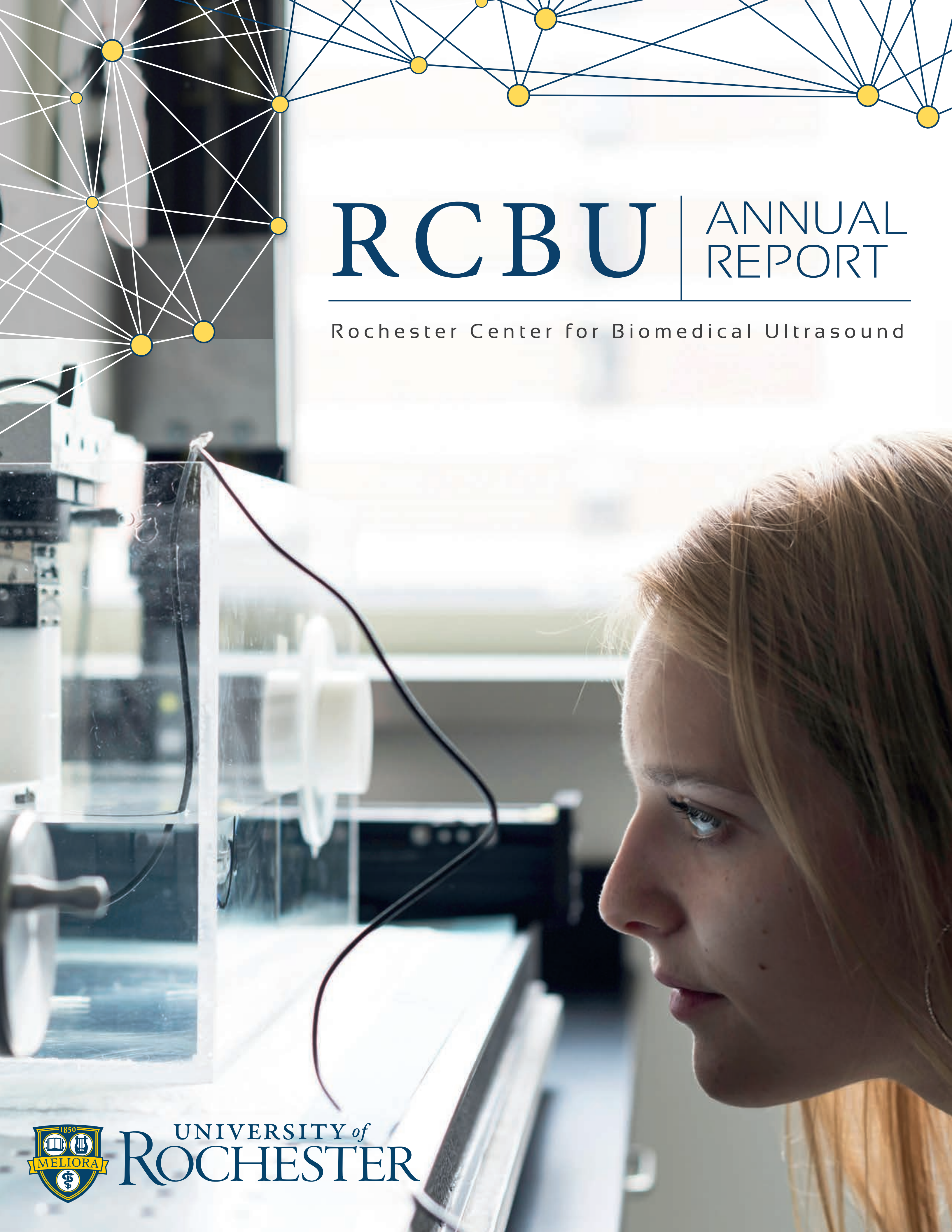


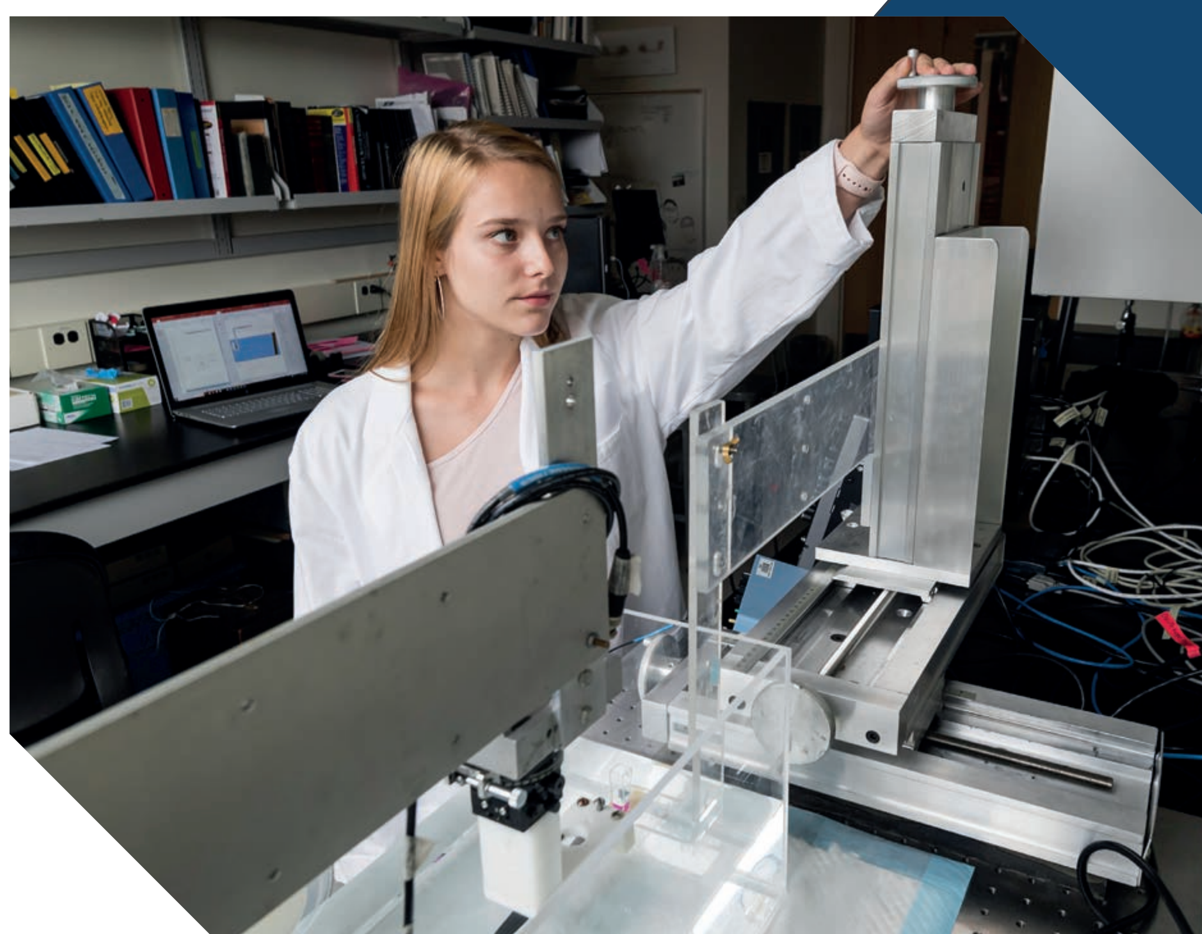
RCBU | ANNUAL REPORT

Rochester Center for Biomedical Ultrasound

UNIVERSITY *of* ROCHESTER

on the COVER

Alyssa Garvin ('21) is a rising senior from Greenfield, Massachusetts. In these photos, she is working in Professor Diane Dalecki's lab on a project that uses ultrasound standing wave fields to non-invasively pattern cells or particles in hydrogels. This project contributes to advancing a novel ultrasound-based technology for fabricating vascularized engineered tissue constructs.



