascular networks within the gels were analyzed. Constructs with loosely aggregated bands of cells developed anastomosing networks with a tortuous morphology within 4 days post-exposure. These networks were present throughout the three-dimensional volume of the construct and were maintained at least 10 days post-fabrication (Figure 2). Anastomosing network formation was delayed until day 10 in constructs initially containing densely packed cells bands. Networks in these samples exhibited a vascular-tree like morphology with large, lumen-containing areas and smaller branching capillary-like structures emerging from these areas (Figure 2). In contrast, any vascular network formation in sham-exposed samples initially containing a homogeneous distribution of cells was confined to a thin layer at the gel bottom and not present throughout the three-dimensional volume of the engineered

tissue (Figure 2). Similar results were observed for constructs fabricated at a different frequency where the initial spacing between adjacent bands of cells was decreased (Figure 2). Taken together, these data indicate that the initial density of USWF-induced cell bands, but not the initial spacing, affects both the rate of formation and morphology of vascular networks within collagen-based engineered tissue. As such, the spatial organization of endothelial cells was shown to influence the vascularization of engineered tissue in vitro. Therefore, not only can we use our USWF technology to produce various spatial patterns of cells within engineered tissue for reconstructing complex tissue organization, USWF-patterning can also be used to effectively and rapidly create vascular networks within engineered tissue with complex network morphologies.

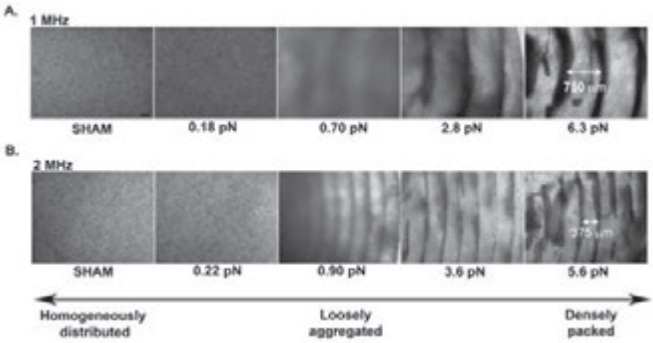


Figure 1. *Various spatial patterns of cells created within three-dimensional engineered tissue using USWF technology. Patterns ranging from homogeneously distributed cells, to loosely aggregated planar bands of cells, to more densely packed cell bands produced at 1 MHz (A) and 2 MHz (B). Scale bar, 200 μm.*

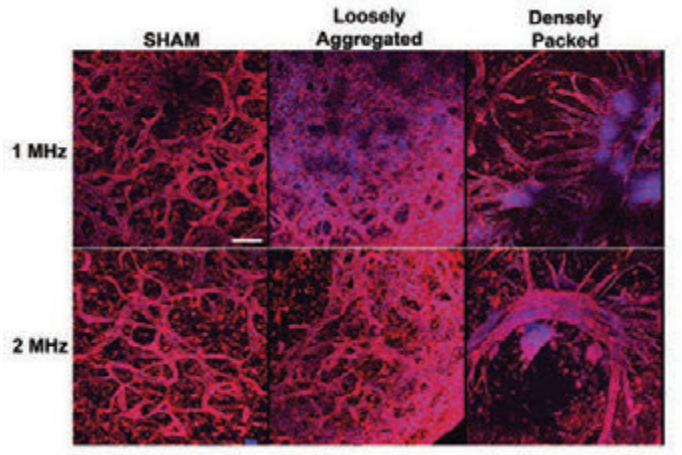


Figure 2. *Various complex vascular network morphologies created within three-dimensional engineered tissue using USWF technology. Multiphoton microscopy images showing vascular network morphology (red, vessel walls; blue, cell nuclei) as dense and tortuous for initially loosely aggregated cell bands but as vascular tree-like for constructs initially containing more densely packed cells bands. Homogeneous cell distributions present in sham samples did not develop networks throughout the three-dimensional construct. Scale bar 200 μm.*

Comparing the performance of plane wave and sparse array elastography imaging systems

Sangmithra Korukonda, MS, and Marvin M. Doyley, PhD

Non-invasive vascular elastography (NIVE) imaging of the carotid artery provides quantitative information on vessel morphology and its mechanical properties. This information may be used to characterize plaque vulnerability. In this work, we compare sparse array and plane wave imaging to perform ultrafast elastographic imaging of the carotid artery. A SONIX RP commercial ultrasound scanner (Ultrasonix Corp., Vancouver, Canada) equipped with an L14–5/38 linear array probe was configured to acquire (1) sparse array data with only 7 active transmit elements and 128 receive elements, and (2) plane wave data by transmitting simultaneously with all 128 elements and receiving in parallel with all elements. Elastographic imaging was performed on vessel phantoms at intra-luminal pressure differences ranging from 4-20 mm Hg. Three-dimensional data sets were acquired by translating the transducer along the long axis of the phantoms in increments of 2 mm. Axial and lateral displacement images were computed by applying 2D cross-correlation to the beam formed radio-frequency (RF) echo frames obtained at different pressures. Radial and circumferential elastograms were obtained from the gradients of the displacement estimates.

Strain elastograms were obtained with both plane wave and sparse array imaging methods over the range of pressures employed in this study. Figure 1 (next page) shows representative examples of elastograms obtained from a cross-section of a phantom containing a soft plaque (4 o'clock). The plaque appears as a localized region of high strain, which is clearly demarcated in the radial (a) and circumferential (b) strain elastograms obtained with the sparse array. In the case of the homogeneous elastograms, higher variance was observed in the plane wave elastograms as compared to the sparse array elastograms, particularly in the lateral sectors. In conclusion, sparse array imaging is a promising elastography technique that can image the carotid artery in real time at ultrafast frame rates. While plane wave imaging has greater speed and higher signal power, sparse array imaging has greater sensitivity to tissue motion, particularly in the lateral direction. In addition, with the high acquisition

speeds, 3D data can be acquired to improve the diagnostic value of this technique.

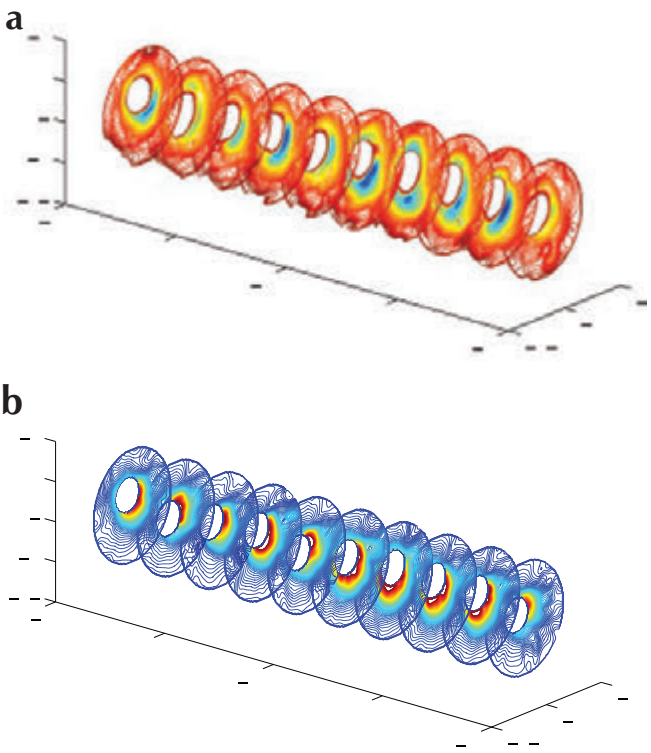


Figure 1. *3-D visualization of strain within a heterogeneous vessel phantom obtained using ultrasound based sparse array elastography. An eccentric soft plaque is located on the phantom's inner lumen at the 4 o'clock cross-section, which is subjected to a 5 mm Hg pressure difference. Pairs of sparse array images (pre- and post-deformation) were acquired along the vessel long axis at increments of 2 mm. Cross-correlation analysis was performed to obtain the displacement estimates between consecutive ultrasound RF image pairs. The displacements were then used to compute radial (a) and circumferential (b) vessel strains. Regions of localized high strain in the 4 o'clock sectors of the vessel clearly indicate the presence of the soft plaque (Plot scales (a) and (b) are [-3 0] and [0 3], respectively).*

