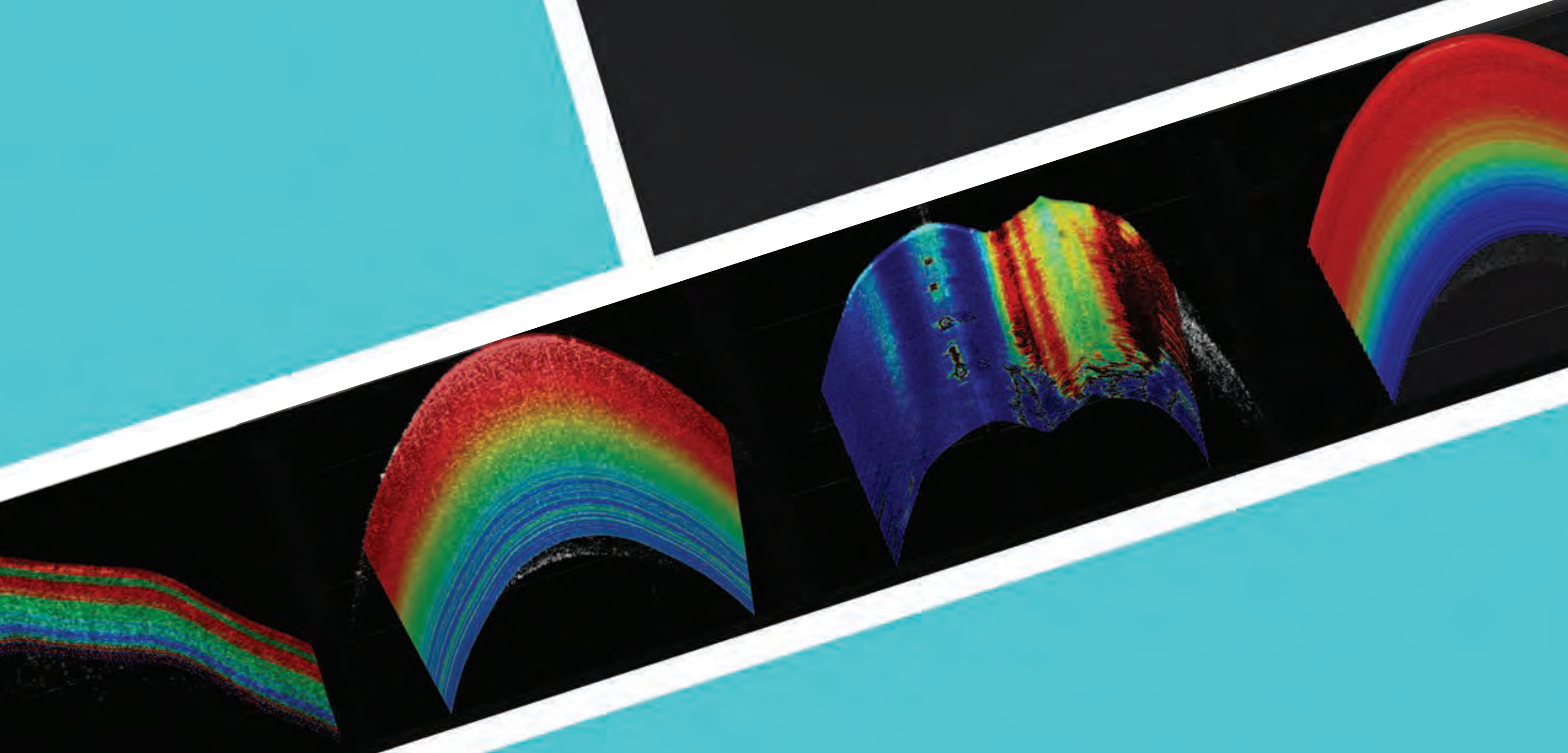
ROCHESTER CENTER FOR BIOMEDICAL ULTRASOUND

RCBU

ANNUAL REPORT



RCBU

ROCHESTER CENTER FOR BIOMEDICAL ULTRASOUND

RCBU Director
Diane Dalecki, Ph.D.

RCBU Associate Director
Deborah J. Rubens, M.D.

RCBU Executive Committee
Diane Dalecki, Ph.D., Vikram S. Dogra, M.D., Morton W. Miller, Ph.D., Kevin J. Parker, Ph.D., and Deborah J. Rubens, M.D.

University of Rochester President
Joel Seligman, Ph.D.

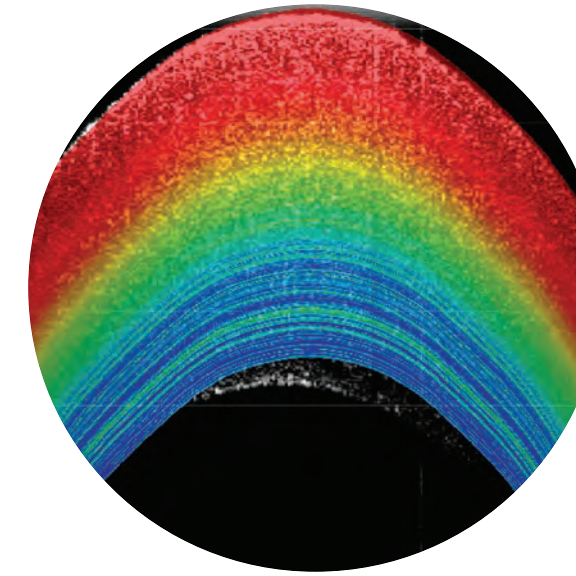
University of Rochester Provost
Robert L. Clark, Ph.D.

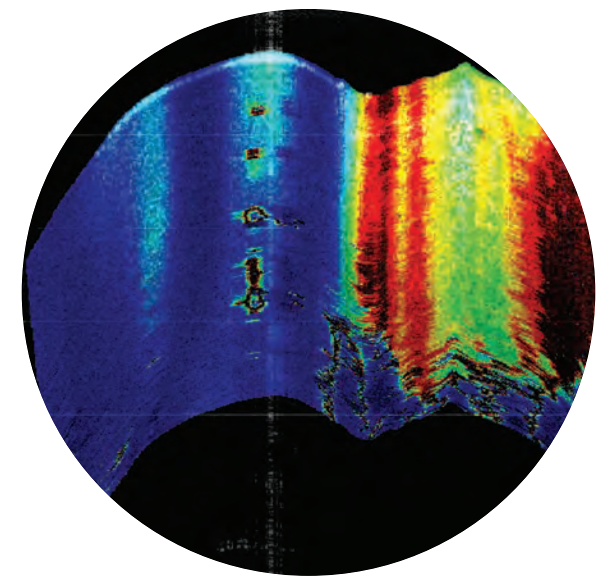
Dean of the School of Medicine and Dentistry; CEO of the University of Rochester Medical Center
Mark B. Taubman, M.D.

Dean of the Hajim School of Engineering and Applied Sciences;
Wendi Heinzelman, Ph.D.

Editing & Graphic Design
Courtney Rieder Nielsen

ABOUT THE COVER





Elastogram 1
Depth-resolved Lamb wave speed map of porcine sclera showing differentiated elastic properties of scleral layers.

Elastogram 2 & 4
Depth-resolved Lamb wave speed map of porcine cornea showing differentiated elastic properties of corneal layers.

Elastogram 3
Lamb wave speed map of cornea-sclera transition showing differentiated elastic properties of cornea and sclera in porcine eyes.

(see story on pg. 8)

CONTACT THE RCBU

Rochester Center for Biomedical Ultrasound
University of Rochester
210A Goergen Hall,
PO Box 270168
Rochester, NY 14627
rochester.edu/rcbu
(585)275-7378

DIANE DALECKI, PH.D.
Director

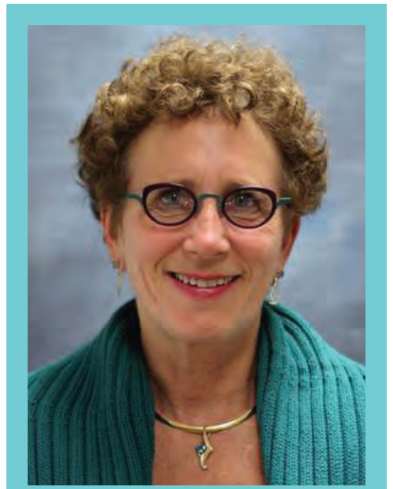
This RCBU report summarizes progress in research, education, and innovation from the Rochester Center for Biomedical Ultrasound. RCBU members continue to advance the development of novel elastography techniques for wide ranging applications, ultrasound technologies for tissue engineering and regenerative medicine, quantitative ultrasound tissue characterization, nonlinear and contrast imaging, and new therapeutic applications of ultrasound.

On a more reflective note, included in this report is a memorial of Ed Carstensen. Professor Carstensen was one of the most important pioneers in the field of biomedical ultrasound, and his work provided the foundation for our understanding of the biological effects of ultrasound fields. He was the Founding Director of the RCBU, a member of the National Academy of Engineers, and recipient of numerous awards and accolades for his scientific achievements. The newly established Edwin and Pam Carstensen Family Endowment will honor the legacy of Ed Carsensten and ensure that his vision for the RCBU endures.

This report also summarizes recent funding news, awards and achievements of RCBU investigators. A list of selected patents by RCBU members in diverse areas of biomedical ultrasound is also included. The UR is consistently rated as one of the best educational institutions in the nation for patent licensing and revenue. Collaborative projects between RCBU clinicians, engineers, and scientists continue to fuel new discoveries in diagnostic and therapeutic applications of ultrasound. Our student members are also an important component of the RCBU. The RCBU provides exciting opportunities for education and research training in biomedical ultrasound. A wide range of relevant course offerings complements the rich environment for collaborative multidisciplinary research in diverse areas of ultrasound. Included within this report are announcements of national awards and fellowships garnered by RCBU student members, highlights of student research, and educational advances by RCBU members. We welcome your comments on any of the enclosed reports.

MEET THE DIRECTORS

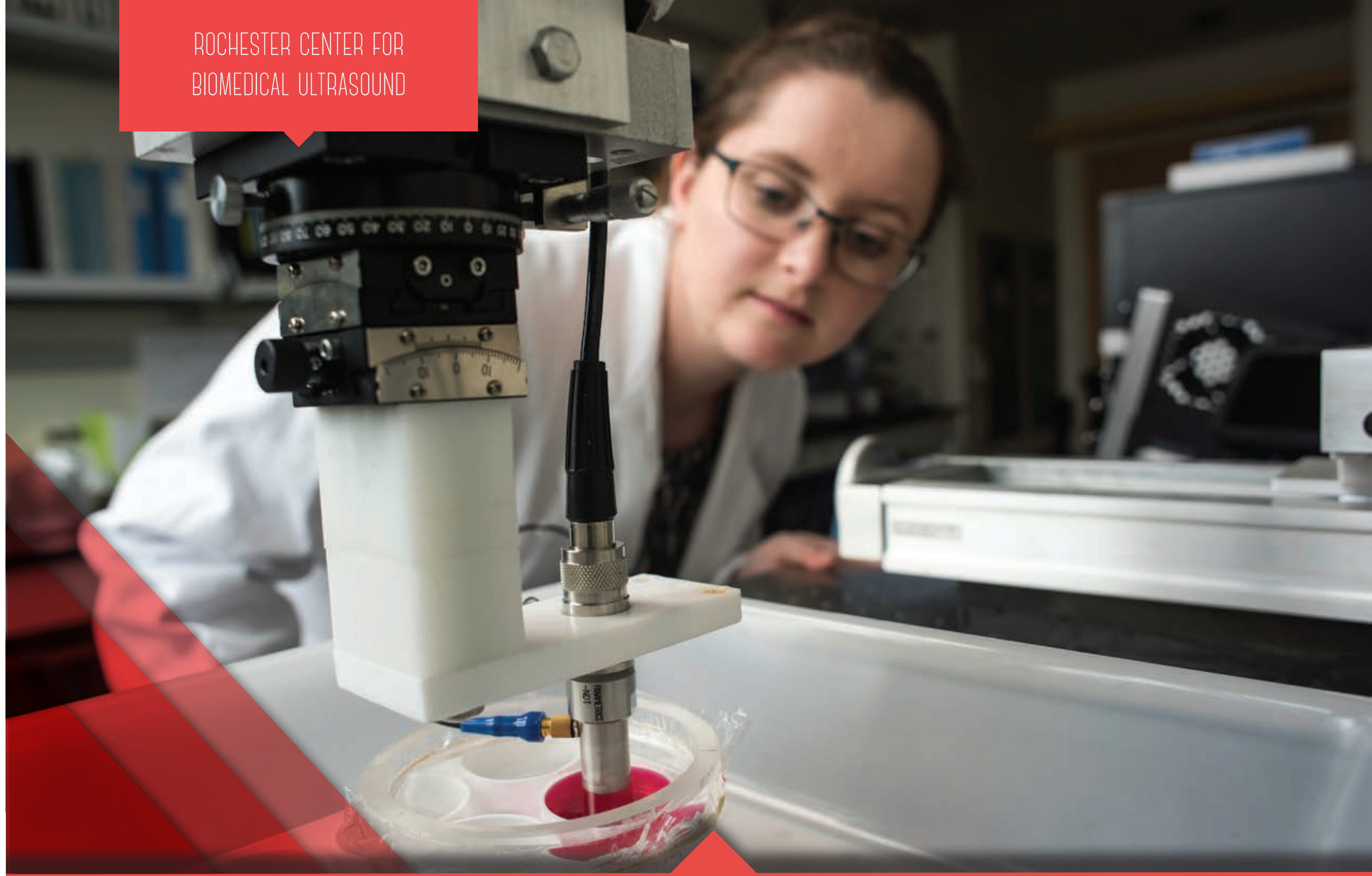
DEBORAH J. RUBENS, M.D.
Associate Director



Ultrasound continues to grow at the University of Rochester Medical Center; by the end of 2016 we were at 31,387 exams for the Imaging Sciences Department. Our clinical enterprise includes Strong West, and out-patient sites at University Imaging at Science Park, Penfield, and our newest outpatient imaging at East River Road. Our affiliate hospitals, Highland Hospital, F.F. Thompson in Canandaigua, Auburn Hospital, and Noyes Hospital in Dansville, are also running busy ultrasound programs, as is the Women's Breast Imaging at Red Creek and our associates at University Medical Imaging. All together these combined facilities perform 83,088 ultrasound examinations/year.

