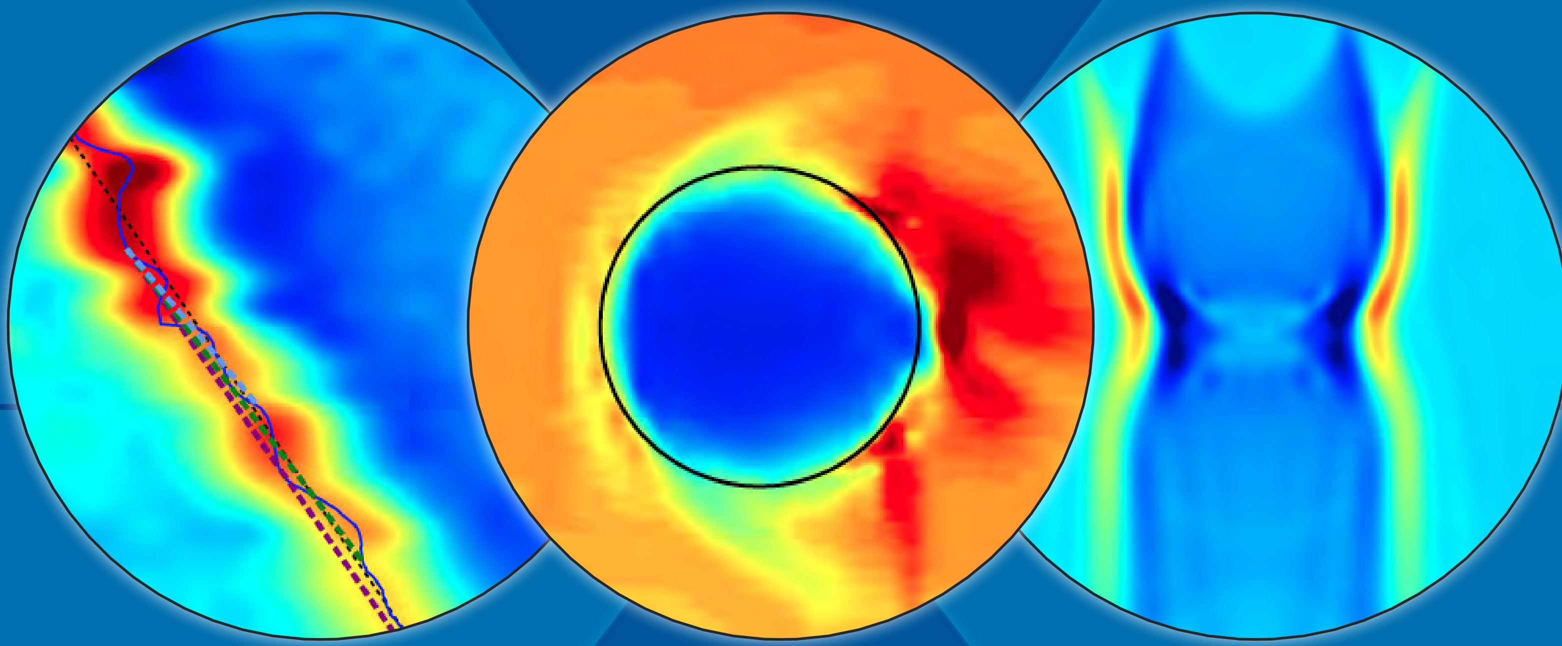
RCBU

ANNUAL REPORT 2015



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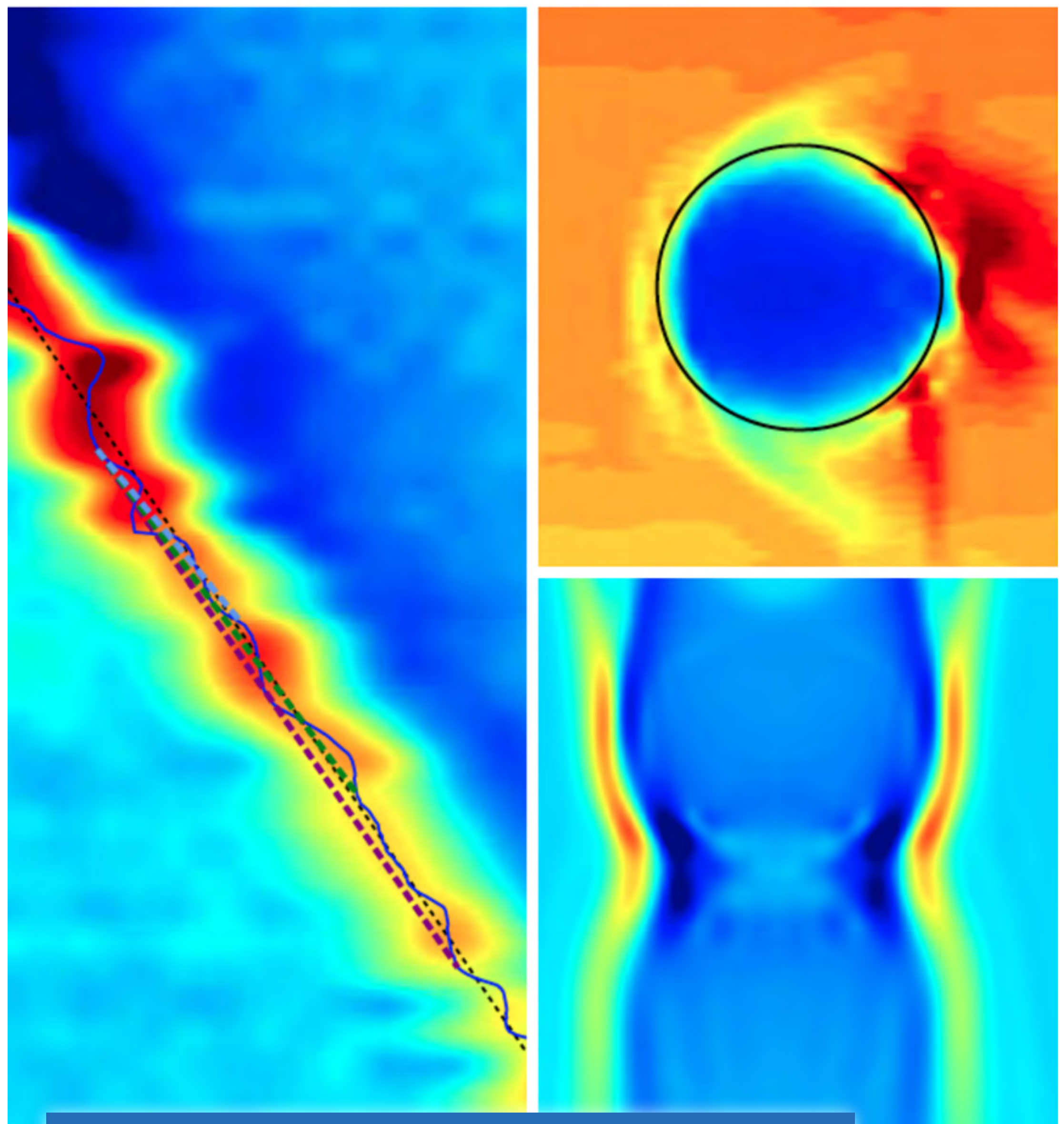
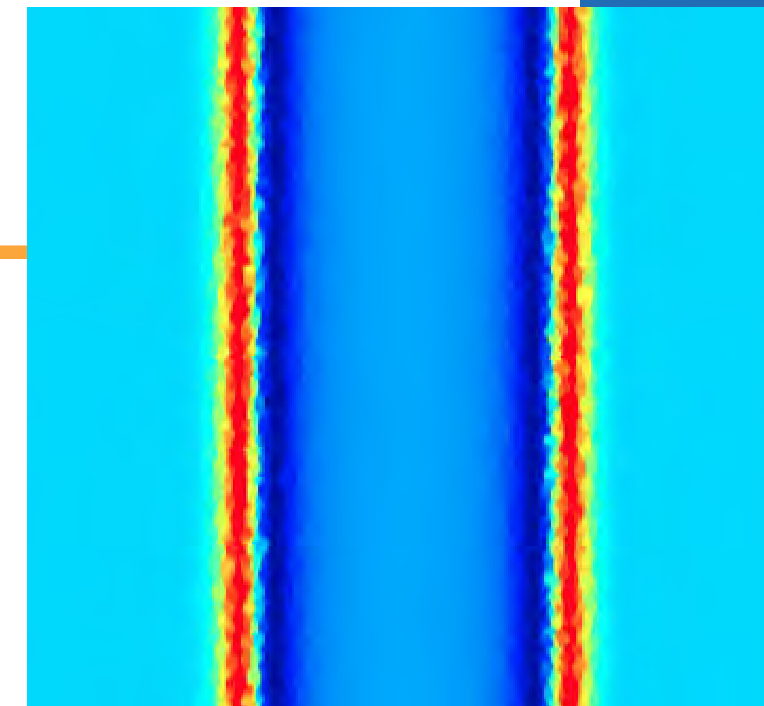


ON THE COVER:

Shear wave elastography is a method of measuring the stiffness of tissue using ultrasound. The shear wave speed is estimated from the particle velocity measured with respect to position and time. This estimation is demonstrated in a tissue mimicking phantom (left). Images may be created by repeating this estimation over a whole region of interest. Custom simulation software can be utilized to create simulated shear wave elasticity images (middle). This software approximates the propagation of shear waves through viscoelastic material (right).



MESSAGE FROM THE DIRECTORS

DIANE DALECKI, PH.D., DIRECTOR

This year's annual report summarizes progress in research, education, and innovation from the RCBU. Recent scientific advances from RCBU laboratories across diverse topics in biomedical ultrasound imaging and therapy are included within this report. 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, non-linear and contrast imaging, and new therapeutic applications of ultrasound. The RCBU continues to play a prominent role in clinical and technological advances in the use of ultrasound for diagnostic imaging and therapy. Nonlinear imaging techniques, sonoelastography, and ultrasound contrast agents all have foundations from innovations within RCBU laboratories. The UR is consistently rated as one of the best educational institutions in the nation for patent licensing and revenue. A list of selected patents by RCBU members in diverse areas of biomedical ultrasound is included within this report. 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.

DEBORAH J. RUBENS, M.D., ASSOCIATE DIRECTOR

Ultrasound continues to grow at the University of Rochester Medical Center, up 20% from 2011, now at 30,595 exams for Imaging Sciences in 2015. Our clinical enterprise now includes Strong West, and out- patient sites at University Imaging at Science Park as well as at Penfield. 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 Imaging site at Red Creek and our associates at University Medical Imaging. All together these combined facilities perform 74,883 ultrasound examinations/year.

On the national and international level, the year has been a busy one, with multiple faculty members lecturing and participating in varied ultrasound endeavors. Dr. Rubens was appointed to the Board of Trustees for the American Registry of Radiologic Technologists (ARRT), which registers and certifies 350,000 imaging technologists in the United States including Ultrasound (US), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), Nuclear Medicine and Radiation Therapy. She will serve a four year term with the specific responsibility as liaison to Ultrasound. Dr. Susan Voci continued her roles as Councilor at the American College of Radiology (ACR) and member of the ACR Ultrasound Section for the Diagnostic Radiology in-training examination. Dr. Rubens was an invited lecturer at Vanderbilt's 39th Annual Diagnostic Sonography Symposium. Collectively, Drs. Bhatt, Dogra, Rubens, Sidhu and Voci 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 lectured for the American Institute of Radiologic Pathology at the 13th Myanmar Radiological Society meeting. She also was a guest speaker at the Mexican Radiology and Imaging Society. Dr. Bhatt presented at the Annual Ultrafest meeting in India and Dr. Dogra spoke in India, Mexico, Kenya, and China.

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 17 and 18 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 research accomplishments in 2015. Selected publications and presentations can be found on pages 25-28.

Visualizing principal strains of the common carotid artery using plane wave imaging

Rohit Nayak, MS, Stephen Huntzicker, PhD, Jacques Ohayon, PhD, Giovanni Schifitto MD, Marvin M. Doyley, PhD

Rupture of lipid-rich plaque in the carotid artery may lead to stroke – a leading cause of death and long-term disabilities. The rupture propensity of plaques is governed by the material properties of the plaque components. Recent work from the laboratory of Professor Marvin Doyley investigated the feasibility of using plane wave imaging to visualize principal strains in vascular tissues. Principal strains represent the largest strain component at any spatial location. Their hypothesis was that principal strain elastograms can detect the early onset of atherosclerosis.

