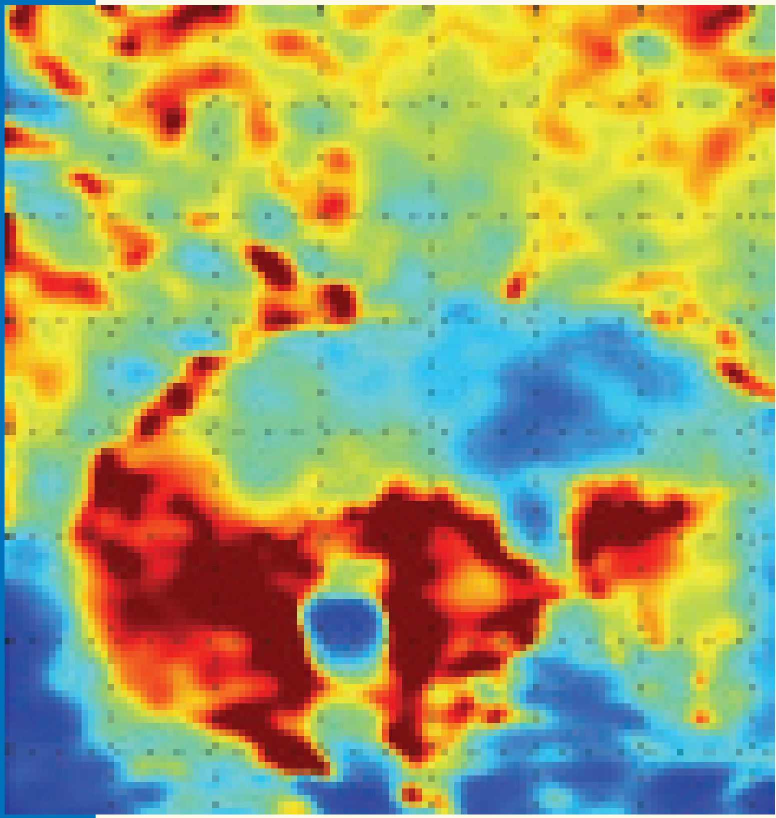

2006 Annual Report

Rochester Center for Biomedical Ultrasound

Cover Image: Shear velocity sonoelastography image in prostate. See the related article on page 15.
Courtesy of Kenneth Hoyt, PhD.

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: Charles E. Phelps, PhD | Dean of the Faculty of Arts, Sciences, and Engineering: Peter Lennie, PhD | Dean, School of Medicine and Dentistry: David S. Guzick, MD, PhD | Editor and Designer: Betsy Christiansen

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From the Directors

From Director Diane Dalecki

This year marked the 20th anniversary since the founding of the Rochester Center for Biomedical Ultrasound by Edwin L. Carstensen in 1986. Through the leadership and vision of directors Edwin Carstensen and Kevin J. Parker, the first twenty years of the RCBU have provided groundbreaking advances in the use of ultrasound in medicine. I am honored to assume directorship of the RCBU and look forward to continuing the Center's role in leading innovations in biomedical ultrasound.

Diane Dalecki

Over the years, the RCBU has played 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 in discoveries and innovations within RCBU laboratories. Today, collaborative projects between RCBU clinicians, engineers, and scientists continue to advance novel scanning techniques, three- and four-dimensional imaging, contrast agents, and new therapeutic applications of ultrasound in medicine.

This year's annual report details progress from RCBU laboratories on diverse topics in biomedical ultrasound, including sonoelastography, acoustic radiation force imaging, ultrasound scattering, acoustic cavitation, and bioeffects. Elasticity imaging continues to expand. The Fifth International Conference on Ultrasonic Measurement and Imaging of Tissue Elasticity, held October 8-11, was attended by more than 150 scientists and clinicians from 20 countries. This annual report also highlights several special celebrations held this year for Center Members Ed Carstensen, Floyd Dunn, and David Blackstock. We welcome your comments on any of the enclosed reports.

From Associate Director Deborah J. Rubens and Chief Sonographer Nancy Carson

The Ultrasound Division of the Department of Imaging Sciences once again experienced an increase in the number of exams performed. During the first half of 2006, the increase was 22% over the first half of 2005 and continued to increase for the second half of the year at a rate of 12% over 2005. The department was able to hire additional staff from RIT's 2006 graduating class.

Deborah Rubens MD.

Early in 2006 the department upgraded its two ATL 5000s to Philips iU22s. The iU22 offers a new generation of SonoCT and XRES that are real-time compounding imaging and speckle reduction. The iU22 also has a 3-1 MHz mulitplanar transducer that allows real-time 3D imaging. Both the Ultrasound and the Interventional Radiology departments will be evaluating this transducer for enhanced needle visualization during biopsies. One of the iU22s will be upgraded to the Vision 2007 software. The department will serve as a testing site for the newest features, including volumetric imaging, iSlice, protocol-driven presets that will increase exam consistency and productivity, and enhanced imaging performance of the multiplanar transducer.

One new GE LOGIQ 9 was also purchased and the existing GE LOGIQ 9 software was upgraded to the latest BTO6 version. This software level continues to improve GE's speckle reduction capabilities and enhances the compounding feature. The new machines are equipped with flat panel monitors and the latest ergonomic improvements such as lighter transducer cables, smaller transducers, and articulating monitors.

In October, two of the sonographers participated in a health fair held at the Dome Center in Henrietta, NY. They provided carotid artery screening to more that 60 patients. Plans for 2007 are to expand the booth to accommodate even more patients.

The department continues to maintain accreditation by both the AIUM and ICAVL. In December of 2006, the department was notified that their AIUM re-accreditation was granted for three more years.

About the Center

The Rochester Center for Biomedical Ultrasound (RCBU) celebrated 20 years at the University of Rochester in 2006. The Center was created in 1986 to unite professionals from the medical, engineering, and applied science communities at the University of Rochester, Rochester General Hospital, and the Rochester Institute of Technology. The RCBU has grown over the years from 30 to more than 70 members, with several visiting scientists from locations around the country.

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

The inside back page of this report shows the diverse departments involved in collaborative ultrasound research.

The Center's objectives include:

Research

Includes interaction with joint laboratories, technical discussion in formal meetings, and communication through a Center newsletter. In addition, interactions with industry, government, and foundations provide an assessment of the needs of the field and encourage mutually beneficial research programs and fellowships.

Education

Includes graduate-level courses in biomedical ultrasound and closely related fields, specialized short courses open to the international community, and post-doctorate collaborations with bioimaging areas within the University.

Innovation

The University of Rochester has a long history of leadership and innovation in biomedical ultrasound. For more than two decades, there has been steady progress in the quality of images of organs within the body which are reconstructed from the echoes of very short pulses of ultrasound.

In the late 1960s, the late Center member Raymond Gramiak led a team that first reported the use of an ultrasound contrast agent. At that time, agitate liquids were injected via a catheter while performing an ultrasound examination of the heart and great vessels. A dramatic increase in echoes was produced from the highly reflective air bubbles contained within the injected solution. Work has progressed through the years in this and other areas. Current projects include: non-linear acoustics, contrast agents, 3D and 4D sonoelastography, ultrasound and MRI fusion, high-intensity focused ultrasound (HIFU), scattering, bioeffects, therapeutics, advanced imaging systems, and more.

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, N.Y., the University's environment gives students exceptional opportunities for interdisciplinary study and close collaboration with faculty. Its College of Arts, Sciences, and Engineering is complemented by the Eastman School of Music, Simon School of Business, Warner School of Education, Laboratory for Laser Energetics, and Schools of Medicine and Nursing.

Celebrating 20 Years of Ultrasound Research

RCBU 20th Anniversary

Diane Dalecki, PhD

The RCBU celebrated its 20th anniversary this year. In 1986, Edwin L. Carstensen, PhD, founded the RCBU with the vision of uniting engineers, physicians, clinicians, and basic scientists to advance the use of ultrasound in medicine and biology. For the past twenty years, that vision has provided a unique foundation for scientific and clinical collaborations among RCBU members.

Founding Director Ed Carstensen

Through monthly meetings, regular short courses with international participation, and monthly newsletters, Founding Director Carstensen established a dynamic collaborative environment for the RCBU. In 1990, Kevin J. Parker, PhD, became the Director of the RCBU. Under Dr. Parker's sixteen years of dedicated leadership, the RCBU continued to grow in membership and scientific impact. Dr. Parker forged advances in new ultrasound imaging modalities, facilitated productive collaborations between RCBU members and industrial colleagues, and established the International Conference on Ultrasonic Measurement and Imaging of Tissue Elasticity. The addition of Deborah Rubens, MD, as Associate Director in 1994 ensured leadership in clinical diagnostic imaging and translation of RCBU research to clinical practice. Through the years, RCBU members have led many advances in the clinical use of ultrasound in diagnostic imaging and therapy, and expanded our fundamental understanding of the interactions of acoustic waves with biological systems.

Director 1990 - 2006 Kevin Parker

Through the devoted leadership and vision of our directors, the first twenty years of the RCBU have provided groundbreaking advances in the use of ultrasound in medicine. As we head to the future, RCBU members will continue to collaborate to discover and advance exciting new technological innovations in ultrasound imaging and therapy.

To receive a special 20th anniversary report highlighting the history of the RCBU, contact Betsy Christiansen at betsyc@ece.rochester.edu.

Current Director Diane Dalecki

New RCBU Director

Diane Dalecki, Ph.D., has been appointed the new Director of the RCBU. Dr. Dalecki is an Associate Professor of Biomedical Engineering at the University of Rochester. She succeeds Kevin J. Parker, PhD, who has been the Director since 1990.

Dr. Dalecki is an expert on the interaction of ultrasound with biological systems. The broad goals of her research are to advance diagnostic ultrasound and discover new therapeutic applications of ultrasound in medicine and biology. Dr. Dalecki completed her education at the University of Rochester, receiving the BS degree in Chemical Engineering and the MS and PhD degrees in Electrical Engineering. A leader in the field of biomedical ultrasound research, Dr. Dalecki is a Fellow of the American Institute of Ultrasound in Medicine (AIUM), and is active in the Acoustical Society of America (ASA), the Biomedical Engineering Society (BMES), and the Institute of Electrical and Electronics Engineers (IEEE). She is currently on the AIUM Board of Governors and has served as Chair of the AIUM Bioeffects Committee.

"We are greatly fortunate to have Diane Dalecki as the next Director of the RCBU," Dr. Parker said. "She has worked closely with the Founding Director, Dr. Edwin Carstensen, over the years, and has established herself as a leading national figure in ultrasound. Her work covers the entire range from sonar to high frequency ultrasound. She was the first person in the world to pace heartbeats with pulsed ultrasound. The RCBU will achieve many important milestones under her direction."

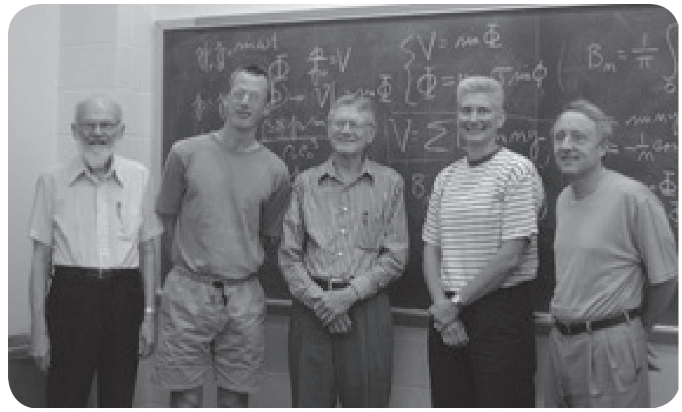
Founding RCBU Director Edwin Carstensen said, "The University and the biomedical ultrasound community are fortunate to have Prof. Diane Dalecki as the Center's new director. In addition to her fundamental contributions to basic knowledge in biomedical ultrasound, she has contributed to many aspects of University life from her days as an undergraduate student here in Chemical Engineering. She is today one of our best teachers and played a key role in the development of the Biomedical Engineering Department. We can look forward to a new surge of excellence in the Center under her direction. I'd like to add my personal thanks to Dean Parker, for more than a decade and a half of excellent leadership and selfless devotion to the Center."