Locally, Dr. Rubens and Dr. Bhatt spoke at the Rochester Ultrasound Society, Rochester Institute of Technology. On the national level, Drs. Bhatt, Dogra, Rubens and Sidhu presented multiple lectures, workshops, posters and papers at the Society of Abdominal Radiology, the American Institute of Ultrasound in Medicine, the American Roentgen Ray Society, the Society of Radiologists in Ultrasound and the Radiologic Society of North America. Internationally, Dr. Rubens was an invited lecturer at University of Gothenburg; Gothenburg, Sweden, as well as the American Institute of Radiologic Pathology GI/GU course in Manchester, Great Britain. Dr. Dogra spoke in India, Italy, Copenhagen and was an International Visiting Professor on behalf of the Radiological Society of North America (RSNA) to Mexico.

Dr. Dogra continues investigation of photoacoustic imaging of the prostate and the thyroid. In the lab a real time thyroid photoacoustic imaging probe has been tailor designed with acoustic lens and implemented using 3D rapid prototyping techniques. Dr. Rubens continues her collaboration with Professor Kevin Parker and General Electric on liver elasticity and steatosis.



ABOUT THE RCBU

The Rochester Center for Biomedical Ultrasound (RCBU) was created at the University of Rochester to unite professionals in engineering, medical, and applied science communities at the University of Rochester, Rochester General Hospital, and the Rochester Institute of Technology. Since its founding in 1986, the RCBU has grown to nearly 100 members, with several visiting scientists from locations around the world. The Center provides a unique collaborative environment where researchers can join together to investigate the use of high frequency sound waves in medical diagnoses and therapy. The Center's mission encompasses **research**, **education**, and **innovation**.

RESEARCH

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

EDUCATION

RCBU laboratories provide a rich environment for graduate training in biomedical ultrasound. Students have access to state-of-the-art research facilities to engage in leading-edge research in ultrasound. The University of Rochester offers graduate level courses in biomedical ultrasound. RCBU laboratories provide opportunities for post-doctoral research in ultrasound and collaborations with other areas of biomedical engineering. The center offers short courses in specialized topics in ultrasound that attract national and international experts.

INNOVATION

The RCBU maintains a long history of leadership and innovation in biomedical ultrasound. RCBU members hold numerous patents in ultrasound and imaging that can be found on pages 23 and 24 of this report. The University of Rochester is a leader in technology revenue income among all higher education institutions in the nation. RCBU innovations have produced steady progress in new imaging modalities and therapeutic applications of ultrasound.

RESEARCH

Research laboratories of RCBU members are advancing the use of ultrasound for diagnosis and therapy. The following pages highlight recent research accomplishments. Selected publications and presentations can be found on pages 25-28.

Abdominal aortic aneurysm elasticity imaging

Michael S. Richards, PhD, Doran S. Mix, MD, Michael C. Stoner, MD

The laboratory of Professor Michael Richards is investigating the mechanics of abdominal aortic aneurysms and developing ultrasound elastography techniques to characterize abdominal aortic aneurysms. Clinical research is in collaboration with Dr. Michael Stoner and Dr. Doran Mix in the Division of Vascular Surgery. The team has collected ultrasound images from over 130 patients (with over 30 follow-up scans) suffering from abdominal aortic aneurysms. Preliminary findings suggest that the presence of high overall pressure normalized strain and high regional differences in pressure normalized strain are indicative of aneurysms with a high growth rate, and that lower pressure normalized strains are characteristic of larger aneurysms. The team's preliminary theory is that there is a multistage evolution of aneurysmal tissue in which, during the disease onset tissue initially gets softer which is followed by higher associated growth, but ultimately stiffens relative to healthy tissue when the aneurysms are large and are perhaps closer to rupture.

The Richards laboratory has also developed a novel algorithm for solving the elastic inverse problem using ultrasound measured displacement fields. This algorithm is adapted from the team's previous work using optimization methods to recover the shear modulus of the imaged tissue, using finite-element models and the measured displacements. This technique requires a soft prior regularization scheme to incorporate geometric segmentation information from the ultrasound images to improve the ill-posedness of the inverse-problem. Preliminary tests have validated the approach in simulation. Further tests in phantoms and with the clinical data are underway.

Ex-vivo human aortic samples have also been obtained from both "healthy" aortas and "aneurysmal" aortas to mechanically test tissue to compare to the team's clinical imaging study. They have successfully measured the dynamic mechanical modulus of abdominal aortic aneurysm tissue, at a physiologic prestress, and found that abdominal aortic aneurysms have increased stiffness. Histological analysis has also shown that abdominal aortic aneurysm tissue shows a marked loss of elastin in the vessel.

Acoustically-modified collagen for the treatment of chronic and hard-to-heal wounds

Emma Grygotis, MS, Diane Dalecki, PhD, Denise C. Hocking, PhD

As a major structural component of many tissues, type I collagen is a valuable building block for a variety of tissue engineering applications. However, techniques to control collagen structure site-specifically to mimic tissue-specific heterogeneity are currently limited. Ongoing studies in the laboratories of Denise Hocking and Diane Dalecki seek to add ultrasound as a valuable tool to control collagen structure and function in vitro.

These studies have demonstrated that solutions of 0.8 mg/mL type I rat tail collagen polymerized in the presence of an 8-MHz ultrasound standing wave field with a spatial peak temporal average intensity (ISPTA) of 10-30 W/cm^2 are characterized by changes in collagen fiber structure, including radial fiber alignment and the introduction of porous networks, compared to sham control conditions. Ultrasound-exposed collagen hydrogels supported collagen fiber reorganization and rapid cell migration when fibronectin-null mouse embryonic fibroblasts were seeded on the surface (Figure 1).

Given the application of collagen as a scaffold material for therapeutic wound dressings, the researchers hope to develop ultrasound as a tool to improve the migratory and proliferative capacity of collagen-based wound dressings. In preliminary studies, 6-mm skin biopsy punches taken from genetically diabetic mice were cultured ex vivo on the surface of collagen hydrogels, polymerized either in the presence of 20 W/cm^2 ultrasound or under sham conditions. The fibroblast-like cells that migrated out of skin explants remodeled the collagen fibrils of acoustically-modified gels to form three-dimensional tissue-like structures. In contrast, explant-derived cells adherent to sham-exposed gels formed two-dimensional cell monolayers. Future studies will pursue the development of an acoustically-modified collagen-based biomaterial to facilitate the closure of chronic and hard-to-heal wounds.

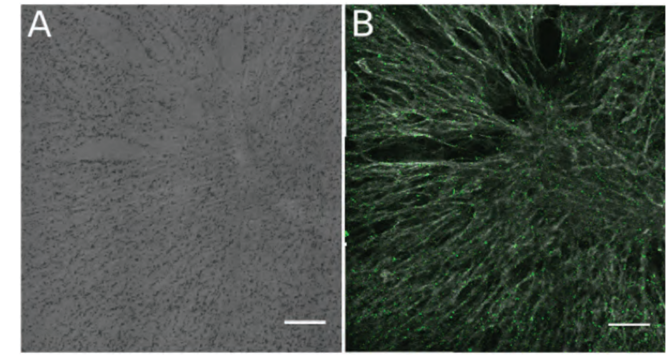


Figure 1. Collagen solutions were exposed to ultrasound (8 MHz, 20 W/cm^2) for 15 min during hydrogel formation. Myofibroblasts were seeded on the surface of polymerized gels and incubated for 24 h. Phase contrast microscopy images (A) and confocal second harmonic generation images (B) were collected. In (B), maximum intensity projections of the upper 250 µm of the gel were collected in 10-µm z-steps. Collagen, white; cells, green. Panoramic images were reconstructed using Photoshop. Scale bar, 500 µm.

Single tracking location viscosity estimation measurements in fibrotic liver phantoms

Stephen A. McAleavey, PhD, Jonathan Langdon, PhD

Tissues are viscoelastic and exhibit frequency-dependent shear wave velocity. This property is potentially diagnostic, but, because the frequency content of shear waves excited by different elastography systems varies, also represents a significant source of system dependent uncertainty and bias in ultrasonic quantitative shear wave imaging if a purely elastic model is assumed. The investigators hypothesize that an appropriate viscoelastic model can yield consistent material property estimates for a range of beam sequence parameters.

The single tracking location viscoelasticity estimation method (STL-VE) tracks tissue motion along a single scan line in response to two separately located ARFI push pulses. As seen in Figure 1, the measured shear waves in response to nearer (blue trace) and more distant (red trace) ARFI pulses differ in shape. This is due both to dispersive effects of the viscoelastic medium, as well as to geometric diffraction effects associated with the extended shear wave source provided by the ARFI beam. In the STL-VE approach, the shear wave from the first location is passed through a filter K, which parametrically models the effect of wave propagation through the additional distance Δx separating the two ARFI beams. Viscoelastic parameters are estimated by finding values which best transform trace 1 to trace 2

This approach was implemented using a Siemens Antares scanner, VF7-3 linear array, and off-line processing. Homogeneous viscoelastic phantoms similar to fibrotic liver were scanned at 4.21 MHz. Plane and cylindrical models were considered for ARFI source geometry, while elastic, Kelvin-Voigt (KV), and Kelvin-Voigt Fractional Derivative (KVFD) models were used for viscoelastic properties.

Investigators gratefully acknowledge the RSNA QIBA SWS Biomarker Committee for loan of viscoelastic phantoms used in this work.

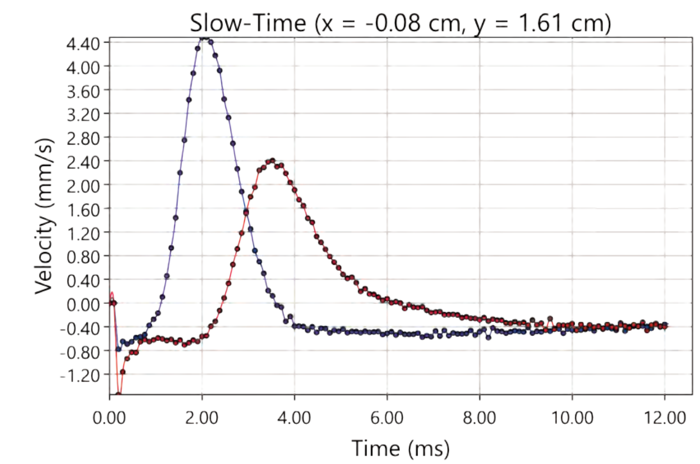


Figure 1. Shear wave traces obtained in rodent liver using STL shear wave elastography. The dispersion of the shear wave is evident, due to the viscoelastic nature of the liver.

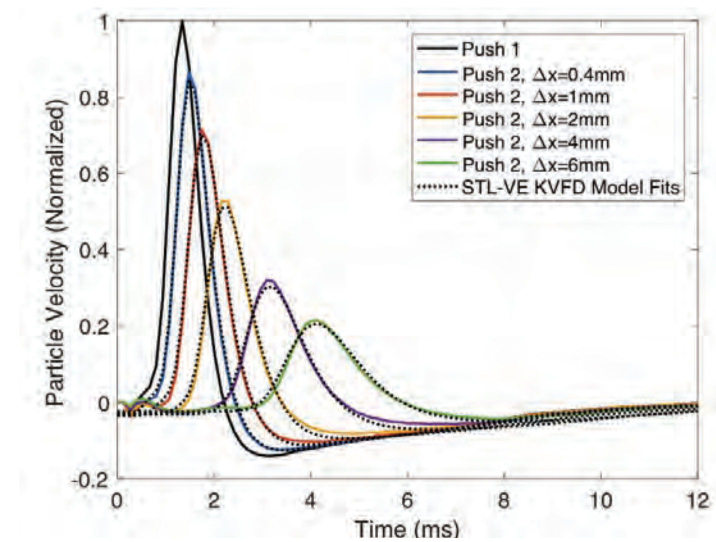


Figure 2. Shear wave traces measured with Siemens Antares system and VF7-3 linear array at 4.21 MHz obtained in a homogeneous viscoelastic phantom (CIRS). Dotted lines represent fit to KVFD model under a cylindrical-source assumption.

Scattering and reflection identification in H-scan images

Kevin J. Parker, PhD

Recent work from Professor Kevin Parker's laboratory has led to the development of a new imaging format, termed H-scan, for visualizing ultrasound backscatter images. Medical ultrasound imaging scanners typically display the envelope of the reflected signal on a log scale. The properties of this image and speckle patterns from collections of scatterers have a number of well-known disadvantages. One is the inability to differentiate between different scatterers that may have fundamentally different frequency-dependent scattering cross sections. The H-scan is based on a simplified framework for characterizing scattering behavior, and visualizing the results as color-coding of the B-scan image (Phys Med Biol L20-L28; 2016). The methodology matches a model of pulse-echo formation from typical situations to the mathematics of Gaussian weighted Hermite functions. Reflections are characterized by their similarity to nth order Hermite polynomials. The results of the technique show an ability to reveal some information otherwise hidden in the conventional envelope display, and can be generalized to more conventional bandlimited pulse functions. This new class of images is termed H-scan where 'H' stands for 'Hermite' or 'hue' to distinguish it from conventional B-scan format. An example of an H-scan is shown in Fig. 1.

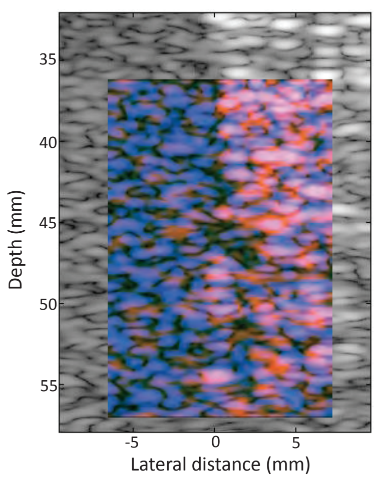


Figure 1. Example of H-scans. Scan of small versus large scatterers in a gelatin phantom. Grey scale shows conventional B-scan, and color insert shows scatterer H-scan.

Comparison of quantitative elastographic techniques for shear-wave speed measurements

Juvenal Ormachea, MS, Stephen A. McAleavey, PhD, Roberto J. Lavarello, PhD, Kevin J. Parker, PhD, Benjamin Castaneda, PhD

Elastography techniques provide tissue stiffness information to characterize the elastic properties of tissue. However, there is still limited literature comparing elastographic modalities for tissue characterization. Recent work from an international collaboration of RCBU investigators, focused on comparing shear wave speed estimations using two quantitative techniques that employ different vibration sources: crawling wave sonoelastography (CWS) and single tracking location shear wave elasticity imaging (STL-SWEI).