Non-contact ultrasound characterization of paper substrates

Maria Helguera, PhD

In collaboration with Ricardo Costa, CENIMAT, Universidade de Nova Lisboa, Portugal, the Helgeura lab is investigating the use of ultrasound for characterization of paper substrates. Latest developments in the field of lignocellulose thin film transistors (LPTFT) have demonstrated that it is possible to construct electronic nanoscale components on top of micrometric structures. There is a need for consistent results and it has been determined that the fiber orientation in commercial papers affect performance. A raster scan of a 2.25 cm^2 region in the paper was investigated using non-contact ultrasound pulse-echo techniques at 1 MHz. Six different classes of papers that have been used in the construction of LPTFT were analyzed. Figures 1a and 1b (below) show results for two paper substrates. It can be seen that the structure of the papers and fiber orientation are easily detected using this technique. The next step in this project entails quantitative analysis of the backscattered data to extract characteristic parameters for each paper sample.

Figure 1a. *From left to right: Paper "D", C-scan of top surface, B-scan image;*

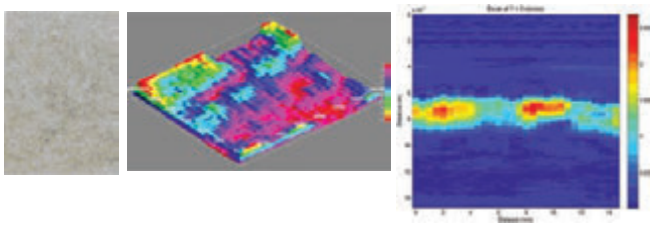
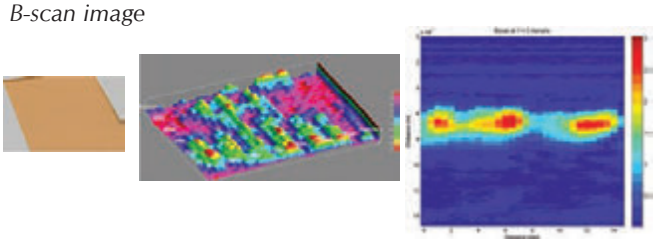


Figure 1b. *From left to right: Paper "E", C-scan of top surface, B-scan image*



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 mediated by complex and dynamic interactions between cells and their surrounding extracellular matrix (ECM). Disruptions in the healing process can lead to chronic wounds that may impair quality of life or result in death. Fibronectin is a principal component of the ECM and is thought to play a role in wound healing. Soluble fibronectin is polymerized into insoluble ECM fibrils via a tightly regulated, cell-dependent process. In turn, ECM fibronectin stimulates several cell functions critical for wound repair, including proliferation. Recent data suggest that ECM fibronectin may exist in various conformational states that produce different cellular behaviors. The Hocking and Dalecki laboratories are investigating whether ultrasound, and its associated mechanical

forces, can be used to promote the healing of chronic wounds. To this end, we developed an in vitro model of tissue formation by combining compliant, polymerized collagen-I substrates with the cell-mediated assembly of fibronectin matrix fibrils. Fibronectin matrix assembly stimulated the formation of multicellular structures with tall ($\sim 50\ \mu$m) dome-like central cores surrounded by cells that extended onto the collagen substrate. Immunofluorescence microscopy studies revealed that fibronectin fibrils were present throughout the microtissues, whereas proliferating cells were confined to the microtissue periphery (Figure 1). Collagen and fibronectin fibrils also co-localized only at the microtissue periphery (Figure 2). Blocking fibronectin-collagen interactions completely inhibited cell proliferation, indicating that cell proliferation in response to fibronectin is dependent on the co-polymerization of collagen and fibronectin fibrils. Ongoing experiments will determine if ultrasound exposure can alter the conformational state of collagen fibrils to enhance fibronectin-collagen interactions and, in turn, stimulate cell proliferation.

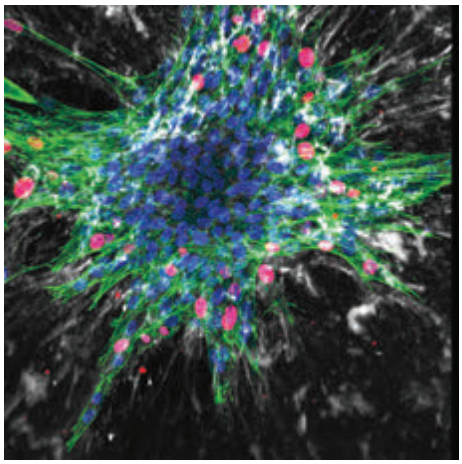


Figure 1. *Immunfluorescence image captured using two-photon microscopy showing the spatial organization of fibronectin (white), proliferating cells (red), and cell nuclei (blue) within three-dimensional microtissues.*

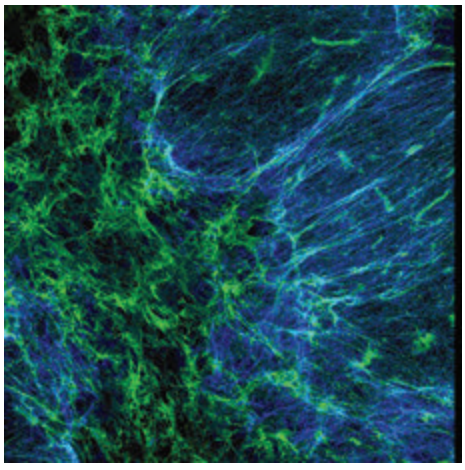


Figure 2. *Immunfluorescence image captured using two-photon microscopy showing fibronectin (green). Collagen fibrils (blue) were visualized using second harmonic generation. Areas of co-localization appear white.*

Measuring circumferential and radial component of displacement using a non-rigid registration based displacement estimator