RCBU Annual Report Contents

message from the directors

Although delivery of this report has been delayed due to the pandemic, I am delighted to share with you the latest updates from the Rochester Center for Biomedical Ultrasound (RCBU). This annual report summarizes progress in research, education, and innovation from the RCBU. RCBU laboratories are advancing biomedical ultrasound for imaging and therapy across diverse areas, such as novel elastography techniques, contrast agents, nonlinear acoustics, ultrasound technologies for regenerative medicine, quantitative ultrasound including the new H-scan technique, and therapeutic ultrasound (pg. 25-33).

The 2019 RCBU Biomedical Ultrasound Symposium Day (pg. 8-13) was a resounding success! This annual symposium showcases advances in ultrasound research and technology, fosters collaborations, and provides a platform for trainees to present their research and network with other scientists, engineers, and clinicians. The Distinguished Edwin L. Carstensen Lecture is a highlight of this event, and this year's lecture was delivered by Michael Bailey, Ph.D. and titled, "Improving Urinary Stone Lithotripsy: One Outgrowth of RCBU Research." The symposium also featured the Distinguished RCBU Alumni Lecture, presented by Benjamin Castaneda Aphan, PhD from Pontificia Universidad Catolica del Peru. A particularly special event at the symposium this year was the announcement of the new endowed Kevin J. Parker Distinguished Professor, and I was honored and humbled to be installed as the first recipient of this professorship (pg.14-15). The RCBU Biomedical Ultrasound Symposium Day was inspired and enabled by the Edwin and Pam Carstensen Family Endowment (pg. 11), which honors the legacy of Ed Carstensen and ensures that his vision for the RCBU endures.

In 2019, we welcomed a new president of the University of Rochester, Sarah Mangelsdorf, and look forward to her leadership (pg. 6-7). This report also summarizes funding news, awards and achievements of RCBU investigators (pg. 21-24), and includes a list of selected patents by RCBU members in areas of biomedical ultrasound (pg. 34-35). The RCBU provides exciting opportunities for education in biomedical ultrasound, and our student members are a vibrant component of the RCBU! Included within this report are awards and fellowships garnered by RCBU student members, highlights of student research, and educational advances by RCBU members (pg. 16-20). Collaborative projects between RCBU clinicians, engineers, and scientists continue to fuel new discoveries in diagnostic and therapeutic applications of ultrasound.

This was an exciting year of research, education, and innovation at the RCBU! Please stay safe and healthy through the coming year.

Diane Dalecki, Ph.D.
RCBU Director

Ultrasound continues to grow at the University of Rochester Medical Center; by the end of 2019 we are now at 48,439 exams for the Imaging Sciences Department, up from 37,360 2018. Our clinical enterprise includes Strong Memorial Hospital and Strong West, and out-patient sites at East River Road and at Penfield. Our affiliate hospitals, Highland Hospital, F.F. Thompson in Canandaigua, Auburn Hospital, Noyes Hospital in Dansville and Saint James in Hornell, are also running busy ultrasound programs, as is the Women's Breast Imaging at Red Creek and our associates at University Medical Imaging. All together these combined facilities perform well over 100,000 ultrasound examinations/year.

Locally Dr. Rubens presented "Ultrasound in Oncology at the Rochester Ultrasound Society Annual RIT Symposium in June. On the national level Drs. Dogra, Oppenheimer Rubens and Sidhu presented multiple lectures, workshops, posters and papers at the Society of Abdominal Radiology, the American Institute of Ultrasound in Medicine, the American Roentgen Ray Society, the Society of Radiologists in Ultrasound and the Radiologic Society of North America. Dr. Rubens continues as faculty for the American Institute of Radiologic Pathology (AIRP), which offers five courses annually for radiology residents and practitioners from throughout the United States, Canada and International attendees. In 2019 this included lectures in Vienna, Madrid, Paris and Lisbon. She also directs the Ultrasound Case Based Review course for the Radiologic Society of North America and participates on the ACR Ultrasound Commission. Dr. Dogra continues his efforts with Medical Imaging Partnership, delivering ultrasound equipment and training in underserved areas throughout the world.