To understand each technique's performance, shear wave speed (SWS) was measured in three different homogeneous phantoms (10%, 13%, and 16% gelatin concentrations) and beef liver tissue ex vivo. Then, the contrast, contrast-to-noise ratio (CNR), and lateral resolution were measured in an inclusion and two-layer gelatin-based phantoms. The SWS values obtained with both modalities were validated with mechanical measurements (MM) which serve as reference. Finally, the Tukey-Kramer test was applied to show differences (or lack of differences) between the methods relative to each other.

The SWS results for the three different homogeneous phantoms (10%, 13%, and 16% gelatin concentrations) and beef liver tissue ex vivo showed good agreement between CWS, STL-SWEI, and MM as a function of frequency. For all gelatin phantoms, the maximum accuracy errors were 2.52% and 2.35% using CWS and STL-SWEI, respectively. For the ex vivo beef liver, the maximum accuracy errors were 9.40% and 7.93% using CWS and STL-SWEI, respectively. The Tukey-Kramer test showed that each modality is able to differentiate between the elastic properties of different materials, the SWS results for each phantom were significantly different ($p<0.05$) (10% vs. 13% vs. 16%).

Additionally, the test showed that the SWS measurements, obtained with each modality, were not significantly different for the same phantom type and the ex vivo liver tissue. For lateral resolution, contrast, and CNR, both techniques obtained comparable measurements for vibration frequencies less than 300 Hz (CWS) and distances of the pushing locations between 3 mm and 5.31 mm (STL-SWEI). The results obtained in this study agreed over a SWS range of 1-6 m/s. They are expected to agree in perfectly linear, homogeneous, and isotropic materials, but the overlap is not guaranteed in all materials because each of the three methods (CWS, STL-SWEI, and MM) have unique features.

It was found that CWS and STL-SWEI give comparable lateral resolution, contrast and CNR. Finally, the results of this study contribute to the limited data currently available for comparing elastographic techniques, especially techniques that use different types of force to generate shear waves inside the material.

Soft tissue vascularity and shear wave speed

Kevin J. Parker, PhD, Juvenal Ormachea, MS

The microchannel flow model (MFM) explicitly accounts for the effect of vascular and fluid channels on the stress-strain behavior of soft tissues. In recent work from the Parker laboratory, the validity of the MFM was assessed by its ability to predict changes in stress-strain behavior due to swelling or vasoconstrictors. The overall goal of the work was to assess the effects of changes in vascularity on the biomechanical response of soft tissues, using experimental and theoretical approaches. Experimental tests of the MFM were made on liver samples where changes in salinity (and therefore cellular swelling, which restricts small channels) were found to change the stress-relaxation curves. Cylindrical cores (~ 25 mm in diameter and 60 mm in length) were acquired from fresh bovine livers using a custom coring tool, and stored at 4ºC for 24 hours in either hypotonic (0.65%) saline, normal (0.9%) saline, or hypertonic (1.15% saline). The osmotic pressure difference can cause swelling or shrinking. In addition, the effect of a vasoconstrictor on living, perfused placentae were measured. The results showed that the four parameter MFM model provided a prediction of change in shear wave speed and dispersion. For the liver, the elastic parameter A has a distinct trend as its value changed as a result of hypotonic swelling (highest, 4.1 kPa) vs. hypertonic swelling (lowest, 1.4 kPa). The power law parameter was in the range of 0.11 – 0.14 for all samples. Similar results were obtained in other soft tissues. For placenta, the dispersion power law parameter increased from 1.4 to 1.6, and the stiffness increased following the administration of a vasoconstrictor. In summary, the MFM predicts a number of ways in which normal soft tissue such as liver can be modified so as to be perceived as less compliant, or hardened. First, an increase in E may be achieved by soaking specimens in formalin, which is known to harden and preserve samples. A second way to harden a sample is by increasing the viscosity of the fluids in the microchannels. Finally, and even less obvious, is hardening caused by constriction of the smallest microchannels. This has a double effect in modifying the relaxation spectrum, and shifting it to the right (longer time constants) according to the theory of the MFM. The net result is a modification that makes the specimen feel more resistant or harder, over long time periods. This was experimentally approximated in liver and placenta; however, in vivo, this could be the net effect of inflammatory responses or edema. This could explain why inflamed regions of skin feel harder than the surrounding normal tissue.

Elastography of porcine cornea by tracking propagation of surface acoustic waves using optical coherence elastography

Fernando Zvietcovich, MS, Jianing Yao, MS, Manuel Ramirez, MS, Mark Buckley, PhD, Jannick Rolland, PhD, Kevin J. Parker, PhD

Measuring the biomechanical properties of the cornea, such as shear modulus, is fundamental to understanding, diagnosing, and monitoring degenerative ocular diseases.

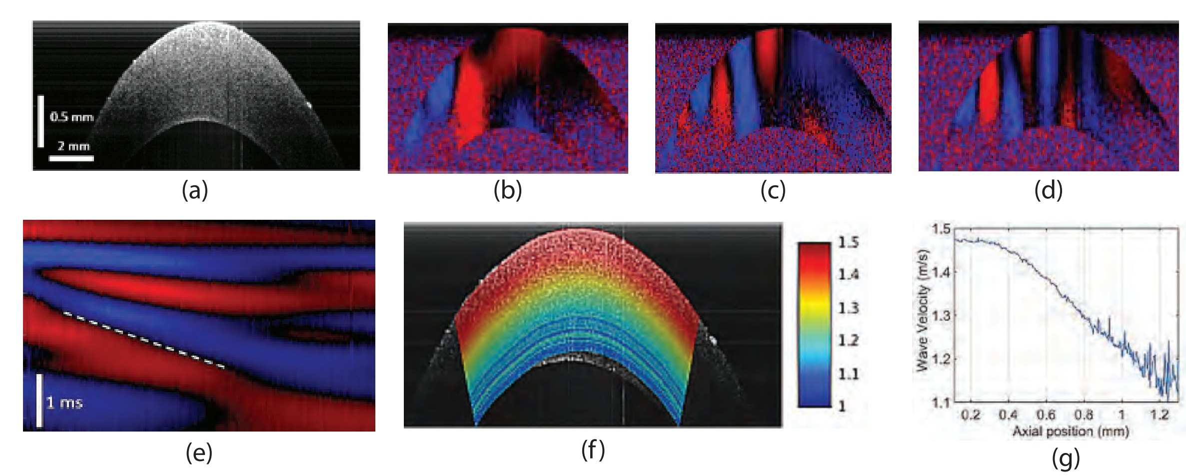


Figure 1. (a) B-mode structural image of a porcine cornea (b-d) Motion 2D snapshots of SAW propagation at various instants (needle located on the left side). (e) Space-time map of SAW propagation. (f) 2D SAW speed map depicting differentiated layers. (g) Depth-resolved SAW speed profile depicting a decreasing tendency.

Current clinically-available elastographic techniques for the cornea suffer from inaccuracy and low depth-resolved resolution. Optical coherence tomography (OCT) has being applied successfully to study of the cornea structure due to its micro-scale resolution and its depth of penetration in millimeters. The application of OCT in elastography can be used to calculate the speed of surface acoustic waves (SAW) in the cornea since it is related to the local shear modulus.

Recent work from a team of RCBU investigators estimated the depth-resolved shear modulus of the cornea in order to identify different elastic layers by tracking the propagation of SAW. A fresh porcine cornea (Fig. 1a) was excited with a rod connected to a piezoelectric actuator in order to produce a tone-burst at 1 kHz propagating from left to right (Fig. 1b-d). Wave propagation was detected using a phase-sensitive OCT system implemented with a swept source laser (HSL-2100-WR, Santec, AicShi, Japan) with a center wavelength of 1318 nm. The tone was sent every 35 ms in order to acquire motion frames at a frame rate of 20 kHz. The region of measurement in the sample consisted of a rectangle 2.5 mm high x 15 mm wide. After the acquisition process was conducted, motion frames were acquired and stored as a video. Subsequently, space-time maps (Fig. 1e) were calculated for each propagation path. Herein, the slope of the main peak trajectory of the tone-burst represents the inverse of the SAW speed, which is related to the elasticity of the sample.

Experiments with porcine cornea revealed differentiated layers as shown in the 2D SAW speed map (Fig. 1 f). Moreover, the investigators found a decreasing tendency with a local maximum close to the cornea surface when a vertical depth-resolved speed profile was analyzed (Fig. 1g). The SAW speed values ranged from 1.10 m/s to 1.47 m/s, which produced shear moduli of 1.34 kPa and 2.39 kPa, respectively. In conclusion, SAW speed can be successfully measured for the identification of differentiated layers in ex vivo cornea using OCT. Further research related to the SAW dispersion is required for the estimation of viscoelastic parameters.

Ultrasound-mediated cell patterning for the development of engineered microvessel networks

Eric Comeau, MS, Denise C. Hocking, PhD, Diane Dalecki, PhD

The goal of tissue engineering is to repair or replace diseased and damaged tissues. Current successes in the field include engineered skin, cartilage, and bladder wall, all of which are naturally thin or avascular. The fabrication of larger, viable, and three-dimensional (3D) tissues has proven to be more difficult because perfused blood vessel networks must be present to supply the entire tissue volume with sufficient oxygen and nutrients. The laboratories of Professor Diane Dalecki and Professor Denise Hocking have developed an ultrasound-based technology to stimulate rapid blood vessel network formation throughout 3D hydrogel scaffolds. The technology utilizes acoustic radiation forces associated with ultrasound standing wave fields (USWFs) to volumetrically pattern endothelial cells into planar bands within 3D collagen hydrogels. In response to USWF-patterning, endothelial cells form lumen-containing, microvessel networks throughout the volume of the hydrogel.

The ability to control the morphological characteristics of blood vessel networks will permit the recreation of complex and tissue-specific vascular architectures. USWF frequency and pressure amplitude provide control over initial spacing and cell density of planar bands, respectively. Importantly, the team found that USWF-controlled variations in initial endothelial cell patterning directly influenced microvessel diameter, alignment, extent of branching, and vessel density. Using USWF-patterning technology, different microvessel morphologies were recreated including capillary-like networks, large-caliber branching vessels, and large-caliber non-branching vessels. The capability to rapidly produce 3D endothelial vessel networks of known morphology is a valuable tool for tissue engineering.

In the body, the formation and function of blood vessels is supported by mural cells, including smooth muscle cells and pericytes, which wrap around the outer surface of vessels. Thus, studies were conducted to determine whether endothelial cells could be co-patterned with smooth muscle cells using USWFs, and if so, whether the addition of smooth muscle cells altered microvessel network morphology. Results indicate that USWF-patterning significantly increases cell viability versus sham-exposure. Microvessel networks underwent extensive sprouting in the presence of smooth muscle cells compared to networks formed with endothelial cells alone. Furthermore, smooth muscle cells localized to the outer surface of resultant microvessels, mimicking the morphological arrangement of smooth muscle cells and endothelial cells in vivo.

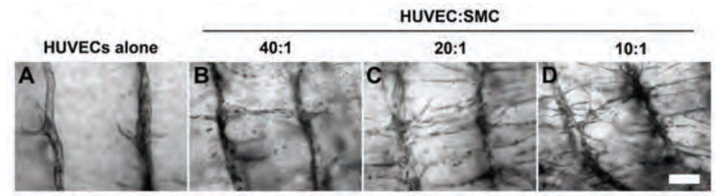


Figure 1: This figure contains four images of MTT-stained vessel networks formed by USWF-exposed HUVECs and SMCs cultured for 10 days. All samples were exposed to 1 MHz, 0.2 MPa USWFs. A) HUVECs alone, B) 40:1 HUVEC:SMC, C) 20:1 HUVEC:SMC, D) 10:1 HUVEC:SMC. Scale bar: 250 μm.

Resolution enhancement of B-mode ultrasound imaging with stabilized inverse filters

Shujie Chen, MS, Kevin J. Parker, PhD

Many pulse-echo imaging systems' lateral resolution is improved by focusing, where the beam width is determined by the choice of source and apodization function, the frequency, and the physics of focusing. Based on the convolution model and Z-transform analysis, inverse filtering can be performed to the RF data to further enhance the resolution. However, this is limited by the need for conditioning due to the instabilities of the inverse filters. In recent work from the laboratory of Professor Kevin Parker, an analysis was developed that defined key constraints on the shape and sampling of lateral beam patterns. Within these constraints are useful symmetric beam patterns which, when properly sampled, can have a stable inverse filter. Specifically, for the approximately Gaussian-apodized broadband focal beam patterns, stable inverse filters are pre-designed with parameterization and applied to the beamformed RF scan lines. The proposed method was applied to B-mode ultrasound images either simulated in Field II or imaged by a Verasonics scanner with an ATL L7-4 transducer operating at 5 MHz. Simulation using Field II showed higher resolution for scatterers, anechoic cysts, hyperechoic lesions, and blood vessels at 50 mm depth. Specifically, scatterers 1.1 mm apart were resolved, and a 3-mm blood vessel was opened from barely visible to ~2.1 mm. Furthermore, imaging of an ATS 535 QA phantom with focus at 50 mm showed that the -20 dB width of a line target was decreased to 1.19 mm from 2.26 mm, and a small 4 mm cyst was opened from 1.4 mm to 3.0 mm. In vivo imaging of the human carotid artery demonstrated the opening of the arterial lumen and a better-defined arterial wall. In summary, an inverse filtering approach has been designed in the context of the convolution model and the Z-transform. A framework for analysis and processing was developed for the enhanced lateral resolution that can be realized. This framework can also be applied to improve axial resolution, where the concept of stabilized inverse filters guides the selection of the pulse shape.

Kevin Parker, (left) the William F. May Professor of Engineering and Miguel Alonso, professor of optics, (right) illustrate the "analytically beautiful mathematical solution" Alonso devised for the new beam pattern they describe in a recent paper. The new beam pattern devised by University of Rochester researchers causes a light or sound wave to collapse inward, forming—during a mere nanosecond or less—an incredibly thin, intense beam before the wave expands outward again. It could bring unprecedented sharpness to ultrasound and radar images, burn precise holes in manufactured materials at a nano scale—even etch new properties onto their surfaces. (University photo / J. Adam Fenster)

Shear wave elastography of the postpartum perfused human placenta

Stephen McAleavey, PhD, Kevin J. Parker, PhD, Juvenal Ormachea, MS, Ronald W. Wood, PhD, CJ Stodgell, PJ Katzman, Eva K. Pressman, MD, Richard K. Miller, Ph.D.