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

Intravascular ultrasound elastography is emerging as an imaging modality that can visualize the radial strain distribution within vascular tissues providing new diagnostic information that cardiologists may use to detect rupture prone atherosclerotic plaques. Since plaques typically rupture in areas where the circumferential stress is high, it should prove useful to develop methods to measure both the radial and circumferential component of displacement. The goal of recent work from the Doyley lab was to investigate the feasibility of developing elastographic methods for visualizing the circumferential strain within vascular tissue using a single-element rotating catheter. In these studies, elastography imaging was performed on homogeneous and heterogeneous vessel phantoms using a commercially available intravascular ultrasound scanner (ILABTM, Boston Scientific) that was equipped with a 40 MHz rotating element catheter. The phantoms were pressurized using a dynamic pressurization system (peak to peak 20 mmHg, 1 Hz) during elastographic imaging. A non-rigid image registration based method was developed to obtain both radial and circumferential displacements, based on which radial and circumferential strain elastograms were computed. Since a single element rotating transducer was used, non-uniform rotation distortion (NURD) exists that will induce additional circumferential motion. The magnitude of NURD is dependent on the catheter position; in this study the magnitude of the non-uniform distortion was estimated to be $+1$-$2°$ from the angular location. To make the method feasible when NURD exists, an incompressibility constraint was introduced in the image registration method procedure. Phantom studies were performed to investigate the feasibility of the method. Figure 1 (next page) shows representative examples of radial and circumferential strain images obtained from a homogeneous vessel phantom. Figure 2 (next page) shows representative examples of radial and circumferential strain images obtained from a heterogeneous phantom that contained a soft

plaque. The result of this preliminary investigation suggests that circumferential strain images can be computed using a registration based displacement estimator with a commercially available IVUS imaging system.

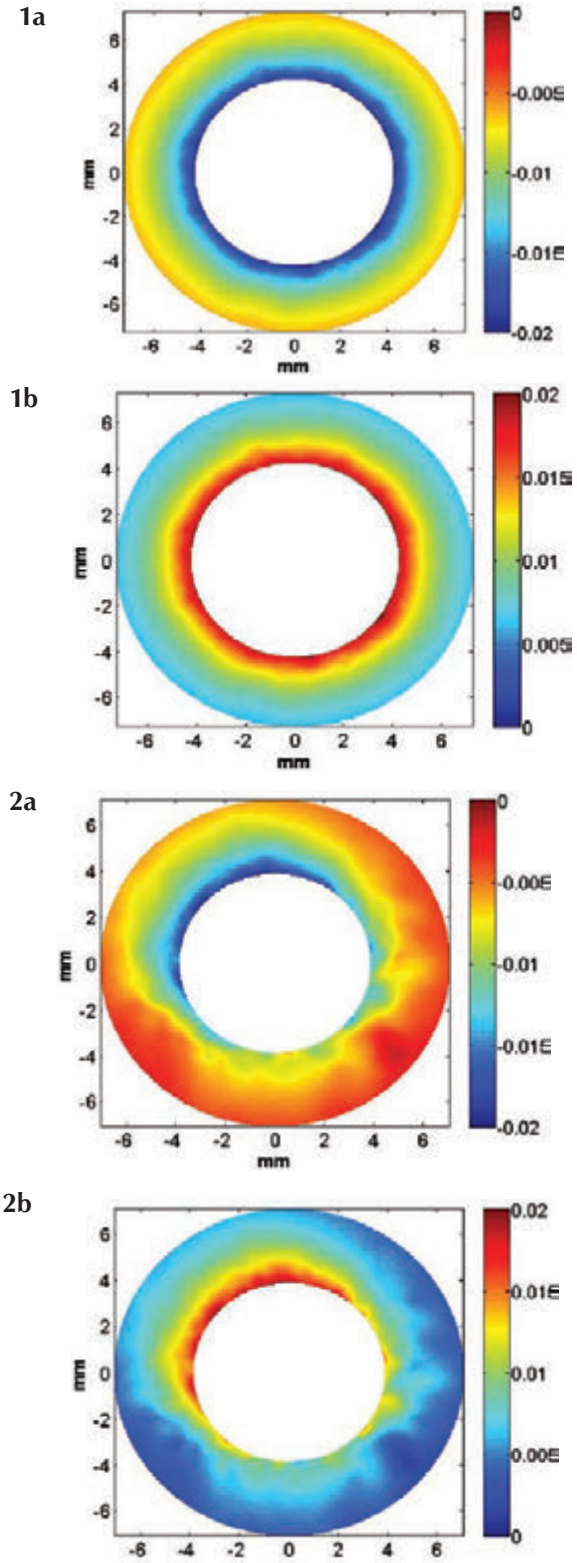


Figure1. *(a) radial strain image of a homogeneous phantom; (b) circumferential strain of a homogeneous phantom.*
Figure2. *(a) radial strain image of a heterogeneous phantom; (b) circumferential strain of a heterogeneous phantom.*

Three-dimensional image analysis and visualization of vasculature in engineered tissues

Maria Helguera, PhD, Mohammed Yousef Hussien, MS, Kelley A. Garvin, MS, Denise C. Hocking, PhD, Diane Dalecki, PhD

The Dalecki and Hocking laboratories have demonstrated that ultrasound standing wave fields can non-invasively control the spatial distribution of cells within three-dimensional, collagen-based engineered tissues (see related story on page 14). Their studies indicated that ultrasound-induced alignment of mouse embryonic myofibroblasts in collagen gels increases cell contractility and cell-mediated extracellular matrix reorganization. Further, noninvasive organization of endothelial cells within collagen gels accelerates the formation of capillary sprouts that mature into branching networks throughout the three-dimensional hydrogel. Multi-photon microscopy imaging techniques were employed to visualize these branching networks, as shown below in Figure 1. Both the rate of formation and morphology of the resultant vascular network are dependent upon the ultrasound field parameters used to produce the cellular alignment.

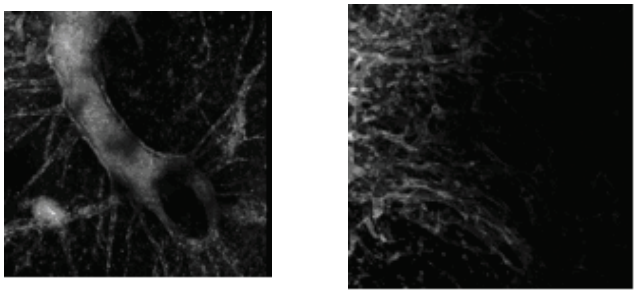


Figure 1. *Multi-photon z-projection microscopy images show different vascular networks produced in response to different ultrasound standing wave field parameters used for cell patterning. Left: 1 MHz, 0.15 MPa, Right: 1 MHz, 0.05 MPa*

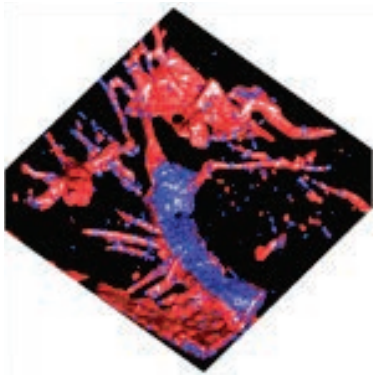


Figure 2. *3-D visualization of two co-registered data sets. Cell nuclei are stained with DAPI (blule) and endothelial cells are stained with anti-CO31 antibodies (red).*

This collaborative multidisciplinary project draws on the expertise of Dr. Maria Helguera to develop image processing approaches to quantify properties of engineered tissues. In one project, the Helguera lab is developing interactive 3-D visualization tools that provide actual volume of vaculature in engineered tissues, as shown in Figure 2 (previous page). Furthermore, Dr. Helguera is investigating 3-D textural and volumetric image analysis techniques for characterizing the multi-photon microscopy image stacks. In recent work, the Helguera lab implemented an algorithm to quantitatively analyze the texture and morphology of vasculature in engineered tissues produced by the Dalecki and Hocking labs. Textural and volumetric parameters were able to differentiate quantitatively the vascular networks produced with different ultrasound standing wave fields of different pressure amplitudes. The Helguera lab is currently working on a stand-alone graphical user interface tool that will support scientists working in this field.