To validate principal strain imaging, the team conducted simulations and studies in vivo. The simulation study was performed with homogeneous and heterogeneous finite element (FE) vessel models with inner and outer radii of 1.5 mm and 6 mm, respectively, and arterial wall stiffness of 45 kPa. The heterogeneous vessel contained an eccentric plaque with a soft lipid core and thin (350 µm) fibrous cap of stiffness 1 kPa and 700 kPa, respectively. The simulated ultrasound system was equipped with a linear transducer array that had 128 elements, each of size 0.2 mm (width) x 4 mm (height); pitch of 0.03 mm, and center frequency of 5 MHz. 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, Analogic, Canada) equipped with a 5-MHz, 128 element transducer array and a parallel data acquisition system (Ultrasonix DAQ, Canada). 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 pre- and post-dilated RF echo frames. Principal strains were estimated by computing the eigenvalues of the full 2D strain tensor. Further, the elastographic contrast-to-noise ratio (CNRe), signal-to-noise ratio (SNRe), and root mean square error (RMSE) were computed to evaluate the quality and accuracy of the principal strain elastograms.

Figure 1. Principal and circumferential strain elastograms obtained from (a, d) homogeneous vessel, (b, e) heterogeneous vessel, and (c, f) healthy subject in vivo.

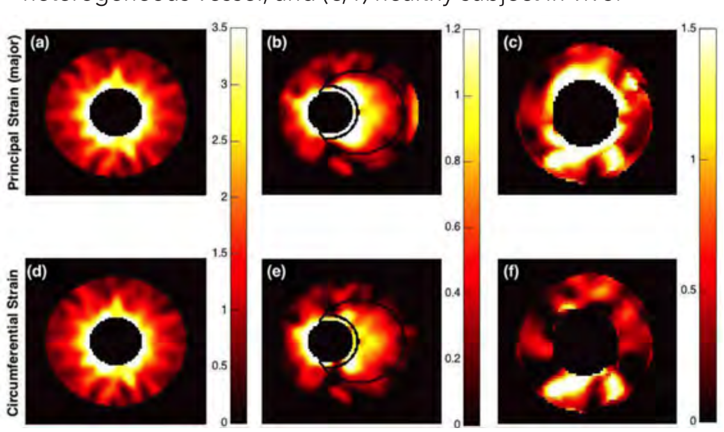


Figure 1(a) is a representative example of a principal strain elastogram obtained from a simulated homogeneous vessel. Figure 1(d) shows the corresponding circumferential strain elastogram, which demonstrates that in the absence of shear strain principal (major) and circumferential strains are equivalent—both were radially symmetric, and decayed inversely with increase in radial distance. In both cases, the SNRe was approximately 16.2 ± 0.44 dB. Figure 1(b) is an example of a principal strain elastogram obtained from a heterogeneous vessel. The corresponding circumferential strain elastogram is shown in Figure 1(e). Principal strain elastograms revealed high strain within the plaque and the interface between the vessel wall and the fibrous cap, which was expected because in these regions the principal strain was dominated by shear strain. Figures 1(c) and 1(f) are principal and circumferential strain elastograms obtained from a healthy volunteer. The principal strain elastogram displays a radially symmetric strain distribution – as expected for a healthy, homogenous vessel (Fig. 1a); however, this was not apparent in the circumferential elastograms because in this case the principal strain elastograms were dominated by radial strains. The results from this preliminary study suggest that principal strain can improve the efficacy of non-invasive vascular elastography, and compounded plane wave imaging can produce clinically useful principal strain elastograms.

Using ultrasound to direct microvessel network formation and morphology

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

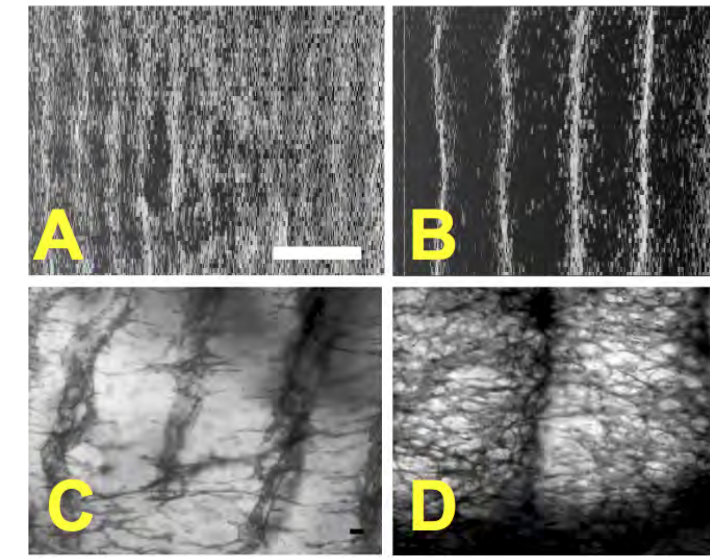
Engineering microvessel networks that structurally and functionally mimic native microvasculature is critical for the fabrication and survival of a wide range of bioengineered tissues. Recent collaborative efforts from the laboratories of Diane Dalecki and Denise Hocking have led to the development of a non-invasive ultrasound-based method to spatially pattern cells within 3D hydrogels, and the team has shown the feasibility of translating this technology to microvascular tissue engineering. Investigations by BME graduate student Eric Comeau have focused on determining how acoustic frequency and amplitude affect initial cell patterning and resulting microvessel network morphologies.

In these studies, human umbilical vein endothelial cells (HUVECs) were suspended in soluble type I collagen, and solutions were exposed to ultrasound standing wave fields (USWFs) generated with acoustic sources of 0.5, 1, and 2 MHz. Samples were exposed for 15 min, during which time cell patterning and collagen polymerization occurred. High-frequency (38-MHz) ultrasound imaging was used to visualize initial cell patterns through the depth of 1-cm thick gels. Gels were also cultured for 10 days and images of microvessel networks were obtained using light microscopy. Image analysis was used to quantify initial cell patterning and resultant microvessel morphology as a function of acoustic frequency and pressure.

USWFs rapidly patterned cells into planar bands. High-frequency ultrasound was used to generate B-scan images of the full depths of USWF-patterned hydrogels (Fig. 1 A, B). B-mode images were used to quantify distances between planar bands of cells and the density of cells within planar bands. Distance between planar bands of cells decreased with increasing acoustic frequency, and cell concentration within each planar band increased with increasing pressure amplitude. After 10 days, microvessel networks were present throughout the volume of USWF-exposed samples. The morphology of the resultant microvessel networks was influenced by acoustic parameters employed for the initial cell patterning (Fig. 1 C, D). Microvessel networks formed in response to patterning with 0.5-MHz USWFs formed capillary-like networks characterized by vessels less than 25 µm in diameter (Fig. 1D). In contrast, three different microvessel morphologies formed in response to 1-MHz USWF patterning. Capillary-like networks formed as a result of 0.1 MPa exposure; minimally branching microvessels with diameters of 50-200 µm formed in response to 0.2 MPa exposure; and hierarchically-branching networks formed in response to 0.3 MPa exposure (Fig. 1C). Microvessel networks formed with 2-MHz USWFs were capillary-like for exposures at 0.05 MPa and branching networks at 0.1 MPa and 0.15 MPa. Sham-exposed samples underwent limited network formation.

Investigations from the team have demonstrated that USWF-patterning of HUVECs leads to rapid formation of 3D microvessel networks within collagen hydrogels. The frequency and pressure amplitude of the USWF control both the initial cell patterning and the resulting microvessel network morphology. Furthermore, high-frequency ultrasound imaging provides a valuable tool to visualize and quantify 3D cell patterning throughout thick collagen gels.

Figure 1. USWF-induced patterning and network formation. B-mode images of cells patterned at 1 MHz (A) and 0.5 MHz (B). Scale bar = 2 mm. C & D) Microscopy images of resultant microvessel networks formed from initial patterning in A and B, respectively. Scale bar = 100 µm.

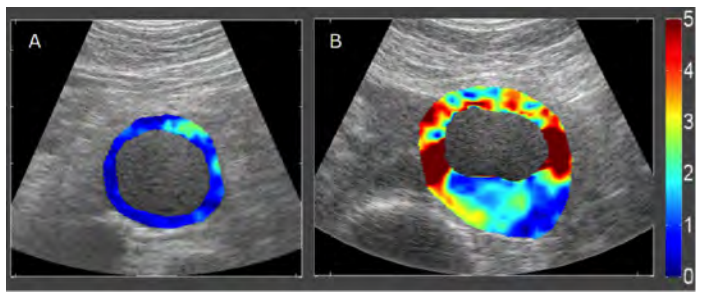


Abdominal aortic aneurysm elasticity imaging

Michael S. Richards, PhD, Doran S. Mix, MD, Michael C. Stoner, MD, Steven W. Day, PhD, Camille C. Johnson, Ling Yang, BS, Nathan Couper, MS, Ben Zarras, BS

As part of a recently awarded NIH R21 grant, the laboratory of Professor Michael Richards is studying the mechanics of abdominal aortic aneurysms (AAA) and developing ultrasound elastography techniques to characterize AAA. The team has developed image registration algorithms to accurately measure accumulated, regional strains from ultrasound images of AAA cross-sections over an entire cardiac cycle. In addition, they have developed novel phantom fabrication techniques to validate and test their image processing methods in vitro. A clinical study, enrolling patients of the vascular surgery clinic with abdominal aneurysms, was also initiated in collaboration with Dr. Michael Stoner and Dr. Doran Mix in the Division of Vascular Surgery at the University of Rochester. This study seeks to use ultrasound images of aortas and elasticity image processing methods (Fig. 1, next page), along with non-invasive blood pressure measurements, to assess the condition or stability of aneurysms more accurately than a size metric alone. Currently, over 100 patients have been enrolled in the study and folow-up scans of approximately 15 patients have been obtained. 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 preliminary theory is that there is a multistage evolution of aneurysmal tissue in which, during the disease onset tissue initially gets softer and this is followed by higher associated growth, but ultimately tissue stiffens relative to healthy tissue when the aneurysms are large and are perhaps closer to rupture. A limited number of ex-vivo human aortic samples have also been obtained from both "healthy" aortas and "aneurysmal" aortas to mechanically test tissue to compare to the clinical imaging study.

Figure 1. Ultrasound measurement of regional strain (%) accumulated between diastole to systole. A) 4.7 cm AAA with 0.1 cm/year growth. B) 4.7 cm AAA with 0.6 cm/year growth.



Ultrasound non-invasively patterns microparticles in situ

Eric Comeau, MS, Carol H. Raeman, AAS, Denise C. Hocking, PhD, Diane Dalecki, PhD

Technologies that enable rapid patterning of cells and microparticles within three-dimensional (3D) hydrogels are needed to advance the fabrication of complex engineered tissues. Ultrasound standing wave fields (USWFs) provide a non-invasive approach for patterning cells and/or microparticles rapidly. Furthermore, USWF-patterning of endothelial cells can accelerate microvessel network formation, and direct microvessel morphology within 3D hydrogel constructs (see related story on pages 5 and 6). Ultrasound propagates through tissue as a focused beam, and thus is ideal for translation in vivo. Recent efforts in the Dalecki and Hocking labs have been dedicated to developing a dual-transducer USWF system to enable rapid, non-invasive, volumetric patterning of cells and microparticles within hydrogels in situ.

A dual-transducer system comprised of two, ultrasound sources was developed to generate an USWF in the region of intersecting sound fields (Fig. 1A). USWFs are characterized by pressure nodes and anti-nodes, and the distance between nodal planes, d, in this system is given by $d = \lambda / [2\sin(\theta/2)]$ where λ is the wavelength of the incident sound field and θ is the angle between propagation paths of the two sources. Thus, the distance between nodal planes can be controlled by choice of θ and/or frequency. Solutions of Sephadex particles suspended in water were exposed to USWFs generated by interfering sound fields with angle θ of 60°, 120°, and 180°. In vitro, USWFs generated by the dual-transducer system rapidly patterned Sephadex microparticles suspended in water into planar bands (Fig. 1B). Distances between planar bands were controlled by adjusting angle (θ), and measured distances (d) were consistent with theoretical predictions.

The dual-transducer system was also tested for its ability to pattern microparticles in situ. Mice were anesthetized and the target region of one flank was precisely positioned within the USWF. Sephadex beads, suspended in type I collagen solutions, were injected subcutaneously into both flanks. One flank was exposed to the USWF and the other served as a sham control. After exposure, USWF patterning within collagen hydrogels injected under the skin of mice was visualized using high-frequency (38-MHz) ultrasound imaging (Fig. 1C, 'USWF'). No patterning was evident in hydrogels in sham-exposed flanks (Fig. 1C, 'Sham').