Despite widespread use of ultrasound imaging and Doppler in obstetrics and gynecology and recent growth of elastographic technologies, little is known about the biomechanical (elastic shear wave) properties of placenta and the range of normal and pathologic parameters that are present. Recent work from a team of RCBU investigators provided initial estimates of placenta stiffness under a range of experimental conditions. Human placentae from healthy, uncomplicated, term pregnancies were obtained immediately following caesarean section delivery, placed in a plastic container, and transported to the perfusion laboratory within 20 minutes. The study used a well-developed protocol for perfusing whole placentas, post-delivery, to maintain tissue integrity and function for hours. In this model, the placenta is living, whole, and maintained within normal physiological parameters such as flow, arterial pressure, and oxygen, throughout examination by ultrasound, and shear wave elastography. Additionally, a titration procedure was applied to evaluate the placenta response to vasoactive agents. Placentae were placed on an acoustically-absorbing pad, immersed in a buffered saline bath at 37°C, and scanned during perfusion. Single tracking location shear wave elasticity imaging (STL-SWEI), an acoustic radiation force based-technique, was applied to measure shear wave speed in placental tissue. Shear wave speed measurements from the fetal side of the perfused tissue were obtained from a typical 1x1cm^2 ROI within the placenta. Shear wave speed data had a mean of 1.92 m/s with a standard error of ± 0.05 m/s and were generally in the range of 1.5-2.5 m/s for normal placental tissue (baseline). An analysis of the measured data using the Tukey-Kramer test showed that the baseline groups were significantly different ($p < 0.05$) from the measurements following vasoconstrictor and vasodilator injections in the placental tissue. In conclusion, these preliminary results indicated that normal placental tissue on the fetal side have shear wave speed in a defined range around 2 m/s, comparable to the tissue elasticity found in animal livers. Shear wave speeds in the placenta were measurably increased by abnormalities, including infarcts and artificial "clots" introduced by perfusing viscous gelatin solutions into the vasculature. Elastography of human placentas will provide a useful clinical tool for discriminating normal versus abnormal regions. Future work includes a determination of the range of normal placental shear wave speed versus gestational age.

Evaluating anisotropy of the carotid artery using principal strain vascular elastography

Rohit Nayak, PhD, Giovanni Schifitto, PhD, Marvin M. Doyley, PhD

The carotid artery (CA) exhibits transversely isotropic mechanical behavior; however, most vascular elastography techniques assume vessels are isotropic. Such an assumption can degrade diagnostic performance, and accuracy of the modulus and stress recovery process. In a recent study from the laboratory of Professor Marvin Doyley, the team assessed the feasibility of estimating fractional anisotropy (FA), a metric for assessing anisotropy within vascular tissues, using principal. The team performed simulations with isotropic and transversely isotropic vessel models, and a pilot study with 10 healthy volunteers to demonstrate its efficacy in identifying isotropic and anisotropic components in vessels.

The study employed two finite element (FE) vessel models with identical geometry (Fig 1.a), having inner and outer radii of 1.5 and 6 mm, respectively, but different mechanical behavior (isotropic vs. transversely isotropic). The arterial wall, lipid-core, and fibrous cap of the isotropic vessel model were assigned a stiffness of 45 kPa, 1 kPa, and 700 kPa, respectively, and a Poisson's ratio of 0.495. The transversely isotropic vessel model was assigned an arterial wall and fibrous cap stiffness of 45 kPa, and 700 kPa, respectively, Poisson's ratio of 0.01 along radial direction, and 450 kPa and 7000 kPa, respectively and Poisson's ratio of 0.27 in the circumferential directions. The plaque was modeled as an isotropic material with Young's modulus of 1 kPa and Poisson's ratio of 0.495. The compounded plane wave ultrasound images were synthesized for 15 transmissions (-14° to 14°, in increments of 2°) using Field II. The simulated ultrasound system was equipped with a 128-element linear transducer array operating at a center frequency of 5 MHz. Gaussian noise of 20 dB was added to the simulated RF channel to mimic transducer noise. The team conducted an in vivo study with 10 healthy volunteers between ages 50-60 years, to evaluate the FA maps acquired with a clinical prototype system. The in vivo echo imaging was performed using a commercial ultrasound scanner (Ultrasonix RP, Analogic Corp., MA, USA) that was equipped with a 5 MHz, 128-element transducer array and a parallel data acquisition system (Sonix DAQ, Analogic Corp., MA, USA). Beamforming was performed off-line using the delay-and-sum technique. Displacement elastograms were computed by applying a 2D cross-correlation-based echo-tracking technique to the echo frames. FA was estimated using the principal strains estimated from Eigen decomposition of the 2D strain tensor. Root mean square error (RMSE) between the simulated and the FE estimates were computed to evaluate the accuracy of the FA maps.

Fig. 1 (b, c) shows FA maps obtained from simulated vessels. FA varied between 0 (isotropic) and 1 (completely anisotropic). Fig. 1 (b) shows the FA map for the isotropic model; FA in the vessel wall and the lipid pool were similar (~0.33). Fig. 1 (c) shows the corresponding FA map for the transversely isotropic vessel with an isotropic plaque, showing low FA in the isotropic lipid pool (~0.35) and high FA (>0.8) in the vessel wall. Isotropic and anisotropic vessel components were discernable in FA maps. Further, there was good agreement between FE-derived FA maps and those estimated from noisy principal strains, with RMSE error < 10%. Figure 1 (d,f) & (e,g) show B-mode and the corresponding FA elastograms associated with two healthy volunteers, respectively. The mean FA of the patient elastograms were > 0.6 which corroborates that the CA shows transversely isotropic mechanical behavior. More specifically, localized areas of low FA values were apparent in the anisotropic maps. This study shows that besides providing coordinate independent strain estimates, principal strain elastography can be used to assess the degree of anisotropy within vascular vessels.

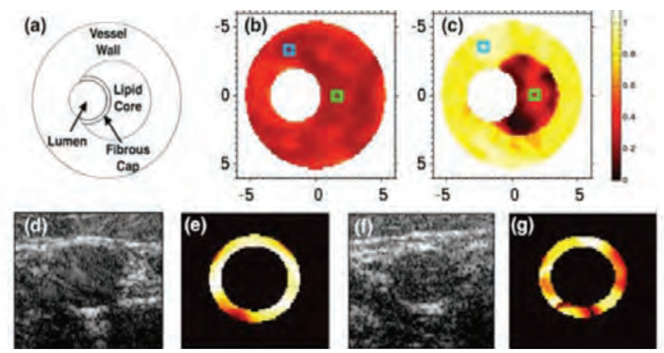


Figure 1. Panels a-c show the geometry and the estimated FA of the simulated vessels. Panels d-g show the B-mode and FA maps of the two healthy volunteers, respectively.

Biological effects of low frequency strain

Edwin L Carstensen, PhD, Kevin J. Parker, PhD, Diane Dalecki, PhD, Denise C. Hocking, PhD

In the later part of his career, Professor Edwin L. Carstensen dedicated his research efforts towards understanding shear wave propagation in tissue. The final paper published by Professor Carstensen (Ultrasound Med Biol 42:1-15, 2016) focused on biological effects of low frequency strain and physical descriptors. This paper investigated, specifically, strains that are produced in tissues from sound and vibration sources. Biological effects of sound and vibration are related directly to what those acoustic exposures do physically to the tissue. Instead of simple compressional strains produced by diagnostic ultrasound, realistic sources of low-frequency vibration produce both fast (1,500 m/s) and slow (1-10 m/s) waves, each of which may have longitudinal and transverse shear components. The paper presents strains produced by longitudinally and transversely oscillating planes, vibrating bubbles, acoustic dipoles, and the case of a sphere moving in translation, i.e., the simplest model of fields produced by realistic sources.

Contrast-enhanced quantitative intravascular elastography: impact of microvasculature on model-based elastography

Stephen J. Huntzicker PhD, Himanshu Shekhar, PhD, Marvin M. Doyley, PhD

Model-based intravascular ultrasound elastography visualizes the stress distribution within vascular tissue-information that clinicians could use to predict the propensity of atherosclerotic plaque rupture. However, there are concerns that clusters of microvessels may reduce the accuracy of the estimated stress distribution. Consequently, a team of investigators from the Doyley lab has developed a contrast-enhanced intravascular ultrasound system to investigate how plaque microvasculature affects the performance of model-based elastography. In simulations, diameters of 200, 400 and 800 µm were used, where the latter diameter represented a cluster of microvessels. In phantoms, the team used a microvessel with a diameter of 750 µm. Peak stress errors of 3% and 38% were incurred in the fibrous cap when stress recovery was performed with and without a priori information about microvessel geometry (UMB 42:1167-1181; 2016). The results indicate that incorporating geometric information about plaque microvasculature obtained with contrast-enhanced ultrasound imaging improves the accuracy of estimates of the stress distribution within the fibrous cap precisely.

Visualizing principal strains of the carotid artery using plane wave imaging

Rohit Nayak, PhD, Prashant Verma, MS, Nancy Carson, Vikram Dogra, MD, Singh Meera, PhD, Maggirwar Sanjay, PhD, Giovanni Schifitto, MD, Marvin M. Doyley, PhD

The simulation study was conducted using heterogeneous finite element vessel models. The in vivo study was conducted on 10 healthy volunteers. All echo imaging was performed by an experienced sonographer using a commercial ultrasound scanner (Ultrasonix RP, Canada) that was equipped with a 5 MHz, 128 element transducer array and a parallel data acquisition system (Ultrasonix DAQ, Canada). The principal strains were estimated by computing the eigenvalues of the full 2D strain tensor. The elastographic contrast-to-noise ratio (CNRe), and root mean square error (RMSE) were computed to evaluate the quality and accuracy of the principal strain elastograms. Principal strain elastograms revealed elevated shear strain at the plaque shoulder – a rupture prone region of the fibrous cap. All elastograms had an CNRe > 25 dB and RMSE < 15%. The principal strain elastogram of the healthy volunteers displayed a radially symmetric strain distribution that was consistent with theory. The results from this preliminary study suggest that principal strain imaging is viable for non-invasive vascular elastography, and compounded plane wave imaging can produce clinically useful principal strain elastograms.

Tendon elasticity imaging

Michael S. Richards, PhD, Mark Buckley, PhD

The laboratories of Professor Michael Richards and Professor Mark Buckley have an ongoing collaboration focused on improving our understanding of the mechanical properties of tendon tissues and the changes associated with diseases such as tendinopathy. The team has found that pathologic tendons experience lower compression due to biomechanical stiffening induced within the tendon, and that it may be transferred compression in the surrounding tissues which causes pain during dorsiflexion. Their work has been extended to study the compression/tension in patellar tendon in children suffering from Apophysitis (Osgood-Schlatter disease). In addition, preliminary work is underway to use elastography techniques to measure the functional mobility of flexor tendons of the hands following injury. This work is focused on measuring tendon excursion and strain in mice tendons using a Visualsonics.

A comparative study of shear wave speed estimation techniques in optical coherence elastography applications

Fernando Zvietcovich, MS, Jianing Yao, MS, Jannick P. Rolland, PhD, Kevin J. Parker, PhD

Optical Coherence Elastography (OCE) is a widely investigated noninvasive technique for estimating the mechanical properties of tissue. In particular, vibrational OCE methods aim to estimate the shear wave velocity generated by an external stimulus in order to calculate the elastic modulus of tissue. Recent work from RCBU investigators, compared the performance of five acquisition and processing techniques for estimating the shear wave speed in simulations and experiments using tissue-mimicking phantoms. Accuracy, contrast-to-noise ratio, and resolution were measured for all cases. The first two techniques make the use of one piezoelectric actuator for generating a continuous shear wave propagation (SWP) and a tone-burst propagation (TBP) of 400 Hz over the gelatin phantom. The other techniques make use of one additional actuator located on the opposite side of the region of interest in order to create an interference pattern. When both actuators have the same frequency, a standing wave (SW) pattern is generated. Otherwise, when there is a frequency difference, df, between both actuators, a crawling wave (CrW) pattern is generated and propagates with less speed than a shear wave, which makes it suitable for being detected by the 2D cross-sectional OCE imaging. If df is not small compared to the operational frequency, the CrW travels faster and a sampled version of it (SCrW) is acquired by the system. Preliminary results suggest that TBP (error < 4.1%) and SWP (error < 6%) techniques are more accurate when compared to mechanical measurement test results.

Investigating strategies for improving plane wave vascular elastography

Prashant Verma, MS, Marvin M. Doyley, PhD

Plane-wave (PW) imaging achieves narrow lateral beam width using boxcar apodization but at the expense of high side-lobes, which degrade the performance of vascular elastography. The goal of a recent study from the Doyley laboratory was to investigate various imaging techniques for improving the performance of PW imaging. More specifically, the investigators evaluated the quality of elastograms produced with: (1) fixed apodization beamforming (FAB) using modified hyperbolic sine (sinh) functions; and (2) minimum variance beamforming (MVB). The profile of sinh functions can be easily manipulated using single parameter (β) and for the case β=1, this function closely resembles spheroidal wave functions that have been shown to produce lowest side-lobes. For MVB, the team performed subarray averaging to obtain well-conditioned covariance matrix for inversion. Simulated plaques were discernible in all elastograms, but MVB elastograms were marginally better than those produced with FAB. Specifically, sinh (β=1.5) and MVB (L=56) produced elastograms with elastographic contrast-to-noise ratios of 2.35 dB and 3.07 dB, respectively.

Obstetrics & Gynecology Ultrasound Unit

Dzhamala Gilmandyar, MD

The UR OB/GYN Ultrasound Unit provides clinical services at multiple sites including Strong Memorial Hospital, Highland Hospital, and FF Thompson Hospital. The physicians of the UR OB/GYN Ultrasound Unit also provide ultrasound interpretation services at Rochester General Hospital, Newark Wayne Hospital (NWH), FF Thompson Hospital and Nicholas Noyes Hospital utilizing a combination of telemedicine and onsite services.

The total number of examinations in 2016 from SMH sites (HH, SMH, FFT, Noyes) included 19,673 abdominal and 3798 vaginal obstetric scans, and 4926 abdominal and 4128 vaginal gynecologic scans. Invasive procedures performed included 116 amniocentesis for karyotype or lung maturity, 57 chorionic villus samplings, 134 sonohysterograms, 268 OR guidance for minor gynecologic procedures, and 28 invasive pregnancy procedures including intrauterine shunt insertions, transfusions, pleurocenteses and other fetal procedures. Additionally, 5251 obstetric and 1948 gynecologic scans were completed at RGH/NWH.

The unit has 19 ultrasound machines within SMH and HH hospitals, all with 3D and 4D capability, plus additional portable scanners. There are 21 sonographers at HH and SMH, 13 of whom are CLEAR certified, and 9 of whom are fetal echocardiography certified. SMH remains an active member of NAFNET (North American Fetal Therapy Network).