Dr. Dogra continues his research investigation of thyroid cancer using photoacoustic imaging. He is editor-in-chief of the Journal of Clinical Imaging Science (JCIS) (https://clinicalimagingscience.org) and also of the American Journal of Sonography (https://Americanjs.com). Dr. Avice O'Connell continues her project entitled "Breast Ultrasound Image Review with Assistance of Deep Learning Algorithms", sponsored by Samsung. Dr. Thomas Marini and Dr. Kate Kaproth-Joslin continue their collaboration with Professor Benjamin Castaneda to deliver ultrasound diagnosis of pneumonia in rural settings. Drs. Rubens, Oppenheimer Marini (Imaging Sciences), Drennan and Toscano (Obstetrics/MFM) and Prof. Castaneda are reviewing pilot data from a telediagnostic ultrasound system in rural Peru where non-medical personnel acquire programmatic volume sweep imaging of thyroid, abdomen or fetal ultrasounds and transmit them for remote interpretation.

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

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 page 34 and 35 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.

The University's first woman president

New president Sarah Mangelsdorf praised by University community

"We were in contact with more than 200 people in developing the pool of possible candidates to find the very best person to be the next president of the University of Rochester. I am thrilled that Sarah Mangelsdorf is that leader. Sarah is a super smart, empowering, compassionate, and kind leader, is expert at managing complexity and overcoming challenges, and will work tirelessly in tandem with our students, faculty, staff, and trustees to make the University of Rochester the best it can be."
-University of Rochester Board Chair Richard Handler

Sarah C. Mangelsdorf became the University of Rochester's eleventh president on July 1, 2019. In her inauguration address, she spoke of the importance of universities and the gravity of her role in continuing the path set by her predecessors. She also emphasized the need for inclusion and openness to people from all backgrounds, and the need for the University to engage and support not just the local community, but communities across the globe where students and faculty are working and studying.

Mangelsdorf, a developmental psychologist with a significant research portfolio, is known for her collaborative and inclusive approach to leadership. The arrival of such a president is a reflection of the search process that brought her here.

Trustees Cathy Minehan '68 and Danny Wegman led a search committee that developed a job description based on numerous town halls with faculty, staff, and students, as well as a University-wide survey seeking the characteristics community members wanted in the next president. Faculty, staff, and student advisory committees were integrated into the search process as well.

Mangelsdorf has earned recognition for her leadership roles with each of those constituencies throughout her career.

"THE UNIVERSITY OF ROCHESTER IS A VERY SPECIAL PLACE, AND I AM TERRIBLY HONORED TO BE TRUSTED WITH ITS STEWARDSHIP AND ITS CONTINUED FORWARD TRAJECTORY."
-SARAH MANGELSDORF, UNIVERSITY PRESIDENT

As the former provost of the University of Wisconsin-Madison, she comes with sterling credentials as a manager of large and complex institutions, and a deep understanding of how to help advance a university's research mission across disciplines. She has also been a recognized leader in fostering institutional diversity and inclusion, and access and affordability for undergraduate students in particular.

Among those who played a role in the search process was Sarah Walters, a doctoral student in optics. Walters cochaired the Student Advisory Committee, made up of undergraduate, graduate students, and postdocs across schools and units of the University.

"You can tell she is a genuine person of high integrity, and she'll be all in and 100 percent invested," said Walters. "She'll pour her heart and soul into this University."

And faculty can claim her as one of their own. Mangelsdorf, a self-described "third-generation academic," continues to embrace her role as a faculty member and comes with an appointment as a professor in the Department of Clinical and Social Sciences in Psychology. So, too, does her husband, fellow developmental psychologist Karl Rosengren, who has a joint appointment with the Department of Brain and Cognitive Sciences.

In her introductory remarks, Mangelsdorf highlighted her appreciation for the role that research universities play in the lives of faculty, students, alumni, and staff, as well as in their home communities and in the larger society.

"Higher education should and does change people's lives," she said, noting that the scientific discoveries, clinical treatments, humanistic scholarship, and performing and visual arts that grow out of academic communities enrich the experiences of people well beyond campus.