In summary, the team has developed and implemented a dual-transducer USWF system for rapid, non-invasive, 3D spatial patterning of microparticles within collagen hydrogels injected in situ.

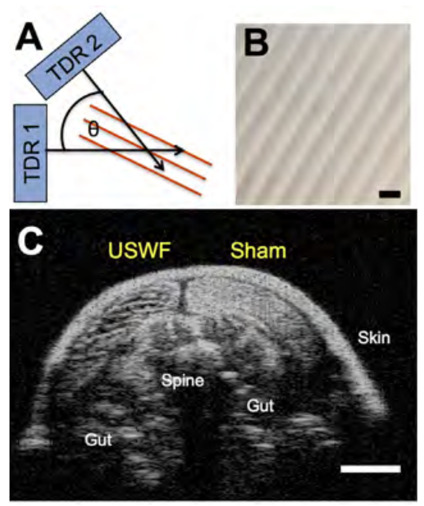


Figure 1.
A) Dual-transducer schematic.
B) Ultrasound transducers angled at 120° produce planar bands of microparticles spaced 840 ± 24 µm apart. Scale bar = 1 mm.
C) High-frequency ultrasound imaging was used to visualize USWF-patterned microparticles in the flank of a mouse. Scale bar = 5 mm.

Shear wave arrival time estimates correlate with local speckle pattern

Stephen A. McAleavey, PhD, Laurentius O. Osapoetra, MS, Jonathan Langdon, PhD

Recent work from the lab of Stephen McAleavey presented simulation and phantom studies demonstrating a strong correlation between errors in shear wave arrival time estimates and the lateral position of the local speckle pattern in targets with fully developed speckle. The team hypothesizes that the observed arrival time variations are largely due to the underlying speckle pattern, and call the effect speckle bias. Arrival time estimation is a key step in quantitative shear wave elastography, performed by tracking tissue motion via cross-correlation of RF ultrasound echoes or similar methods. Variations in scatterer strength and interference of echoes from scatterers within the tracking beam result in an echo that does not necessarily describe the average motion within the beam, but one favoring areas of constructive interference and strong scattering. A swept-receive image, formed by fixing the transmit beam and sweeping the receive aperture over the region of interest, is used to estimate the local speckle pattern. Metrics for the lateral position of the speckle are found to correlate strongly ($r > 0.7$) with the estimated shear wave arrival times both in simulations and in phantoms. Lateral weighting of the swept-receive pattern improved the correlation between arrival time estimates and speckle position. The simulations indicate that high RF echo correlation does not equate to an accurate shear wave arrival time estimate—a high correlation coefficient indicates that motion is being tracked with high precision, but the location tracked is uncertain within the tracking beam width. The presence of a strong on-axis speckle is seen to imply high RF correlation and low bias. The converse does not appear to be true—highly correlated RF echoes can still produce biased arrival time estimates. The shear wave arrival time bias is relatively stable with variations in shear wave amplitude and sign (−20 µm to 20 µm simulated) compared with the variation with different speckle realizations obtained along a given tracking vector. The team showed that the arrival time bias was weakly dependent on shear wave amplitude compared with the variation with axial position/ local speckle pattern. Apertures of f/3 to f/8 on transmit and f/2 and f/4 on receive were simulated. Arrival time error and correlation with speckle pattern were most strongly determined by the receive aperture.

Visualizing stress distribution within vascular tissues using intravascular ultrasound elastography

Michael S. Richards, PhD, Renato Perucchio, PhD, Marvin M. Doyley, PhD

A methodology for computing the stress distribution of vascular tissue using finite element-based, intravascular ultrasound (IVUS) reconstruction elastography was described by a team of RCBU researchers. This information could help cardiologists detect life-threatening atherosclerotic plaques and predict their propensity to rupture. The calculation of vessel stresses requires the measurement of strain from the ultrasound images, a calibrating pressure measurement and additional model assumptions. In this work, the team conducted simulation studies to investigate the effect of varying the model assumptions, specifically Poisson's ratio and the outer boundary conditions, on the resulting stress fields. In both simulation and phantom studies, we created vessel geometries with two fibrous cap thicknesses to determine if they could detect a difference in peak stress (spatially) between the two. The results revealed that (i) Poisson's ratios had negligible impact on the accuracy of stress elastograms, (ii) the outer boundary condition assumption had the greatest effect on the resulting modulus and stress distributions and (iii) in simulation and in phantom experiments, their stress imaging technique was able to detect an increased peak stress for the vessel geometry with the smaller cap thickness. This work is a first step toward understanding and creating a robust stress measurement technique for evaluating atherosclerotic plaques using IVUS elastography.

Oestreicher and elastography

Edwin L. Carstensen, PhD, Kevin J. Parker, PhD

A recent paper (JASA 138:2317-2325; 2015) by RCBU Founding Director, Edwin Carstensen, and Kevin Parker (Past RCBU Director) discussed the analytical solution of Hans Oestreicher (JASA 23:704-714; 1951) for the particle displacement field and impedance of a sphere, oscillating in translation in a viscoelastic medium. Oestreicher's analytical model gives an understanding of the transverse and longitudinal, fast and slow waves that are generated. The authors discuss how this analytical model can provide valuable insight into the displacement fields that are produced with elastography techniques. The results suggest several ways to determine the absorption coefficients of tissues, which together with phase velocity permit the computation of both the real shear modulus and the shear viscosity as functions of frequency.

Ultrasound-induced pro-migratory effects on collagen

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

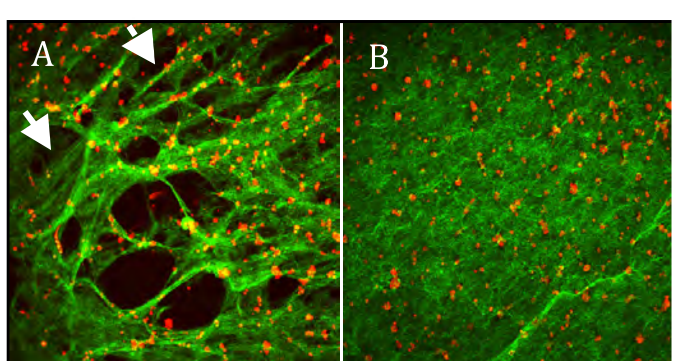
Tissue engineered dermal replacement materials are a promising strategy for treating chronic wounds when conventional therapies fail. Currently, collagen I is used widely in wound dressings and for skin substitutes. Although several such materials have been approved for clinical use, many rely on cell-mediated assembly of an extracellular matrix (ECM) scaffold, resulting in labor-intensive manufacturing and high costs. Advances from the laboratories of Denise Hocking and Diane Dalecki have demonstrated that exposing soluble collagen to ultrasound during collagen gel polymerization influences collagen fiber length, diameter, alignment, and porosity of resultant hydrogels. Recently, this team has focused on understanding underlying mechanisms for the ability of ultrasound to produce pro-migratory collagen microstructures.

In a recent set of experiments, ice-cold solutions of 0.8 mg/mL type I rat tail collagen were prepared, then transferred to 6-well bioflex membrane plates for ultrasound exposures. Collagen hydrogels were polymerized for 15 min in the presence of an 8-MHz ultrasound standing wave field (USWF) with spatial peak temporal average intensity (I_{SPTA}) of 0, 10, 20, or 30 W/cm^2. Temperature increases associated with each exposure condition were measured using thermocouples. In subsequent experiments, a temperature-controlled water bath was used to replicate USWF-induced heating in the absence of ultrasound exposure (i.e. temperature control shams). Following polymerization, fibronectin-null mouse embryonic fibroblasts were seeded on the surface of collagen gels and allowed to migrate for 24 h. Phase contrast microscopy was used to visualize cell distribution 20 min and 24 h post seeding, and cell migration was quantified as the difference in area of the cell-free regions between the two time points. Second harmonic generation (SHG) microscopy was used to visualize collagen microstructure prior to and 24 h after cell seeding; cells were visualized using intrinsic autofluorescence.

The magnitude of ultrasound-induced heating was proportional to I_{SPTA}. Rapid, directional cell migration was observed on collagen gels fabricated with USWF at 10 and 20 W/cm^2, and was not observed on temperature-controlled sham gels or gels exposed to USWF at 30 W/cm^2. Collagen gels that supported cell migration were characterized by radially-aligned collagen fibers that were further remodeled by cells (Fig. 1A, arrows). In contrast, temperature-controlled sham gels consisted of dense, randomly oriented fibers, and contained smaller pores (Fig. 1B) than ultrasound-exposed gels.

Exposure of soluble collagen to ultrasound during polymerization resulted in structural changes (increased fiber alignment and porosity) that correlated with the ability of collagen to support cell migration. These effects were not observed in temperature controlled, sham gels. Future studies will investigate the contributions of mechanical effects of ultrasound on fiber alignment, pore size, and cell behavior in collagen hydrogels.

Figure 1. Collagen gels fabricated in an USWF generated with an 8-MHz acoustic source at 20 W/cm^2 (A), or in a 33°C waterbath without ultrasound exposure (B) were seeded with cells and incubated 24 h prior to fixation. Two-photon imaging was used to detect both the collagen SHG (green) and cellular autofluorescence (red) signals. Z-slices were collected from the gel surface in 5-μm steps and are displayed as maximum intensity projections. Arrows indicate examples of regions of radial fiber alignment around the acoustic focus (out of frame to left of image). Scale bar 200 μm.



Analysis and visualization of microvessel networks in engineered tissues

Amy Becker, Eric Comeau, MS, Denise C. Hocking, PhD, Diane Dalecki, PhD, María Helguera, PhD

Professor Maria Helguera is developing new texture analysis software tools to rapidly visualize and quantify structures within engineered tissues. These tools are of particular value to Professor Diane Dalecki and Professor Denise Hocking for their collaborative projects focused on developing 3D microvessel networks within engineered tissue constructs using ultrasound (see related story on pages 5 and 6). Together, this multidisciplinary team is advancing new image processing approaches to visualize and quantify properties of engineered microvessel networks fabricated with ultrasound technologies.

The software tool provides quantitative textural and morphometric analyses of microscopy images of ultrasound-induced microvasculature in 3D engineered tissues. The tool also provides capability for fast 3D volume rendering of microvessel network structure and morphology. Confocal microscopy images or multi-photon immunofluorescence microscopy images are first pre-processed to suppress noise.

Two different textural analysis techniques (gray level co-occurrence matrix, GLCM, and gray level run length matrix, GLRLM) are combined to provide a comprehensive quantification of microvessel network structure. GLCM textural parameters are computed in nine spatial orientations and include entropy, energy, contrast and homogeneity. GLRLM methods provide quantification of vessel length and branching, and volumetric analyses are used to quantify vessel growth direction and volume percentage. Results indicate the methods are capable of quantitatively characterizing morphological differences in microvessel network structures. Among the parameters for the GLCM analysis, it was shown that homogeneity and contrast were the two most indicative of vessel structure. Among the parameters for the GLRLM analysis, it was concluded that gray-level non-uniformity (GLNU) was best suited for characterizing texture. The algorithms can be implemented through a stand-alone graphical user interface to facilitate rapid analyses of large volumes of date, and provide 3D vessel network and image projection capabilities.

Shear wave dispersion in lean versus steatotic rat livers

Christopher T. Barry, MD, Christopher Hazard, PhD, Zaegyoo Hah, PhD, Gang Chen, PhD, Alexander Partin, PhD, Robert A. Mooney, PhD, Kuang-Hsiang Chuang, PhD, Wenqing Cao, PhD, Deborah J. Rubens, MD, Kevin J. Parker, PhD

The precise measurement of fat accumulation in the liver, or steatosis, is an important clinical goal. This RCBU team's previous studies in phantoms and mouse livers support the hypothesis that, starting with a normal liver, increasing accumulations of microsteatosis and macrosteatosis will increase the lossy viscoelastic properties of shear waves in a medium. This increase results in an increased dispersion (or slope) of the shear wave speed in the steatotic livers. In a recent paper (JUM 34:1123-1129; 2015), the team moved to a larger animal model, investigated lean versus obese rat livers ex vivo, and employed a higher-frequency imaging system to estimate the shear wave speed from crawling waves. The results of their investigations showed elevated dispersion in obese rats and a separation of the lean versus obese liver parameters in a 2-dimensional parameter space of the dispersion (slope) and shear wave speed at a reference frequency of 150 Hz. The team has confirmed in 3 separate studies the validity of their dispersion hypothesis in animal models.