RCBU Celebrates Blackstock's Nonlinear Acoustics

In June, the RCBU celebrated **David Blackstock's** 40 years of research in nonlinear acoustics. In 1966, while a Professor in the Electrical Engineering Department at the University of Rochester, Dr. Blackstock published his groundbreaking paper, "Connection Between the Fay and Fubini Solutions for Plane Sound Waves of Finite Amplitude." It provided the foundation for the development of nonlinear acoustics in biomedical ultrasound. The abstract is below. Currently, Dr. Blackstock is Professor Emeritus of Mechanical Engineering at the University of Texas at Austin, and an Adjunct Professor in the Department of Electrical and Computer Engineering at the University of Rochester. "For many years, Dr. Blackstock has been spending his summers at the University of Rochester, teaching a summer acoustics course and collaborating with RCBU members on diverse research projects. We are greatly fortunate to have Dr. Blackstock at the UR during the summer months. His insights and expertise have stimulated and advanced many diverse research projects," said Diane Dalecki.

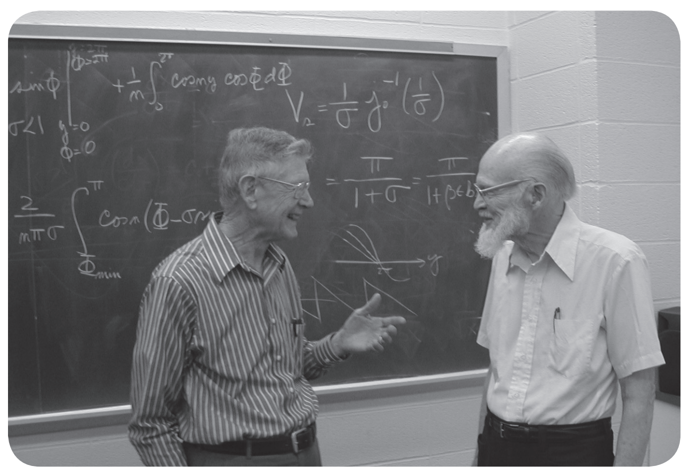
Abstract

Plane, progressive, periodic sound waves of finite amplitude are considered. The well-known solutions of Fay and Fubini are reviewed. At first glance, the two solutions seem contradictory, but, actually, each holds in a different region of the flow, the Fubini solution close to the source and the Fay solution rather far from the source. In the intermediate, or transition, region, neither solution is valid. A more general solution is obtained by using a method commonly employed for waves containing weak shocks. For distances up to the shock-formation point, the general solution reduces exactly to the Fubini solution. For distances greater than about 3.5 shock-formation lengths, the general solution is practically indistinguishable from the sawtooth solution, which, in turn, is the limiting form of Fay's solution for strong waves. The form of the general solution shows clearly how, in the transition region, the Fubini solution gives way to the sawtooth solution. The problem of an isolated cycle of an originally sinusoidal wave is also considered. Finally, some limitations on the weak-shock method are discussed. In the periodic-wave problem, the general solution is found to be inaccurate for distances greater than $1/\alpha$, approximately, where α is the small-signal absorption coefficient.



Edwin Carstensen, Ted Christopher, David Blackstock, Diane Dalecki, and Kevin Parker

David and Marjorie Blackstock



David Blackstock and Edwin Carstensen

Citation: Connection Between the Fay and Fubini Solutions for Plane Sound Waves of Finite Amplitude J. Acoust. Soc. Am. Vol. 39(6) 1966 p. 1019-1026.

2006 Research

Ultrasound contrast agents and cardiac arrhythmias

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

An active area of research in our laboratory focuses on developing an understanding of the physical mechanisms responsible for ultrasound-induced arrhythmias. Early work from our lab demonstrated that a single pulse of ultrasound could produce a premature cardiac contraction. Recent work has concentrated on investigating this bioeffect when ultrasound contrast agents are present in the blood. Ultrasound contrast agents are suspensions of gas-filled microbubbles used to enhance diagnostic imaging. Microbubble contrast agents can increase the likelihood of bioeffects of ultrasound associated with acoustic cavitation. Results of several investigations from our lab are consistent with the hypothesis that acoustic cavitation is the mechanism for the production of premature cardiac contractions with ultrasound and microbubble contrast agents. The acoustic pressure threshold for premature beats was significantly lower with microbubble contrast agents present in the blood than without. With microbubbles, the threshold for premature beats was below the current output limits of diagnostic devices. The threshold was not significantly dependent upon contrast agent type and was not influenced by contrast agent dose over three orders of magnitude. The dependence of the threshold on acoustic frequency was consistent with the frequency dependence of acoustic cavitation. Furthermore, for mice injected with contrast agent, a passive cavitation detector (PCD) was used to measure the acoustic emissions produced within the hearts in vivo when exposed to ultrasound pulses. We observed a direct correlation between the amplitude of the PCD and the percentage of ultrasound pulses producing a premature beat, consistent with cavitation as a mechanism for this bioeffect. Taken together, these results indicate that ultrasound-induced arrhythmias are produced by intravascular microbubble activity. Ongoing work continues to investigate ultrasound-induced bioeffects of microbubble contrast agents in the cardiovascular system. Collaborations with Sheryl Gracewski in the Mechanical Engineering Department provide unique capabilities to simulate the response of a microbubble to sound exposure within a confining blood vessel.

Semi-automatic measurement of thermal ablated lesions in sonoelastography images

Benjamin Castaneda, MS, Man Zhang, MS, Kevin Bylund, BS, Jared Christensen, MD, Wael Saad, MD, Deborah J. Rubens, MD, Kevin J. Parker, PhD

Objectives

To process the large amount of images generated in sonoelastography, an accurate and fast method for measuring the size and shape of the lesions is needed. This work proposes a semi-automatic segmentation algorithm for sonoelastography data. The aim of the algorithm is to reduce the variability and processing time involved in manual segmentation while keeping comparable results.

Methods

Radiofrequency ablation was used to create 11 lesions in 5 porcine livers. Sonoelastography images were acquired in vivo. The animal was sacrificed after imaging and lesions were harvested and measured. These measurements were considered ground truth and ranged from 20 mm^2 to 250 mm^2. Three independent observers manually measured the lesions in the sonoelastography images. The images were also processed by the semi-automatic algorithm. The algorithm requires an initialization step in which the user selects the center of the lesion. This initialization was performed by three different observers. Based on the user's input, a region-growing technique based on initial watershed segmentation is applied to define an estimate of the area of the lesion. Then, level-set methods are used to refine the final shape of the lesion.

Results

Measurements of lesion size (area) were analyzed. The correlation coefficients and average and maximum errors were computed with respect to ground truth. Results showed that the semi-automatic algorithm outperformed manual segmentation. Inter-observer coefficients of variation indicated that the algorithm increases repeatability. The processing time was reduced significantly.

Conclusions

A semi-automatic segmentation algorithm for processing sonoelastography images is presented. Results show that the algorithm outperforms manual segmentation in accuracy, speed, and repeatability. These results suggest that measurement of lesions in sonoelastography images can be processed in real-time with minimal human intervention.

Numerical study of ultrasound bio-effects by solving gas-liquid-solid interaction problems with coupled FEM and BEM

Hongyu (Jacky) Miao, PhD, advised by Sheryl Gracewski, PhD

The following abstract is from the PhD thesis that Jacky Miao successfully defended in November 2006.

Abstract

Various independent investigations indicate that acoustically-excited microbubbles may increase the likelihood of hemolysis and hemorrhage. To explore potential damage mechanisms that might occur during bubble expansion and collapse, one- and two-dimensional models were developed to investigate spherical bubble dynamics, asymmetric bubble dynamics, and interactions between a bubble and a nearby structure.

First, a one-dimensional Gilmore model combined with gas diffusion was used to predict maximum bubble radii and maximum collapse pressures over a range of acoustic frequencies, pressures, and bubble sizes. The results indicated gas diffusion had little influence on the maximum bubble radius, but significant influence on maximum collapse pressure for inertial cavitation. Also, it might be possible to separate the effects of bubble expansion and collapse on premature ventricular contractions for higher acoustic frequencies.

A commercial axisymmetric boundary element model (2DynaFS by DynaFlow Inc.) was employed to investigate the interactions between an ultrasonically-excited bubble and a rigid or deformable object. The effects of the distance between the bubble and the object and the geometrical shape of the object on the pressure field near the object surface were investigated. The interactions between a bubble and a deformable sphere were simulated to predict the cell areal expansion during bubble expansion. The predicted areal expansion was much less than the cell lysis threshold and indicated that the bubble expansion was unlikely to cause hemolysis.

A coupled finite element and boundary element code was developed, validated, and employed to solve axisymmetric bubble-vessel interaction problems in acoustic fields. The effects of vessel dimensions, material properties, ultrasound frequencies, and pressure amplitudes on tube dilation were investigated. The maximum principal stress during bubble expansion was greater than the value during bubble collapse. The hoop stress was mainly investigated as the maximum principal stress during bubble expansion. The pressure drop across the tube wall could contribute to tube dilation. As vessel thicknesses, vessel radii, and acoustic frequencies decreased, or as pressure amplitudes, elastic moduli, and Poisson's ratios increased, the maximum hoop stresses increased, indicating a higher potential of hemorrhage. This research of interactions between bubbles and deformable structures is important for understanding ultrasound-induced bioeffects.

Coded waveforms

Michael Sealander, BS, advised by Edward Titlebaum, PhD and Stephen McAleavey, PhD

The research we are currently conducting extends over several projects in diagnostic ultrasound, including the use of coded waveforms, array processing techniques, speckle reduction, and information-theoretic image formation.

Coded waveforms have enjoyed wide success in sonar and radar applications for decades and have only recently been investigated by the ultrasound community. This is largely due to the formidable obstacles inherent to their use in diagnostic ultrasound that are either not present or mitigated in the other applications. These include propagation through inhomogeneous media, multipath propagation, frequency dependent attenuation, and nonlinear propagation effects. We are currently exploring different mechanisms of combining many of these previously problematic effects in the transmission and processing stages of image formation, including active and passive phase conjugation and novel array processing algorithms. Additionally, stochastic analysis of the wave propagation process is leading to novel methods of speckle reduction that combine many of the concomitantly developing waveform coding techniques.

Currently, there is also widespread interest in the research community in obtaining information about the functional and structural properties of tissue other than echogenicity. Efforts are underway to combine more of this data, especially tissue elasticity, in the image formation process, facilitating segmentation and characterization to maximize the diagnostic information available to the clinician.

Real-time sonoelastography detection of hepatic radiofrequency ablation lesions in an in vivo porcine model

Jared Christensen, MD, Man Zhang, MS, Benjamin Castaneda, MS, Wael Saad, MD, Deborah Rubens, MD

Objectives

1. Prospectively evaluate the accuracy of two-dimensional (2D) sonoelastography (SE) versus conventional gray scale B-mode ultrasound (US) in the detection of hepatic thermal lesions in an in vivo porcine model.
2. Determine the viscoelastic properties of radio frequency ablation (RFA) lesions relative to normal hepatic tissue.

Methods and Materials

A total of 15 hepatic RFA lesions were created in vivo in 5 pigs using a standard LeVeen needle with variable tip tine diameter up to 2 cm. Lesions smaller than 0.2 cc on gross pathology were not included. Lesions were imaged in two planes with US, followed by vibration induced SE produced by frequencies from 120-200 Hz, depending on lesion depth, and imaged with a real-time Doppler variance map simultaneously acquiring elastography and gray scale images for perfect registration. The liver was resected. RFA lesions were excised and measured to determine true size and volume with gross specimens forming the gold standard. Matched 2D US and SE images for each lesion were identified and categorized as (1) no visible lesion, (2) partially obscured lesion boundary, or (3) completely visualized. Partial and completely visible lesions were then measured with the size obtained in long and orthogonal short axes and the lesion area calculated by boundary mapping. Lesion characteristics for US and SE were compared against gross pathology specimens. Biomechanical properties of untreated liver and RFA lesions were subsequently determined by the Kelvin-Voigt Fractional Derivative (KVFD) model.

Results

Of 15 hepatic RFA lesions, the average lesion long axis was 16.0 mm (range: 8-22.6 mm) with an average area of 173.2 mm^2 (range: 26.4 - 280.5 mm^2). All lesions were completely visualized by SE (100%) vs. 5 by US (33.3%). Remaining lesions categorized on US: 7 partially circumscribed (46.7%) and 3 not visualized (20%). For completely visualized lesions, US underestimates RFA lesion size by 43.2% versus only 1.1% for SE. When including partially visualized lesions, the discrepancy increases slightly (44.4% for US). SE reliably visualizes hepatic RFA lesions and accurately approximates true lesion size (R^2=0.9924).