Assessing weight gain by the 2009 Institute of Medicine Guidelines and perinatal outcomes of twin pregnancy

Tulin Ozcan, MD, Stephen J Bacak, DO, MPH, Paula Zozzaro-Smith, DO, Dongmei Li, PhD, Seyhan Sagcan, MD, Neil Seligman, MD, Christopher J Glantz, MD, MPH

The objective of this study was to estimate the impact of maternal weight gain outside the 2009 Institute of Medicine recommendations on perinatal outcomes in twin pregnancies. Twin pregnancies with two live births between January 1, 2004 and December 31, 2014 delivered after 23 weeks Finger Lakes Region Perinatal Data System (FLRPDS) and Central New York Region Perinatal Data System were included. Women were classified into three groups using pre-pregnancy body mass index (BMI). Perinatal outcomes in women with low or excessive weekly maternal weight gain were assessed using normal weekly weight gain as the referent in each BMI group.

Low weight gain increased the risk of preterm delivery, birth weight less than the 10th percentile for one or both twins and decreased risk of macrosomia across all BMI groups. There was a decreased risk of hypertensive disorders in women with normal pre-pregnancy weight and an increased risk of gestational diabetes with low weight gain in obese women. Excessive weight gain increased the risk of hypertensive disorders and macrosomia across all BMI groups and decreased the risk of birth weight less than 10th percentile one twin in normal pre-pregnancy BMI group.

Among twin pregnancies, low weight gain is associated with low birth weight and preterm delivery in all BMI groups and increased risk of gestational diabetes in obese women. This study did not reveal any benefit from excessive weekly weight gain with potential harm of an increase in risk of hypertensive disorders of pregnancy. Normal weight gain per 2009 IOM guidelines should be encouraged to improve pregnancy outcome in all pre-pregnancy BMI groups.

Education

BME Senior Design Teams Focused on Ultrasound Projects

BME seniors gain real-world experience with solving biomedical engineering problems through the two-semester Senior Design course taught by RCBU member Professor Amy Lerner and Professor Scott Seidman. In the 2016-2017 academic year, one team of seniors is working on a project to develop a phantom for photoacoustic imaging that mimics the optical and acoustical properties of tissue. The students on this "OPTI Phanton Team" are Zachary Sia, Nick Vohra, Vincent Ching-Roa and Amanda Smith. The supervisors for this team are Navalgund Rao and Vikram Dogra. In the 2015-2016 academic year, one team of seniors embarked on a project to develop techniques to monitor sonographer position and posture during typical ultrasound imaging procedures. The "Ultranomics" team consisted of BME students Mary Bucklin, Gregory Palis, Megan Routzong, and Yanwen Zhai, and the supervisor for this project was Diane Dalecki.

Maria Helguera Teaches in Mexico and Peru

Maria Helguera left her primary faculty appointment at the Rochester Institute of Technology looking for opportunities to work and teach in other parts of the world. In fall of 2016, she headed to Lagos de Moreno, Jalisco, Mexico where she joined the Instituto Tecnológico Mario Molina in Lagos de Moreno, Jalisco, Mexico. Lagos is a quaint small city where her family originates. The institute is making an effort to create a research group and one of Maria's first tasks has been to identify projects and faculty. The first project that they are launching strives to reduce waste in the cheese industry. They will use whey as a liquid ingredient in baked products, which may not be a novelty by itself, however, they are designing a microfluidic system to apply a thin cover that will minimize the waste of material and enhance the freshness of flavor. Dough and cover will be characterized via image processing. In the fall semester, she taught Calculus I to engineering freshmen. In her free time, she is establishing a community center where they are planning to introduce a wide range of activities, from drip irrigation to electronics, to help families to supplement their income. In spring 2017, Maria headed to Perú for 4 months to join the Pontificia Universidad Católica de Perú. There she is teaching a course on medical imaging systems for biomedical engineering students and a project-based course for electrical engineering juniors. She will also continue ongoing research collaborations with RCBU member Benjamín Castaneda and his lab on a project to design and implement an automated system for the detection and diagnosis of TB in sputum samples.

Summer Acoustics Course

David Blackstock again offered his popular summer acoustic course at the UR for students with wide-ranging interests in acoustics and biomedical ultrasound. Dr. Blackstock, from the University of Texas at Austin, is a long-standing RCBU member. He is an expert in acoustics and author of leading textbooks in physical acoustics and nonlinear acoustics. For over 20 years, this course has provided a unique opportunity for RCBU students to learn from one of the world's leading experts in acoustics.

TRAINING COMPLETED

Jonathan Langdon completed his MD/PhD training at the University of Rochester. Jonathan will proceed to a preliminary year at Hofstra University, followed by a residency in Radiology at Yale University. Jonathan completed the PhD portion of his training in biomedical engineering under the mentorship of Professor Stephen McAleavey. The title of his thesis was "Development of Single Track Location Shear Wave Viscoelasticity Imaging for Real-Time Characaterization of Biological Tissues."

Hexuan (April) Wang received her M.S. in Electrical and Computer Engineering from the University of Rochester. Her thesis, titled "Visualizing Total Tissue Stress in Pancreatic Cancer Microenvironment," was supervised by Professor Marvin Doyley.

Alexander Bensch received his M.S. in Computer Engineering from the Rochester Institute of Technology (RIT). His thesis is titled, "Toward Real-time Video-Enhanced Augmented Reality for Medical Visualization and Simulation." This work describes the implementation and evaluation of a video-based augmented reality visualization approach that enables the viewer to "see" underlying, internal anatomy information by means of superimposing computer graphics models of the internal anatomy extracted from medical images onto the real-time video view of the organ acquired using a laparoscopic camera. The work presents both a camera-only augmented reality environment designed as an inexpensive and versatile solution for simulation and training, as well as a more accurate implementation that employs high performance, clinical-grade surgical tracking systems developed by Northern Digital Inc. His research was supervised by Professor Cristian Linte.

Aditya Daryanani received his M.S. in Computer Engineering from the Rochester Institute of Technology. His thesis is titled, "Left Ventricle Myocardium Segmentation from 3D Cardiac MR Images using Combined Probabilistic Atlas and Graph Cut-based Approaches." This work describes the development and validation of a novel, robust and efficient technique for segmenting the left ventricle anatomy from 3D and 4D magnetic resonance images using hybrid atlas and graph cut-based approach. The proposed method combines the benefits of atlas-based training with the accuracy and computational efficiency of graph cut segmentation, enabling fast and reliable extraction of anatomical features and construction of anatomical models for enhanced computer-assisted diagnosis, surgical planning, visualization an computer-assisted interventions and therapy. His research was supervised by Professor Cristian Linte.

STUDENT AWARDS

Rohit Nayak received the First Place Award for the poster titled "Visualizing principal strains of carotid artery using plane wave imaging", presented at the University of Rochester Center for Integrated Research Computing (CIRC) Poster Session. Rohit is doctoral candidate in Electrical and Computer Engineering supervised by Professor Marvin Doyley.

Jonathan Langdon was the recipient of the Outstanding Dissertation Award for Engineering at the University of Rochester. Jonathan's thesis, titled "Development of Single Track Location Shear Wave Viscoelasticity Imaging for Real-Time Characaterization of Biological Tissues", was recognized for outstanding advances in new ultrasound elastography technologies for measuring and visualizing viscoelastic properties of tissues.

RELATED COURSES

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.

Ultrasound Imaging

(BME 452) 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, velocity estimation, and flow imaging.

Medical Imaging - Theory & Implementation

(ECE 452) Provides an introduction to the principles of X-ray, CT, PET, MRI, and ultrasound imaging. The emphasis is on providing linear models of each modality, which allows linear systems and Fourier transform techniques to be applied to analysis problems.

Fundamentals of Acoustical Waves

(ECE 432) Introduces acoustical waves. Topics include acoustic wave equation; plane, spherical, and cylindrical wave propagation; reflection and transmission at boundaries; normal modes; absorption and dispersion; radiation from points, spheres, cylinders, pistons, and arrays; diffraction; and nonlinear acoustics.

Digital Image Processing

(ECE 447) Digital image fundamentals. Intensity transformation functions, histogram processing, fundamentals of spatial filtering. Filtering the frequency domain. Image restoration and reconstruction. Multi-resolution processing. Morphological image processing. Image segmentation.

Viscoelasticity in Biological Tissues

(BME 412) Viscoelastic materials have the capacity to both store and dissipate energy. As a result, properly describing their mechanical behavior lies outside the scope of both solid mechanics and fluid mechanics. This course will develop constitutive relations and strategies for solving boundary value problems in linear viscoelastic materials. In addition, the closely-related biphasic theory for fluid-filled porous solids will be introduced. An emphasis will be placed on applications to cartilage, tendon, ligament, muscle, blood vessels, and other biological tissues. Advanced topics including non-linear viscoelasticity, composite viscoelasticity and physical mechanisms of viscoelasticity will be surveyed.

Biosolid Mechanics

(BME 483) This course examines the application of engineering mechanics to biological tissues, including bone, soft tissue, cell membranes, and muscle. Other topics include realistic modeling of biological structures, including musculoskeletal joints and tissues, investigations of the responses of biological tissues to mechanical factors, and experimental methods and material models.

Elasticity

(ME 449) 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.

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.

Applied Vibration Analysis

(ME 443) Vibrations of both discrete (one, two, and many degrees-of-freedom systems) and continuous (strings, beams, membranes, and plates) will be studied. Focus is on free and forced vibration of undamped and damped structures. Analytical, numerical, and experimental methods will be covered. Approximate methods (Rayleigh, Rayleigh-Ritz) for obtaining natural frequencies and mode shapes will also be introduced.

Nonlinear Finite Element Analysis

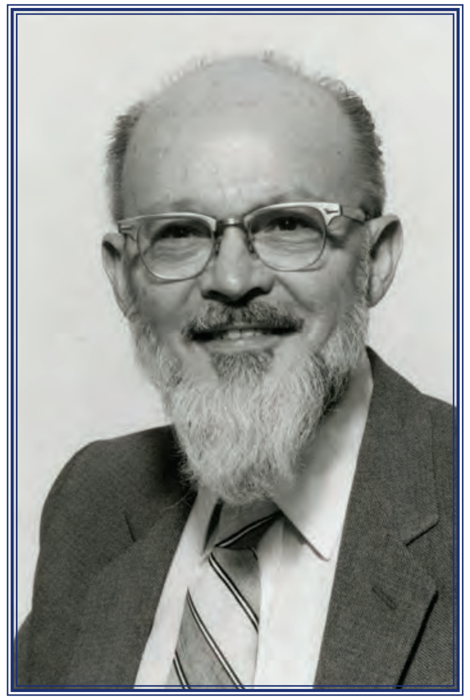
(BME 487) The theory and application of nonlinear FE methods in solid and structural mechanics, and biomechanics. Topics: review and generalization of linear FE concepts, review of solid mechanics, nonlinear incremental analysis, FE formulations for large displacements and large strains, nonlinear constitutive relations, incompressibility and contact conditions, hyperelastic materials, damage plasticity formulation, solution methods, explicit dynamic formulation.

Computational Methods

(ECE 492) Covers computational techniques for the solution of numerical problems with applications of the techniques in acoustic and electromagnetic wave propagation and scattering.

Remembering Ed Carstensen

A Pioneer in the Bioeffects of Ultrasound



Edwin Carstensen, professor emeritus of electrical engineering at Rochester, was a trailblazing researcher. His contributions to understanding the biological effects of ultrasound and extremely low frequency electric fields won him widespread acclaim during a career that spanned almost 50 years.

Ed died in June in Rochester, the city that had been his home since 1961. Ed arrived at the University that year, and quickly became the director of the nascent biomedical engineering program. He was awarded one of the first three NIH Training Grants in Biomedical Engineering (the other two went to counterparts at Penn and Duke). In 1986, he became the founding director of the Rochester Center for Biomedical Ultrasound, one of the largest groups of MD and PhD researchers active in medical ultrasound.

Ed came from modest roots. He grew up in rural Nebraska, where his parents, August and Opal Carstensen, ran a hardware store. His early life was centered on family, farm, school, and church. He was inspired by his father's keen but intuitive ability to fix radios, and this sparked his interest in science and math. Anticipating the possibility of a career in teaching, he attended Nebraska State Teacher's College, where he majored in physical science and minored in math, biological science, and music.

At the recommendation of his physics professor, however, Ed chose to pursue graduate study. After a stint at the Navy's Underwater Sound Reference Laboratory in Orlando, Ed enrolled in a PhD program at the University of Pennsylvania, where he completed his thesis on the ultrasonic properties of blood.

From his initial appointment in electrical engineering at Rochester, Ed made pioneering contributions to the understanding and development of ultrasound contrast agents, lithotripsy systems, high intensity focused ultrasound, nonlinear tissue imaging, and thresholds for tissue exposures. He won multiple awards during his career from such organizations as the Acoustical Society of America, the American Institute of Ultrasound in Medicine, and the IEEE, of which he was a life fellow. In 1987, he was elected to the National Academy of Engineering.

Ed's expertise was in high demand. Working with a committee established by the National Institutes of Health, he helped set the worldwide standards for ultrasound exposure. His landmark book, Biological Effects of Transmission Line Fields (1987), was widely influential in legal and government actions related to exposures to electromagnetic fields.

Ed and his wife, Pam, raised five children, including one College alumnus, Laura Carstensen '78, director of Stanford University's Center on Longevity. His family grew to include seven grandchildren and two great-grandchildren. His devotion to documenting his family's genealogy will ensure that his grandchildren are well acquainted with several thousand ancestors. His "academic descendants" are many, including Diane Dalecki, professor and chair of biomedical engineering at Rochester. Those of us who worked with Ed share a sense of profound gratitude for his encouragement, brilliant insights, and gentle, unfailingly positive guidance.

—David Blackstock, Diane Dalecki, and Kevin Parker

THE EDWIN AND PAM CARSTENSEN FAMILY FUND

A generous gift from the family of the late Edwin L. Carstensen, renowned scientist and founder of the Rochester Center for Biomedical Ultrasound (RCBU), will enable the Center to invite a leading expert from the field to the University of Rochester campus each year to present a seminar, interact with faculty, and deliver a distinguished Carstensen lecture.

"Our intent is to grow the fund, so that eventually it will support a full biomedical ultrasound symposium day, kicking off with the distinguished Carstensen lecture, but also featuring a series of local speakers, student poster sessions, and interactions with local industry, all related to biomedical ultrasound," said Professor Diane Dalecki, current director of the center and chair of the Department of Biomedical Engineering. "Over time, we'd like to support student scholarships as well."