Mangelsdorf's experience at Wisconsin working with a major academic health center makes her particularly suited to leading Rochester, said Mark Taubman, dean of the School of Medicine and Dentistry and chief executive officer of the Medical Center.

"I think she has a wonderful sense of what it means to be a research-intensive university," Taubman told the Democrat and Chronicle. "She has, I think, a very good understanding of what some of the challenges are for supporting research in the current environment, the importance of research in terms of the reputation of the institution and also for what it does nationally."

Jeffrey Tucker, an associate professor of English and a member of the University Advisory Committee, said it became clear during the process that Mangelsdorf was the ideal choice. "We asked, 'what personal characteristics are you looking for?' The top answers were 'trustworthiness, integrity, and collegiality.' All of those traits are evident in Sarah."

About President Mangelsdorf

An experienced academic leader, Mangelsdorf served as provost at the University of Wisconsin–Madison before coming to Rochester. She is a professor of psychology who is internationally recognized for her research on social and emotional development. President Mangelsdorf is known for her work on issues of academic quality, educational access, and diversity and inclusion at some of the nation's leading public and private institutions.

Professor Diane Dalecki hands the University mace to Sarah Mangelsdorf, the 11th University president, at the inauguration ceremony on October 4. The presentation of the mace, a four-foot-long, 6.4 pound silver and mahogany staff, is a centerpiece of the investiture, and a ritual to mark the entrustment of authority to the new president.

Contributing authors: Jim Mandelaro, Karen McCally, and Lindsey Valich

The RCBU Biomedical Ultrasound Symposium is an annual day devoted to sharing advances in biomedical ultrasound. The symposium is designed to showcase ultrasound research, foster collaboration, and provide a platform for trainees to present their research and connect with scientists, engineers, and clinicians from Rochester, other institutions, and industry partners. The symposium features the Distinguished Edwin L. Carstensen Lecture and the Distinguished RCBU Alumni Lecture. The day's events also include special lectures, a scientific poster session, lunch, and networking. Support for the RCBU Biomedical Ultrasound Symposium Day is provided by the Edwin and Pam Carstensen Family Endowment, the Rochester Center for Biomedical Ultrasound, and the Department of Biomedical Engineering at the University of Rochester.

2019 RCBU Biomedical Ultrasound Symposium Day

Tuesday, November 7, 2019
8:00am-5:00pm

agenda

Welcome & Introduction of Distinguished Lecturer
Diane Dalecki, Ph.D.
Director, Rochester Center for Biomedical Ultrasound
Chair and Distinguished Professor of Biomedical Engineering
University of Rochester

Distinguished Edwin L. Carstensen Lecture
Improving Urinary Stone Lithotripsy: One Outgrowth of RCBU Research
Michael Bailey, Ph.D.
Center for Industrial and Medical Ultrasound, Applied Physics Laboratory
Departments of Mechanical Engineering, and Urology
University of Washington

Trainee Presentations
Moderator: Stephen A. McAleavey, Ph.D.
Associate Professor of Biomedical Engineering
University of Rochester

Clinical Challenges
Giovanni Schifitto, M.D., M.S.
Professor of Neurology, and Imaging Sciences
University of Rochester

Lunch, Scientific Posters, and Networking

Introduction of Distinguished RCBU Alumni Lecturer
Diane Dalecki, Ph.D.

Distinguished RCBU Alumni Lecture
Tele-Ultrasound Deployment in Rural Areas of Peru
Benjamin Castaneda Aphan, Ph.D.
Department of Biomedical Engineering
Pontificia Universidad Católica del Perú

Trainee Presentations
Moderator: Denise C. Hocking, Ph.D.
Professor of Pharmacology and Physiology
University of Rochester