Stress-relaxation testing with curves fit to the KVFD model reveals an elasticity contrast ratio of 7.2:1 for RFA lesions versus normal hepatic tissue (Young's modulus values of 21,091.5 and 2,933.5 Pa, respectively).

Conclusion

SE reliably and more accurately images hepatic RFA lesions in vivo in comparison to conventional US. This is partly attributable to the differential elasticity of RFA lesions versus normal hepatic tissue. In patients undergoing RFA for treatment of hepatic malignancy, SE may potentially display treated lesion boundaries in real-time to assure adequate therapy. Furthermore, SE could be used to monitor RFA and any other methods of thermal lesion ablation (i.e., high intensity focused ultrasound) that create sufficient tissue stiffness contrast for lesion detection.

A ring transducer system for medical ultrasound research

Robert Waag, PhD, RJ Fedewa, PhD

An ultrasonic ring transducer system was developed for experimental studies of scattering and imaging. The transducer consists of 2048 rectangular elements with a 2.5 MHz center frequency, a 67% 6 dB bandwidth, and a 0.23 mm pitch arranged in a 150 mm diameter ring with a 25 mm elevation. At the center frequency, the element size is 0.30 lambda x 42 lambda and the pitch is 0.38 lambda. The system has 128 parallel transmit channels, 16 parallel receive channels, a 2048:128 transmit multiplexer, a 2048:16 receive multiplexer, independently programmable transmit waveforms with 8-bit resolution, and receive amplifiers with time variable gain independently programmable over a 40 dB range. Receive signals are sampled at 20 MHz with 12-bit resolution. Arbitrary transmit and receive apertures can be synthesized. Calibration software minimizes system nonidealities caused by noncircularity of the ring and element-to-element response differences. Application software enables the system to be used by specifying high-level parameters in control files from which low-level, hardware-dependent parameters are derived by specialized code. Use of the system is illustrated by producing focused and steered beams, synthesizing a spatially limited plane wave, measuring angular scattering, and forming B-scan images.

Effects of underwater sound fields on lung

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

The Dalecki lab continues to investigate the interaction of underwater sound fields with biological tissues. The U.S. Navy and the Naval Submarine Medical Research Laboratory (NSMRL) in Groton, CT support our projects in this area. Our efforts aim to develop a greater understanding of the response of biological tissues to both continuous wave and impulse underwater sound. Results of our studies have direct relevance to safety guidelines for swimmers, divers, and marine mammals exposed to underwater sound fields.

The air-filled lung is particularly sensitive to underwater sound exposure. Medical ultrasound at diagnostic frequencies (i.e., > 1 MHz) is known to produce lung hemorrhage in numerous mammalian laboratory animals. In comparison, when the wavelength of the sound field is much greater than the radius of the lung, the whole lung is exposed to a homogenous sound field. Over the years, the Dalecki lab has been working to quantify the thresholds for lung hemorrhage over a broad range of acoustic frequencies (~100 Hz to 10 MHz) and identify the physical mechanisms for sound-induced lung hemorrhage. Our lab has demonstrated that, in response to exposure to low-frequency underwater sound, the whole lung oscillates and lung injury can result from mechanical forces associated with these pressure fields. The resonance frequency of adult murine lung is ~325 Hz. At the resonance frequency, the response of lung to sound exposure is maximized and the threshold for lung hemorrhage is lowest. Mammalian lung can also be damaged by exposure to low-frequency sound above resonance frequency. Using an open tube exposure system, our lab determined the thresholds for murine lung hemorrhage from exposure to continuous wave underwater sound at frequencies ranging from ~2.5-1000 kHz. The equation $P_{thresh} = 0.01f^{0.64}$, where P_{thresh} is the threshold pressure in MPa and f is the acoustic exposure frequency in kHz, represents a best-fit to our experimental lung threshold data over the 2.5-1000 kHz range. Ongoing studies continue to characterize the response of lung to sound at frequencies below lung resonance.

Our recent series of experiments, performed at the resonance frequency of the murine lung, investigated the dependence of sound-induced lung hemorrhage on total exposure duration. Results of these studies demonstrated that the extent of lung hemorrhage increases with increasing exposure duration. For exposure durations of 1 min and 3 min, the extent of damage for a given pressure amplitude and the threshold for lung damage are relatively independent of exposure amplitude. However, at shorter exposure durations (i.e., 10 s), the threshold for lung damage increases and the extent of lung damage at a given pressure amplitude decreases compared to exposure durations greater than or equal to 1 min. Lung damage and rupture of the lung were observed for exposure durations as short as 5 s. For exposures above threshold, longer exposure durations increase the extent of lung hemorrhage and the likelihood of lung rupture. Further studies in our lab continue to characterize the response of lung to continuous wave sound exposures of short duration.

We have recently begun a new line of investigation focusing on effects of low frequency, underwater impulses on mammalian lung. Underwater acoustic impulses are produced with an air gun source system. To generate and test the bioeffects of these impulse fields, the Dalecki lab has developed collaborations with Rochester-based Hydroacoustics, Inc. (see the box below). The Dalecki lab plans to characterize acoustic impulse fields in a laboratory setting and determine the effects of these impulse fields on mammalian lung.

Dalecki Lab Collaborates with Hydroacoustics, Inc.

The Dalecki lab and Hydroacoustics, Inc. (HAI) are working together to investigate the effects of underwater acoustic impulses on biological systems, particularly mammalian lung. HAI manufactures and supports unique low frequency, continuous wave and impulsive underwater sound sources. The HAI facility includes 12,000 square feet of laboratory space dedicated to acoustic research and testing of underwater sound sources. Air gun technology and measurement facilities at HAI are used to generate underwater acoustic impulses in a laboratory setting. The Dalecki lab will undertake a series of tests to identify the bioeffects of these high amplitude, low frequency acoustic impulses. This work is sponsored by the U.S. Naval Submarine Medical Research Laboratory (NSMRL).

Acoustic radiation force and brachytherapy research

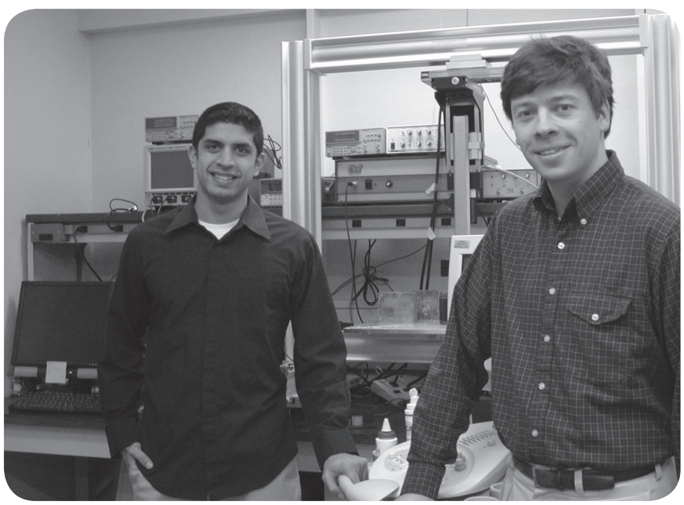
Stephen McAleavey, PhD

The work in the McAleavey lab in 2006 concentrated on the development of imaging techniques for prostate imaging. We presented new methods for imaging brachytherapy seeds through magnetically induced vibration and methods for artifact compensation. We have presented our first ex vivo acoustic radiation force impulse (ARFI) images of prostates and found that measureable displacements may be induced in the prostate with standard transducers, and that a useful degree of ARFI-visible stiffness contrast exists between healthy prostate and cancerous lesions.

Acoustic radiation force impulse imaging of excised human prostates

Stephen McAleavey, PhD, Manoj Menon, MS, Deborah Rubens, MD

We present initial results in acoustic radiation force impulse (ARFI) imaging of excised human prostates. Prostates were obtained from seven patients undergoing prostatectomy for prostate cancer. All men had a positive biopsy prior to surgery and had consented to allow elastographic imaging of the excised tissue. The prostates were obtained immediately after surgery and immersed and scanned in an isotonic saline bath at room temperature. Scanning was performed with a Siemens Antares scanner using a VF10-5 linear array. Tissue displacement was induced with pushing pulses of 30 μs duration at 6.67 MHz and an Isppa of < 1kW/cm^2. Pushing beams were focused at 2 cm with an F/# of 3.5. RF data were collected and processed off-line using cross correlation methods to obtain displacement estimates. Low-resolution displacement images were obtained in near real time (~3 s/frame) to guide image acquisition. The saved RF data were later processed to produce displacement images with improved SNR. Prostates were scanned free-hand, looking for interesting B-mode or ARFI targets. Peak displacements in healthy tissue were in the range of 6-12 μm. Cancerous lesions were stiffer and showed smaller displacements.



Manoj Menon and Steve McAleavey in the lab

Magnetically vibrated brachytherapy seeds: ferromagnetic core models and image reconstruction methods

Stephen McAleavey, PhD, Scott White, Manoj Menon, MS

Magnetically induced motion imaging (MIMI) uses an oscillating magnetic field and ultrasonic motion-tracking techniques to vibrate and identify brachytherapy seeds in situ. The efficacy of the technique relies on the ability to generate and detect seed vibration, and distinguish this vibration signal from other motion sources. The vibration of the seed depends on the torque generated by a ferromagnetic core in the seed. A design goal is to maximize the torque for the limited amount of core material that can be placed within a seed. We have developed 3D finite-element models for two seed core geometries, an ellipsoid and a rod capped by two semi-hemispheres. Both seed cores have identical volumes (7.4 x 10-10 m^3), length (4 mm), and permeability (μr = 4000). Calculation by the Maxwell Stress Tensor method yields a torque for the rod 1.4 times that of the ellipsoidal core, demonstrating the substantial sensitivity of torque on core geometry.

The oscillating seeds act as dipole shear wave sources, with maximum vibration amplitude at the ends of the seed and a vibration minimum at the center of length. This gives rise to a characteristic vibration amplitude distribution in the surrounding tissue, with two lobes per seed. By taking advantage of the opposing phase of the seed ends, we demonstrate a method that links these lobes. A compounding technique for suppressing ring-down artifact is demonstrated. These methods are demonstrated on RF data acquired from seeds in beef muscle tissue. We presented 3D vibration isosurface maps of seed vibration amplitude and found those to be in good agreement with previously reported simulations.

Congruence of sonoelastography crawling waves and mechanical measurements for estimation of viscoelastic properties of soft tissues

Benjamin Castaneda, MS, Man Zhang, MS, Zhe Wu, PhD, Deborah J. Rubens, MD, Kevin J. Parker, PhD

Aims

The first aim of the study is to measure reliably and accurately the viscoelastic properties of soft tissue. The second aim is to compare the results of two techniques: sonoelastography crawling waves (CrW), and mechanical measurement (MM) results fitted into a Kelvin-Voigt fractional derivative (KVFD) model.

Methods

Fresh and thermal-treated veal liver tissue samples (approximately 500 cc volume) as well as excised prostate glands were directly placed in between a pair of shear wave sources. The wavelengths of shear wave interference patterns in sonoelastography images were measured in a range from 100 to 280 Hz using a model-based algorithm. The algorithm pre-processes the image to increase the region of interest, which is then projected into its horizontal axis. The projection is fitted to a cosine-squared model, which provides the estimation of the wavelength and, therefore, the estimation of the shear wave velocity and the Young's modulus of the tissue.

For the MM, cylindrical cores (10 mm diameter, 8 mm length) were acquired from fresh/thermal-treated liver and prostate tissues. Five percent compressional strain was applied over 1000 seconds. The stress-relaxation curve of each sample was fitted to a KVFD model. Finally, the complex elastic modulus at any frequency was obtained by the Fourier transform of the time domain response.

Results

Table 1 shows the estimated Young's modulus for raw liver, thermal-treated liver, and human prostate using CrW and MM. Fig. 1 shows the comparison of CrW and MM for a prostate gland where particular care was taken to extract cores from the region where CrW were measured. Both methods provide similar results.

Conclusions

The CrW method provides estimations of the Young's moduli of the fresh veal liver, thermal-treated liver and human prostate, which are congruent with the MM results. The new model-based image-processing algorithm improves the measurements obtained from CrW. These results suggest that CrW can be adapted for in vivo use to measure tissue properties. The stress-relaxation test produces repeatable results, which fit well to the KVFD model. The methodology used in this study can be applied to other soft tissues.

Acknowledgements: This study was partly supported by NIH grant 5 RO1 AG016317-05.

