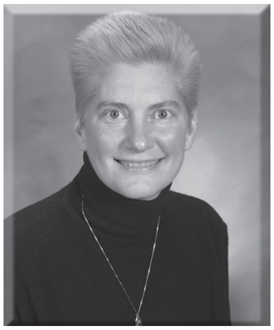
FROM THE DIRECTORS

Diane Dalecki, PhD, Director



Diane Dalecki

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

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

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

Deborah J. Rubens, MD, Associate Director

Deborah Rubens MD.

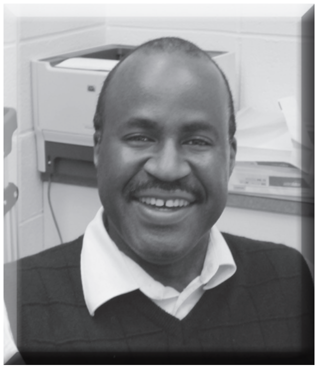
The Imaging Sciences Ultrasound Department experienced more than 5% growth in exam and patient volumes in 2009; performing over 20,000 exams. The unit continued to expand its clinical coverage; adding more sonographer positions to manage the increased demand.

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

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

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

RCBU FUNDING NEWS



Above: Marvin Doyley, PhD

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

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

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

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

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

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

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

Above: Maria Helguera, PhD

Below: Denise Hocking, PhD

Above: Diane Dalecki, PhD

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

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

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

2009 RESEARCH

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

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

Manoj Menon, MS and Stephen McAleavey, PhD

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

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

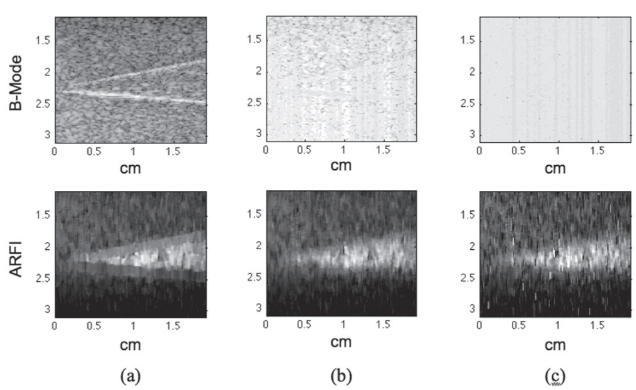


Figure 1. *B-mode and ARFI images using cross-correlation (a) without normalization, (b) partial normalization, and (c) full normalization. The center frequency is 5.33 MHz, the maximum displacement (white) is 2 μm, the correlation window length was 0.77 mm, and the tracking pulse length was 2 λ.*

In vivo prostate cancer detection using sonoelastography: Preliminary results

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

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

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

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

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

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

Methods for generating crawling waves with radiation force from ultrasonic beam

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

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

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

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

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

Resonance frequencies of bubbles in tubes

Sheryl M. Gracewski, PhD

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

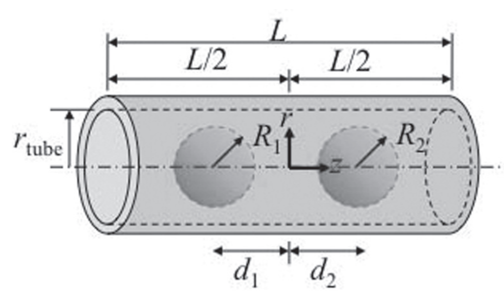


Figure 1. Schematic of 2 bubbles inside a circular cylindrical tube immersed in a liquid. This is a model of interacting bubbles in a vessel, e.g. echo contrast agents in a capillary, excited by ultrasound.

Backscatter imaging by shear wave induced phase encoding

Stephen McAleavey, PhD

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

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

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

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

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

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

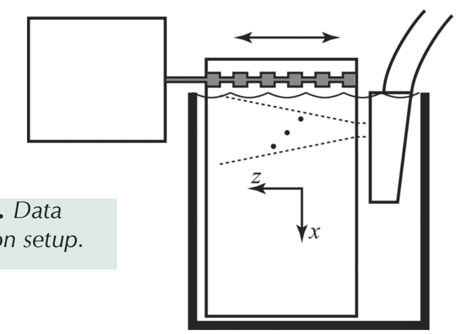


Figure 1. *Data acquisition setup.*

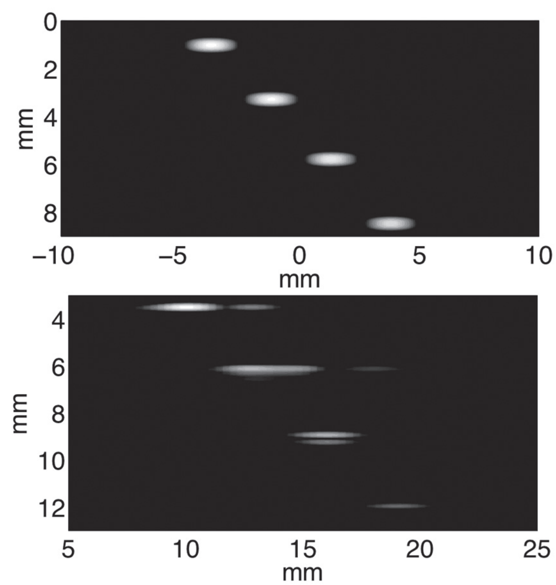


Figure 2. *Simulated (top) and experimentally acquired (bottom) images of wire targets in an elastic gel using the proposed method.*