Ultrasound strain mapping of the Achilles tendon

Michael S. Richards, PhD, Mark R. Buckley, PhD, Ruth L. Chimenti, PhD, Meghan Kelly, MD, A. Samuel Flemister, MD, John Ketz, MD, Mary Bucklin, BS

The laboratories of Professor Michael Richards and Professor Mark Buckley are collaborating in ongoing investigations focused on improving the understanding of mechanical properties of tendon tissues and changes in tissue mechanical properties associated with diseases such as tendinopathy. One of the most frequent sites of tendon pathology is the Achilles, and pathologies that involve tendon insertion are termed insertional Achilles tendinopathy (IAT). Professor Buckley's lab is dedicated to understanding the role of mechanics in the onset, progression, and treatment of several diseases, including those that affect tendon and cartilage, while Professor Richards' lab is focused on developing and implementing new elastography techniques for clinical diagnoses. Together, the team is advancing new applications of ultrasound elastography to noninvasively image and measure tendon mechanical properties to provide clinicians with new diagnostic information.

The clinical portion of their work involves patients, previously diagnosed with IAT, who are undergoing therapy to improve the condition of the disease and prevent the need for more invasive treatments (i.e. surgery). To improve clinical outcomes for IAT patients, there is a need to develop new and effective conservative treatments for IAT, and the team hypothesizes that understanding the role of tendon compression will aid in the development of these therapies. In recent work, the team quantified tendon compression using ultrasound to examine the effects of heal lifts on tendon compression during dorsiflexion, and assess the compressive strain of the Achilles tendon in individuals with IAT during dorsiflexion compared to healthy subjects. Regional strains within and around the Achilles tendon were measured during exercise in patients with and without IAT (Figs. 1 & 2). Preliminary findings suggest that IAT tendons experience lower compression due to biomechanical stiffening induced within the tendon, that may be transferred to compression in the surrounding tissues thereby causing pain during dorsiflexion.

Figure 1. Task 1: A→B, Task 2: A→C, Task 3: A→B→D

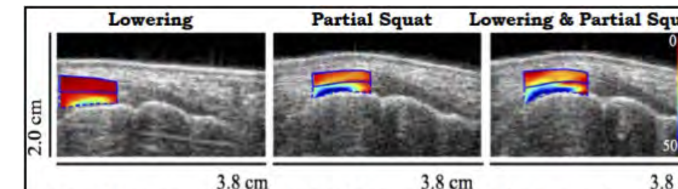


Figure 2. Compressive strain in the Achilles insertion for 1 subject, 3 tasks.

Remotely accessible microscope

Megan Laftrati, BS, Rose Rustowicz, BS, María Helguera, PhD

Professor Maria Helgeura and undergraduate students in her laboratory have designed and built a portable, low cost, WiFi accessible microscope (20x to 200x) that fits inside an incubator for microscopic cell visualization in real time. The system is based on a Raspberry Pi microcomputer and can hold two cell culture plates for simultaneous scanning and time-lapse studies. The system can be adapted to perform 2D or 3D scans, still images or video, gray scale or color. The system facilitates remote microscopic visualization, minimizes manipulation and removal of samples from an incubator, and decreases risk of contamination.

Control and image processing software have been created in Python. The control graphical user interface (GUI) provides an image of the cell culture plates on which the user selects the desired well position by click of the mouse. Motors move the microscope/camera unit to the desired position while a window displays the field of view. Fine position adjustments can be done using the arrows in the keyboard. The GUI also controls the illumination system, mounted on the microscope/camera unit. Image processing algorithms to enhance, segment and count cells are available through another GUI. Other quantitative analyses protocols may include gray-scale textural and volumetric analyses, cell tracking, etc. The system is easily customized for different applications. This project won both the 2014-2015 CIS Faculty Award Celebrating Excellence, and the 2015 UNYTE–Hitting the Accelerator:

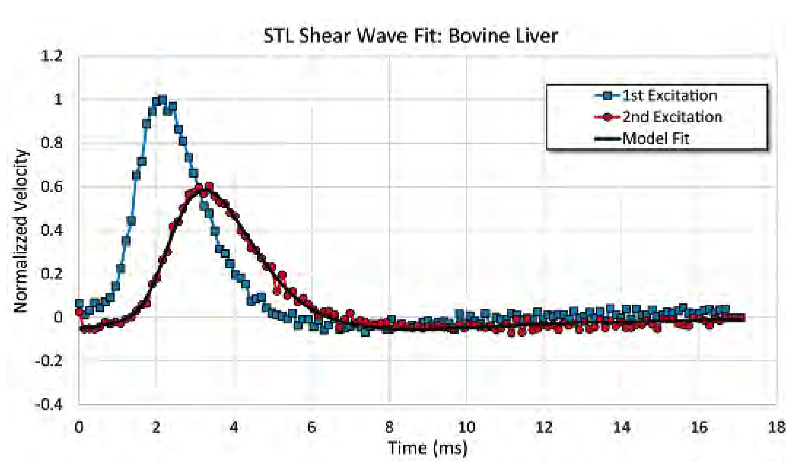
Health Research Innovation through Data Science Best Student Poster Award.

Single tracking location acoustic radiation force impulse viscoelasticity estimation (STL-VE): A method for measuring tissue viscoelastic parameters

Jonathan H. Langdon, PhD, Etana Elegbe, PhD, Stephen A. McAleavey, PhD

Single tracking location (STL) shear wave elasticity imaging (SWEI) is a method for detecting elastic differences between tissues. It has the advantage of intrinsic speckle bias suppression compared with multiple tracking location variants of SWEI. However, the assumption of a linear model leads to an overestimation of the shear modulus in viscoelastic media. A new reconstruction technique from the McAleavey Lab, denoted single tracking location viscosity estimation (STL-VE), is introduced to correct for this overestimation. This technique utilizes the same raw data generated in STL-SWEI imaging. In recent work, the STL-VE technique was developed by way of a maximum likelihood estimator for general viscoelastic materials. The method was then implemented for the particular case of the Kelvin–Voigt model. Using simulation data, the STL-VE technique was demonstrated and the performance of the estimator was characterized. Finally, the STL-VE method was used to estimate the viscoelastic parameters of ex vivo bovine liver. The team found good agreement between the STL-VE results and the simulation parameters, as well as between the liver shear wave data and the modeled data fit.

Figure 1. Example shear wave pairs obtained in bovine liver. The STL-VE result of applying the calculated wave filter to the first shear wave is shown as the model fit overlaying the second shear wave. The ROI contains 464 total shear wave pairs. Using STL, the MLE method yielded $\mu = 1.22$ kPa and $\eta = 0.46$ Pa·s.



Crawling waves speed estimation based on the dominant component analysis paradigm

Renan Rojas, MS, EE, Juvenal Ormachea, MS, Arthur Salo, MS, Paul Rodrigues, PhD, Kevin J. Parker, PhD, Benjamin Castaneda, PhD

A novel method for estimating the shear wave speed from crawling waves based on the amplitude modulation–frequency modulation model was proposed in a recent paper led by RCBU members Professor Kevin Parker and Professor Benjamin Castenda (Ultrason Imaging 37:341-355; 2015). Their method consists of a two-step approach for estimating the stiffness parameter at the central region of the material of interest. First, narrowband signals are isolated in the time dimension to recover the locally strongest component and to reject distortions from the ultrasound data. Then, the shear wave speed is computed by the dominant component analysis approach and its spatial instantaneous frequency is estimated by the discrete quasi-eigenfunction approximations method. Experimental results on phantoms with different compositions and operating frequencies show coherent speed estimations and accurate inclusion locations.

ElasticityLab: A GPU-accelerated simulation tool for ARFI-based viscoelastic shear wave elastography

Jonathan H. Langdon, PhD, Stephen A. McAleavey, PhD

Development and validation of imaging techniques requires testing with targets of known properties, as in phantoms and resolution test objects. Viscoelastic phantoms for ultrasound elastography are challenging to fabricate and limited by the range of available materials. Simulation tools can greatly aid the development of imaging techniques by modeling the response of a system with defined properties.

ElasticityLab is an integrated software tool for shear wave elastography under development in the McAleavey laboratory. It simulates in 3D both the generation of shear waves due to the acoustic radiation force of ultrasound tonebursts from a specified aperture, and the propagation of these shear waves through viscoelastic media. This tool allows for 3D full wave simulation of single-tracking-location shear wave elastography (STL-SWEI) as well as other radiation force based shear wave elastography methods, including supersonic shearwave imaging (SSI), multiple tracking location (MTL) SWEI and time to peak (TTP). This solver was used to evaluate the single tracking location viscoelastic estimator (STL-VE) developed in the lab of Stephen McAleavey. The simulator allows the effect of tracking bias, viscoelasticity, and beam geometry on shear wave elastography algorithms to be evaluated.

Simulations are performed in two steps – an acoustic wave simulation to model the propagation of the "push" pulse and the radiation force developed, and a full-wave elastodynamic simulation to model shear wave propagation. The acoustic wave simulation is performed in the velocity stress formulation implemented on a staggered grid. Perfectly matched layers are included at the boundary of the model to avoid reflections of the push pulse. The push aperture is described in terms of amplitude and phase as a function of position in the aperture, allowing a variety of beam profiles to be simulated. The elastic wave simulation is similar, but calculates the entire stress tensor, rather than just the pressure as in the acoustic case. The source of the shear wave can be the result of the acoustic simulation described above, or can be described as a function of position in 3D space. As an example, Figure 1 shows a comparison of shear waves resulting from push apertures of two sizes, and matched phantom shear wave data. Material properties may be varied as a function of position in both simulations, allowing the modeling of shear wave reflections, behavior around cysts, and other complex interactions. The result of the elastodynamic simulation is a file describing particle velocity as a function of space and time. The results can viewed directly as shear wave movies, or can be passed to the SWEI algorithm to generate images. ElasticityLab allows effects of speckle bias to approximated without a full ultrasound imaging simulation though the addition of coherent bias errors to the shear wave data.

ElasticityLab takes advantage of recent developments in general purpose computing on graphics cards (GPU), which allow for massively parallel computation on inexpensive personal computers. The McAleavey Lab developed a new implementation of the Elastodynamic Finite Integration Technique (EFIT) optimized for the GPU using the OpenCL language. The development of simulation libraries based in OpenCL allows continuous development of ElasticityLab and its deployment across a wide variety of hardware.

Image-based quantification and analysis of longitudinal lung nodule deformations

Kfir Ben-Zikri, MS, Nathan Cahill, PhD, María Helguera, PhD

Lung cancer is the leading cause of cancer related-deaths in the U.S., accounting for 28% of all cancer-related mortality in 2012, and having a 16% five-year survival rate. If lung cancer is diagnosed at an early stage when the cancer is still localized in small lesions or nodules, the five-year survival rate improves to 52%. It is impractical and risky, however, to biopsy every lesion that may be found in a computed tomography (CT) scan. To mitigate this risk, longitudinal scans are collected to determine the growth rates of individual lesions in order to determine if they are consistent with growth rates of known types of malignancies. Maria Helguera, PhD, in collaboration with Kitware, Inc and the University of North Carolina, is advancing new image processing and registration techniques to quantify longitudinal lung nodule deformations. Ground glass opacity (GGO) lesions are especially difficult to analyze, as they feature a variety of non-solid components that may be influenced by lung deformation. Compensating for background lung deformation across longitudinal scans (via image registration) is vital to enable accurate estimation of lesion growth rate. Recent work from the Helguera lab tested four clinical cases and demonstrated that registration over a region of interest (ROI) centered around the lesion yielded lower target registration errors (TRE) than registration over the entire lung. In 3 of 4 cases for lesion ROIs, the median TRE was less than 1 mm. Registration based on lesion ROIs had better performance in 3 of 4 cases, suggesting that a limited ROI enables registration algorithms to converge to the correct global minimum. It was found that affine registration outperformed rigid registration in all four cases, both when lung and lesion ROIs were used.