Raw Veal Liver					
Frequency (Hz)	100	120	150	180	
E CrW (kPa)	5.5	8.2	10.7	11.1	
E MM (kPa)	11.2	11.5	11.8	12.0	
Thermal Ablated Veal Liver					
Frequency (Hz)	150	180	200	220	240
E CrW (kPa)	247	405	365	360	476
E MM (kPa)	351	363	370	376	382
Human Prostate					
Frequency (Hz)	100	120	140	160	180
E CrW (kPa)	20.8	24.0	24.9	25.4	26.3
E MM (kPa)	20.7	21.7	22.6	23.5	24.2

Table 1. Young's moduli estimation using CrW and MM.

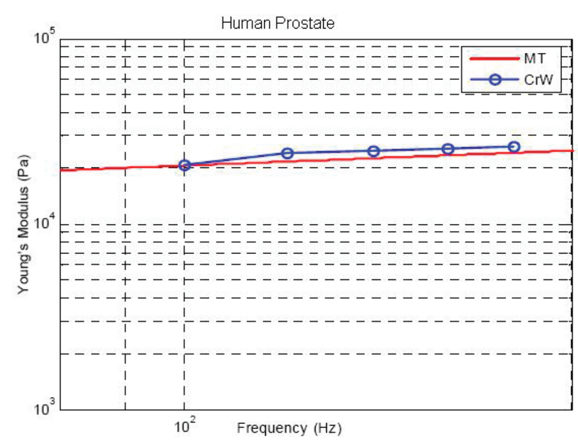


Figure 1. Frequency dependent elastic moduli of the human prostate.

Obstetrics and Gynecology Ultrasound Unit

Eva K. Pressman, MD

The OB/GYN Ultrasound Unit continues to be involved in busy clinical practice and multiple research endeavors. We continue to expand the availability of first trimester screening for aneuploidy, with nine physicians and sonographers now certified in obtaining nuchal translucency measurement. Additional equipment has been obtained to increase the utilization of three- and four-dimensional scanning in both obstetrics and gynecology. Research areas have expanded to include fetal anthropometrics as related to maternal habitus and prediction of abnormal pregnancy by first trimester blood flow evaluation.

The unit performed more than 17,700 obstetric and gynecologic procedures in 2006. In addition to diagnostic sonograms, the unit performed 500 amniocenteses, 85 chorionic villus samplings, 228 sonohysterograms, and 6 fetal blood samplings and transfusions.

Recently completed research projects include postnatal follow-up of prenatally diagnosed fetal renal anomalies and evaluation of fetal growth in obese patients. (See below.)

Third trimester ultrasound for fetal pyelectasis is a better predictor of the need for postnatal surgery than second trimester ultrasound

Introduction: The ability to predict the need for postnatal surgery based on fetal renal pyelectasis in a second or third trimester prenatal ultrasound is limited. We sought to determine if the timing of prenatal pyelectasis can predict the need for postnatal surgery.

Methods: A database query for all patients with at least one fetal kidney with pyelectasis was performed. Study patients received ultrasounds during the second and third trimesters and postnatally. Postnatal surgery was at the discretion of their physicians. A cutoff of >7 mm for renal pelvis anterior-posterior diameter for the second trimester and >10 mm for the third trimester was used to define pyelectasis. The kidneys were analyzed independently based on pyelectasis in the second and/or third trimesters and correlated with the grade of postnatal hydronephrosis and the need for postnatal surgery using Fisher's exact test.

Results: A total of 59 patients with 116 kidneys were identified. Second trimester pyelectasis correlated with degree of postnatal hydronephrosis (grade 3 or 4) but not the need for postnatal surgery ($p = .61$). Third trimester pyelectasis also correlated with postnatal hydronephrosis but did correlate with surgical intervention ($p < 0.0001$). The positive predictive value of pyelectasis for postnatal surgery was 9% in the second trimester and 20% in the third trimester pyelectasis. The negative predictive value was 95% and 100% in the second and third trimesters, respectively.

Conclusions: Third trimester ultrasound for fetal pyelectasis is a better predictor of postnatal surgery than second trimester ultrasound.

Accuracy of sonographic birth weight prediction in obese parturients using the gestation-adjusted projection method

Objective: Birth weight (BW) prediction by ultrasound was shown to be most accurate if assessed between 34.0-36.9 weeks gestation and extrapolated using the gestation-adjusted projection (GAP) method. As maternal body mass increases (BMI), accurate ultrasound measurements can become difficult and may be less accurate. We sought to assess the accuracy in BW prediction in obese pregnant women as compared with non-obese controls.

Study Design: We preformed a retrospective review of 1377 women with singleton pregnancies who underwent sonograms between 34.0 and 36.9 weeks. Patients were divided into four groups, based on their BMI. Analysis of variance compared the differences between the predicted and actual BW.

Results: A total of 352 obese women and 1025 controls were included in the study. The distribution of obese patients was: 158 Class I (BMI 30-35), 103 Class II (BMI 35-40) and 91 Class III (BMI >40). Birth weights ranged from 1735 to 5370 g. Birth weights were overestimated in control patients and Class I and II obese patients, and minimally underestimated in patients with Class III obesity. The absolute error in BW prediction was greater in the most obese patients but the absolute percent error did not differ with the degree of maternal obesity. Post-hoc power analysis indicates 99% power to detect a difference of 1% in absolute percent BW error.

Conclusion: The GAP method is able to predict BW within 10% from sonograms performed between 34.0 and 36.9 weeks regardless of BMI. Overall, the GAP method is accurate in obese parturients.

Sonoelastographic shear velocity imaging: application of crawling waves

Kenneth Hoyt, PhD

The objective of this study was to develop a novel sonoelastographic technique for estimating local shear velocities from propagating shear wave interference patterns termed crawling waves. It has been shown that interfering shear waves could produce slowly propagating interference patterns with an apparent velocity much less than the underlying true shear velocity. These crawling waves can be visualized in real-time using sonoelastography, which depicts the vibrational response of soft tissue owing to dynamic mechanical excitation. In general, crawling wave images describe shear wave propagation patterns and allow estimation of spatial elastic properties in tissue, namely, shear velocity distributions. Since changes in tissue elasticity are indicative of an abnormal pathological process, imaging parameters such as shear velocity distributions may prove feasible for differentiating normal from abnormal tissues.

To evaluate our novel shear velocity estimation technique, a 1D sonoelastographic simulation program was developed. Simulation studies analyzed tradeoffs between various system-level parameters and imaging conditions. A GE LOGIQ 9 scanner equipped for sonoelastography was used for experimental studies. Demodulated IQ colorflow data was transferred to an external computer for shear velocity image generation. In experiments, shear velocity images were generated using two homogeneous phantoms of different stiffness with true shear velocities obtained using time-of-flight measurements. Results from a heterogeneous phantom were compared to true shear velocities derived from mechanical measurements. Finally, shear velocity images were obtained from an in vitro prostate and compared to the final pathological diagnosis. For all experimental studies, crawling waves were induced using a pair of bending piezoelectric elements positioned on opposite sides of the phantoms or embedded tissue sample vibrating at offset frequencies (e.g., 200 and 200.15 Hz) parallel to the ultrasound scan plane.

Simulation results demonstrate that increasing kernel window size reduces shear velocity estimator noise, but compromises spatial resolution due to the moving window estimation approach. Increasing the source vibration frequency was shown to reduce estimator variance, but shear wave attenuation also increases at higher vibration frequencies owing to viscoelastic effects. Since attenuation effectively reduces the shear wave signal-to-noise ratio (SNR), this variable was assessed, revealing that lower SNR levels produced substantial variability in shear velocity estimates. The effects of amplitude quantization were evaluated and results indicated that 4-bit display resolution produced more variability in the shear velocity estimates than that obtained using either 8-bit or 16-bit quantization (16-bit being the most accurate). Results from homogeneous phantoms demonstrated the ability of sonoelastographic shear velocity imaging to quantify the true underlying shear velocity distributions (less than 7% error) as verified using time-of-flight measurements. Furthermore, heterogeneous phantom results revealed the capacity for lesion detection (1 cm diameter inclusion) and shear velocity quantification as validated from mechanical measurements. Experimental results obtained from a prostate specimen depict two high-contrast regions of elevated shear velocity (Fig. 1) that were confirmed as focal adenocarcinomas by pathology.

In conclusion, a novel sonoelastographic shear velocity imaging technique was developed and shown to produce results consistent with true shear velocities in simulation and phantom studies. High-contrast visualization of focal carcinomas was demonstrated, introducing the clinical potential.

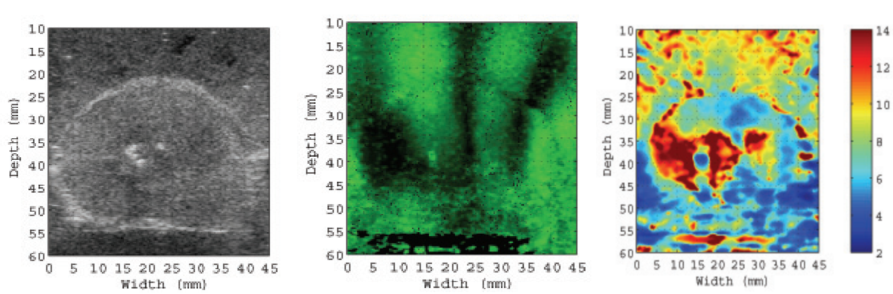


Figure1. Matched B–mode ultrasound (left), crawling wave sonoelastogram where green corresponds to high vibrational amplitude and vice versa for black (middle), and shear velocity image (right) in prostate.

Sonoelastography data generation and processing

Benjamin Castaneda, MS

Research in 2006 focused on the generation of 3D sonoelastography data and its semi-automatic processing to collect location, volume, and shape information from a detected tumor. Mr. Castaneda developed a system capable of generating volumes from 2D ultrasound (US) and sonoelasticity images based on a magnetic positioning sensor. It was successfully used for in vivo experiments (Fig. 1, 2). To process the many images generated in sonoelastography, an accurate and fast method for measuring the size and shape of the lesions is needed. He implemented a semi-automatic segmentation algorithm for sonoelastography data to reduce the variability and processing time involved in manual segmentation, while keeping comparable results (Fig. 3). He also developed a model-based algorithm for estimating elasticity modulus in a homogenous tissue from crawling waves. This algorithm was used to establish the congruence between crawling waves and mechanical methods for estimating elasticity modulus.

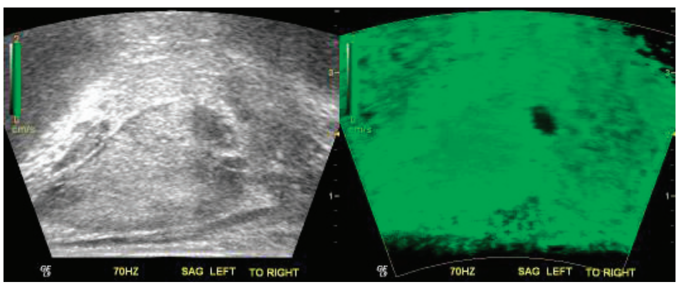


Figure 1. B-mode US image (left) and sonoelasticity image (right) of an in vivo experiment. Notice the detected tumor (void) in the middle of the sonoelasticity image corresponding to a hypoechoic structure in the US image.

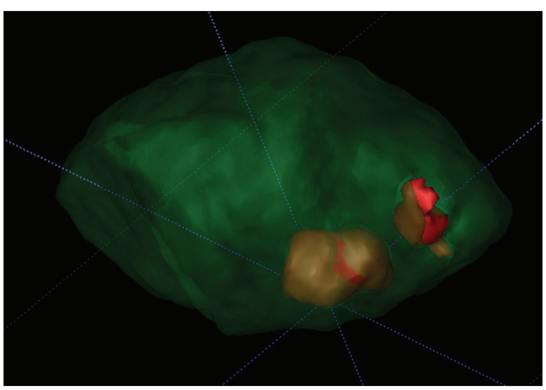


Figure 2. 3D reconstruction of a prostate gland from an in vivo experiment showing two cancerous tumors (in red) to the left.

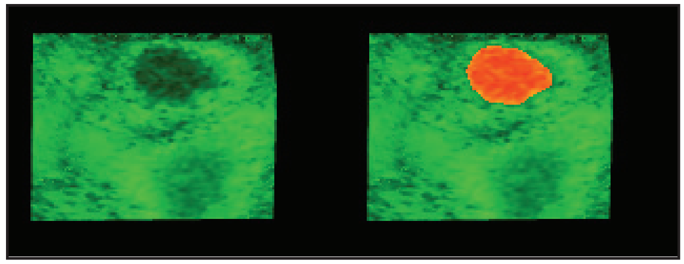


Figure 3. Original sonoelasticity image (left) and the result of the semi-automatic segmentation algorithm (right).