Dr. Carstensen was the Arthur Gould Yates Professor Emeritus of Engineering and Senior Scientist in Electrical and Computer Engineering at the University of Rochester. His illustrious career, spanning nearly 50 years, was celebrated during a special session at the annual conference of the Acoustical Society of America in June. Students and colleagues celebrated his life and work in acoustics, especially as applied to biomedical acoustics, physical acoustics, and selected problems in underwater sound.

The Edwin and Pam Carstensen Family Fund was announced during the special session, to advance the RCBU's goal to provide a unique, collaborative environment for engineering, medical, and applied science professionals in the Rochester area to investigate the use of high frequency sound waves in medical diagnoses and therapy.

"Ed Carstensen was a pioneer in the field of ultrasound and the development of biomedical engineering as a field," Professor Dalecki said. "He was a wonderful mentor to many students, and was a valued colleague, not only at Rochester but also across the world. This fund will help ensure that his legacy endures."

Contributions to the Edwin and Pam Carstensen Family Fund can be made by contacting Eric Brandt at (585) 273-5901 or eric.brandt@rochester.edu.

Dr. Carstensen's contributions to understanding the biological effects of ultrasound and extremely low frequency electric fields won him widespread scholarly acclaim. He was a member of the National Academy of Engineering and the recipi ent of key awards from the Acoustical Society of America, the American Institute of Ultrasound in Medicine, and IEEE.

After joining the University of Rochester in 1961, he became director of the biomedical engineering program. In 1986, he founded the Rochester Center for Biomedical Ultrasound, one of the largest groups of MD and PhD researchers active in medical ultrasound.

The Center has since grown to nearly 100 members, with several visiting scientists from locations around the country. Its laboratories are advancing the use of ultrasound in diagnosis and are discovering new therapeutic applications of ultrasound in medicine and biology. The Center's research spans a wide range of topics in diagnostic and therapeutic ultrasound including sonoelastography, ultrasound contrast agents, 3D and 4D ultrasound imaging, tissue characterization techniques, lithotripsy, acoustic radiation force imaging, novel therapeutic applications, multi-modal imaging, nonlinear acoustics, and acoustic cavitation.

The ASA Carstensen Special Session

The Acoustical Society of America (ASA) honored Edwin L. Carstensen with two special sessions at the Joint Meeting of the Acoustical Society of America and the European Acoustics Association in Boston, MA, on June 28, 2017. The sessions were organized and co-chaired by David T. Blackstock (The University of Texas at Austin) and Gail ter Haar (Royal Marsden Hospital), and were sponsored by the Biomedical Acoustics, Physical Acoustics, and Underwater Acoustics Technical Sections of the ASA. Titles and speakers of the sessions are below.

Edwin L. Carstensen, A scientist's life. David T. Blackstock (The Univ. of Texas at Austin)

Edwin L. Carstensen, the father. Laura L. Carstensen (Stanford Univ.)

Ed Carstensen—Elucidating the physical mechanisms for biological effects of ultrasound. Diane Dalecki (Univ. of Rochester)

From A-mode to virtual beam: 50 years of diagnostic ultrasound. Frederick W. Kremkau (Wake Forest Univ.)

Professor Ed Carstensen—A personal University of Rochester perspective. Robert M. Lerner (Rochester General Hospital)

Cavitation nucleation in medical ultrasound. Lawrence Crum, Michael R. Bailey, Oleg Sapozhnikov, Julianna C. Simon (Univ. of Washington)

Ed Carstensen and the recognition of nonlinear acoustics in biomedical ultrasound. Thomas G. Muir (The Univ. of Texas at Austin)

Carstensen's contributions to shear stress in strain and tissues. Kevin J. Parker (Univ. of Rochester)

Edwin Carstensen's unique perspective on biological effects of acoustically-excited bubbles. Sheryl Gracewski (Univ. of Rochester)

Bioeffects of microsecond pulses of ultrasound—Launching a new era in diagnostic ultrasound safety. Jeffrey B. Fowlkes (Univ. of Michigan)

The role of cavitation in vascular occlusion. Gail ter Haar (Royal Marsden Hospital), Ian Rivens, John Civale (Inst. Of Cancer Res., London), Caroline Shaw, Dino Giussani (Cambridge Univ.), and Christoph Lees (Imperial College)

Defining ultrasound for bio-effects at all frequencies. Francis Duck (Univ. of Bath)

Ed Carstensen, advisor and mentor to the shockwave lithotripsy program project group. James McAteer, Andrew P. Evan, James E. Lingeman, Lynn R. Willis, Philip M. Blomgren, James C. Williams, Rajash Handa, Bret A. Connors (Indiana Univ.), Lawrence Crum, Michael Bailey, Tom Matula, Vera A. Khokhlova, Oleg A.Sapozhnikov (Univ. of Washington), Robin Cleveland (Univ. of Oxford), Tim Colonius (California Inst. of Technol.), and Yuri A. Pishchalnikov (Burst Labs)

Innovative strategies for improved outcomes in nephrolithiasis. Michael Bailey, Julianna C. Simon, Wayne Kreider, Barbrina Dunmire, Lawrence Crum, Adam D. Maxwell, Vera Khokhlova, Oleg A. Sapozhnikov (Univ. of Washington), Robin Cleveland (Univ. of Oxford), Tim Colonius (California Inst. of Technol.), James E. Lingeman, James McAteer, James C. Williams (Indiana Univ.), and Jonathan Freund (Univ. of Ilinois, Urbana)

Biliary lithotripsy and what we learned from Carstensen. E. Carr Everbach (Swarthmore College)

Edwin Carstensen's contributions to early research at the Navy's Underwater Sound Reference Laboratory. David A. Brown (Univ. of Massachusetts Dartmouth)

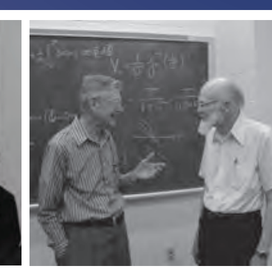
Low frequency sound scattering from a submerged bubble cloud: The Seneca Lake experiment. Ronald Roy (Univ. of Oxford)

The acoustic characteristics of bubbly liquids near the individual bubble resonance frequency. Preston S. Wilson (The Univ. of Texas at Austin, and Ronald Roy (Univ. of Oxford)

Ultrasound in air: Today's guidelines have an insufficiently solid basis for today's exposures. Tim Leighton (Univ. of Southampton)

Exposure measurements for ultrasound in air. Craig N. Dolder, Sarah R. Dennison, Michael Symmonds, Tim Leighton (Univ. of Southampton)

Ultrasonic activated stream cleaning of a range of materials. Tim Leighton, Thomas Secker, Craig N. Dolder, Mengyang Zhu, David Voegeli, William Keevil (Univ. of Southampton)



The Edwin and Pam Carstensen Family Endowment

The Edwin and Pam Carstensen Family Fund was established to honor the legacy of Edwin L. Carstensen and ensure that his vision of the Rochester Center for Biomedical Ultrasound endures. Edwin L. Carstensen was a pioneer in the field of biomedical ultrasound and internationally recognized throughout his career for his advances in understanding the interaction of ultrasound fields with biological tissues. He was the Founding Director of the Rochester Center for Biomedical Ultrasound (RCBU), a multidisciplinary research center dedicated to advancing the use of biomedical ultrasound in imaging and therapy. Professor Carstensen, the Arthur Gould Yates Professor Emeritus of Engineering, was a member of the Department of Electrical and Computer Engineering at the University of Rochester for over fifty years. Professor Carstensen was a member of the National Academy of Engineering, and his outstanding scientific achievements were widely recognized with numerous awards and honors. The fund was enabled by a generous seed gift from the Carstensen family. To contribute to the Edwin and Pam Carstensen Family Fund, please contact Eric Brandt at (585) 273-5901 or eric.brandt@rochester.edu.

FUNDING

Stephen McAleavey (BME) was the recipient of a new NIH grant titled "Quantification of Shear Wave Strain Dependence in Breast Tissues." The goal of this project is to improve the power of ultrasound imaging and elastography to predict if a breast lesion is benign or malignant, by using a novel, high-resolution technique to non-invasively map the nonlinear mechanical properties of breast tissue. Co-investigators are **Marvin Doyley** (Electrical and Computer Engineering), Linda Schiffhauer (Pathology and Laboratory Medicine), and Avice O'Connell (Imaging Sciences).

Mark Buckley (BME) received a grant from the American Orthopaedic Foot & Ankle Society for his research project titled "In Vitro Assessment of the Role of Mechanical Strain in the Pathogenesis and Reversal of Insertional Achilles Tendinopathy (IAT)." With co-investigator **Michael Richards** (Surgery), the project seeks to elucidate how mechanical deformations occurring in the Achilles tendon insertion can lead to IAT pathogenesis, and whether IAT-associated changes can be reversed in vitro by specific mechanical loading regimens.

Diane Dalecki (BME) and **Denise Hocking** (Pharmacology and Physiology) were recipients of a UR Technology Development Fund Award for their project titled "Ultra-Collagen for Enhanced Wound Healing." The project aims to develop an ultrasound-based technology to fabricate bioactive collagen-based wound dressings to promote wound healing.

Marvin Doyley (ECE) was the recipient of two University Research Awards. One project, titled "Early Detection of Chronic Kidney Disease" will compare the viscoelastic properties of normal versus diseased kidneys using quasi-static elastography and ultrasound imaging to discern how metabolic acidosis accelerates kidney disease. The second project, titled "Molecular Imaging of Arterial Occlusion in Mice" will use vascular elastography to explore a novel molecular biomarker for arterial occlusion in mice.

Stephen McAleavey (BME) and **Mark Buckley** (BME) received funding from Carestream Health, Inc. and the Center for Emerging and Innovative Sciences for the research project titled "Towards Automated Clinical Evaluation of Tendon Through Shear Wave Elastography." This project will advance ultrasound elastography techniques to image and characterize shear wave propagation in tendon.

Zeljko Ignjatovic (ECE) received funding from Carestream Health, Inc. and the Center for Emerging and Innovative Sciences for the research project titled "Compressive Beamforming for Portable Ultrasound." The project will develop a compressive parallel-beamforming ultrasound imaging technique to improve diagnostic ultrasound imaging.

Michael Richards (Surgery) and **Marvin Doyley** (ECE) received funding from Carestream Health, Inc. and the Center for Emerging and Innovative Sciences for the research project titled "Plane Wave and Elastographic Imaging of AAA and Carotid Arteries." This project will develop plane wave and elastography techniques to characterize the structure of abdominal aortic aneurisms and blockages in carotid arteries to more accurately assess the risk of ruptures.

Pictured from right to left: Prof. Marvin Doyley, Dr. Maggie Zhang, Dr. Deborah Rubens, Prof. Kevin Parker, Prof. Ken Hoyt, and Dr. Clark Wu gather at the AIUM Annual Convention, Orlando, 2017. Clark Wu and Maggie Zhang are both former UR PhD students supervised by Prof. Parker; Ken Hoyt was a former Postdoctoral scholar in Prof. Parker's lab.

Stephen McAleavey (BME) is a PI on a new project titled "Assistive and Autonomous Breast Ultrasound Screening: Improving Positive Predictive Value and Reducing Repetitive Stress Injury." The project aims to develop a sonographer-supervised robotic system for breast ultrasound imaging using quantitative elastography, with the purpose of improving the positive predictive value of ultrasound screening. Use of a robotic arm will further advance the goal of reducing sonographer repetitive stress injuries associated with ultrasound imaging. The project is funded as a Breakthrough Award by the Congressionally Directed Medical Research Program (CDMRP) Breast Cancer Research Program. Co-investigators on the project include Thomas Howard (ECE), Marvin Doyley (ECE), and Avice O'Connell (Imaging Sciences).

Denise Hocking (Pharmacology and Physiology) received a Program of Excellence Pilot Award for her project titled "Fibronectin-Driven Mechanisms of Embryonic Tendon Development." The project aims to determine how the cell-mediated co-assembly of fibronectin and collagen fibrils within the extracellular matrix influences tendon development.

STUDENT FELLOWSHIPS

Geoffrey Rouin received a University Research and Innovation Grant to support his summer research in the laboratory of Professor Diane Dalecki. Research and Innovation Grants allow students to pursue their own academic interests beyond the classroom. Geoffrey, a BME undergraduate student, is researching the interaction of ultrasound with collagen hydrogels.

Amanda Smith was the recipient of a Xerox Undergraduate Research Fellowship. Amanda was a BME undergraduate student working in the laboratory of Professor Diane Dalecki on a project focused on acoustic streaming. She presented her project titled, "Characterization of ultrasound-induced changes in collagen microstructure using high frequency quantitative ultrasound" at the David T. Kearns Center Research Symposium held at the University of Rochester. The Xerox Undergraduate Fellowship is a highly selective program that provides research experience for undergraduates during the summer and continuing through the academic year.

Awards and Honors

Robert Waag, professor emeritus of electrical and computer engineering, receives the Hajim School Lifetime Achievement Award from Dean Wendi Heinzelman.

Robert Waag was honored as the recipient of the Lifetime Achievement Award from the Hajim School of Engineering and Applied Sciences at the University of Rochester. Professor Waag joined the University of Rochester in 1969 as an assistant professor in the Department of Electrical Engineering, and became the Arthur Gould Yates Professor of Engineering in 1994. For more than 45 years, Professor Waag worked at the leading edge of research in biomedical ultrasound. Through his work, he made seminal contributions to the field in a number of ultrasound areas, including cardiac imaging, scattering from tissue, Doppler signal processing, tissue characterization, wave propagation in inhomogeneous tissue, and aberration correction for imaging systems. Over the years, Professor Waag received awards in recognition of his scientific and engineering achievements from the Radiological Society of North America, National Institutes of Health, World Federation for Ultrasound in Medicine and Biology, Alexander von Humbolt Foundation, the American Institute of Ultrasound in Medicine, and the Japan Society of Ultrasonics in Medicine. He is a fellow of the Acoustical Society of America, the Institute of Electical and Electronic Engineers, and the American Institute of Ultrasound in Medicine.