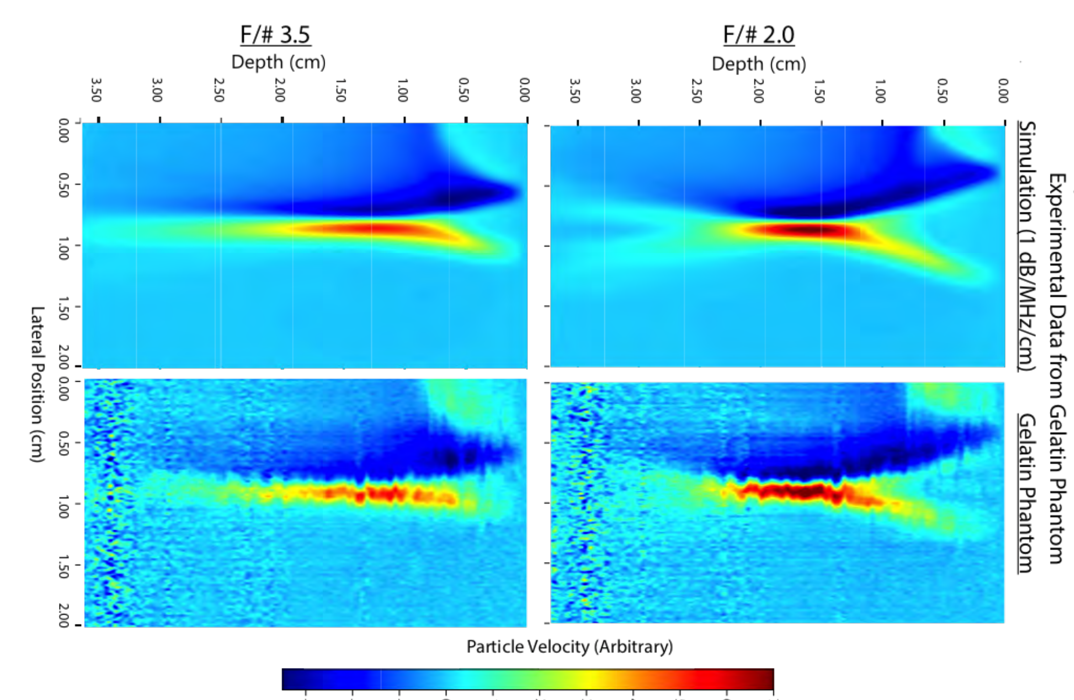
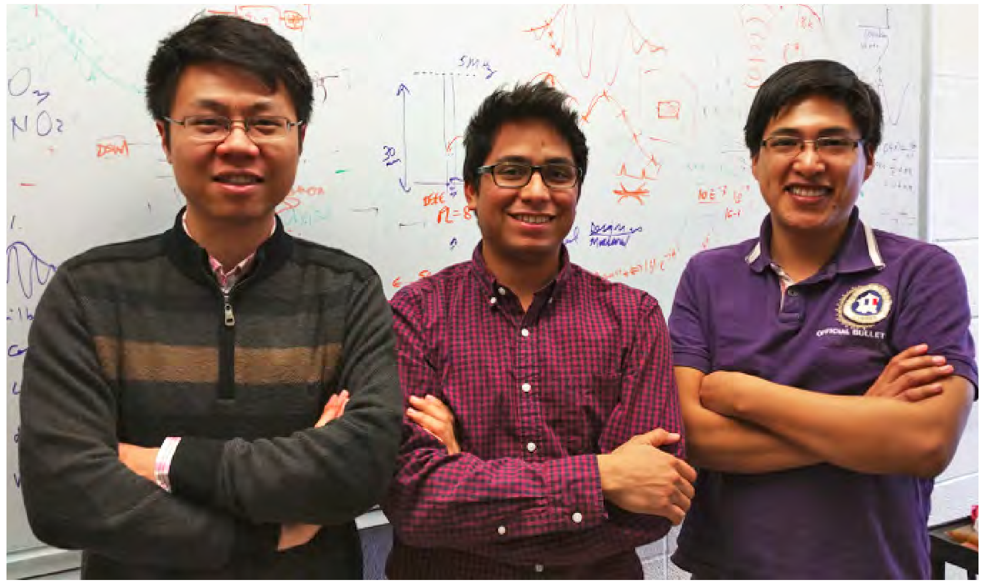


Figure 1. Shear wave movie frames from a 2 kPa simulated phantom (left column) are presented next to matched gelatin phantom frames with F/# 2.0 (top row) and F/# 3.5 (bottom row) cases. The velocity scale for the simulated data is arbitrary and chosen to match the magnitude of the velocities in the experiment. Distortions due to speckle tracking and velocity estimation noise are seen in the phantom images but are not simulated.



Current Ph.D. candidates in the Parker Lab: Shujie Chen, Fernando Zvietcovich, Juvenal Ormachea (left to right)

- Shujie Chen: Conducting research in the area of superresolution
- Fernando Zvietcovich: Conducting research in the area of OCT/OCE
- Juvenal Ormachea: Conducting research in the area of sonoelastography

Experimental evaluations of the microchannel flow model

Kevin J. Parker, PhD

Recent advances have enabled a new wave of biomechanics measurements, and have renewed interest in selecting appropriate rheological models for soft tissues such as the liver, thyroid, and prostate. The microchannel flow model was recently introduced to describe the linear response of tissue to stimuli such as stress relaxation or shear wave propagation. This model postulates a power law relaxation spectrum that results from a branching distribution of vessels and channels in normal soft tissue such as liver. In a recent article by Professor Kevin Parker (Phys Med Biol 60(11)4227-4242, 2015), the derivation is extended to determine the explicit link between the distribution of vessels and the relaxation spectrum. In addition, liver tissue is modified by temperature or salinity, and the resulting changes in tissue responses (by factors of 1.5 or greater) are reasonably predicted from the microchannel flow model, simply by considering the changes in fluid flow through the modified samples. The 2 and 4 parameter versions of the model were considered, and shown that in some cases the maximum time constant (corresponding to the minimum vessel diameters), could be altered in a way that has major impact on the observed tissue response. This could explain why an inflamed region is palpated as harder compared to surrounding normal tissue.

Obstetrics & Gynecology Ultrasound Unit

Loralei L. Thornburg, MD

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

The total number of examinations in 2015 from Strong Memorial Hospital sites (HH, SMH, FFT, Noyes) included 11,057 abdominal and 3086 vaginal obstetric scans, and 2424 abdominal and 2148 vaginal gynecologic scans. Invasive procedures performed included 94 genetic amniocentesis for karyotype or lung maturity, 48 chorionic villus samplings, 68 sonohysterograms, 40 OR guidance for minor gynecologic procedures, and 38 invasive pregnancy procedures including intrauterine shunt insertions, transfusions, pleurocenteses and other fetal procedures. Additionally, 5,011 obstetric and 1,878 gynecologic scans were completed at RGH/NWH.

The unit has 16 ultrasound machines within SMH and HH hospitals, all with 3D and 4D capability, plus additional portable scanners. There are 17 sonographers at HH and SMH, all of whom are CLEAR certified, and 5 of whom are fetal echocardiography certified. SMH remains an active member of NAFNET (North American Fetal Therapy Network). Some examples of recent research projects are provided below.

Prediction of macrosomic newborn from ultrasound biometry and maternal characteristics

L Gray, MD, M Mongelli, MB, BS, DM, LL Thornburg, MD, L Mack, RDMS, MPH, JC Glantz, MD MPH, EK Pressman, MD, TO Ozcan, MD

The objective of this work was to predict macrosomia >4000 g from maternal characteristics and ultrasound biometry taken before delivery. The dataset included all term vaginal deliveries from 2004-2013 at a single U.S. institution with an ultrasound ≤ 4 weeks from delivery. Maternal characteristics included age, weight, height, prepregnancy body mass index (BMI), weight gain, and parity. Femur length (FL), abdominal circumference (AC), head circumference (HC), estimated fetal weight (EFW), gender, and birth weight were included. EFW, biometry measurements, and ratios including HC: AC, FL: AC, BPD: FL and AC: maternal height were converted into their respective z-scores. Binary logistic regression analysis (stepwise forward conditional) was used to select the best predictive model. Model performance was validated by calculating the ROC curve and sensitivities and specificities. $P<0.05$ was considered significant.

There were 3788 cases available for analysis including 298 newborns with macrosomia. The mean gestational age at ultrasound and the mean interval from ultrasound to delivery were 38.1 weeks and 9.7 days, respectively. Mothers of macrosomic infants were significantly older, heavier, taller and had greater weight gain, higher BMI, and higher parity on univariate analyses. The z-scores for EFW and biometry were higher in the macrosomia group. Ratios (except for HC: FL) were significantly different between groups. Males were more likely to be macrosomic. A combination of gestational age at delivery, parity, and z-EFW predicted macrosomia with a sensitivity of 72.5%, false positive rate (FPR) of 10%. This is significantly better than using the z-score of the EFW alone (sensitivity 63%, FPR of 10%). In conclusion, the prediction of macrosomia can be improved by combining maternal characteristics with ultrasound biometry.

Completed sonographic anatomic surveys: The exception rather than the rule

J Glantz

The aim of this study was to determine how often fetal organ systems are imaged completely and whether this varies by hospital. All initial anatomic ultrasounds between 16-24 weeks from 3 hospitals (perinatal designation level I, II, and III) from Jan 2012 through Dec 2013 were identified in their AS-OBGYN report databases, focusing on 36 anatomic fields. Structures were grouped into regions: brain, face, spine, heart, abdomen, and extremities. Rates of complete visualization of each structure, structure grouping, and total were calculated, and compared using chi-square testing.

From 7211 exams (2578 from level I, 986 from level II, and 3647 from level III), the completion rate was 16.8% (I: 20.6%; II: 20.0%: III 13.2%, $p<0.00001$). Brain and extremity imaging was complete ≥85% of the time, but spine only 62.4% (sacrum consistently lowest). Completeness rates varied significantly ($P<0.00001$) for face (28.1% to 64.4%, due to low rates of clearing lips at the level III and of the level I not clearing profiles), heart (37.3% to 56.1%; level I<II<III), and abdomen (65.2% to 85.7%, due to lower rates of clearing kidneys at the level I). Completion of both heart and spine was 32% (I: 23%; II: 25.4%; III: 40.2%; $p<0.00001$).

With a comprehensive reporting system, completion rates for full anatomic sonograms are low. Facial, cardiac, and spinal structures are least complete, and follow-up exams often remain incomplete. Completion benchmarks would be helpful because "incomplete" studies lead to repeat exams that increase health care costs.

Prediction of small for gestational age (SGA) newborn from ultrasound biometry and maternal characteristics

L Gray, MD, M Mongelli, MB, BS, DM, LL Thornburg, MD, L Mack, RDMS, MPH, JC Glantz, MD, MPH, EK Pressman, MD, TO Ozcan, MD

The aim of this study was to predict SGA newborn (< 10th percentile) from ultrasound biometry and maternal characteristics taken before delivery. The dataset included all term vaginal deliveries from 2004-2013 at a single U.S. institution with an ultrasound ≤ 4 weeks from delivery. Maternal characteristics included age, weight, height, prepregnancy body mass index (BMI), weight gain, and parity. Femur length (FL), abdominal circumference (AC), head circumference (HC), estimated fetal weight (EFW), gender, and birth weight were included. EFW, biometry measurements, and ratios including HC:AC, FL:AC, BPD:FL, and AC:maternal height were converted into respective z-scores. $P<0.05$ was considered significant. Binary logistic regression (stepwise backward conditional) was used to select the best predictive model. Model performance was validated by calculating the ROC curve and sensitivities and specificities.

There were 3788 cases available for analysis including 158 SGA newborns. The mean gestational age at ultrasound and the mean interval from ultrasound to delivery were 38.1 weeks and 9.7 days, respectively. Mothers of SGA infants were significantly younger, lighter, shorter, and had lower weight gain and lower BMI. The zscores for EFW, HC, BPD, AC, FL, and AC:maternal height were lower in the SGA group. All biometric ratios were significantly different except the HC:FL. Primiparity and female gender were more likely associated with SGA. The combination of maternal height, infant gender, HC:AC, HC:FL, AC: maternal height, and z-scores of BPD and HC predicted SGA with a sensitivity of 84.5% at a false positive rate (FPR) of 10%. This is significantly better than the zscore of the EFW(sensitivity 80%, at FPR 10%). In conclusion, ultrasound biometry and maternal characteristics can predict SGA newborns better than EFW alone.

AWARDS

STUDENT HONORS

Rohit Nayak was awarded the Best Graduate Student Poster at the University of Rochester Center for AIDS Research World AIDS Day Symposium in December 2015. Rohit is a Ph.D. candidate in Electrical and Computer Engineering working in the laboratory of Professor Marvin Doyley. Rohit was recognized for his presentation titled "Visualizing principal strains of the carotid artery using plane wave imaging". Co-authors were **Marvin Doyley** (ECE), **Rifat Ahmed** (ECE), **Prashant Verma** (Physics & Astronomy), **Nancy Carson** (Imaging Sciences), **Vikram Dogra** (Imaging Sciences), Meera Singh (Microbiology & Immunology), Sanjay Maggirwar (Microbiology & Immunology), and Giovanni Schifitto (Neurology).