Measurement of pelvic osteolytic lesions in follow-up studies after total hip arthroplasty

Benjamin Castaneda, MS, Jose Gerardo Tamez-Pena, PhD, Saara Totterman, PhD, Regis O'Keefe, MD, R. John Looney, MD

Previous studies have demonstrated the plausibility of using volumetric computerized tomography to provide an accurate representation and measurement of volume for pelvic osteolytic lesions following total hip joint replacement. These studies have been performed manually (or computed-assisted) by expert radiologists with the disadvantage of poor reproducibility of the experiment. The purpose of this work is to minimize the effect of user interaction in these experiments by introducing Laplacian level-set methods in the volume segmentation process and using temporal articulated registration to follow the evolution of a lesion over time. Laplacian level set methods reduce the inter- and intra-observer variability by attaching the segmented contour to edges defined in the image while keeping smoothness. The registration process allows the information of the lesion from the first visit to be used in the segmentation process of the current visit. This work compares the automated results from seven volunteers versus the volume measured manually. Results have shown that the proposed technique is able to track osteolytic lesions and detect changes in volume over time. Intra-reader and inter-observer variabilities were reduced.

Sonoelastograpy and mechanical measurements

Man Zhang, PhD candidate

Research in 2006 focused on three major projects:

1. In vivo sonoelastography of thermal lesions (RFA lesions and HIFU lesions) in a swine model. This project was completed in December. Very good agreement on lesion dimensions and volume were found between sonoelastography and gross pathology.
2. Congruence of sonoelastography crawling wave estimator and mechanical measurements of viscoelastic properties of soft tissues.
3. Ex vivo and in vivo prostate imaging and mechanical measurement of normal and cancerous prostate tissues. Prostate imaging is an ongoing project, and the study on prostate mechanical properties was completed.

Three-dimensional sonoelastography for thermal lesion detection in an in vivo swine model

Man Zhang, MS, Benjamin Castaneda, MS, Jared Christensen, MD, Wael Saad, MD, Deborah Rubens, MD, Kevin J. Parker, PhD

In the last two decades, sonoelastography has been tested and verified in theoretical studies, acoustical phantoms, and thermal ablation studies in liver tissue in vitro. Radiofrequency ablation (RFA), a minimally invasive thermal therapy, has been under investigation as an alternative to surgery for treating liver tumors. This study investigates the feasibility of detecting RFA lesions using in vivo three-dimensional (3D) sonoelastography, which presents unique imaging challenges due to respiratory and cardiac motion. Furthermore, establishing efficacy in an in vivo animal model is an important step towards clinical implementation in humans. The aim of this study is to investigate the detectability of in vivo thermal lesions in porcine liver using real-time 2D and 3D sonoelastography. The pig is anesthetized and the abdomen is prepared and draped in the standard surgical manner. The liver is exposed through a midline incision. A RFA needle is then inserted into the porcine liver under ultrasound B-scan guidance. A lesion is created about 1 cm beneath the liver surface. Two mini-shakers (Bruel & Kjaer, Denmark) are applied on the liver surface. A sonoelastography volume is generated by acquiring a series of 2D images using a motorized tracking device (Velmex Inc., Bloomfield, NY). After in vivo imaging, the animal is sacrificed and the liver is excised for ex vivo study. RFA lesions are harvested and measured with calipers and fluid displacement. The elastic contrast between the RFA lesion and untreated liver is obtained by viscoelastic testing. A total of 12 RFA lesions were created in 3 porcine livers, with volumes ranging from 0.2 cc to 3 cc. Preliminary results showed good correlation of lesion dimensions and volume between sonoelastography images and gross pathology for lesions of different sizes. For instance, the volume of a RFA lesion measured by fluid displacement was 3.0 cc while the sonoelastography volume of the same lesion was 2.94 cc. Fig. 1 shows the B-mode and sonoelastography image of a 1.5 cc lesion. Its major axes are 14.87 mm and 10.52 mm when measured in the sonoelastography image, while in gross pathology they are 14.78 mm and 10.57 mm, respectively. A RFA lesion as small as 0.2 cc was also detected successfully in vivo. Preliminary results show good correlation between 3D sonoelastography and gross pathology, supporting the feasibility of sonoelastography for lesion detection and volume estimation. In vivo 2D sonoelastography images of different-sized RFA lesions were acquired, showing the potential of sonoelastography as a real-time method to accurately monitor thermal therapy of tumors. More experiments are ongoing to advance our results.

Acknowledgements: This study was supported by Fischer Fund Grant 4-50275.

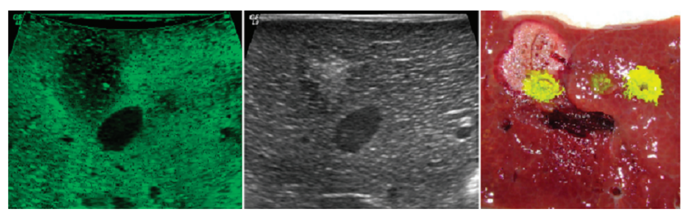


Figure 1. Sonoelastography image of a RFA lesion in vivo (left). Corresponding B-mode image of the lesion (center). Gross pathology of the lesion (right).

Curing characterization of polymer-based coatings on metallic plates using pulse-echo ultrasound and plate-guided waves

Raj Pananandiker, PhD candidate, advised by Navalgund Rao, PhD

The aim of this study was first to establish a relationship between the mechanical properties of a polymer coating on a metallic plate, determined by the extent of its curing, and a set of parameters, including acoustic velocity, attenuation, and nominal frequency shifts extracted using various ultrasonic investigative systems. Second, to investigate additional signal transformation phenomena observed during pulse-echo experiments. Test specimens were generated using a powder-coating system to coat the metallic plates with a polyester-based powder formulation and then heating the coated plates for different lengths of time in an oven. The heating time affects the extent of curing of the polymer and consequently its material properties vis-à-vis the resulting ultrasonic signal.

Characterizing parameters extracted from the signal included amplitude at nominal frequency, peak frequency, full width at half maximum (FWHM) and peak to side-lobe ratio. Additionally, differences were also observed in the V(z) curves of the set of plates. V(z) curves arise due to the interference of Rayleigh waves generated in the polymer-plate system and the specularly reflected longitudinal wave component in the coupling medium. Current investigations are aimed towards relating these Rayleigh waves to characteristic signal transformation phenomena observed in the pulse-echo experiments.

Non-contact ultrasound characterization of paper substrates

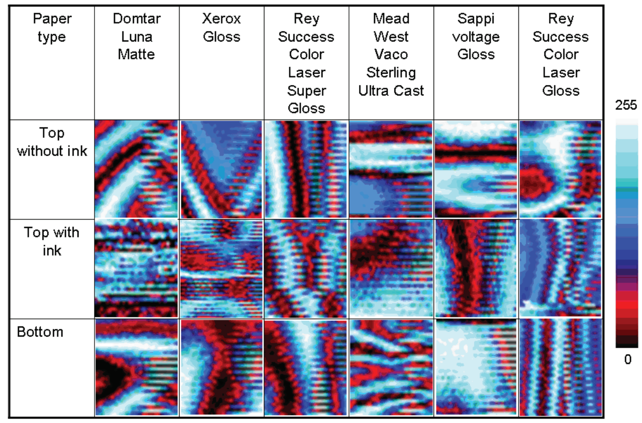
Maria Helguera, PhD

Different kinds of paper varying in basis weight, thickness, etc. and finishing characteristics such as cast, gloss, and matte were analyzed with and without deposited ink. A 1.7 MHz Ultran non-contact ultrasound focused transducer was operated in the pulse-echo mode to investigate the samples following a raster scan on a 1.5 cm by 1.5 cm area. Both sides of each sample were imaged under this protocol.

A pre-designed pattern consisting of some text and a rectangular solid block was printed on the front side of the samples using a Xerox Nuvera120 laser printer and the imaging protocol was repeated.

C-scan images created from the envelope detected data provide a promising means to investigate and visually differentiate the mechanical properties of the samples as ink is deposited, as well as to differentiate front and back sides of each sample.

The second normalized intensity moment and signal-to-noise ratio (SNR) of the signal envelope were investigated to test their validity to discriminate between different kinds of paper as well as differences in scattering properties when ink is deposited. Results are illustrated below.



Reduction of variance in spectral estimates for correction of ultrasonic aberration

Jeffrey Astheimer, PhD, Wayne Pilkington, PhD, Robert Waag, PhD

A variance reduction factor is defined to describe the rate of convergence and accuracy of spectra estimated from overlapping ultrasonic scattering volumes when the scattering is from a spatially uncorrelated medium. Assuming that the individual volumes are localized by a spherically symmetric Gaussian window and that the centers of the volumes are located on orbits of an icosahedral rotation group, the factor is minimized by adjusting the weight and radius of each orbit. We examined conditions necessary for the application of the variance reduction method, particularly for statistical estimation of aberration. The smallest possible value of the factor is found by allowing an unlimited number of centers constrained only to be within a ball rather than on icosahedral orbits. Computations using orbits formed by icosahedral vertices, face centers, and edge midpoints with a constraint radius limited to a small multiple of the Gaussian width show that a significant reduction of variance can be achieved from a small number of centers in the confined volume. This reduction is nearly the maximum obtainable from an unlimited number of centers in the same volume.

Lung damage induced by acoustic excitation and the subharmonic response of bubbles

Jonathan Young, MS, Sheryl Gracewski, PhD, Diane Dalecki, PhD

In May 2006, Jonathan Young completed his MS in Mechanical Engineering. His thesis, "The Relation Between Lung Damage Induced by Acoustic Excitation and the Subharmonic Response of Bubbles," was supervised by Sheryl Gracewski. This work contributes to ongoing collaborative efforts in the Gracewski and Dalecki labs to identify the acoustic mechanism for lung hemorrhage produced by low-frequency underwater sound. Following is the abstract from the thesis.

Abstract

Continuous wave excitation of murine lung at its resonance frequency leads to lung hemorrhaging when exposed above an applied acoustic pressure threshold. The mechanism for lung hemorrhaging was hypothesized to be dependent on the presence of subharmonic frequencies of order one-half in the displacement amplitude of the lung wall. The presence of subharmonics suggests a dependence on the stability of non-spherically symmetric modes given by the spherical harmonic functions.

To approximate the behavior of murine lung, a spherically symmetric balloon model was developed. The theory of bubble dynamics given by the Rayleigh-Plesset equation was generalized to include the effect of an elastic membrane surrounding a spherically symmetric bubble to model the spherically symmetric balloon. Balloons were made using a latex-rubber finger cot 0.09 mm thick and a 10 mm equilibrium radius.

The modal contribution of the spherical harmonic is a solution of the Mathieu equation. Numerical simulations of the Mathieu equation were used to determine the stability of specific modes to predict the onset of the subharmonic of the balloon models. The results gave an average applied pressure amplitude threshold of 0.87 kPa for the balloon models.

To test the simulations, the resonance frequencies of four balloons were measured. Displacement measurements at a point on the balloon surface were taken while increasing the applied acoustic pressure amplitude. A threshold for the onset of large amplitude subharmonic modes was found to be 0.5 ± 0.05 kPa, when forced at the resonance frequency of the balloon.

A second model of the murine lung that was investigated consisted of an air cavity of equilibrium radius 11 mm enclosed in 3% agar. Two 3% agar gel models were constructed and the resonance frequencies were measured and surface displacement amplitudes were recorded as functions of applied acoustic pressure amplitude. However, no evidence of a subharmonic frequency or a threshold for the onset of large amplitude displacements was observed.

Finally, four mice were tested for resonance frequency and were then exposed to underwater sound at resonance. Displacement amplitude measurements were recorded as a function of applied pressure amplitude. Again, the subharmonic was not observed. Despite this absence, a threshold for large amplitude displacements was found to be 1.0 ± 0.2 kPa.