A coded excitation technique for functional imaging of coronary atherosclerosis using ultrasound contrast agents

Himanshu Shekhar, MS, Marvin M. Doyley, PhD

Acute coronary syndromes may occur when life–threatening atherosclerotic plaques rupture in the advanced stages of cardiovascular disease. There is increasing evidence that plaque neovascularization accelerates the progression and disruption of atherosclerotic plaque. Plaque neovessels may be detected by subharmonic intravascular ultrasound (IVUS) imaging with ultrasound contrast agents (UCAs). The assessment of plaque neovascularity and perfusion at high spatial and contrast resolution may help identify those most at risk of acute coronary syndromes. While theoretical considerations dictate the use of high peak pressures and long excitation pulses for obtaining high contrast subharmonic IVUS images, microbubble disruption and the risk of hemorrhage limit the peak pressures practical. Moreover, the use of long pulses degrades the axial resolution achievable. In recent work from the Doyley lab, a novel excitation strategy using preemphasized chirps for microbubble insonation was employed to significantly enhance subharmonic signal from UCA. Therefore, low peak pressures can be employed to obtain high contrast resolution and the axial resolution can be restored by pulse compression. This technique was validated by numerical simulations and flow studies at high transmit frequencies (20 MHz). High spatial and contrast resolution achievable by this technique may significantly enhance the clinical potential for functional imaging of coronary atherosclerosis.

ECE graduate student, Himanshu Shekhar

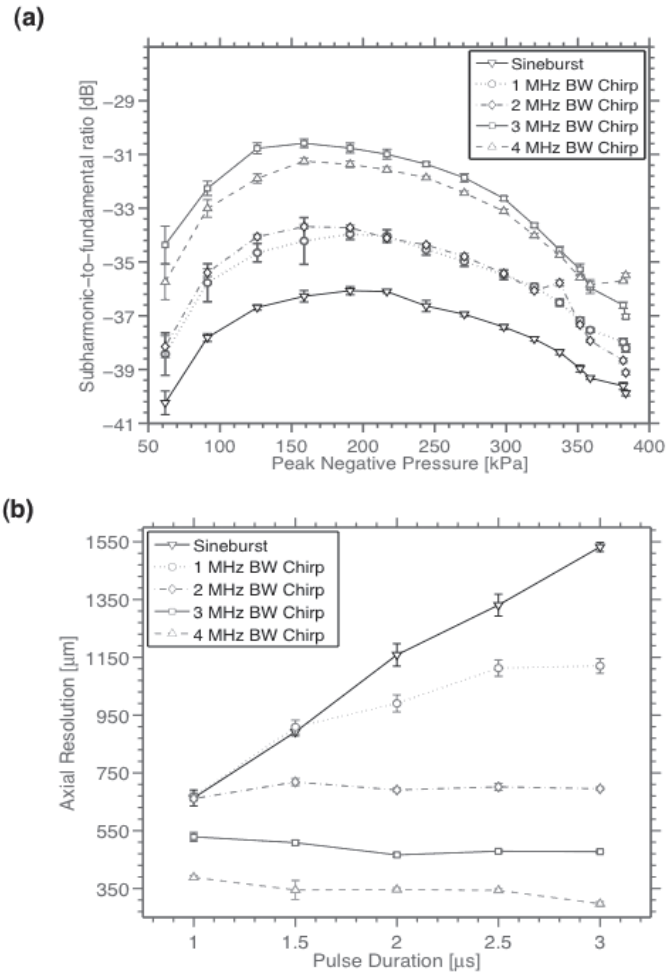


Figure 1. *Demonstrattion that chirp-coding of the ultrasonic transmitted pulse can improve the sensitivity and axial resolution of high-frequency subharmonic imaging. Chirp-coded excitation shows improved subharmonic to fundamental ratio computed from the frequency response of ultrasound contrast agent backscatter (a), and improves the axial resolution by almost two-fold (b).*

Crawling wave detection of prostate cancer: Preliminary in vitro results

Liwei An, PhD, Brady Mills, BS, Zaegoo Hah, PhD, Shuo Mao, MS, Jorge Yao, MD, Jean Joseph, MD, Deborah Rubens, MD, John Strang, MD, Kevin J. Parker, PhD

A focus of investigation in the Parker laboratory is to develop signal and image processing methods to derive an accurate estimation of local tissue elasticity using the crawling wave (CrW) sonoelastography method. The task is to reduce noise and to improve the contrast of the elasticity map. The protocol of the CrW approach was first tested on heterogeneous elastic phantoms as a model of prostate cancers. Then the contrast-to-noise ratio of the estimation was calculated iteratively with various sequences of algorithms to determine the optimal signal processing settings. Finally, the optimized signal processing was applied to ex vivo prostate cancer detection. The comparison of the segmented elasticity map and the histology tumor outline was made by quadrants to evaluate the diagnostic performance of the protocol. Furthermore, the CrW approach was combined with amplitude-sonoelastography to achieve a higher specificity.

Results of this study demonstrated the feasibility of the proposed approach for clinical applications. In the application to ex vivo prostate cancer detection, the established approach was tested on 43 excised prostate glands. The combination of the CrW approach and amplitude-sonoelastography achieved an accuracy of over 80% for finding tumors larger than 4 mm in diameter. The elasticity values and contrast found by the CrW approach were in agreement with the previous results derived from mechanical testing. In summary, crawling waves can be applied to detect prostate cancer with accuracy approaching 80% and can quantify the stiffness or shear modulus of both cancerous and noncancerous tissues. The technique therefore shows promise for guiding biopsies to suspect regions that are otherwise difficult to identify.

Interactions of underwater sound fields and biological tissues

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

Underwater sound fields are used for numerous commercial and military applications, including imaging, oil exploration, mapping the ocean floor, and harbor surveillance. 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 Naval Submarine Medical Research Laboratory (NSMRL) in Groton, CT have been collaborators and supporters of 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.

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 over four orders of magnitude (i.e., ~100 Hz to 1000 kHz). Sheryl Gracewski has developed both analytical and computational models to predict the acoustic fields within the exposure chambers of our experimental acoustic systems. 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.
Through a collaborative project, the Dalecki lab and Hydroacoustics, Inc. (HAI) investigated the effects of underwater acoustic impulses on mammalian systems. Air gun technology, water tanks, and measurement facilities at HAI were used to generate underwater acoustic impulses for our bioeffects investigations. The Dalecki lab completed a series of experimental investigations on the effects of underwater acoustic impulses on murine lung in vivo. 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.

TISSUE ELASTICITY CONFERENCE HIGHLIGHTS

Celebrating its Tenth Anniversary, the International Tissue Elasticity Conference displayed mugs from the the previous conferences.

The Tenth International Tissue Elasticity Conference was held in Arlington, Texas from October 12–15, 2011. 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 **Alex Partin, Michael Richards, Kevin J. Parker,** and **Marvin Doyley** attended the conference.