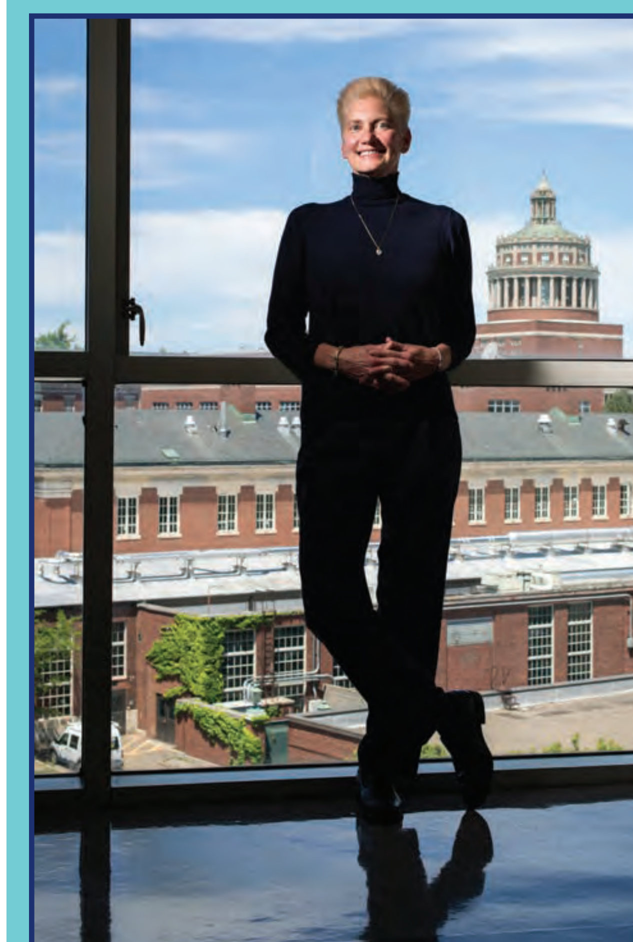
Denise C. Hocking (Pharmacology and Physiology, BME) was elected a Fellow of the American Institute for Medical and Biological Engineering. She was recognized for her outstanding contributions to understanding the extracellular matrix, and for engineering matrix-based therapies to promote tissue function and regeneration. Professor Hocking's research lab is dedicated to understanding mechanisms by which extracellular matrix proteins affect cell and tissue functions that are critical for wound repair and tissue development. Areas of focus in her lab include developing novel ultrasound technologies for tissue engineering, and therapeutic approaches to promote tissue regeneration.

Kevin Parker was named a Fellow of the National Academy of Inventors. "Election to NAI Fellow status is the highest professional distinction accorded solely to academic inventors who have demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development, and the welfare of society" (NAI). Professor Kevin Parker, the William F. May Professor in Engineering was recognized for his outstanding contributions to innovation, discovery, and technology development. His numerous patents have had significant impact broadly across the field of imaging. Professor Parker is inventor on many patents related to sonoelasticity imaging and ultrasound imaging techniques. He and his former graduate student, Theophano Mitsa, Ph.D., are inventors of the Blue Noise Mask, a widely adopted halftoning technique that prints shades of gray in less time and at a higher quality than traditional methods. Professor Parker also holds numerous patents in the area of medical imaging and signal processing. Furthermore, as past Dean of the School of Engineering and Applied Sciences, Professor Parker inspired, and continues to inspire, an environment of innovation for faculty and students throughout the university.

Diane Dalecki was named the Distinguished Professor of Biomedical Engineering. "Diane has become one of the leading experts on the interaction between ultrasound and biological systems," said Joel Seligman, President, CEO, and G. Robert Witmer, Jr. University Professor. The distinguished professorship was established by the University through royalties from the Blue Noise Mask invented by Kevin Parker, Ph.D., the William F. May Professor in Engineering, and Theophano Mitsa '88 (MS), '91 (PhD). "Funding made possible by the Blue Noise Mask underscores the importance of recognizing world-class work and retaining world-class people," said Robert L. Clark, senior vice president for research and dean of the Hajim School of Engineering and Applied Sciences.

Pictured from right to left: Peter Lennie, Dean of the Faculty of Arts, Science and Engineering; Diane Dalecki, Distinguished Professor of Biomedical Engineering and Director of the Rochester Center for Biomedical Ultrasound; Kevin Parker, William May Professor in Engineering and inventor of the Blue Noise Mask, and Joel Seligman, University President & CEO

New Appointments



Diane Dalecki was appointed Chair of the Department of Biomedical Engineering. The department, established in 2000, is a joint program shared by the Hajim School of Engineering and Applied Sciences and the School of Medicine and Dentistry at the University of Rochester. It consists of 18 primary faculty members with expertise spanning biomechanics, biomaterials, tissue engineering and regenerative medicine, neuroengineering, nanotechnology, imaging, and biomedical optics. The department enrolled 368 undergraduates and 70 graduate students during the 2015-16 academic year and led the Hajim School's female undergraduate enrollment with 48 percent.

Maria Helguera became Emeritus Professor and Research Scientist in the Chester F. Carlson Center for Imaging Science at the Rochester Institute of Technology (RIT). She is a long-standing member of the RCBU with expertise in medical imaging, quantitative ultrasound imaging, and non-destructive characterization of materials. Professor Helguera is now pursuing teaching and research opportunities in other parts of the world. She has an appointment in the Instituto Tecnologico Mario Molina in Lagos de Moreno, Jalisco, Mexico where she is focused on expanding the research mission of the institute. In addition, she often teaches at Pontificia Universidad Catolica de Peru with fellow RCBU member and UR alumnus, Ben Castaneda. For more on the new educational and research initiatives undertaken by Professor Helguera, please see the related story on page 14 of this report.

The RCBU is continually advancing novel concepts in ultrasound technology. For more information, visit the UR Ventures website at www.rochester.edu/ventures/

Innovation

UR: A Leader in Technology Commercialization

The University of Rochester has a long-standing tradition of being at the forefront of innovation and scientific research. In 2016, 142 invention disclosures were received from 201 inventors from 48 University departments and divisions. Forty-four external collaborators from 27 institutions, agencies, and corporations were also named as inventors. Three copyright registrations and 210 patent applications were filed in FY 2016. Of the patent filings, 67 were new matter filings, while 143 were continuations of applications filed in previous years. In FY 2016, the UR was granted 48 U.S. patents and 21 foreign patents. These 67 patents cover 56 different technologies. In FY 2016, the UR also executed 31 new license and options agreements and monitored 137 active agreements.

The University of Rochester is one of only eight universities nationwide to rank in the top 20 each year over the last decade in licensing revenue. The University of Rochester is consistently rated as one of the best educational institutions in the nation for patent licensing and revenue, according to the Association for University Technology Managers (AUTM). The AUTM U.S. Licensing Activity Survey is an annual report of the technology transfer activity of top universities, research institutions, and teaching hospitals across the nation. The technological advances of members of the Rochester Center for Biomedical Ultrasound continue to contribute to the UR's success.

New Patents Issued for RCBU Member Inventions

The patent titled "Superresolution Imaging of Scatterers in Pulse-Echo Imaging" (US 9,453,908) was issued September 27, 2016. The patent has been assigned to the University of Rochester with inventor Kevin J. Parker. The technology in the patent uses an inverse filter approach to eliminate speckle and poor resolution dependency on pulse length and width to produce superresolution ultrasound images. The technology has applications for creating higher resolution images for ultrasound, radar, sonar, and other pulse-echo imaging systems.

U.S. Patents

Superresolution Imaging of Scatterers in Pulse-Echo Imaging. U.S. Patent No. 9,453,908	Kevin J. Parker September 27, 2016
Chimeric Fibronectin Matrix Mimetics and Uses Thereof, U.S. Patent No. 9,072,706	Denise C. Hocking and Daniel Roy July 7, 2015
Photodynamic Therapy with Spatially Resolved Dual Spectroscopic Monitoring, U.S. Patent No. 9,044,140	Thomas H. Foster, et al. June 2, 2015
Methods and Systems for Spatially Modulated Ultrasound Radiation Force Imaging, U.S. Patent No. 8,753,277	Stephen McAleavey June 17, 2014
Low-cost Device for C-scan Acoustic Wave Imaging, U.S. Patent Nos. 8,870,770 (2014) and 8,353,833 (2013)	Vikram S. Dogra and Navalgund Rao 2013
Sonoelastographic Shear Velocity Imaging using Crawling Wave Excitation, U.S. Patent No. 8,267,865	Kenneth Hoyt and Kevin J. Parker September 18, 2012
Statistical Estimation of Ultrasonic Propagation Parameters for Aberration Correction, U.S. Patent No. 7,867,166	Robert C. Waag and Jeffrey P. Astheimer January 11, 2011
Ultrasound Imaging of Tissue Stiffness by Spatially Modulated Acoustic Radiation Force Impulse (SM-ARFI), U.S. Patent No. 8,225,666	Stephen McAleavey May 9, 2008
Real Time Visualization of Shear Wave Propagation in Soft Materials with Sonoelastography, U.S. Patent No. 7,444,875	Zhe Wu and Kevin J. Parker November 4, 2008
Method of Treating Neurodegenerative Disease Using Ultrasound, U.S. Patent No. 7,211,054	Charles W. Francis and Valentina Suchkova May 1, 2007
Finite Amplitude Distortion-Based Inhomogeneous Pulse Echo Ultrasonic Imaging, U.S. Patent No. 7,104,956	Ted Christopher September 12, 2006
Ultrasound Distortion Compensation using Blind System Identification, U.S. Patent No. 6,699,189	Feng Lin and Robert C. Waag March 2, 2004
System and Method for 4D Reconstruction and Visualization, U.S. Patent No. 6,169,817	Kevin J. Parker, Saara Totterman, Jose Tamez-Pena January 2, 2001
System for Model-Based Compression of Speckle Images, U.S. Patent No. 5,734,754	Kevin J. Parker March 31, 1998
Thin-Film Phantoms and Phantom Systems, U.S. Patent No. 5,756,875	Daniel B. Phillips and Kevin J. Parker May 26, 1998
Smart Endotracheal Tube, U.S. Patent No. 5,785,051	Jack Mottley and Randy Lipscher July 29, 1998
Blue Noise Mask, U.S. Patent Nos. 5,111,310 (1992); 5,477,305 (1995); 5,543, 941 (1996); 5,708,518 (1998); and 5,726,772 (1998)	Kevin J. Parker and Theophano Mitsa
Ultrasmall Porous Particles for Enhancing Ultrasound Backscatter, U.S. Patent Nos. 5,741,522 (1998); 577,496 (1998)	Michael R. Violante and Kevin J. Parker
Multiple Function Infant Monitor, U.S. Patent No. 5,479, 932	Joseph Higgins, E. Carr Everbach, Kevin J. Parker January 2, 1996
Butterfly Search Technique, U.S. Patent No. 5,419,331	S. Kaisar Alam and Kevin J. Parker May 30, 1995

Selected Publications

Chimenti RL, Chimenti PC, **Buckley MR**, Houck JR, Flemister AS. Utility of ultrasound for imaging osteophytes in patients with insertional Achilles tendinopathy. Arch Phys Med Rehabil, 97:1206-1209 ; 2016.

Chimenti RL, Flemister AS, Ketz KP, Bucklin M, **Buckley MR**, **Richards MS**. Ultrasound strain mapping of Achilles tendon compressive strain patterns during dorsiflexion. J. Biomech, 49:39-44; 2016.

Bah I, Kwak S, **Chimenti RL**, **Richards MS**, Ketz JP, Flemister AS, **Buckley MR**. Mechanical changes in the Achilles tendon due to insertional Achilles tendinopathy. J Mech Behav Biomed 53:320-328; 2016.

Carstensen EL, **Parker KJ**, **Dalecki D**, **Hocking DC**. Biological effects of low frequency shear strain: Physical descriptors. Ultrasound Med Biol, 42:1-15; 2016.

Chen S, **Parker KJ**. Enhanced resolution pulse-echo imaging with stabilized pulses. J Med Imaging, 3:027003-1-027003-13; 2016.

Dalecki D, **Mercado KP, Hocking DC**. Quantitative ultrasound for nondestructive characterization of engineered tissues and biomaterials. (Invited for Special Issue on Nondestructive Characterization of Biomaterials for Tissue Engineering and Drug Delivery) Annals of Biomedical Engineering, 44:636-648; 2016.

Dalecki D, **Hocking DC**. "Advancing Ultrasound Technologies for Tissue Engineering" in Handbook of Ultrasonics and Sonochemistry. Editor, Muthupandian Ashokkumar, Springer, pgs. 1101-1126, 2016.

Harris GR, Church CC, **Dalecki D**, Ziskin MC, Bagley JE. A comparison of thermal safety practice guidelines for diagnostic ultrasound exposures. Ultrasound Med Biol, 42:345-357; 2016.

Huntzicker SJ, **Shekhar H**, **Doyley MM**. Contrast-enhanced quantitative intravascular elastography: impact of microvasculature on model-based elastography. Ultrasound Med Biol, 42:1167-1181; 2016.

McAleavey S, **Parker KJ**, **Ormachea J**, Wood RW, Stodgell CJ, Katzman P, **Pressman EK**, Miller RK. Shear wave elastography in the living, perfused, post-delivery placenta. Ultrasound Med Biol, 42:1282-1288; 2016.

Meemon P, Yao J, Chu Y, Zvietcovich F, **Parker KJ**. Crawling wave optical coherence elastography. Opt Lett, 41:847-850; 2016.

Miller RK, **McAleavey S**, **Ormachea J**, **Pressman E**, **Thornburg L**, Dombroski D, **Zhong J**, Doyley M, Wood RW, Carrol-Nellenback J, Hyrien O. The human placenta: Function and morphological assessments using ultrasound and magnetic resonance elastography. Placenta, 45:74; 2016.

Ormachea J, Lavarello RJ, **McAleavey SA**, **Parker KJ**, **Castaneda B**. Shear wave speed measurements using crawling waves sonoelastography and single tracking location shear wave elasticity imaging for tissue characterization. IEEE Trans Ultrason Ferroelectr Freq Control, 63:1351-1360; 2016

Parker KJ. Scattering and reflection identification in H-scan images. Phys Med Biol, L20-L28, 2016.

Parker KJ. The H-scan format for classification of scattering. OMICS J Radiol, 5:1000236; 2016.

Parker KJ, Alonso MA. The longitudinal iso-phase condition and needle pulses. Opt Express, 24:28669-28677; 2016.

Parker KJ, **Ormachea J**, **McAleavey SA**, Wood RW, Carroll-Nellenback JJ, **Miller RK** . Shear wave speed dispersion behaviors of soft, vascularized tissues from the microchannel flow model. Phys Med Biol, 61:4890-4903; 2016.

Shekhar H, **Huntzicker S**, **Awuor I**, **Doyley MM**. Chirp-coded ultraharmonic imaging with a modified clinical intravascular ultrasound system. Ultrason Imaging, 38:403-419; 2016.