BME/Optics Building Nears Completion

The University of Rochester's newest engineering building, Goergen Hall, will be completed in spring 2007. The 92,000 square foot facility will house the Department of Biomedical Engineering and provide expanded space for the Institute of Optics. The RCBU administrative office will move to this new building, along with the research laboratories of RCBU members Diane Dalecki, Amy Lerner, Steve McAleavey, and Rick Waugh. The facility also houses state-of-the-art biomedical engineering teaching laboratories, classrooms, lecture halls, and student and faculty offices, thus providing exciting opportunities for collaborative research and education. An enclosed walkway connects the new building with the Computer Studies Building and the Carlson Engineering Library. Building dedication and opening celebrations are scheduled for May 2007.

People, Promotions, and Awards

Shweta Bhatt, Deborah Rubens, and **Vikram Dogra** won first prize for their poster, "Color Flow Doppler Evaluation of Testicular Torsion and Its Pitfalls" at the AIUM Annual Meeting in March.

David Blackstock of the University of Texas taught a Nonlinear Acoustic Waves graduate course at the University of Rochester in summer 2006.

Edwin Carstensen was honored in a celebration session by the Acoustical Society of America (ASA) on June 8, 2006. (See article on page 21.)

Hannah Chang, Kristina Siddall, **Deborah Rubens**, Patrick Fultz, and **Vikram Dogra** won third prize for their poster, "Tricks and Pitfalls of Ovarian Torsion Imaging" at the AIUM Annual Meeting in March.

Diane Dalecki was appointed Director of the RCBU. Dr. Dalecki also received the Undergraduate Engineering Professor of the Year award from the University of Rochester Students' Association Senate.

Sheryl Gracewski, Professor of Mechanical Engineering, became a fellow of the Acoustical Society of America. Dr. Gracewski is recognized for her contributions to advancing our understanding of acoustic cavitation in biomedical ultrasound.

Maria Helguera, in collaboration with VirtualScopics, received a CAT-EIS 2006 award to fund development of an alternative approach to arriving at an imaging protocol using simulated magnetic resonance images.

Maria Helguera's graduate student, Stephanie Shubert, was awarded a Graduate Research Fellowship by the National Science Foundation (NSF).

Ken Hoyt, postdoctoral fellow in the Department of Electrical and Computer Engineering, was selected by the NIH for the Clinical Research Loan Repayment Program (LRP), based on his research proposal for three-dimensional sonoelastographic imaging for prostate cancer. Dr. Hoyt also was Co-Chair of the scientific session on Signal and Image Processing at the Fifth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Snowbird, Utah, October 2006.

Stephen McAleavey received the Professor of the Year award from the Biomedical Engineering Society (BMES) Student Chapter.

Deborah Rubens, Associate Director of the RCBU, will serve as the distinguished scientist in the Department of Radiologic Pathology at the Armed Forces Institute of Pathology (AFIP) for the 2006-2007 academic year.

The career of Floyd Dunn, an honorary RCBU member, was celebrated in a special day-long session of the 4th Joint Meeting of the Acoustical Society of America and the Acoustical Society of Japan on November 30 in Honolulu, Hawaii. Invited speakers spoke on Dr. Dunn's contributions to biomedical ultrasound, including ultrasound absorption, nonlinear phenomena, and biological effects of ultrasound.

ASA Celebration for Edwin Carstensen

On June 8, 2006, the Acoustical Society of America (ASA) held a special celebration session to honor the achievements of **Edwin L. Carstensen**. Carstensen was the Founding Director of the RCBU. He is an internationally recognized expert on the impact of ultrasonic waves and of electromagnetic waves on biological systems. The special session, held in Providence R.I., was organized by Diane Dalecki, Larry Crum (University of Washington), Leon Frizzell (University of Illinois), and Fred Kremkau (Wake Forest University). At the session, Marv Ziskin (Temple University) presented Ed Carstensen with a Meritorious Achievement Award from the World Federation of Ultrasound in Medicine (WFUMB).

Throughout his career, Dr. Carstensen has made outstanding and wide-ranging contributions to the field of biomedical ultrasound. His work pioneered our understanding of ultrasound absorption mechanisms, nonlinear propagation of ultrasound in tissues, acoustic cavitation in vivo, and biological effects of ultrasound and lithotripter fields. Dr. Carstensen's scientific achievements have been recognized through many awards and honors, including the Joseph H. Holmes Pioneer Award from the American Institute of Ultrasound in Medicine (AIUM), and membership in the National Academy of Engineering.

At the full-day ASA celebration session, colleagues, former students, and leading researchers in the field presented 25 lectures on many topics, including nonlinear acoustics, bioeffects, lithotripsy, and diagnostic imaging. Abstracts of presentations by RCBU members are provided below.

Sally Child, Ed Carstensen, Carol Raeman, and Diane Dalecki

Abstracts

Nonlinear acoustics in E. L. Carstensen's career.
David T. Blackstock, Univ. of Texas at Austin
HIFU and harmonic imaging are hallmarks of present day biomedical ultrasound. But it wasn't always this way. At one time linear theory ruled supreme. Although by the early 1970s nonlinear acoustics had made its way into many areas of acoustics, e.g., physical acoustics, underwater sound, and aeroacoustics, biomedical ultrasound remained a safe haven for small signalists. Ed Carstensen changed all that. By the mid-1970s he realized that linear theory could not account for certain phenomena he observed. At the 1978 Allerton Conference his invited talk entitled "Nonlinear Aspects of Ultrasonic Absorption" may have been the first public disclosure that nonlinear effects are important in biomedical ultrasound. His first archival work appeared as two papers in 1980; Tom Muir was a co-author for both. During the next decade, Ed and a series of colleagues showed that absorption could easily be dominated by nonlinear propagation effects. In turn, the increased absorption causes increased heating, an important practical application. Ed's pioneering work paved the way for many of the well-known applications today.

Medical imaging using nonlinear ultrasound and the role of Edwin Carstensen. *Kevin J. Parker*
In the 1960s, with the development of weak shock theory by Blackstock and other advances, nonlinear acoustics found growing importance and applications in the atmosphere and underwater. By comparison, during this timeframe the field of medical ultrasound remained largely focused on linear mechanisms. Three major subfields within medical ultrasound eventually developed major nonlinear theory and applications: cavitation, lithotripsy, and imaging. Edwin Carstensen's collaborative research and directorship of the Rochester Center for Biomedical Ultrasound played an important role in these developments. This talk focuses on the development of nonlinear acoustics to clinical imaging, tracing benchmark developments from the 1960s to the early 2000s, under the guiding influence of Ed Carstensen.

Acoustic radiation force imaging of prostate: initial results. *Stephen McAleavey*
Dr. Edwin Carstensen has contributed significantly to the understanding of the mechanical forces produced by acoustic waves in biological tissues, including work on cavitation and tactile perception of acoustic radiation force. This work presents some initial results in using radiation force for remote palpation of prostate tissue. Acoustic radiation

force impulse (ARFI) images of excised human prostates are presented. Fresh prostates obtained immediately after surgery were scanned in an isotonic saline bath at room temperature. Scanning was performed with a Siemens Antares scanner and VF10-5 linear array. Tissue displacement was induced by "pushing" pulses of 30 to 75 μm s duration at 6.67 MHz and an I_{sppa} on the order of 1 kW. Observed peak displacements in healthy tissue were in the range of 6-12 μm. Most prostates were scanned freehand. One specimen was scanned with a transducer mounted to a single axis stage and imaged at 1mm steps. The resulting images are presented with matching histology images and show good correspondence. This work was supported by the Wallace H. Coulter Foundation Early Career Award for Translational Research Program.

Thresholds for sound-induced lung hemorrhage for frequencies from 100 Hz to 1 MHz.
Diane Dalecki, Sally Z. Child, and Carol H. Raeman
Edwin L. Carstensen has made outstanding and wide-ranging contributions to the field of biomedical ultrasound. His many achievements span the areas of bioeffects of ultrasound, acoustic cavitation, lithotripsy, thermal and mechanical mechanisms, and nonlinear acoustics. In 1990, Carstensen first reported that pulsed ultrasound at diagnostic exposure conditions could produce mammalian lung hemorrhage (Child et al., *Ultrasound Med. and Biol.* 16, 817–825 1990). Recent work from our lab has quantified the thresholds for murine lung hemorrhage over a range of acoustic frequencies from approximately 100 Hz to 1 MHz. Various exposure systems were used to generate acoustic fields over this broad frequency range in the laboratory. Through several different investigations, we have shown that murine lung responds to low-frequency underwater sound as a resonant structure. The resonance frequency of adult murine lung is approximately

Marv Ziskin congratulates Edwin Carstensen after presenting him with a WFUMB Meritorious Achievement Award.

325 Hz, and the pressure threshold for lung hemorrhage is lowest at the resonance frequency. The threshold increases for frequencies above lung resonance. The equation $P_{th} = 0.01f^{0.64}$, where P_{th} is the threshold pressure in MPa and f is the acoustic exposure frequency in kHz, approximates our experimental lung threshold data, for long pulse durations, over the 2.5-1000 kHz range.

Stress, strain, and flow produced by a vibrator in or on the surface of a soft solid. *Wesley L. Nyborg and Harold M. Frost, Univ. of Vermont*
The field of biomedical ultrasound is greatly indebted to Edwin Carstensen for important contributions, without number, that he and his associates have made to understanding the subject. These contributions have dealt not only with linear and nonlinear propagation of ultrasound in biological materials, but also with effects produced by ultrasound through various thermal and nonthermal mechanisms. Such understanding is important for advancing benefits and minimizing risks in applications of ultrasound. Many therapeutic applications discussed in the literature utilize focused beams of megahertz frequency, while others employ lower frequencies. In this talk, some findings will be presented from experiments in which a vibrating source of frequency in the range 20-90 kHz is brought into contact with the surface of a soft viscoelastic solid and information is obtained on resulting fields of strain. Under some conditions the mechanical properties of the solid are altered by an exposure, in an apparent change of internal structure, and the change is maintained and recorded until erased by a later sonication. The role of radiation force and other mechanisms in producing such effects will be discussed, as well as their possible relevance to ultrasonic angioplasty and other applications.

Statistical estimation of ultrasonic propagation path parameters for aberration correction.
Robert C. Waag and Jeffrey P. Astheimer
Parameters in a linear filter model for ultrasonic propagation are found using statistical estimation. The model employs an inhomogeneous-medium Green's function that is decomposed into a homogeneous-transmission term and a path-dependent aberration term. Power and cross-power spectra of random-medium scattering are estimated over the frequency band of the transmit-receive system by using closely situated scattering volumes. The frequency-domain magnitude of the aberration is obtained from a normalization of the power spectrum. The corresponding phase is reconstructed from cross-power spectra of subaperture signals at adjacent receive positions by a recursion. The subapertures constrain the receive sensitivity pattern to eliminate measurement system phase contri-

butions. The recursion uses a Laplacian-based algorithm to obtain phase from phase differences. Pulse-echo waveforms were acquired from a point reflector and a tissue-like scattering phantom through a tissue-mimicking aberration path from neighboring volumes having essentially the same aberration path. Propagation path aberration parameters calculated from the measurements of random scattering through the aberration phantom agree with corresponding parameters calculated for the same aberrator and array position by using echoes from the point reflector. The results indicate the approach describes, in addition to time shifts, waveform amplitude and shape changes produced by propagation through distributed aberration under realistic conditions.

Vessel damage mechanisms by ultrasound or shock wave pulses. *Sheryl M. Gracewski, Hongyu Miao, and Diane Dalecki*
Edwin L. Carstensen has been one of the pioneers investigating not only the thresholds for bioeffects of ultrasound, but also determining mechanisms for these bioeffects, especially when air cavities are involved. Previous studies have demonstrated that hemorrhage or endothelial layer damage can occur when the blood vessels are exposed to lithotripter shock waves or to ultrasound in the presence of echo contrast agents. The presence of bubbles is often necessary for the damage to occur. Two main hypotheses describing the mechanism of vessel damage by acoustically excited microbubbles have been proposed. The vessel could be damaged by the high pressures and/or temperatures generated by the violent collapse of cavitation bubbles. Alternatively, the vessel could rupture upon bubble expansion. Here, a simple model is presented for vessel rupture upon bubble expansion and calculations are presented for parameters corresponding to two recently published experimental observations of vessel rupture and of endothelial cell damage to try to distinguish between these two mechanisms.