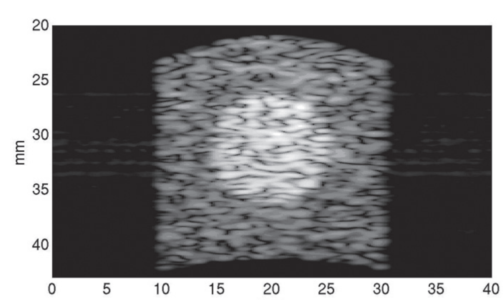


Figure 3. *Simulated +12 dB hyperechoic lesion in elastic medium with the proposed method. The displayed dynamic range is 40 dB.*

Obstetrics & Gynecology Ultrasound Unit

Tulin Ozcan, MD

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

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

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

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

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

The effect of vaginal progesterone in patients with active preterm labor

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

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

Tumor pathology report in 3D dynamic image format

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

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

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

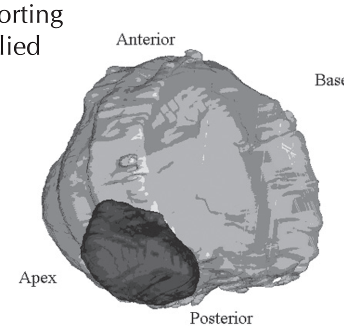


Figure 1. *3D model of the prostate gland (light gray) with a carcinoma (dark gray).*

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

Manoj Menon, MS and Stephen McAleavey, PhD

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

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

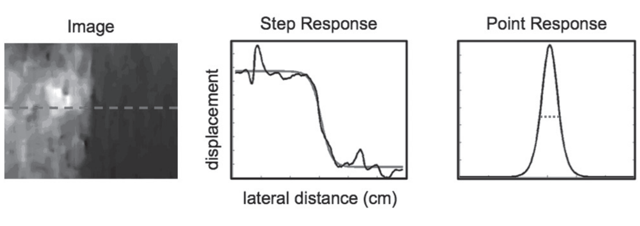


Figure 1. *Nonlinear least squares fit, full-width half maximum resolution estimation using an ARFI image of a step phantom.*

Spatially modulated ultrasound radiation force (SMURF) imaging

Stephen A. McAleavey, PhD

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

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

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

Studying biofilms with ultrasound

Maria Helguera, PhD and Michael Pichichero, MD

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

The University of Rochester/Pontificia Universidad Catolica del Peru Collaboration

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

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

The goal of the program is to:

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

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

Effects of ultrasound on microvessel tone

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

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

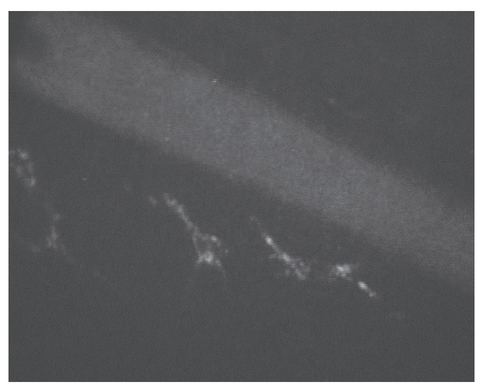


Figure 1. *Intravital confocal microscopy shows that fluorescently-labeled fibronectin is rapidly taken up from the blood and assembled into fibrils within the connective tissue surrounding blood vessels.*

TISSUE ELASTICITY CONFERENCE HIGHLIGHTS

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

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

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

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

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

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

The conference had 17 sessions, including:

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

RCBU MEMBERS

RCBU Remembers Edward L. Titlebaum

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

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

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

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

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

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

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

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

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

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

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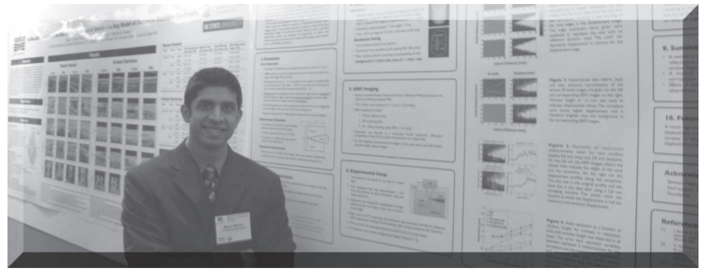

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