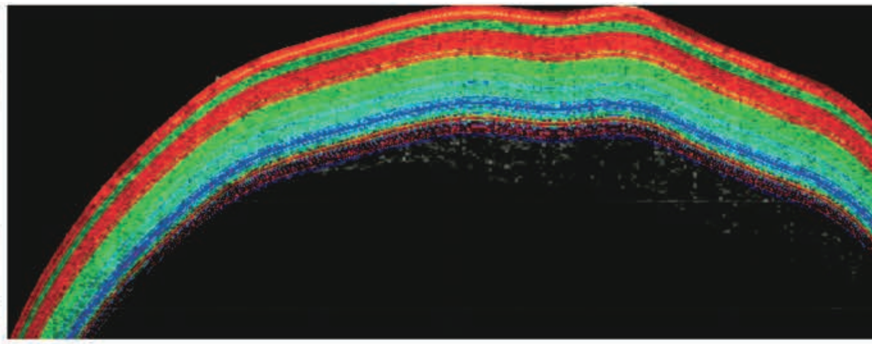
Installation of Diane Dalecki as the Kevin J. Parker Distinguished Professor in Biomedical Engineering

Poster Session, Networking, and Refreshments

Distinguished Lectures

Distinguished Edwin L. Carstensen Lecture
Improving Urinary Stone Lithotripsy: One Outgrowth of RCBU Research
Michael Bailey, Ph.D.
Center for Industrial and Medical Ultrasound, Applied Physics Laboratory
Departments of Mechanical Engineering, and Urology
University of Washington

Michael Bailey is a Senior Principal Engineer at the Applied Physics Laboratory, and Associate Professor of Mechanical Engineering and Adjunct Associate Professor of Urology at the University of Washington. His research interests include cavitation, shock wave lithotripsy, high intensity focused ultrasound, and ultrasound imaging. He is a Fellow of the Acoustical Society of America (ASA). He has served on the Board of the International Society for Therapeutic Ultrasound (ISTU), the Bioeffects Committee of the American Institute for Ultrasound in Medicine (AIUM), and the ASA Executive Council. He received the R. Bruce Lindsay Award from ASA in 2004, and the Frederic Lizzi Early Career Award from ISTU in 2008. Dr. Bailey serves as program director of an NIH NIDDK program project grant on kidney stone lithotripsy, which is entering its 25th year.



Distinguished RCBU Alumni Lecture
Tele-Ultrasound Deployment in Rural Areas of Peru
Benjamin Castaneda Aphan, Ph.D.
Department of Biomedical Engineering
Pontificia Universidad Católica del Perú

Benjamin Castaneda is Professor and Chair of Biomedical Engineering, and founder of the Medical Imaging Laboratory, at the Pontificia Universidad Católica del Perú (PUCP). Dr. Castaneda's research expertise includes quantitative elastographic imaging, computed aided diagnosis tools, and telemedicine. In 2013, Dr. Castaneda received the Academic Innovator Award from the Peruvian Government for his continuous work in the development of medical technology, and that same year, he won the Best Patent from the Peruvian Government for an automated staining system for tuberculosis detection. The same invention received a silver medal at the International Exhibition of Inventions of Geneva in 2014. Dr. Castaneda is the founder of Medical Innovation & Technology, a Peruvian start-up focused on development of telemedicine technology for rural areas. He is currently a member of the Peruvian Committee for Health.

2019 RCBU Biomedical Ultrasound Symposium Day

The RCBU Biomedical Ultrasound Symposium was funded in part by the Edwin and Pam Carstsensen Family Endowment. To contribute to the Edwin and Pam Carstensen Family Endowment, visit rochester.edu/rcbu/carstensen.html or contact Derek Swanson at derek.swanson@rochester.edu or 585.273.1341

The Edwin and Pam Carstensen Family Endowment

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

RCBU Symposium Poster Presentations

Poster Presentation Winners
(highlighted below)
1st Place: Fernando Zvietcovich
2nd Place: Melinda Vander Horst
3rd Place: Luis Eduardo Chahua Salgueran

Sparse ML Based Inverse Reconstruction for Elastography
Abrar Faiyaz, Marvin M. Doyley

Testing the Feasibility of Acoustic Patterning in the Near-field for Tissue Engineering
Alyssa Garvin, Sarah Wayson, Denise C. Hocking, Diane Dalecki

Effect of Underlying Bone on Tendon Shear Wave Elastography
Ananya Goyal, Hannah Goldring, Soumya Goswami, Rifat Ahmed, Stephen McAleavey, Mark Buckley