Emma Grygotis was awarded the Outstanding Presentation Award at the Therapeutic Ultrasound Winter School held at Ecole de Physique des Houches in Les Houches France in March 2015. Emma presented an overview of her studies focused on developing ultrasound technologies to fabricate bioactive collagen hydrogels for wound repair. Emma is a Ph.D. candidate in the Department of Pharmacology and Physiology, and her research is supervised by **Professor Denise Hocking** and **Professor Diane Dalecki**.

Rose Rustowicz *Megan Iafrati*


Rose Rustowicz and **Megan Iafrati** received the Best Student Poster Award at the Rochester Global Health Symposium & UNYTE Scientific Session. Their poster, titled "Remotely Accessible Microscope (RAM)", described the development of a low-cost, low-profile microscope system that can be remotely accessible. Rose and Megan were undergraduate students in Imaging Sciences at RIT. The ongoing project is supervised by **Professor Maria Helguera**.

Jonathan Langdon

Jonathan Langdon was awarded First Place in the Best Student Paper Competition in the Biomedical Acoustics Section at the 169th Meeting of the Acoustical Society of America held in Pittsburgh PA in May 2015. Jonathan was recognized for his presentation titled "Compensating for Scholte waves in single trackling location shear wave elasticity imaging," with co-authors Karla Mercado, **Diane Dalecki**, and **Stephen McAleavey**. Jonathan is an MD/PhD trainee in the laboratory of Professor McAleavey.

FACULTY ACHIEVEMENTS

The latest collaborative research by **Diane Dalecki** (BME) and **Denise Hocking** (Pharmacology and Physiology) was recognized with the Best Paper Award at the Micro- and Nanotechnology Sensors, Systems, and Applications Conference of the SPIE Defense + Security Symposium held in Baltimore MD in April 2015. Their invited paper, titled "Guiding tissue regeneration with ultrasound in vitro and in vivo" detailed three biomedical ultrasound technologies under development in their laboratories to stimulate tissue formation and regeneration. Co-authors of the paper included RCBU members **Sally Child** and **Carol Raemen**, and BME graduate students **Eric Comeau** and Laura Hobbs. These ultrasound technologies offer new solutions to key challenges currently facing the fields of tissue engineering, biomaterials fabrication, and regenerative medicine.

Cristin Linte was the recipient of the IET JA Lodge Early Career Award in Biomedical Engineering from the Institution of Engineering and Technology (IET)–Healthcare Technologies Network. Dr. Linte is an Assistant Professor in Biomedical Engineering at the Rochester Institute for Technology. His Biomedical Modeling, Visualization, and Image-Guided Navigation Laboratory focuses on the discovery and development of innovative image processing, navigation, and visualization techniques and instrumentation to improve the understanding, diagnosis, and treatment of diseases through minimally invasive or non-invasive approaches.

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 2015, 151 invention disclosures were received from 253 inventors from 56 University departments and divisions. Fifty-eight external collaborators from 31 institutions, agencies, and corporations were also named as inventors. Eight copyright registrations and 241 patent applications were filed in FY 2015. Of the patent filings, 76 were new matter filings, while 165 were continuations of applications filed in previous years. In FY 2015, the UR was granted 53 U.S. patents and 21 foreign patents. These 74 patents cover 61 different technologies. In FY 2015, the UR also executed 24 new license and options agreements and monitored 120 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 "Chimeric Fibronectin Matrix Mimetics and Uses Thereof" (US 9,072,706) has recently been assigned to the UR with inventors Denise C. Hocking, Ph.D. and Daniel Roy, Ph.D. The patent relates to a series of recombinant fibronectin peptide mimetics developed to promote wound repair. The technology falls under a new and exciting class of therapies known as wound biologics. The primary commercial application for this technology is to promote the healing of chronic wounds, including diabetic, venous, and pressure ulcers, which impose a significant health care burden worldwide.

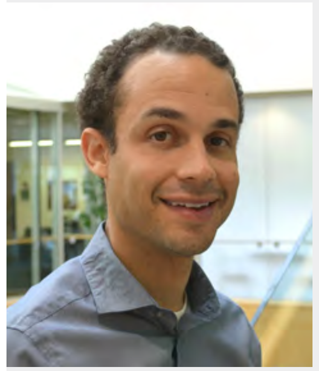
Professor Thomas Foster and colleagues were inventors on a new patent assigned to the UR titled "Photodynamic Therapy with Spatially Resolved Dual Spectroscopic Monitoring" (US 9,044,140). This patent describes an apparatus and method to determine photodynamic therapy dosimetry in real-time in vivo.

U.S. PATENTS

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

RCBU FUNDING NEWS & NEW APPOINTMENTS

Mark Buckley, PhD



Mark Buckley is PI on a new NIH grant titled "Tracking Achilles Tendon Compression to Monitor Insertional Achilles Tendinopathy". Professor Buckley is an assistant professor of biomedical engineering at the University of Rochester and his research lab is dedicated to understanding mechanics underlying the progression and treatment of diseases that affect cartilage, tendon, cornea, sclera and other connective tissues. In this NIH-sponsored project, Professor Buckley and collaborators will develop and test an ultrasound imaging approach to track compression of the Achilles tendon against the heal during ankle rotation as a tool to assess the severity of insertional Achilles tendinopathy.

Professor Buckley also received support from the Valerie and Frank Furth Fund for his proposal titled "The Role of Mechanics in Disease and Disease Therapies." The Furth Fund promotes natural and biological science research by funding young scientists in the College of Arts, Sciences, & Engineering and the UR Medical Center.

Michael Richards, PhD

Michael Richards received a new NIH grant titled "Abdominal Aortic Aneurysm Ultrasound Elasticity Imaging". As PI on this grant, Professor Richards will lead a research program focused on developing new ultrasound techniques to predict the risk of abdominal aortic aneurysm rupture. Novel elastography approaches will be developed to assess stress within the abdominal aorta over the cardiac cycle. Experimental measurements will be compared to numerical simulations and validated using unique anatomically accurate phantoms fabricated using combined X-ray CT imaging and 3D printing technology.

Cristian Linte, PhD

Cristian Linte's project, titled "Exploring Advanced Image Processing and Segmentation Tools for Patient-Specific Anatomical Modeling and 3D Printing for Advanced Therapy Planning, Simulation and Guidance", was supported by a grant from the NY State Center for Emerging and Innovative Sciences (CEIS) and Carestream Health. Professor Linte and colleagues also received a Dean's Research Initiation Grant for their project titled "Virtual Medical Imaging Augmentation and Simulation for Surgery and Therapy: Evaluating New Paradigms for Anatomy Teaching and Training."

Stephen McAleavey, PhD

Stephen McAleavey was the recipient of a UR Pump Primer Award for his project titled "Towards Diagnostic Ultrasonic Imaging of Tissue Non-Linearity: Strain Dependence of Shear Wave Velocity in Liver and Breast Tissue". The goal of this project is to improve the positive predictive value of ultrasound imaging in identifying breast cancers by developing a system to measure and image the nonlinear mechanical properties of breast tissue. The project is a step towards a long-term goal of characterizing nonlinear mechanical properties of tissues in vivo with non-invasive ultrasound techniques.

Denise C. Hocking was promoted to Professor of Pharmacology and Physiology, and of Biomedical Engineering at the University of Rochester. 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. Areas of focus in her lab include developing novel ultrasound technologies for tissue engineering, and therapeutic approaches to promote tissue regeneration in chronic wounds.

Diane Dalecki (BME) was elected to a two-year term as Vice Chair of the Bioeffects Committee of the American Institute of Ultrasound in Medicine (AIUM). The AIUM Bioeffects Committee provides information and guidance to the AIUM on matters relating to the biological effects and safety of ultrasound.

Deborah Rubens was appointed to the Board of Trustees for the American Registry of Radiologic Technologists (ARRT), which registers and certifies 350,000 imaging technologists in the United States including Ultrasound (US), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), Nuclear Medicine and Radiation Therapy. She will serve a four year term with the specific responsibility as liaison to ultrasound.

Marvin Doyley (ECE) was promoted to a secondary appointment as Associate Professor of Biomedical Engineering. Professor Doyley holds a primary appointment as Associate Professor of Electrical and Computer Engineering.

Courtney R. Nielsen joined the RCBU and the Department of Biomedical Engineering at the University of Rochester as the communications specialist in June of 2015. She was previously the assisant director of communications at the University of Virginia School of Engineering.

Robert C. Waag Retires after 45-Year Career in Biomedical Ultrasound Research

Robert C. Waag, the Arthur Gould Yates Professor of Engineering, professor of electrical and computer engineering, and professor of imaging sciences, retired on June 30, 2015.

Born in Pennsylvania, Professor Waag attended Cornell University, where he received BEE and MS degrees in electrical engineering and a PhD degree in communications engineering in 1961, 1963, and 1965, respectively. After being awarded his doctoral degree, he served as an officer in the United States Air Force.

In 1969, Professor Waag joined the faculty at the University of Rochester as assistant professor of electrical engineering. His academic career continued here with a joint appointment in the Department of Radiology in 1973 and promotions to associate professor in 1975, professor in 1985, and the Arthur Gould Yates Professor of Engineering in 1994. During his early years at Rochester, Professor Waag was introduced to the field of diagnostic ultrasound, which was to be the major field of his academic work for decades to come.

For more than 45 years, Professor Waag worked at the leading edge of research in medical 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.

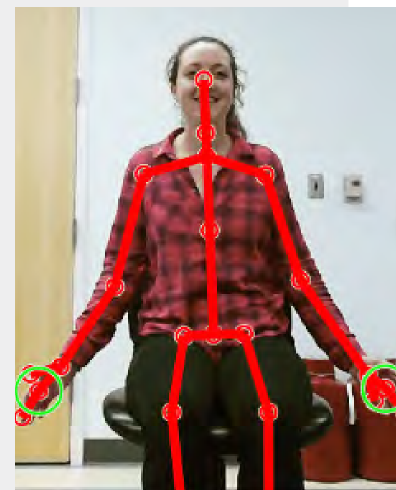
He has received awards from the Radiological Society of North America, National Institutes of Health, World Federation for Ultrasound in Medicine and Biology, Alexander von Humboldt Foundation, the American Institute of Ultrasound in Medicine, and the Japan Society of Ultrasonics in Medicine. He served as a visiting professor at Ruhr-Universität Bochum in Germany, University of Paris, Tokyo Institute of Technology, and Ecole Supérieure de Physique et de Chemie Industrielles de laVille de Paris.

Professor Waag held leadership positions in the American Institute of Ultrasound in Medicine and the Institute of Electrical and Electronics Engineers. He is a fellow of the Acoustical Society of America, the Institute of Electrical and Electronics Engineers, and the American Institute of Ultrasound in Medicine. He is also a member of Eta Kappa Nu, Tau Beta Pi, Phi Kappa Phi, and Sigma Xi.

Professor Waag served on the editorial boards of the Journal of Clinical Ultrasound, Journal of Ultrasound in Medicine, Journal of Ultrasound in Medicine and Biology, and IEEE Transactions on Biomedical Engineering. In 1975, he coedited, with Raymond Gramiak, one of the earliest textbooks in the ultrasound field, Cardiac Ultrasound. He has since authored or coauthored many publications in premier peer-reviewed archival journals, presented numerous lectures at international conferences, collaborated with professionals across the globe, and guided many graduate students. He holds two U.S. patents.

EDUCATION

ULTRANOMICS SENIOR DESIGN TEAM



BME seniors gain real-world experience with solving biomedical engineering problems through the two-semester Senior Design course taught by RCBU member **Amy Lerner** and Scott Seidman. 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 senior design team consisted of BME students Mary Bucklin, Gregory Palis, Megan Routzong, and Yanwen Zhai. In the 2014-2015 academic year, another senior design team undertook a project to develop an ultrasound-based technique to detect dental cracks in teeth. RCBU Director **Diane Dalecki** supervised these projects.

UR RANKED AMONG BEST BME GRADUATE PROGRAMS ACCORDING TO STUDENT REVIEWS

The UR Biomedical Engineering Department was ranked 16th on the Graduate Programs Fall 2015 Rankings of Top Biomedical Engineering Graduate Programs. This list highlights the best graduate programs in the country in a variety of disciplines based solely on the ratings and reviews from current or recent graduate students posted on graduateprograms.com. The rankings encompass reviews posted by more than 75,000 students participating in over 1,600 graduate programs nationwide.

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

Steven Huntzicker received his Ph.D. in Electrical and Computer Engineering from the University of Rochester. His thesis, titled "Quantitative Vascular Elastography: Stiffness and Stress Estimation for Identifying Rupture-Prone Plagues," was supervised by **Professor Marvin Doyley.**

Jonathan Langdon received his Ph.D. in Biomedical Engineering from the University of Rochester. His thesis, titled "Development of Single Track Location Shear Wave Viscoelasticity Imaging for Real-Time Characterization of Biological Tissues," was supervised by **Professor Stephen McAleavey**.