Distinguished presenters at Carstensen ASA celebration

A possible noncavitational mechanism of ultrasound-accelerated thrombolysis in fibrin clots.
E. Carr Everbach, Swarthmore College, Irina N. Chernysh and John W. Weisel, Univ. of Pennsylvania
Blood clots made of human plasma or purified fibrin with and without the addition of rt-PA were insonified with 1 MHz pulsed ultrasound on a microscope slide placed in a spectrophotometer. Clot dissolution times were measured by absorption of light at 350 nm wavelength passing through the clot. Dissolution times were halved for ultrasound-exposed clots versus shams. Clots with no rt-PA present showed a small but significant thrombolysis effect in the presence of ultrasound which could be prevented by the addition of factor XIII, which effectively binds the fibrin. Ultrasound pulse parameter variations showed a broad maximum effectiveness at 0.5 MPa peak negative pressure, 1 ms duration, and 50 Hz PRF. Concentration of protein in solution was elevated as much as a factor of 10 following insonification of clots without rt-PA, suggesting that ultrasound affects the kinetics of fibrin remodeling. A possible explanation that does not involve bubble activity is relative motion between the clot fibers and the interstitial fluid.

The relation between lung damage induced by acoustic excitation and the subharmonic response of bubbles. *John Young, Sheryl Gracewski, Steve McAleavey, Diane Dalecki*
Edwin L. Carstensen has made significant contributions to determining thresholds for and understanding mechanisms of mammalian lung hemorrhage caused by both ultrasound and lithotripter shock waves. The work presented here extends this knowledge base to investigate mechanisms of lung damage caused by acoustic excitation at the lung resonance frequency. This situation is relevant to divers exposed to high amplitude, low-frequency sonar. Based on preliminary experiments, it was hypothesized that the threshold for lung hemorrhage at resonance occurs when lung surface oscillations at the subharmonic frequency of order one-half become unstable, producing significantly larger lung displacements. A balloon model was developed to approximate the behavior of small mammalian lung. The theoretical model for surface mode oscillations of a bubble was modified to account for the initial tension in the balloon membrane and used to investigate the stability of subharmonic oscillations. Reasonable agreement between the theoretical model and experimental measurements of the balloon surface displacements were obtained. In addition, a sharp pressure threshold for the presence of subharmonic oscillations was observed in the displacement data for the balloon model. The relevance of these simulations and measurements to murine lung hemorrhage will be discussed.

Student Profile: Maggie Zhang

Therapeutic ultrasound, especially high-intensity focused ultrasound (HIFU), is growing rapidly and is getting more important, according to Man (Maggie) Zhang, a Biomedical Engineering (BME) graduate student expected to receive her PhD in May 2007. "Elasticity and molecular imaging are the future," she said.

Ms. Zhang, advised by Kevin Parker, is working on her dissertation, titled "The Application of Three Dimensional Sonoelastography: Measurement of Soft Tissue Viscoelastic Properties and Imaging of Thermal Lesions in the Liver."

Ms. Zhang became interested in ultrasound as a BME MS student after her lab rotations with Diane Dalecki and Dr. Parker. She studied tissue engineering in China before coming to the University of Rochester. Ms. Zhang said she finds ultrasound research "quite interesting" because of its clinical applications. She likes that in clinical research, results are immediate, unlike tissue engineering, where results take longer to see. Ms. Zhang's medical background means ultrasound research is well-suited for her, leading to her keen interest in radiology.

While at the UR, Ms. Zhang has worked as a research assistant in the Parker lab, where she has proposed and performed sonoelastography of HIFU and RFA lesions in an in vivo swine model, conducted ex vivo imaging and mechanical measurements of human prostate, and evaluated ultrasound thin-film calibration phantoms with Field II simulation and on-site assessment.

Ms. Zhang received her MS in Biomedical Engineering in May 2003 from the University of Rochester. Before coming to Rochester in 2001, she studied at Southeast University, in Nanjing, China, receiving her MEng in Biomedical Engineering and her Bachelor in Clinical Medicine from Nanjing Medical University in 2001. Prior to that, she received her BEng in Biomedical Engineering in July 1998 from Southeast University in Nanjing.

Ms. Zhang chose the University of Rochester for several reason. She had a friend who graduated from the BME Department and recommended the program to her. She liked that BME was a small department at that time. "It was relatively young and developing, which provided me more opportunities to discuss research with the professors in person," she said.

She also liked that in the first year, there were three lab rotations, which she thought was a great way to know more about the program and to help her decide on the best field for future research. Another incentive to come to UR was that both she and her husband, Peng Wang, received BME fellowships.

Ms. Zhang has presented at several professional conferences since coming to the UR, including several American Institute of Ultrasound in Medicine (AIUM) annual conventions and several International Conferences on the Ultrasonic Measurement and Imaging of Tissue Elasticity.

After she earns her PhD, Ms. Zhang plans to look for a position with one of the major healthcare imaging manufacturers or secure a post-doctoral position in a clinical setting at a leading university.

When she is not working on her research studies, Ms. Zhang stays active by hiking, swimming, and playing racquet sports. She also enjoys fishing.

Tissue Elasticity Conference Highlights

The Fifth International Conference on Ultrasonic Measurement and Imaging of Tissue Elasticity was held October 8-11, 2006 in Snowbird, Utah. More than 150 people from 20 countries attended the conference. While the conference has always attracted ultrasound researchers and developers, this year saw an increase in participation from industry, physicians, students, and research groups in related disciplines.

Several RCBU members participated in the conference, including Deborah Rubens, Kevin Parker, Kenneth Hoyt, Benjamin Castaneda, and Clark Wu. Their presentations are listed on page 29.

The number of abstracts submitted to the conference has increased each year—this year, there were 121 accepted abstracts. There has also been a steady increase in the number of clinical papers presented at the conference.

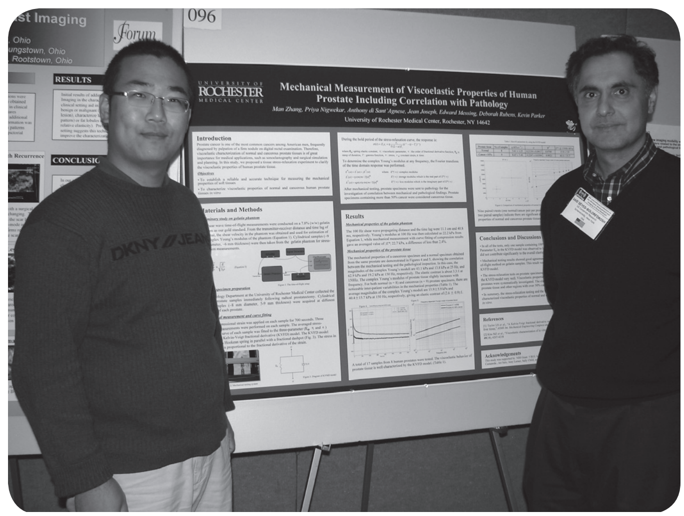
In addition to research presentations and posters, two tutorials were presented on the progress and prospects of basic and clinical science of imaging the elastic properties of tissue. Dr. Armen Sarvazyan from Artann Laboratories in Trenton, NJ presented "Tissue Viscoelasticity: Past and Future, Unexplored Areas and Brave Projections." Dr. Brian Garra from the University of Vermont in Burlington presented "Imaging of Tissue Elasticity: Will It Become an Important Clinical Tool?"

The conference is jointly sponsored and organized by the RCBU and the Ultrasonics Laboratory in the Department of Diagnostic and Interventional Imaging at the University of Texas Medical School at Houston.

In 2007, the conference will also be held in Santa Fe, New Mexico from November 2-5.

For more information, visit the conference Web site: http://www.ece.rochester.edu/projects/rcbu/conference/

Jonathan Ophir from the University of Texas and Kevin Parker.



Clark Wu and Said Seyed-Bolorforosh of GE with Maggie Zhang's poster presentation.

Benjamin Castaneda of UR, Tomy Varghese of the University of Wisconsin - Madison, and Arun Kumar of the University of Texas Health Science Center.

RCBU Seminars

Radiation force imaging methods

RCBU members attended a seminar on September 7 presented by Gregg Trahey, PhD, from Duke University. Dr. Trahey is a professor in the Departments of Medical Physics and Biomedical Engineering at Duke University and the Department of Radiology at Duke University Medical Center. He was named the James L. and Elizabeth M. Vincent Chaired Professor at Duke in 2000. He received his Ph.D. from Duke in 1985. Professor Trahey is a fellow of the American Institute of Ultrasound in Medicine and the American Institute for Medical and Biological Engineering.

At the seminar, Dr. Trahey reviewed current efforts at Duke University to develop radiation force imaging methods and the results of ongoing clinical studies in the liver, vasculature, heart, and breast. He described beamforming techniques designed to optimize the measurements of tissue response to ultrasonic radiation force and hardware challenges in implementing radiation force imaging on commercial ultrasonic scanners. New efforts to track shear waves generated by radiation force and a new method to track shear wave velocities on a scanner with limited parallel receive beamforming were discussed. He presented the results of studies that assess the role of radiation force imaging in guiding radio-frequency ablation procedures in the heart and liver. Last, he reviewed safety issues related to radiation force imaging.

Gregg Trahey and Steve McAleavey

EchoSens and FibroScan

Laurent Sandrin, Technical Director of EchoSens, gave a presentation to RCBU members December 18. EchoSens, headquartered in Paris, France, has developed medical imaging equipment for ultrasound elastography, called FibroScan®. Cecile Guiducci, International Marketing Director, and Luc Talini, Technical Development Manager, accompanied Dr. Sandrin.

Laurent Sandrin presents to RCBU members.

The first application for the FibroScan unit is measurement of hepatic fibrosis. EchoSens is taking a position in the new, promising market for non-invasive diagnosis of liver fibrosis, the consequence of chronic diseases such as hepatitis B and C and alcohol dependence. Robert Lerner, RCBU member from Rochester General Hospital, set the stage for the presentation with a brief overview of liver biopsy, specifically, applications for the hepatitis C virus (HCV). Liver biopsy is the current gold standard for the assessment of HCV disease status and progression. Dr. Lerner discussed the grading, staging, and limitations of liver biopsies.

Dr. Sandrin provided a review of the technology behind FibroScan. He also discussed the quantification of hepatic fibrosis. He said it is highly important to evaluate the fibrosis stage of HCV patients, explaining that liver biopsy, although it is the gold standard, is invasive, expensive, and lacks reproducibility.

The FibroScan unit, Dr. Sandrin explained, is based on 1D transient elastography, since liver fibrosis deposition is homogenous in patients with HCV. He provided a comparison between the liver biopsy scoring system and liver stiffness measurement.

Dr. Sandrin concluded by stating the benefits of FibroScan over liver biopsy: it is non-invasive, rapid, and cost efficient, as well as reliable, quantitative, and easy to use.

Education

Biomedical Ultrasound (BME 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.

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.

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.

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.

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.

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.

Microhydrodynamics (BME 466). Develops insight into the motion of small particles in a viscous fluid. Such problems are found in biology, biotechnology, and composite materials processing. Specific topics include flow past spheres and arbitrary bodies (thermally driven), motion of bubbles and drops, slendor body theory, and leading-order inertial corrections.

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.

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.

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.

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

Selected Publications

JP Astheimer, WC Pilkington, **RC Waag**. Reduction of variance in spectral estimates for correction of ultrasonic aberration. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2006 Jan;53(1):79-89.

S Bhatt, E Kocakoc, **VS Dogra**. Endometriosis: sonographic spectrum. *Ultrasound Q*. 2006 Dec;22(4):273-80.

S Bhatt, R Simon, **VS Dogra**. Gamna-Gandy bodies: sonographic features with histopathologic correlation. *J Ultrasound Med*. 2006 Dec;25(12):1625-9.

S Bhatt, **DJ Rubens**, **VS Dogra**. Sonography of benign intrascrotal lesions. *Ultrasound Q*. 2006 June 22(2), 121-36.

B Castaneda, JG Tamez-Pena, S Totterman, R O'Keefe, RJ Looney. Measurement of pelvic osteolytic lesions in follow-up studies after total hip arthroplasty. *Proceedings of SPIE International Symposium on Medical Imaging*, San Diego, CA, 2006.

M Helguera, J Kastner Eds. *Imaging in the Physical Sciences*. Kendall-Hunt, 2006.

M Helguera, Medical Imaging and What Lies Ahead. *Advanced Imaging,* September 2006. (Cover Story)

K Hoyt, F Forsberg, J Ophir. Analysis of a hybrid spectral strain estimation technique in elastography. *Phys Med Biol*. 2006 Jan 21;51(2), 197-209.

K Hoyt, F Forsberg, J Ophir. Comparison of shift estimation strategies in spectral elastography. *Ultrasonics*. 2006 Jan;44(1), 99-108.