Tacheau A, Le Floc'h S, Finet G, **Doyley MM**, Pettigrew RI, Cloutier G, Ohayon J. The imaging modulography technique revisited for high-definition intravascular ultrasound: theoretical framework. Ultrasound Med Biol, 42:727-741; 2016.

Torres G, Chau GR, **Parker KJ**, **Castaneda B**, Lavarello RJ. Temporal artifact minimization in sonoelastography through optimal selection of imaging parameters. J Acoust Soc Am, 140:714-717; 2016.

Selected Presentations

Bucklin M, **Buckley MR**, **Richards MS**, Ketz J, Flemister AS, **Chimenti RL**. Controlling for limb dominance with ultrasound imaging measures of lower leg muscle thickness. Combined Sections Meeting, American Physical Therapy Association, Anaheim, CA, February 2016.

Chen S, **Parker KJ**. Resolution enhancement of B-mode ultrasound imaging with stabilized inverse filters. 41st International Symposium on Ultrasonic Imaging and Tissue Characterization, Arlington, VA, June 2016.

Chen S, **Parker KJ**. Super-resolution and lateral beampatterns. American Institute of Ultrasound in Medicine Annual Convention, New York, NY, March 2016.

Comeau ES, **Dalecki D**, **Hocking DC**. Ultrasound as a tool to direct microvessel network formation and morphology. European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society, Uppsala, Sweden, June 2016.

Comeau ES, **Raeman CH**, **Hocking DC**, **Dalecki D**. Ultrasound fields to non-invasively pattern microparticles in situ. European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society, Uppsala, Sweden, June 2016.

Doyley M, Nieskoski M, Wang H, Baidya R, Gunn J, Marra K, Pogue B. Elastographic assessment of stromal changes in pancreatic cancer. IEEE International Ultrasonics Symposium, Tours, France, September 2016.

Gonzalez EA, **Ormachea J**, **Parker KJ**, **Castaneda B**. Wavelength average velocity estimator for ultrasound elastography. IEEE International Symposium on Biomedical Imaging, Prague, Czech Republic, April 2016.

Grygotis E, **Dalecki D**, **Hocking DC**. Mechanical bioeffects contribute to ultrasound-induced pro-migratory collagen activity. Annual Meeting of the Biomedical Engineering Society, Minneapolis, MN, October 2016.

Hocking DC, **Raeman CH**, **Dalecki D**. Therapeutic effects of ultrasound on dermal wound healing in diabetic mice. European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society, Uppsala, Sweden, June 2016.

Langdon J, **McAleavey S**. Measurement of liver stiffness using single tracking location shear wave elasticity imaging in a rat model. IEEE International Ultrasonics Symposium, Tours, France, September 2016.

Selected Presentations Cont.

Larson K, **McAleavey S**. Investigating methods of signal interpolation in synthetic aperture ultrasound imaging. Annual Meeting of the Biomedical Engineering Society, Minneapolis, MN, October 2016.

McAleavey S, **Parker KJ**, **Ormachea J**, Wood RW, Stodgell CJ, Katzman PJ, **Miller RK**. Elastography of the post-partum perfused human placenta. American Institute of Ultrasound in Medicine Annual Convention, New York, NY, March 2016.

Miller RK, **McAleavey S**, Wood RW, Carroll-Nellenback J, **Ormachea J**, Hyrien O, Katzman P, Stodgell CJ, **Pressman E**, **Thornburg L**, Szlachetka K, **Parker KJ**. Predicting fetal and newborn health: the role of the placenta and its Imaging. 56th Annual Meeting of the Teratology Society: New Horizons in Birth Defects Research, San Antonio, TX, June 2016.

Miller RK, **McAleavey S**, **Ormachea J**, **Pressman E**, **Thornburg L**, Dombroski D, **Zhong J**, **Doyley M**, Wood RW, Carroll-Nellenback J, Hyrien O, Katzman P, Stodgell C, Szlachetka K, Wang H, **Parker K**. The human placenta: function and morphological assessments using ultrasound and magnetic resonance elastography. International Federation of Placenta Associations Annual Meeting, Portland, OR, September 2016.

Mix DS, Bah I, Toth SA, Stoner MC, Doyle AJ, Ellis JL, Glocker RJ, Knight P, Goldmen BI, **Buckley MC**, **Richards MS**. Viscoelastic material properties of aneurysmal human thoracic and abdominal aortic tissue. International Society for Applied Cardiovascular Biology Biannual Meeting, Alberta, Canada, September 2016.

Mix DS, Arabadjis I, Atene L, Stoner MC, **Richards MS**. Ultrasound detection of heterogeneous accumulated strain within 3D printed patient specific abdominal aortic aneurysms. Vascular Annual Meeting, Washington, D.C., June 2016.

Mix DS, Bah I, Toth SA, Stoner MC, Doyle AJ, Ellis JL, Glocker RJ, Goldmen BI, **Buckley MC**, **Richards MS**. Increased dynamic mechanical energy dissipation in human abdominal aortic aneurysm. AHA: Arteriosclerosis, Thrombosis, and Vascular Biology Annual Meeting, Nashville, TN, May 2016.

Mix DS, Trakimas LE, Stoner MC, Ellis JL, Doyle AJ, Glocker RJ, **Richards M**. Heterogeneous wall strain is associated with increased abdominal aortic aneurysm growth rate. 44th Annual Society for Clinical Vascular Surgery, Las Vegas, NV, March 2016.

Mix DS, Bah I, Toth SA, Stoner MC, Doyle AJ, Ellis JL, Glocker RJ, Goldmen BI, **Buckley MC**, **Richards MS**. Increased dynamic mechanical energy dissipation in human abdominal aorticaneurysm. Vascular Research Initiatives Conference, Nashville, TN, May 2016.

Nayak R, Ohayon J, Schifitto G, **Doyley MM**. Principal strain vascular elastography using compounded plane wave imaging. IEEE International Ultrasonics Symposium, Tours, France, September 2016.

Nayak R, Schifitto S, **Doyley MM**. Evaluating anisotropy of the carotid artery using principal strain vascular elastography. International Tissue Elasticity Conference, Fairlee, VT, October 2016.

Olson RE, Weyand GE, Bucklin M, **Chiment RL**, **Richards MS**, **Buckley MR**. Assessment of strain in the Achilles tendon insertion during exercise using ultrasound elastography. Annual Meeting of the Biomedical Engineering Society, Minneapolis, MN, October 2016.

Ormachea J, **McAleavey SA**, Lavarello RJ, **Parker KJ**, **Castaneda B**. Comparison of quantitative elastographic techniques for shear-wave speed measurements. 41st International Symposium on Ultrasonic Imaging and Tissue Characterization, Arlington, VA, June 2016.

Ormachea J, **McAleavey SA**, Wood RW, Stodgell CJ, Katzman PJ, **Pressman EK**, **Miller RK**, **Parker KJ**. Placenta tissue characterization using single tracking location shear-wave elasticity imaging. 41st International Symposium on Ultrasonic Imaging and Tissue Characterization, Arlington, VA, June 2016.

Parker KJ. Does soft tissue vascularity influence elasticity? American Institute of Ultrasound in Medicine Annual Convention, New York, NY, March 2016.

Parker KJ. Hermite function pulses for scatterer identification. American Institute of Ultrasound in Medicine Annual Convention, New York, NY, March 2016.

Parker KJ, **Ormachea J**, **Zvietcovich F**, **Castaneda B**. Reverberant shear wave fields in tissues. 15th International Conference on the Ultrasonic Measurement of Tissue Elasticity, Fairlee, VT, October 2016.

Parker KJ, **Ormachea J**. Soft tissue vascularity and shear wave speed. 15th International Conference on the Ultrasonic Measurement of Tissue Elasticity, Fairlee, VT, October 2016.

Stone J, Fidalgo A, Park J, Candela B, Mix DS, **Richards MS**, **Erturk E**, and Ghazi A. Full immersion simulated percutaneous nephrolithotomy using 3D printing technology. American Urologic Association Annual Meeting, San Diego, CA, May 2016.

Toth S, Mix DS, Bah I, Stoner MC, Doyle AJ, Glocker RJ, **Buckley M**, Goldmen BI, **Richards MS**. Loss of normal fiber orientation in human abdominal aortic aneurysmal tissue and increased energy loss. Vascular Annual Meeting, Washington, D.C., June 2016.

Wang H, **Parker K**. The human placenta: function and morphological assessments using ultrasound and magnetic resonance elastography. International Federation of Placenta Associations Annual Meeting, Portland, OR, September 2016.

Verma P, **Doyley MM**. Investigating strategies for improving plane wave vascular elastography. IEEE International Ultrasonics Symposium, Tours, France, September 2016.

Verma P, **Doyley MM**. Minimum variance beamforming with spatial compounding for improved performance of plane wave vascular elastography. International Tissue Elasticity Conference, Fairlee, VT, October 2016.

Zvietcovich F, Yao J, Chu Y, Meemon P, Rolland JP, **Parker KJ**. A comparative study of shear wave speed estimation techniques in optical coherence elastography applications. SPIE Photonics West, San Francisco, CS, 13-18 February 2016. (Proc. SPIE 9710, Optical Elastography and Tissue Biomechanics III, 97100Y (March 9, 2016); doi:10.1117/12.2211174)

Zvietcovich F, Yao J, Rolland JP, **Parker KJ**. Experimental classification of surface waves in optical coherence elastography. SPIE Photonics West, San Francisco, CA, February 2016.

Zvietcovich F, Yao Ramirez JM, **Buckley M**, Rolland J, **Parker KJ**. Elastography of porcine cornea by tracking the propagation of surface acoustic waves using optical coherence elastography. 15th International Conference on the Ultrasonic Measurement of Tissue Elasticity, Fairlee, VT, October 2016.

RCBU Members

University of Rochester

Anesthesiology
Paul Bigeleisen, M.D.
Janine Shapiro, M.D.
David Stern, M.D.
Jacek Wojtczak, M.D.

Biomedical Engineering
Mark Buckley, Ph.D
Sally Child, M.S.
Eric Comeau, M.S.
Diane Dalecki, Ph.D.
Melinda Vander Horst, M.S.
Jonathan Langdon, Ph.D
Amy Lerner, Ph.D.
Stephen McAleavey, Ph.D.
Laurentius Osapoetra, M.S.
Carol Raeman, A.A.S.
Richard Waugh, Ph.D.
Sarah Wayson, M.S.

Biophysics/Biochemistry
Scott Kennedy, Ph.D.

Cardiology Unit
James Eichelberger, M.D.
Karl Schwarz, M.D.
Sherry Steinmetz, R.D.M.S.

Center for Vaccine Biology & Immunology
Mitra Azadniv, Ph.D.

Dermatology
Alice Pentland, M.D.

Earth & Environmental Sciences
Asish Basu, Ph.D.

Electrical & Computer Engineering
Rifat Ahmed, M.S.
Yong Thung Cho, Ph.D.
Marvin Doyley, Ph.D.
Andrew Hesford, Ph.D.
Steven Huntzicker, Ph.D.
Zeljko Ignjatovic, Ph.D.
Jack Mottley, Ph.D.
Rohit Nayak, M.S.
Prashant Verma, M.S.
Kevin Parker, Ph.D.
Alexander Partin, Ph.D.
Jason Tillett, Ph.D.
Robert Waag, Ph.D.

Emergency Medicine
Jefferson Svengsouk, M.D.

Imaging Sciences
Mark James Adams, M.D.
Shweta Bhatt, M.D.
Vikram Dogra, M.D.
Thomas Foster, Ph.D.
Nina Klionsky, M.D.
Deborah Rubens, M.D.
John Strang, M.D.
Susan Voci, M.D.
Eric Weinberg, M.D.
Jianhui Zhong, Ph.D.

Immunology/Rheumatology
Ralf Thiele, M.D.

Mechanical Engineering
Stephen Burns, Ph.D.
Alfred Clark, Jr., Ph.D.
Sheryl Gracewski, Ph.D.
Renato Perucchio, Ph.D.

Obstetrics & Gynecology
Morton Miller, Ph.D.
Richard Miller, M.D.
Tulin Ozcan, M.D.
Eva Pressman, M.D.
James Woods, M.D.

Pathology
P. Anthony di Sant' Agnese, M.D.

Pharmacology & Physiology
Emma Grygotis, B.S.
Denise Hocking, Ph.D.

Radiation Oncology
Paul Okunieff, M.D.

Surgery
Christopher Barry, M.D.
Michael Richards, Ph.D.

Urology
Robert Davis, M.D.
Erdal Erturk, M.D.
Irwin Frank, M.D.
Jean Joseph, M.D.
Robert Mayer, M.D.
Jeanne O'Brien, M.D.

Vascular Medicine
Charles Francis, M.D.

Rochester General Hospital

Radiology
Robert Lerner, M.D., Ph.D.

Rochester Institute of Technology

Center for Imaging Sciences
Maria Helguera, Ph.D.
Navalgund Rao, Ph.D.

Biomedical Engineering
Cristian Linte, Ph.D.
Daniel Phillips, Ph.D.

Visiting Scientists

David Blackstock, Ph.D.
University of Texas at Austin

Benjamín Castañeda, Ph.D.
Pontificia Universidad
Catolica del Peru

E. Carr Everbach, Ph.D.
Swarthmore College

Zhe Wu, Ph.D.
University of California, San Diego

Graduate Training Opportunities at the RCBU

The Rochester Center for Biomedical Ultrasound (RCBU) provides exciting opportunities for graduate and post-graduate research and training in the field of biomedical ultrasound. Research at the RCBU spans a wide range of topics in diagnostic imaging and therapeutic applications of ultrasound. With access to RCBU laboratories at the University of Rochester's River Campus, Hajim School of Engineering and Applied Sciences, UR Medical Center, and Rochester Institute of Technology, students can tailor their own interdisciplinary training experiences.

Students can pursue advanced degrees (M.S. and Ph.D.) through various departments of engineering and basic science with a research focus in biomedical ultrasound. A wide range of relevant course offerings enhance the rich research environment. Students tailor their formal coursework individually to complement their research focus and meet requirements of their home department.

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

Students have access to state-of-the-art research facilities to engage in leading-edge research in ultrasound. Core facilities in Goergen Hall include an ultrasound teaching laboratory, imaging and bioinstrumentation equipment, cell and tissue culture facilities, biomedical microscopy equipment, and mechanical testing apparatus. For more information, please contact Diane Dalecki at ddalecki@ur.rochester.edu.

Research Areas

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

UNIVERSITY of ROCHESTER

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

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

RCBU

ANNUAL REPORT