Alex Partin received his Ph.D. in Electrical and Computer Engineering from the University of Rochester. His thesis, titled "Shear Wave Imaging and Tissue Characterization using Vibration Elastographic Techniques," was supervised by **Professor Kevin Parker**.

Alexander Bensch received his M.S. in Computer Engineering from the Rochester Institute of Technology. His thesis, titled "Toward Real-Time Video-Enhanced Augmented Reality for Medical Visualization and Simulation," was supervised by **Professor Cristian Linte**.

Ying-Ju Chu received her M.S. in Biomedical Engineering from the University of Rochester. Her thesis, titled "Development of Crawling Wave Optical Coherence Elastography," was co-supervised by **Professor Kevin Parker** and Professor Jannick Rolland.

Aditya Daryanani received his M.S. in Computer Engineering from the Rochester Institute of Technology. His thesis, titled "Left Ventricle Myocardium Segmentation from 3D Cardiac MR Images using Combined Probabilistic Atlas and Graph Cut-based Approaches," was supervised by **Professor Cristian Linte**.

David Narrow
Sonavex CEO

UR BME ALUMNUS IS CO-FOUNDER OF SONAVEX, INC.

David Narrow, an alumnus of the University of Rochester Biomedical Engineering program (2012) and co-founder and CEO of Sonovex, was named one of Forbe's Magazine's "30 under 30" entrepreneurs in the health care industry in 2015. Sonovex has developed its EchoSure system to facilitate ultrasound monitoring of clot formation in arteries or veins after reconstructive, transplant, or vascular surgery procedures. The EchoSure system combines a bioabsorbable polymeric implant (EchoMark) placed underneath at-risk blood vessels at the time of surgery, and ultrasound software (EchoFind) to quantify blood flow within the target vessels. Blood flow information provided by the EchoSure system assists in early clot detection. Narrow also runs MonoMano Cycling, a company that makes bikes suited for stroke survivors, amputees and others with disabilities.

SONAVEX

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.

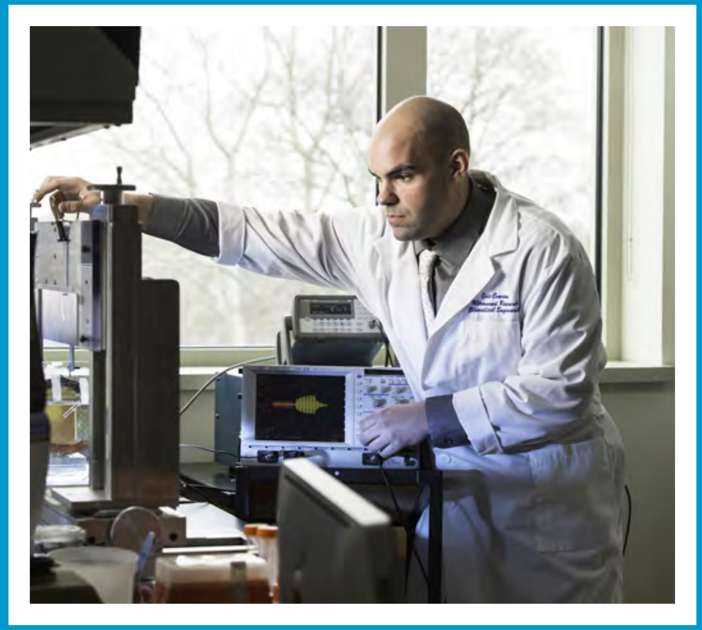
Nonlinear Finite Element Analysis

(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.

STUDENT FELLOWSHIPS



Eric Comeau was the recipient of an American Heart Association Pre-Doctoral Fellowship. This prestigious two-year fellowship will support Eric's research focused on developing new ultrasound-based technologies for cell patterning and microvessel network formation within three-dimensional, engineered tissue constructs. Eric is a Ph.D. candidate in the Department of Biomedical Engineering, and his research is co-mentored by **Professor Diane Dalecki** and **Professor Denise Hocking**.

Tristan Ford was the recipient of a Xerox Undergraduate Research Fellowship. Tristan is a BME undergraduate student working in the laboratory of **Professor Diane Dalecki** on a project focused on acoustic streaming. The Xerox Undergraduate Fellowship is a highly selective program that provides research experience for undergraduates during the summer and continuing through the academic year.

Alexander Dawson-Elli received an SPIE Medical Imaging Undergraduate Student Fellowship from the International Society of Optics and Photonics–SPIE Medical Imaging Symposium. Alexander's research was supervised by **Professor Cristian Linte**.

SELECTED PUBLICATIONS

Barry C, Hazard C, Hah Z, Cheng G, **Partin A**, Mooney RA, Chuang K, Cao W, **Rubens DJ**, Parker KJ. Shear wave dispersion in lean versus steatotic rat livers. J Ultrasound Med, 34:1123-1129; 2015.

Batchu S, Xia J, Ko KA, **Doyley MM**, Abe J, Morrell CN, Korshunov VA. Axl modulates immune activation of smooth muscle cells in vein graft remodeling. Am J Physiol Heart Circ Physiol, 309:H1048-H1058; 2015.

Camp JJ, **Linte CA**, Rettmann ME, Sun D, Packer DL, Robb RA, Holmes III DR. The effect of elastic modulus on ablation catheter contact area. SPIE Medical Imaging – Image-guided Procedures, Robotic Interventions and Modeling, 9415: 941506-1-8; 2015.

Carstensen EL, Parker KJ. Oestreicher and elastography. J Acoust Soc Am, 138:2317-2325; 2015.

Cuckle H, Platt LD, **Thornburg LL**, Bromley B, Fuchs K, Abuhamad A, Benacerraf B, Copel JA, Depp R, D'Alton M, Goldberg J, Okeeffe D, Spitz J, Toland G, Wapner R. Nuchal translucency quality review (NTQR) program: First one and half million results. Ultrasound in Obstetrics & Gynecology, 45:199-204; 2015.

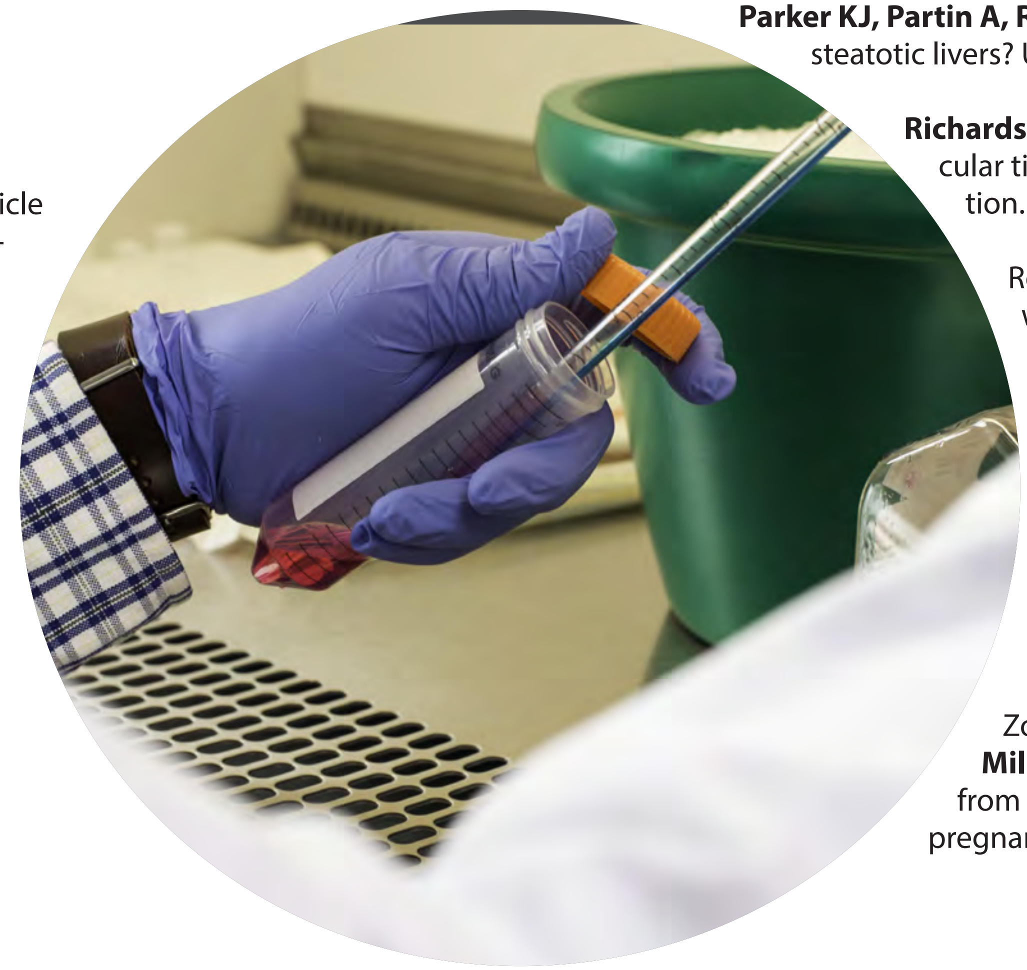
Dalecki D, Hocking DC. Ultrasound technologies for biomaterials fabrication and imaging. (Invited for Special Issue on Scaffolds for Regenerative Medicine) Annals of Biomedical Engineering, 43:747-761; 2015.

Dangi S, Ben-Zikri, YK, Lamash Y, **Schwarz KQ, Linte CA.** Automatic LV feature detection and blood-pool tracking from multi-plane TEE time series. Functional Imaging and Modeling of the Heart. Lect Notes Comput Sci, 9126:29-39; 2015.

Dangi S, Ben-Zikri YK, **Schwarz KQ**, Cahill N, **Linte CA.** Endocardial left ventricle feature tracking and reconstruction from tri-plane TEE data for computer-assisted image guidance and cardiac function assessment. Proc. SPIE Medical Imaging – Image-Guided Procedures, Robotic Interventions and Modeling, 9415:941505-1-9; 2015.

Langdon JH, Elegbe E, McAleavey SA. Single tracking location acoustic radiation force impulse viscoelasticity estimation (STL-VE): A method for measuring tissue viscoelastic parameters. IEEE Trans Ultrason Ferroelect Freq Control, 62:1225-1244; 2015.

Linte CA. Virtual and augmented medical imaging environments: Applications to simulation, training, surgical planning and interventional guidance. In Computation Vision and Medical Image Processing V–Tavares & Jorge Editors. Taylor & Francis Group, London.



Linte CA, Camp JJ, Augustine K, Holmes III DR, Robb RA. Virtual platform for spine surgery planning: Initial assessment and clinical experience. J of Computer Meth Biomech Biomed Engin: Imaging & Visualization, 3:204-12; 2015.

McAleavey SA, Osapoetra LO, Langdon J. Shear wave arrival time estimates correlate with local speckle pattern. IEEE Trans Ultrason Ferroelect Freq Control, 62:2054-2067; 2015.

Mercado KP, Helguera M, Hocking DC, Dalecki D. Noninvasive quantitative imaging of collagen microstructure in three-dimensional hydrogels using high-frequency quantitative ultrasound. Tissue Engineering, Part C: Methods, 21:671-682; 2015.

Mercado KP, Langdon J, Helguera M, McAleavey SA, Hocking DC, Dalecki D. Scholte wave generation during single tracking location acoustic radiation force impulse imaging of engineered tissues. J Acoust Soc of Am, 138:EL138-EL144; 2015.

Parker KJ. Could linear hysteresis contribute to shear wave losses in tissues? Ultrasound Med Biol, 41:1100-1104; 2015.

Parker KJ. Experimental evaluations of the microchannel flow model. Phys Med Biol, 60:4227-4242; 2015.

Parker KJ, Partin A, Rubens DJ. What do we know about shear wave dispersion in normal and steatotic livers? Ultrasound Med Biol, 41:481-1487; 2015.

Richards MS, Perucchio R, Doyley MM. Visualizing the stress distribution within vascular tissues using intravascular ultrasound elastography: A preliminary investigation. Ultrasound Med Biol, 41:1615-1631; 2015.

Rojas R, **Ormachea J**, Salo A, Rodriguez P, **Parker KJ, Castaneda B.** Crawling waves speed estimation based on the dominant component analysis paradigm. Ultrason Imaging, 37:341-355; 2015.

Rojas KD, Montero ML, Yao J, Messing E, Fazili A, Joseph J, Ou Y, **Rubens D, Parker K**, Davatzikos C, **Castaneda B.** Methodology to study the 3D spatial distributions of prostate cancer and their dependence on clinical parameters. J Med Imaging. 2:037501-1–037502-13; 2015.