Dr. Parker, along with co-founder Jon Ophir, provided the opening remarks at the conference. In their joint welcoming statement in the proceedings, Dr. Parker and Dr. Ophir wrote, "This year we celebrate the 10th Anniversary of the annual International Tissue Elasticity Conference. In the 1990s we saw a remarkable development of technologies and approaches for imaging various elastic properties of tissues. The 2000's have seen a continuation of innovative approaches, with the addition of a major step. That important step was the creation of specialized scanners for conducting clinical research on thousands of patients in some of the most highly respected medical centers around the world. In retrospect, the evolution of the field is a superb case study of translational research, developing from 'bench to bedside.' This conference series has, by design, served as the place where researchers, clinicians, industry leaders, and students from around the world could trade ideas and discuss the latest advances, while creating an archival record of their progress. The international participation in the Conference now includes virtually all global entities engaged in research, development, commercialization and practice in the field."

Conference Co-Founder Kevin J. Parker

As with previous conferences, the tutorial series on the technical and clinical progress over the last 10 years as well as potential for the future was continued by Drs. Jeffrey Bamber (UK) and Mark Palmeri (US). The conference also included the popular format of the formal Poster Session, where each presenter has the opportunity to give a brief oral summary of his/her poster.

Next year's conference will be held October 2–5, 2012 in Deauville, France. Please visit www.elasticityconference.org for more in formation.

RCBU members Alex Partin, Michael Richards, Kevin J. Parker, and Marvin Doyley at the Tenth International Tissue Elasticity Conference in Arlington, Texas in October 2011.

RCBU NEWS

In Memoriam: Wesley Nyborg

The biomedical ultrasound community sadly lost one of its most important pioneers. Wesley Nyborg passed away on September 24, 2011 at the age of 94. Wes was a member of the Physics Department at the University of Vermont for over 50 years. Wes' seminal theoretical and experimental work forms the foundation for our understanding of the biological effects of ultrasound. He developed fundamental theories of the physical mechanisms of interaction of ultrasound with tissues including acoustic cavitation, ultrasound heating, and acoustic radiation force. He was a member of the National Academy of Engineering, and was recognized with the highest awards from numerous scientific societies. Wes was a Charter Member of the RCBU and was a long-time friend and colleague for many of us.

Dr. Edwin Carstensen, Founding Director of the RCBU, remembered Dr. Nyborg thus: "Wes was my longest and in many ways my most important professional friend. Wes rightly deserves the title, father of bioacoustics. Others dabbled in the field before him but in total selfless effort and intellectual superiority he was the first and best. After a flurry of interest in the mid-20th century, there was a time in the late '60s when he and Floyd Dunn kept the field alive. As it later flourished and became a mainstay of diagnostic medicine, he almost singlehandedly forced the ultrasound community to consider the safety of ultrasound exposure.

"There really aren't words adequate to praise Wes as a friend. He was always positive and helpful in his interactions with colleagues. Our decade together producing the bioeffects volumes for National Council for Radiation Protection was one of the richest scientific experiences of my life."

The RCBU and the wider biomedical ultrasound community will miss Wes dearly.

New Ultrasound Patent

Robert C. Waag and Jeffrey P. Astheimer have been issued a new patent. Patent US 7,867,166, ***Statistical estimation of ultrasonic propagation parameters for aberration correction,*** was issued on January 11, 2011, and the abstract was published in July, 2011 (J Acoust Soc Am. 2011, 130(1):641).

Maria Helguera was invited to join the Scientific Advisory Board of the International Conference on Education, Research and Innovation, Madrid, Spain.

Denise Hocking was appointed to serve a four-year term on the Bioengineering, Technology, and Surgical Sciences (BTSS) Study Section of the National Institutes of Health (NIH) Center for Scientific Review (CSR).

Vikram Dogra was appointed editor-in-chief of ***The Journal of Clinical Imaging Science*** (JCIS) (www.clinicalimagingscience.org). This peer-reviewed, multidisciplinary journal covers all aspects of imaging, including technical innovations, review articles, case reports, original research, and pictorial essays, enabling radiologists to clearly comprehend concepts and practices, and encouraging further research and technical advances. The primary aim of *The Journal of Clinical Imaging Science* is to provide free access to medical information, especially to developing countries that do not have the resources to join the imaging societies or subscribe to the journals.

Marvin Doyley was invited to join the Editorial Board of the Journal of Electronic Imaging as an expert in ultrasound imaging.

RCBU AWARDS

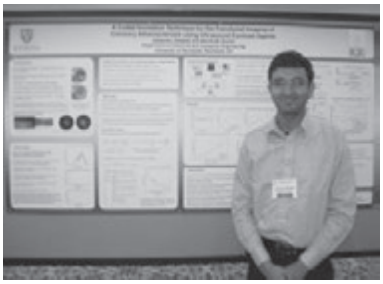
Kevin Parker Receives Lifetime Achievement Award

Left: Kevin J. Parker, Dean Emeritus of the School of Engineering and Applied Sciences, and Right, Rob Clark, Dean of the Hajim School of Engineering and Applied Sciences

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 awarded the Hajim School Lifetime Achievement Award. The award recognizes Professor Parker's long-standing contributions to the School of Engineering and Applied Sciences. Dean Rob Clark presented the award and recognized Professor Parker's outstanding scientific research accomplishments, patents, teaching, and dedicated service to the university, including Dean of the School of Engineering and Applied Sciences, Chair of the Department of Electrical and Computer Engineering, and Director of the Rochester Center for Biomedical Ultrasound.

Student Research Recognized at Acoustical Society of America Meeting

RCBU student member **Himanshu Shekhar** was awarded Second Place in the Best Student Paper in the Biomedical Acoustics Competition at the 161st Meeting of the Acoustical Society of America, held in June in Seattle, Washington. Himanshu was recognized for his research titled, *A Coded Excitation Technique for the Functional Imaging of Coronary Atherosclerosis Using Ultrasound Contrast Agents.*



Himanshu Shekhar

Students Awarded at Undergraduate Research Exposition

The work of several RCBU students was recognized at the annual University of Rochester Undergraduate Research Exposition 2011. Aaron Zakrzewski (ME 2011), a UR/Xerox Undergraduate Fellow mentored by Mechanical Engineering **Professor Sheryl Gracewski**, gave an oral presentation of his research titled *Natural frequency of bubbles within rigid and compliant tubes,* which received a Deans' Award for Undergraduate Research in Engineering and Applied Sciences. Jasmine Carvalho (BME 2011) from the **Dalecki Lab** presented her work titled *Investigations of Ultrasound Parameters to Promote Spatial Organization of Cells in Three-Dimensional Engineered Tissues.* Vlabhav Kakkad (BME 2011) from the **McAleavey Lab** presented his work titled *Experimental Implementation of Shear Wave Induced Phase Encoding Imaging.*

Speaking at the Engineering and Applied Sciences Symposium Talks: (left to right) Benjamin Freedman (BME 2011), Kelli Summers (BME 2011), and Aaron Zakrzewski (ME 2011).

Vlabhav Kakkad (BME 2011) with his poster, Experimental Implementation of Shear Wave Induced Phase Encoding Imaging.