AL Lerner, BH Kenknight, A Rosenthal, PG Yock. Design in BME: challenges, issues, and opportunities. *Ann Biomed Eng*. 2006 Feb;34(2):200-8.

EP Lin, J Marshall, **S Bhatt**, R Simon, R Davis, **VS Dogra**. Penile schwannoma: sonographic features. *J Ultrasound Med.* 2006 Nov;25(11):1447-50.

BK Markhardt, **DJ Rubens**, J Huang, **VS Dogra**. Sonographic features of biliary hamartomas with histopathologic correlation. *J Ultrasound Med*. 2006 Dec;25(12):1631-3.

C Rota, **CH Raeman**, **SZ Child**, **D Dalecki**. Detection of acoustic cavitation in the heart with microbubble contrast agents in vivo: A mechanism for ultrasound-induced arrhythmias. *J. Acoust. Soc. Am*. 120:2958-2964; 2006.

DJ Rubens, Y Yu, AS Barnes, **JG Strang**, R Brasacchio. Image-guided brachytherapy for prostate cancer. *Radiol Clin North Am*. 2006 Sep;44(5), 735-48.

WE Saad, MG Davies, CK Ryan, **DJ Rubens**, NC Patel, DE Lee, LG Sahler, DL Waldman. Incidence of arterial injuries detected by arteriography following percutaneous right-lobe ultrasound-guided core liver biopsies in human subjects. *Am J Gastroenterol.* 2006 Nov;101(11):2641-5.

WE Saad, CK Ryan, MG Davies, P Fultz, **DJ Rubens**, NC Patel, LG Sahler, DE Lee, T Kitanosono, T Sasson, DL Waldman. Safety and efficacy of fluoroscopic versus ultrasound guidance for core liver biopsies in potential living related liver transplant donors: preliminary results. *J Vasc Interv Radiol*. 2006 Aug 17(8), 1307-12.

J Yao, PD Funkenbusch, J Snibbe, M Maloney, **AL Lerner**. Sensitivities of medial meniscal motion and deformation to material properties of articular cartilage, meniscus and meniscal attachments using design of experiments methods. *J Biomech Eng.* 2006 Jun;128(3):399-408.

J Yao, J Snibbe, M Maloney, **AL Lerner**. Stresses and strains in the medial meniscus of an ACL deficient knee under anterior loading: a finite element analysis with image-based experimental validation. *J Biomech Eng*. 2006 Feb;128(1):135-41.

R Waag, RJ Fedewa. A ring transducer system for medical ultrasound research. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2006 Oct;53(10):1707-18.

Z Wu, **K Hoyt**, **DJ Rubens**, **KJ Parker**. Sonoelastographic imaging of interference patterns for estimation of shear velocity distribution in biomaterials. *J Acoust Soc Am*. 2006 Jul 120(1), 535-45.

T Podder, D Clark, J Sherman, D Fuller, **E Messing**, **DJ Rubens**, **J Strang**, R Brasacchio, L Liao, WS Ng, Y Yu. Vivo motion and force measurement of surgical needle intervention during prostate brachytherapy. *Med Phys.* 2006 Aug;33(8):2915-22.

L Fu, H Liu, WS Ng, **DJ Rubens**, **J Strang**, **E Messing**, Y Yu. Hybrid dosimetry: feasibility of mixing angulated and parallel needles in planning prostate brachytherapy. *Med Phys*. 2006 May;33(5):1192-8.

Selected Presentations

KG Baum, **M Helguera**, JP Hornak, JP Kerekes, ED Montag, MZ Unlu, DH Feiglin, and A Krol. Techniques for Fusion of Multimodal Images: Application to Breast Imaging, 2006 IEEE International Conference on Image Processing.

KG Baum, **M Helguera**, and A Krol. Genetic Algorithm Automated Generation of Multivariate Color Tables for Visualization of Multimodal Medical Data Sets, IS&T/SID's Fourteenth Color Imaging Conference, 2006.

S Bhatt and **VS Dogra**. Urologic Emergencies: Role of Sonography, RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

S Bhatt and **VS Dogra**. Acute Gynecological Presentations with Emphasis on Color Flow Doppler Evaluation, RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

S Bhatt and **VS Dogra**. Imaging of Uterine Abnormalities with Color Flow Doppler, RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

S Bhatt, ZH Jafri, NF Wasserman, and **VS Dogra**. Non-Neoplastic Intratesticular Masses, RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

S Bhatt, **DJ Rubens**, RC Vyas, **J Strang**, MS Orloff, A Bozorgzadeh, **VS Dogra**. Significance of High Resistive Indices During the Immediate Post–Liver Transplant Period in Predicting Transplant Outcome, American Institute of Ultrasound in Medicine (AIUM) Annual Meeting, March 22 – 26, 2006.

B Castaneda, **M Zhang**, **Z Wu**, **DJ Rubens**, **KJ Parker**. Congruence of Sonoelastography Crawling Waves and Mechanical Measurements for Estimation of Viscoelastic Properties of Soft Tissues, Fifth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, October, 2006.

B Castaneda. Clinical Applications of Sonoelastography, invited presentation at Hospital Nacional Edgardo Rebagliatti, Lima, Peru, July 2006

B Castaneda. Sonoelastography applied to Prostate Cancer Detection, invited presentation at Rochester Institute of Technology, Rochester, NY, February 2006.

H Chang, **N Carson**, **S Bhatt**, **DJ Rubens**, **VS Dogra**. Is Venous Compression Necessary in Deep Venous Thrombosis Evaluation of Lower Extremities? AIUM Annual Meeting, March 22 – 26, 2006

JD Christensen, **M Zhang**, **B Castaneda**, W Saad, **DJ Rubens**. Real-Time Sonoelastography Detection of Hepatic Radiofrequency Ablation Lesions in an In Vivo Porcine Model, Society of Radiologists in Ultrasound Annual Meeting, San Francisco, CA, 2006

VS Dogra. Genitourinary Doppler Ultrasound Update: Non-invasive Therapy of Myomas, AIUM Annual Meeting, March 22 – 26, 2006

M Helguera. Non-Contact Ultrasound Characterization of Paper Substrates, 9th European NDT Conference, Berlin, September 2006

K Hoyt, **KJ Parker**, and **DJ Rubens**. Sonoelastographic Shear Velocity Imaging: Experiments on Tissue Phantom and Prostate, IEEE International Ultrasonics Symposium, October 2006.

K Hoyt. Ultrasonic Methods for Imaging the Elastic Properties of Tissue, International Congress of Imaging Science (ICIS), May 2006.

K Hoyt, **KJ Parker**, **DJ Rubens**. Sonoelastographic Shear Velocity Imaging: An Application of Crawling Waves, Fifth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, October, 2006.

EP Lin, **S Bhatt**, **DJ Rubens**, **VS Dogra**. Monophasic Venous Waveforms: What Do They Mean? (Selected for the Resident Research Award), RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

S McAleavey, **M Menon**, **DJ Rubens**. Acoustic Radiation Force Impulse Imaging of Excised Human Prostates, IEEE International Ultrasonics Symposium, October 2006.

S McAleavey, S White, **M Menon**. Magnetically Vibrated Brachytherapy Seeds: Ferromagnetic Core Models and Image Reconstruction Methods, IEEE International Ultrasonics Symposium, October 2006.

L Pallwein, H Steiner, M Schurich, D zur Nedden, F Frauscher, **VS Dogra**, Sonoelastography of Testicular Masses: Initial Experience. AIUM Annual Meeting, March 22 – 26, 2006

W Pilkington, **RC Waag**, Computation Reduction for Ultrasonic Aberration Correction. AIUM Annual Meeting, March 22 – 26, 2006

C Sides, **S Bhatt, DJ Rubens**, **VS Dogra**, Color Flow Doppler Evaluation of Testicular Torsion and Its Pitfalls, RSNA 92nd Scientific Assembly and Annual Meeting, Nov 26 – Dec 1, 2006.

JC Tillett, **RC Waag**, Correction of Ultrasonic Transmit Focus Aberration Caused by Propagation Through a Tissue-Mimicking Phantom. AIUM Annual Meeting, March 22 – 26, 2006

M Zhang, **B Castaneda**, J Christensen, W. Saad, **DJ Rubens**, **KJ Parker**. Three-Dimensional Sonoelastography for Thermal Lesion Detection in an In Vivo Swine Model. Fifth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, October, 2006.

M Zhang, P Nigwekar, **PA di Sant'Agnese**, **J Joseph**, **EM Messing**, **DJ Rubens**, **KJ Parker**. Mechanical Measurement of Viscoelastic Properties of Human Prostate Including Correlation with Pathology. Fifth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, October, 2006.

M Zhang, **B Castaneda**, **Z Wu**, **DJ Rubens**, **KJ Parker**, Congruence of Sonoelastography Shear Wave Interference Estimates and Mechanical Measurements for Estimation of Viscoelastic Properties of Soft Tissues. AIUM Annual Meeting, March 22 – 26, 2006

Patents

The RCBU is continually working on novel concepts in ultrasound research. Some of the patents that originated at the Center are summarized below. For more information, call the University of Rochester Technology Transfer office at (585) 275-3998.

New patent

A third patent was issued on September 12, 2006 to former RCBU member Ted Christopher, PhD. The title of the invention is **Finite Amplitude Distortion-Based Inhomogeneous Pulse Echo Ultrasonic Imaging**. The first patent was issued in March 2001 and the second in February 2006. Dr. Christopher received his PhD in Electrical Engineering at the University of Rochester in 1993. US Patent No. 7,104,956

Additional patents issued to RCBU members are listed below.

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. Parker on May 26, 1998.

System and Method for 4D Reconstruction and Visualization
US Patent No. 6,169,817 issued to Kevin J. Parker, Saara SM 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
US Patent No. 5,479, 932 issued to Joseph Higgins, E. Carr Everbach, Kevin J.Parker on January 2, 1996

Apparatus for Bone Surface-Based Registration
US Patent No. 6,106,464 issued to WA Bass, RL Galloway, Jr., CR Maurer, Jr, and RJ Maciunas on August 22, 2000

Sonoelasticity Imaging Estimators
US Patent No. 5,086,775, issued to Ron Huang, Robert Lerner, and Kevin Parker on February 11, 1992

Butterfly Search Technique
US Patent No. 5,419, 331 issued to S. Kaisar Alam and Kevin Parker on May 30, 1995

Smart Endotracheal Tube
US Patent No. 5,785,051 issued to Jack Mottley and Randy Lipscher on July 29, 1998.

Center Members

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Janine Shapiro, MD
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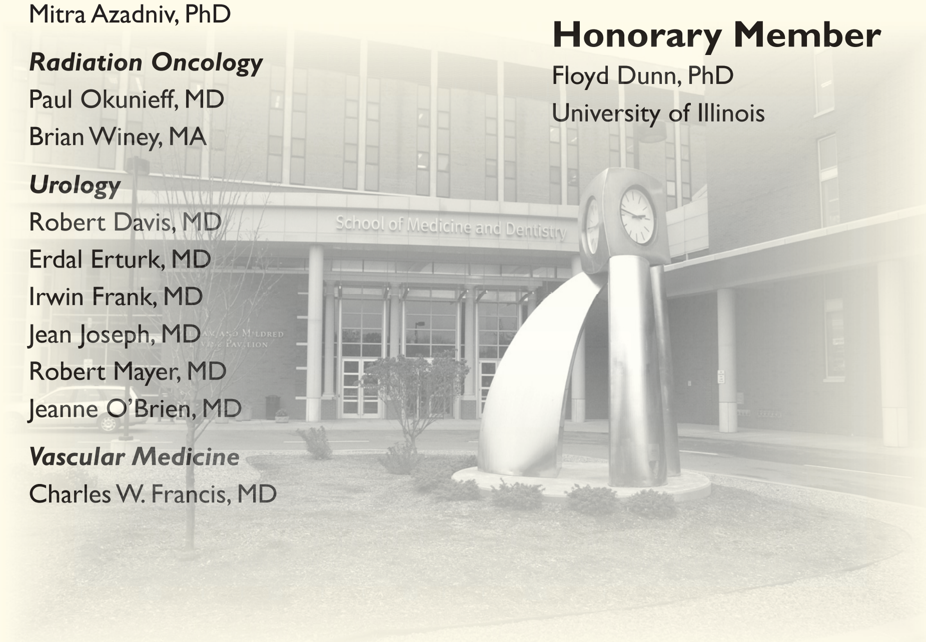

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