Thompson JP, **Bhatt S, Rubens D.** Identify before orchiectomy: Segmental testicular infarct. Ultrasound Quarterly, 31:198-201; 2015.

Zozzaro-Smith PE, Bushway ME, Gerber SA, Herbert D, **Pressman EK**, Lord EM, **Miller RK**, Murphy SP. Whole mount immunofluorescence analysis of placentas from normotensive versus preeclamptic pregnancies. Placenta, 36:1310-1317; 2015.

SELECTED PRESENTATIONS

Ben-Zikri K, **Helguera**, Fetzer D, Chittajallu D, Aylward S, Niethammer M, Cahill N. Longitudinal registration of ground glass opacity lesions in CT scans. International Symposium on Biomedical Imaging (ISBI), April 2015.

Chimenti RL, Flemister AS, Ketz J, Bucklin M, **Buckley MR**, **Richards MS**. Ultrasound strain mapping for measuring Achilles tendon compression in patients with insertional Achilles tendinopathy. International Tissue Elasticity Conference, Verona, Italy, September 2015.

Comeau ES, Hocking DC, Dalecki D. Designing ultrasound fields to control the morphology of engineered microvessel networks. 169th Meeting of the Acoustical Society of America, Pittsburgh, PA, May 2015.

Comeau ES, Vander Horst M, Raeman CH, Hocking DC, Dalecki D. Using acoustic fields to pattern cells or microparticles in collagen hydrogels in situ. Annual Meeting of the Biomedical Engineering Society, Tampa, FL, October 2015.

Comeau ES, Dalecki D, Hocking DC. Acoustic fields as a tool for fabricating three-dimensional microvascular networks. Annual Meeting of the Biomedical Engineering Society, Tampa, FL, October 2015.

Dalecki D, Comeau ES, Hocking DC. Applications of acoustic radiation force for microvascular tissue engineering. Presented at the 169th Meeting of the Acoustical Society of America, Pittsburgh, PA, May 2015.

Dalecki D, Hocking DC. Guiding tissue regeneration in vitro and in vivo with ultrasound technologies. SPIE–Defense and Security: Micro- and Nanotechnology Sensors, Systems, and Applications Conference, Baltimore, MD, April 2015.

Gomez CK, Sidhu R, **Bhatt, Rubens DJ.** Multimodality approach to cystic lesions in the pelvis: What to do and when. Radiological Society of North America 101st Scientific Assembly and Annual Meeting, Chicago, IL, December 2015.

Gray LG, Seligman N, **Ozcan ST**, Berghella V. Transvaginal cervical length ultrasound: A cost analysis of screening and treatment strategies in high-risk women. Society of Maternal-Fetal Medicine. San Diego, CA, February 2015

Gray L, Mongelli M, **Thornburg LL**, Mack L, Glantz JC, **Pressman EK, Ozcan TO.** Prediction of macrosomic new-born from ultrasound biometry and maternal characteristics. ISOUG, October 2015.

Gray L, Mongelli M, **Thornburg LL**, Mack L, Glantz JC, **Pressman EK**, **Ozcan TO.** Prediction of small for gestational age (SGA) newborn from ultrasound biometry and maternal characteristics. ISOUG, October 2015.

Glantz J. Completed sonographic anatomic surveys: The exception rather than the rule. Society for Maternal-Fetal Medicine, San Diego, CA, February 2015.

Hocking DC, Dalecki D. Ultrasound technologies for the fabrication of artificial microvascular networks. 44th Annual Symposium of the Ultrasonic Industry Association, Washington DC, April 2015.

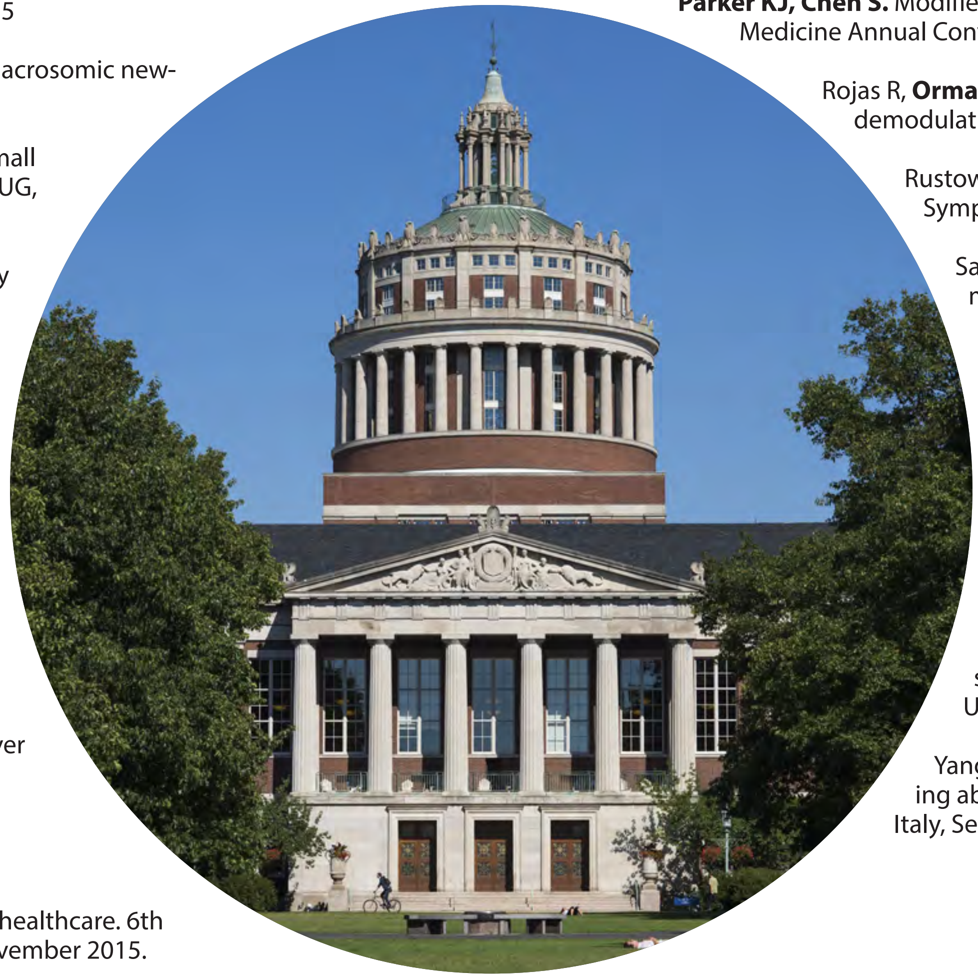
Kessler A, **Rubens DJ, Bhatt S,** Sasson T. Multimodal approach to AV fistulas and grafts: Interpretation and pitfalls. Radiological Society of North America 101st Scientific Assembly and Annual Meeting, Chicago, IL, December 2015.

Langdon J, Mercado K, Dalecki D, McAleavey S. Compensating for Scholte waves in single tracking location shear wave elasticity imaging. 169th Meeting of the Acoustical Society of America, Pittsburgh, PA, May 2015.

Langdon J, Osapoetra L, Ford T, **Elegbe E, McAleavey S**. Comparison and analysis of multiple tracking location and single tracking location shear wave elasticity imaging in a rat model of liver fibrosis. BMES Annual Meeting, Tampa, FL, October 2015

Linte CA. Minimally invasive surgery & therapy revisited: Tools for virtual visualization and guidance. IET Annual Healthcare Technologies Lecture, London, UK, November 2015.

Linte CA. Multi-modality medical imaging applications and computer/information science for healthcare. 6th IET International Conference on Wireless, Mobile, and Multimedia-Networks. Beijing, China, November 2015.



Linte CA. Patient-specific multi-modality visualization environments for minimally invasive image-guided interventions. 5th ECCOMAS Thematic Conference on Computational Vision, Visualization, and Medical Image Processing. Canary Islands, Spain, October 2015.

McAleavey SA. Using acoustic radiation force to probe tissue mechanical properties: Challenges and strategies. 169th Meeting of the Acoustical Society of America, Pittsburgh, PA, May 2015.

McAleavey SA, Langdon JH. Simulation of shear wave elasticity imaging including speckle and refraction effects. 170th Meeting of the Acoustical Society of America, Jacksonville, FL, November 2015.

Nayak R, Huntzicker SJ, Ohayon J, Schifitto G, **Doyley MM**. Visualizing principal strains of the common carotid artery using plane wave imaging. International Tissue Elasticity Conference, Verona, Italy, September 2015.

Nayak R, **Verma P**, Ahmed R, **Carson N, Dogra V**, Singh M, Maggirwar S, Schifitto G, **Doyley MM**. Visualizing principal strains of the common carotid artery using plane wave imaging. University of Rochester Center for AIDS Research World AIDS Day Scientific Symposium, Rochester, NY, December 2015.

Osapoetra LO, Langdon JH, McAleavey SA. On the use of local speckle field as a correction factor for shear modulus estimates based on multiple-track-locations methods. 169th Meeting of the Acoustical Society of America, Pittsburgh, PA, May 2015.

Parker KJ. What do we know about shear wave dispersion in normal and steatotic livers? American Institute of Ultrasound in Medicine Annual Convention, Orlando, FL, March 2015.

Parker KJ. A microchannel flow model for soft tissues. American Institute of Ultrasound in Medicine Annual Convention, Orlando, FL, March 2015.

Parker KJ, Chen S. Modified apodization functions for superresolution imaging. American Institute for Ultrasound in Medicine Annual Convention, Orlando, FL, March 2015.

Rojas R, **Ormachea J, Parker KJ**, **Castaneda B.** Shear wave estimation using null space pursuit and AM-FM demodulation. IEEE International Ultrasonics Symposium, Taipei, Taiwan, October 2015.

Rustowicz R, Iafrati M, **Helguera M**. Remotely accessible microscope (RAM). Rochester Global Health Symposium & UNYTE Scientific Session, May 2015.

Sasson T, Gilani S, Brhel D, Mitra S, Foster T, Kashyap R, Wing R, **Rubens DJ**, Waldman DL. Assisted maturation for dialysis access: Are the ends worth the means? A retrospective analysis of our institutional experience. Society of Interventional Radiology 40th Annual Meeting, Atlanta, GA, March 2015.

Torres G, **Ormachea J**, Lavarello R, **Parker KJ, Castaneda B.** Effects of data acquisition parameters on the quality of sonoelastographic imaging. 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Milano, Italy, August 2015.

Torres G, **Parker KJ, Castaneda B**, Lavarello R. Effects of aberration in crawling wave sonoelastography. IEEE International Ultrasonics Symposium, Taipei, Taiwan, October 2015.

Vander Horst M, Comeau ES, Hocking DC, Dalecki D. Development of a dual transducer system for ultrasound standing wave field-induced particle banding. 29th Annual National Undergraduate Research Conference (NCUR), Eastern Washington University, WA, April 2015.

Yang L, Johnson CC, Couper N, Zarras B, Mix DS, **Richards MS.** Ultrasound elastography for assess-ing abdominal aortic aneurysmal rupture risk. International Tissue Elasticity Conference, Verona, Italy, September 2015.

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.
Ruth Chimenti, Ph.D.
Eric Comeau, M.S.
Diane Dalecki, Ph.D.
Jonathan Langdon, Ph.D
Amy Lerner, Ph.D.
Stephen McAleavey, Ph.D.
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Carol Raeman, A.A.S.
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Sherry Steinmetz, R.D.M.S.

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Mitra Azadniv, Ph.D.

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Robert Waag, Ph.D.

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Sheryl Gracewski, Ph.D.
Renato Perucchio, Ph.D.

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Richard Miller, M.D.
Tulin Ozcan, M.D.
Eva Pressman, M.D.
James Woods, M.D.

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Denise Hocking, Ph.D.

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Michael Richards, Ph.D.

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Jean Joseph, M.D.
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Jeanne O'Brien, M.D.

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Rochester General Hospital

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Rochester Institute of Technology

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Navalgund Rao, Ph.D.

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Daniel Phillips, Ph.D.

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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 complements 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 the new Goergen Hall include an ultrasound teaching laboratory, imaging and bioinstrumentation equipment, cell and tissue culture facilities, biomedical microscopy equipment, and mechanical testing apparatus. For more information, contact Diane Dalecki at ddalecki@ur.rochester.edu.

RESEARCH AREAS

- Lithotripsy
- Acoustic cavitation
- Harmonic imaging
- Nonlinear acoustics
- Diagnostic imaging
- Doppler ultrasound
- Tissue characterization
- High frequemcy 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

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