Jasmine Carvalho (BME 2011) in front of her poster, Investigations of Ultrasound Parameters to Promote Spatial Organization of Cells in Three-Dimensional Engineered Tissues.

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

- **Statistical Estimation of Ultrasonic Propagation Parameters for Aberration Correction**
  U.S. Patent No. 7,867,166 issued to **Robert Waag** and Jeffrey Astheimer on January 11, 2011
- ***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
- ***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 2011 fiscal year, the University received $415 million in research funding. The UR Offices of Technology Transfer received over 120 invention disclosures, including several non-invasive diagnostic and therapeutic methods and tools. The University was granted 27 new U.S. patents, 22 foreign patents, and successfully completed 22 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.

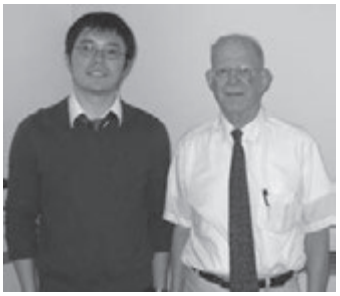
The UR is consistently rated as one of the best educational institutions in the nation for patent licensing and revenue, according to the Association for University Technology Managers (AUTM). The AUTM U.S. Licensing Activity Survey is an annual report of the technology transfer activity of top universities, research institutions, and teaching hospitals across the nation. In 2011, UR royalty revenue exceeded $41.8 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 2011 UR Technology Commercialization Annual Report, visit the University of Rochester Office of Technology Transfer at http://www.urmc.rochester.edu/technology-transfer/.

RCBU MEMBER EDUCATION

Training Completed

Wei Jiang received his Ph.D. degree in Electrical and Computer Engineering,from the University of Rochester in May 2011. His PhD dissertation, *Ultrasound Focusing by Use of Apertures with Different Pitches and Ultrasound Imaging by Use of a Hemispheric Transducer Array* was supervised by **Robert C. Waag, PhD.**



Wei Jiang, Ph.D. and Robert C. Waag, Ph.D.

New Ultrasound Course Offered

RCBU member **Andrew Hesford** offered a new course, ECE 492—Computational Methods. The course covered computational techniques for the solution of numerical problems with applications of the techniques in acoustic and electromagnetic wave propagation and scattering. Professor Hesford is a Research Assistant Professor in the Department of Electrical and Computer Engineering and his areas of expertise include diagnostic ultrasound imaging, acoustic aberration estimation and correction, acoustic and electromagnetic forward and inverse scattering, fast algorithms, parallel systems, computational wave physics, and general-purpose GPU computing.

RCBU member **Shweta Bhatt, M.D.** participated in the creation of the Maintenance of Certification examination for the American Board of Radiology, and RCBU Associate Director **Dr. Deborah Rubens** and **Dr. Bhatt** were oral board examiners in ultrasound.

RCBU member **Dr. Vikram Dogra,** along with international colleagues, continues his leadership with 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.

BME Senior Design Students Tackle Ultrasound Problem

For the last ten years, senior biomedical engineering students have helped real-life customers solve bioengineering problems through a two-semester Senior Design course taught by RCBU member **Amy Lerner** and Scott Seidman. In 2011, BME seniors Andreana Echter, Eileen Hansen, Katherine Prokop, and Frank Yeung became interested in a problem presented by RCBU members **Professor Marvin Doyley** and **Michael Richards, Ph.D**. The Doyley Lab is working to develop image processing techniques for Intravascular Ultrasound (IVUS) as a tool to better understand plaque structure and to predict the likelihood of plaque rupture. The senior design team, supervised by RCBU Director **Diane Dalecki, Ph.D.,** developed CoroFlow, a coronary artery perfusion system.

The CoroFlow Team designed and developed a prototype device to perfuse the coronary arteries of excised hearts for IVUS imaging of atherosclerotic plaques. The perfusion systems consist of two primary units. The Heart Unit is comprised of a holder to secure an excised heart for IVUS imaging, and a chamber to submerge the heart in a bathing fluid. The Plumbing Unit provides flow through the coronary artery via a specially designed cannula system that incorporates the IVUS transducer and allows for contrast agent infusion. The final prototype was delivered to the Doyley Lab at the end of the semester.

Summer Acoustics Course

Once again RCBU visiting professor **David Blackstock** offered his popular summer acoustics course. Dr. Blackstock, from the University of Texas at Austin, is a leading expert in acoustics and the author of one of the leading textbooks in physical acoustics.

"I loved this class," says **Karla Mercado**, a BME graduate student and member of the Dalecki lab. "Dr. Blackstock took complicated concepts and made them easy to understand. I definitely benefited from the course because it laid the basic foundation for ultrasound, and what I learned will help me with the rest of the my research by providing me with a more intuitive understanding of ultrasound research. We were blessed to have Dr. Blackstock to teach this summer."

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 2011 PUBLICATIONS

Alvarez DM, **Bhatt S**, **Dogra VS**. Sonographic spectrum of tunica albuginea cyst. J Clin Imaging Sci. 1:5; 2011.

An L, Mills B, Hah Z, Mao S, Yao J, Joseph J, **Rubens DJ**, **Strang J**, **Parker KJ**. Crawling wave detection of prostate cancer: Preliminary in vitro results. Med Phys. 38:2563-71; 2011.

Barry CT, Mills B, Hah Z, Mooney RA, Ryan CK, **Rubens DJ, Parker KJ**. Shear wave dispersion measures liver steatosis. Ultrasound Med Bio. 38:2: 75-182; 2011.

Baum KG, Menezes G, **Helguera M**. Simulation of high-resolution magnetic resonance images on the IBM Blue Gene/L supercomputer using SIMRI. International Journal of Biomedical Imaging. doi:10.1155/2011/305968, 2011.

Bhatt S, Jafri SZ, Wasserman N, **Dogra VS**. Imaging of non-neoplastic intratesticular masses. Diagn Interv Radiol.17:52-63; 2011.

Carstensen EL, Gracewski SM, Dalecki D. Shear strain from irrotational tissue displacements near bubbles. J Acoust Soc Am. 130:3467-71; 2011.

Elegbe EC, Menon MG, McAleavey SA. Comparison of two methods for the generation of spatially modulated ultrasound radiation force. IEEE Trans Ultrason Ferroelectr Freq Control. 58:1344-54; 2011.

Garvin KA, Dalecki D, Hocking DC. Vascularization of three-dimensional collagen hydrogels using ultrasound standing wave fields. Ultrasound Med Biol. 37:1853-64; 2011.

Hah Z, Hazard C, **Mills B, Barry C**, **Rubens D, Parker K**. Integration of crawling waves in an ultrasound imaging system. Part 2: Signal processing and applications. Ultrasound Med Bio. 38: 312-323; 2011.

Hazard C, **Hah Z, Rubens D, Parker K.** Integration of crawling waves in an ultrasound imaging system. Part 1: System and design considerations. Ultrasound Med Bio. 38: 2; 296-311; 2011.

Hedegard WC, **Bhatt S**, Saad W, **Rubens D, Dogra V**. Hepatic arterial waveforms on early posttransplant Doppler ultrasound. Ultrasound Q. 27:49-54; 2011.

Helguera M, Baum KG, Schmidt E, Rafferty K, Krol A. Evaluation of novel genetic algorithm generated schemes for PET/MRI image fusion. Journal of Digital Imaging. 24:1031-1043; 2011.

Hesford AJ, Waag RC. Reduced-rank approximations to the far-field transform in the gridded fast multipole method. J Comput Phys. 230:3656-3667; 2011.

Hubeny CM, Sykes JB, O'Connell A, **Dogra VS**. Pilomatrixoma of the adult male breast: A rare tumor with typical ultrasound features. J Clin Imaging Sci. 1:12; 2011.

Jang NW, Zakrzewski A, Rossi C, **Dalecki D, Gracewski S**. Natural frequencies of two bubbles in a compliant tube: Analytical, simulation, and experimental results. J Acoust Soc Am. 130:3347-56; 2011.

Korukonda S, Doyley MM. Estimating axial and lateral strain using a synthetic aperture elastographic imaging system. Ultrasound Med Biol. 37:1893-908; 2011.

Lee V, Alvarez MD, **Bhatt S, Dogra VS**. Median arcuate ligament compression of the celiomesenteric trunk. J Clin Imaging Sci. 1:8; 2011.

Lefort CT, Wojciechowski K, **Hocking DC**. N-cadherin cell-cell adhesion complexes are regulated by fibronectin matrix assembly. J Biol Chem. 26:286:3149-60; 2011.

Loberant N, Bhatt S, Messing E, **Dogra VS**. Bilateral testicular epidermoid cysts. J Clin Imaging Sci. 1:4; 2011.

Mihmanli I, Kantarci F, **Dogra VS**. Endoanorectal ultrasonography. Ultrasound Q. 27:87-104; 2011.

Onur MR, Wandtke B, Yao JL, **Dogra VS**. Paratesticular solitary plasmacytoma. J Clin Imaging Sci. 1:52; 2011.

2011 PUBLICATIONS

Parker KJ. The evolution of vibration sonoelastography. Current Medical Imaging Reviews. 7:283-291; 2011.

Parker KJ, Doyley MM, Rubens DJ. Imaging the elastic properties of tissue: The 20 year perspective. Phys Med Biol. 56:R1-R29; 2011.

Paspulati RM, Turgut AT, **Bhatt S,** Ergun E, **Dogra VS**. Ultrasound assessment of premenopausal bleeding. Obstet Gynecol Clin North Am. 38:115-47.; 2011.

Perera E, Bhatt S, **Dogra VS**. Complications of denver shunt. J Clin Imaging Sci. 1:6; 2011.

Perera E, Bhatt S, **Dogra VS**. Cystic duct remnant syndrome. J Clin Imaging Sci. 1:2; 2011.

Perera E, Bhatt S, **Dogra VS**. Traumatic ectopic dislocation of testis. J Clin Imaging Sci. 1:17; 2011.

Richards MS, Doyley MM. Investigating the impact of spatial priors on the performance of model-based IVUS elastography. Phys Med Biol. 21;56:7223-46; 2011.

Rothschild J, Bhatt S, **Dogra VS**. Renal collision tumor in association with xanthogranulomatous pyelonephritis. J Clin Imaging Sci. 1:9; 2011.

Roy DC, Wilke-Mounts SJ, **Hocking DC**. Chimeric fibronectin matrix mimetic as a functional growth- and migration-promoting adhesive substrate. Biomaterials 32:2077-87; 2011.

Wang H, Weaver JB, Perreard II, **Doyley MM**, Paulsen KD. A three-dimensional quality-guided phase unwrapping method for MR elastography. Phys Med Biol. 56:3935-52; 2011.

2011 PRESENTATIONS

Barry C, Mills B, Hah Z, Mooney R, Safadjou S, Ryan C, **Rubens D, Parker K**. Ex vivo and in vivo ultrasonographic hepatic steatography measurements correlate with histologic estimates of liver fat content. Presented at the American Association for the Study of Liver Diseases: The Liver Meeting, San Francisco, CA, November 2011.

Barry C, Mills B, Hah Z, Mooney R, Safadjou S, Ryan C, **Rubens D, Parker K**. Ultrasonic hepatic steatography: A noninvasive method to measure intrahepatic fat content. Presented at the American Transplant Congress, Philadelphia, PA, May 2011.

Castaneda B, Westesson K, **An L**, Yao J, Baxter L, **Joseph J,** Hoyt K, **Strang J**, **Rubens D, Parker K.** Prostate cancer detection using 3-dimensional vibration sonoelastography: Ex vivo and in vivo results. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Doyley MM. A model-based approach to quasi–static, harmonic and transient elastography. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Doyley MM. Model-based elastography: Problems and opportunities. Presented at the Workshop on Biomechanical Engineering, Renssalaer Polytechnic Institute Inverse Problems Center, Troy, NY, April 2011.

Eisenbrey J, Sridharan A, Lobel B, deMuinck E, Forsberg F, **Doyley M**. Comparison of parametric contrast-enhanced fundamental and subharmonic intravascular ultrasound for plaque identification. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Garvin KA, Carvalho JJ, Hocking DC, Dalecki D. Ultrasound technology for cell patterning and vascularization of three-dimensional engineered tissue. Presented at the Tissue Engineering and Regenerative Medicine International Society Annual Meeting, Houston, TX, December 2011.

Garvin KA, Dalecki DC, Hocking D. Vascular network formation within collagen hydrogels fabricated with different spatial organizations of endothelial cells using ultrasound-based cell patterning techniques. Presented at the North American Vascular Biology Organization's Vascular Matrix Biology and Bioengineering Workshop III, Hyannis, MA, October 2011.

SELECTED 2011 PRESENTATIONS

Hah Z, Mills B, Hazard C, **Parker K, Rubens D.** Measuring dispersion of a biological medium with crawling waves synthesized from ultrasonic radiation force. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Hah Z, Hazard C, **Mills BN**, Yao J, **Rubens DJ, Parker KJ**. Local shear speed estimation of ex–vivo prostate using acoustic crawling waves (arc) generated from radiation forces. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Jing S, Richards MS, Doyley MM. Measuring circumferential and radial component of displacement using a non-rigid registration based displacement estimator. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Kaproth-Joslin K, **Rubens D.** Beyond portal hypertension: Abnormalities of the portal venous system. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Kaproth-Joslin K, **Francis C**, Hobbs S, **Rubens D.** Predictive risk score for venous thromboembolism in patients with malignancy: A role for prophylactic screening. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Korukonda S, Doyley MM. Comparing the performance of plane wave and sparse array elastography imaging systems. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Korukonda S, Doyley MM. Ultrafast elastography imaging of the carotid artery using sparse arrays. Presented at the IEEE International Ultrasonics Symposium, Orlando, FL, October 2011**.**

McAleavey S, Kakkad V. Shear wave induced phase encoding imaging with enhanced resolution. Presented at the 2011 IEEE International Ultrasonics Symposium, Orlando, FL, October 2011.

Mills B, Barry C, Hah Z, Rubens DJ, Parker KJ. Using crawling wave sonoelastography for the measurement of intrahepatic fat content. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Parker K. Three-dimensional vibration elastography and crawling waves. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Parker KJ, Hah Z. Dispersion and distortion of shear wave pulses. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Parker KJ, Hah Z, **Rubens D.** Vibration elastography: Overview and clinical results. Presented at the Symposium on Ultrasonic Imaging and Tissue Characterization, Rosslyn, VA, June 2011.

Partin A, Hah Z, Mills BN, Rubens DJ, Parker KJ. A hand-held system for quantitative mapping of elastic properties within a biomaterial from crawling waves generated on the surface. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Richards MS, Doyley MM. Minimally constrained reconstructions in intravascular ultrasound elastography: Initial clinical investigation. Presented at the Tenth Annual International Tissue Elasticity Conference, Arlington, TX, October 2011.

Sevilla C, Dalecki D, Hocking DC. Fibronectin-collagen interactions promote cell proliferation and determine microtissue structure. Presented at the Tissue Engineering and Regenerative Medicine International Society Annual Meeting, Houston, TX, December 2011.

Shekhar H. A coded excitation technique for the functional imaging of coronary atherosclerosis using ultrasound contrast agents. Presented at the 161st Meeting of the Acoustical Society of America, Seattle, WA, June 2011.

Sridharan A, Eisenbrey JR, DeMuinck ED, **Doyley MM**, Forsberg F. Intravascular subharmonic imaging of atherosclerosis: An in vivo pilot study. Presented at the Symposium on Ultrasonic Imaging and Tissue Characterization, Rosslyn, VA, June 2011.

Tillett J, Astheimer J, **Waag R.** Aberration estimation and correction in ultrasound imaging. Presented at the AIUM Annual Convention, New York, NY, April 2011.

Vaidya, K, Hatfield K, **Helguera M**, Pichichero M. Building parametric images of biological materials using high frequency ultrasound. International Conference on Biomedical Engineering, Manipal University, India, 2011.

Walsh JM, **Mills B, Rubens D, Parker JK, An L, Miller M, Hah Z**. Crawling wave sonoelastography of benign and malignant thyroid nodules. Presented at the American Academy of Otolaryngology Head and Neck Surgery Foundation Annual Meeting, San Francisco, CA, September 2011.

Rochester Center for Biomedical Ultrasound Members

University of Rochester/ Strong Memorial Hospital

Anesthesiology
Paul Bigeleisen, MD
Janine Shapiro, MD
David Stern, MD
Jacek Wojtczak, MD

Biomedical Engineering
Nicholas Berry, BS
Sally Child, MS
Diane Dalecki, PhD
Etana Elegbe, MS
Kelley Garvin, MS
Jonathan Langdon, BS
Amy Lerner, PhD
Stephen McAleavey, PhD
Karla Mercado, MS
Carol Raeman, AAS
Maria Randazzo, BA
Carlos Sevilla, MS
Richard Waugh, PhD

Biophysics/Biochemistry
Scott Kennedy, PhD

Cardiology Unit
James Eichelberger, MD
Karl Schwarz, MD
Sherry Steinmetz, RDMS

Center for Vaccine Biology and Immunology
Mitra Azadniv, PhD

Dermatology
Alice Pentland, MD

Earth and Environmental Sciences
Asish Basu, PhD

Electrical and Computer Engineering
Edwin Carstensen, PhD
Yong Thung Cho, PhD
Marvin Doyley, PhD
Zaegyoo Hah, PhD
Andrew Hesford, PhD
Steven Huntzicker, MS
Sanghamithra Korukonda, MS
Jack Mottley, PhD
Rohit Nayak, BS
Kevin Parker, PhD
Alexander Partin, BS
Michael Richards, PhD
Michael Sealander, MS
Himanshu Shekhar, MS
Jason Tillett, PhD
Robert Waag, PhD

Emergency Medicine
Jefferson Svengsouk, MD

Imaging Sciences
Mark James Adams, MD
Shweta Bhatt, MD
Nancy Carson, MBA, RDMS, RVT
Vikram Dogra, MD
Thomas Foster, PhD
Nina Klionsky, MD
Deborah Rubens, MD
John Strang, MD
Susan Voci, MD
Eric Weinberg, MD
Jianhui Zhong, PhD

Immunology/Rheumatology
Ralf Thiele, MD

Mechanical Engineering
Stephen Burns, PhD
Alfred Clark, Jr., PhD
Sheryl Gracewski, PhD
Neo Jang, MS
Renato Perucchio, PhD

Obstetrics and Gynecology
Morton Miller, PhD
Richard Miller, MD
Tulin Ozcan, MD
Eva Pressman, MD
James Woods, MD

Pathology
P. Anthony di Sant'Agnese, MD

Pharmacology and Physiology
Denise Hocking, PhD

Radiation Oncology
Paul Okunieff, MD

Surgery
Christopher Barry, MD

Urology
Robert Davis, MD
Erdal Erturk, MD
Irwin Frank, MD
Jean Joseph, MD
Robert Mayer, MD
Jeanne O'Brien, MD

Vascular Medicine
Charles Francis, MD

Rochester General Hospital

Radiology
Robert Lerner, MD, PhD

Rochester Institute of Technology

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

Biomedical Engineering
Daniel Phillips, PhD

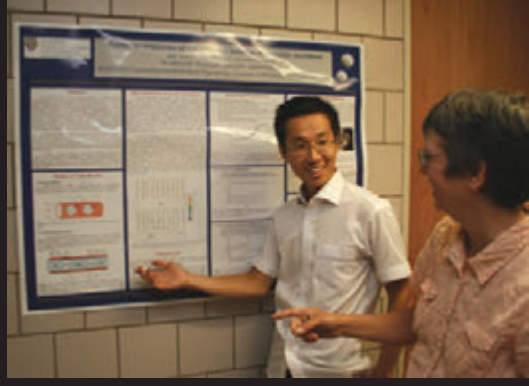
Visiting Scientists

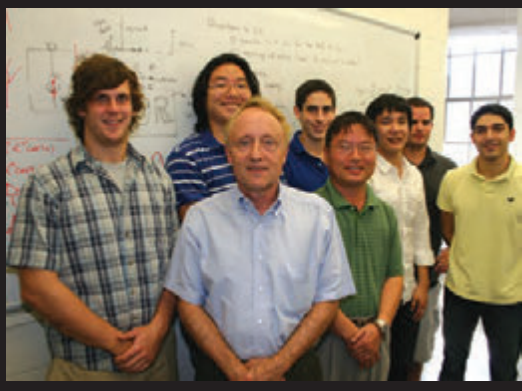
David Blackstock, PhD
University of Texas at Austin
E. Carr Everbach, PhD
Swarthmore College
Benjamin Castaneda, PhD
Pontificia Universidad Catolica del Peru
Zhe Wu, PhD
University of California, San Diego

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.

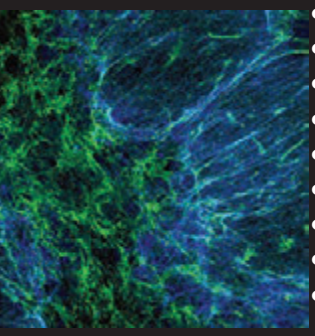
The Ultrasound Journal Club is attended by an interdisciplinary group of students and faculty interested in biomedical applications of ultrasound.

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 for 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

UNIVERSITY of ROCHESTER

Rochester Center for Biomedical Ultrasound
PO Box 270168
Rochester, NY 14627

Nonprofit
U.S. Postage Paid
Rochester, NY
Permit No. 780

Rochester Center for Biomedical Ultrasound

2011 Annual Report