Ultrasound in Liquid Metals
Bitong Wang, Douglas H. Kelley, Andrew H. Caldwell, Antoine Allanore

Tendon Thickness and Impingement in Insertional Achilles Tendinopathy and the Influence of Exercise
Anthony N. Aggouras, Ruth L. Chimenti, Laura C. Slane, Michael S. Richards, Mark R. Buckley

Simulation of Multiple Tracking Location Shear Wave Elasticity Imaging Using K-Wave Toolbox
Fan Feng, Soumya Goswami, Siladitya Khan, Stephen A. McAleavey

Shear Wave Speed Estimation and Assessment of the Elasticity of the Foot Using Reverberant Fields
Fernando Gutierrez, Juvenal Ormachea, Benjamin Castaneda

Reverberant 3D Optical Coherence Elastography Maps the Elasticity of Individual Corneal Layers
Fernando Zvietcovich, Pornthep Pongchalee, Panomsak Meemon, Jannick P. Rolland, Kevin J. Parker

Characterizing Thyroid Tissue Using H-scan Ultrasound Imaging
Gary R. Ge, Rosa Laimes, Joseph Pinto, Jorge Guerrero, Himelda Chavez, Claudia Salazar, Roberto J. Lavarello, and Kevin J. Parker

An Initial Study to Evaluate Reverberant Shear Wave Generation: Analysis Applying Different Amount of External Vibration Sources at Different Locations
Gilmer Flores Barrera, Juvenal Ormachea, Benjamin Castaneda

Acoustic Patterning of Neural Cells in Hydrogels
Holly Eyrich, Denise C. Hocking, Diane Dalecki

Development of Longitudinal, Non-invasive Ultrasonography to Measure Tensile Mechanical Properties in Tendon Healing
Marlin H. Myers, Michael S. Richards, Alayna E. Loiselle

A Method for Direct Measurement of Ultrasound Contrast Agent Shell Properties
Jeff Rowan, James McGrath, Richard Waugh, Marvin Doyley

Pulsed Ultrasound for the Treatment of Chronic Wounds
Melinda A. Vander Horst, Carol H. Raeman, Diane Dalecki, Denise C. Hocking

Synthetic Transmit Focusing for High Quality Shear Wave Elasticity Imaging
Rifat Ahmed, Marvin M. Doyley

A New Deep-Learning Network for Mitigating Limited-View and Undersampling Artifacts in Ring-shaped Photoacoustic Tomography
Huijuan Zhang, Hongyu Li, Nikhila Nyayapathi, Depeng Wang, Leslie Ying, Jun Xia

Ultrasound Assessment of the Mechanical Environment in the Mouse Achilles Tendon Insertion
Keshia E. Mora, Samuel J. Mlawer, Albert Bae, Michael S. Richards, Alayna Loiselle, Mark R. Buckley

2-D Shear Wave Dispersion Images Using the Reverberant Shear Wave Field Approach: Application in Tissues Exhibiting Power Law Response
Juvenal Ormachea, Richard G. Barr, Kevin J. Parker

Pilot Testing of a Telemedicine Ultrasound System for Use in Rural Areas
Luis Chahua, Thomas Marini, Lorena Tamayo, Rosemary Quinn, Thomas Chaumont, Italo Fernandez, Jorge Guerrero, Brian Garra, Benjamin Castaneda

Obstetrics Volume Sweep Imaging: Preliminary Comparison with Traditional Obstetric Ultrasound
Joseph Salcedo, Thomas Marini, Jonah Kan, Raymond Lay, Lorena Tamayo, Timothy Baran, Miguel Egoavil, Bertha Ramos, Hubertino Diaz, Jorge Guerrero, Jorge Hurtado, Brian Garra, Benjamin Castaneda

Dual-scan Mammoscope: A Photoacoustic-based Breast Cancer Imaging System
Nikhila Nyayapathi, Huijuan Zhang, X.Cynthia Fan, Ermelinda Bonaccio, Kazuaki Takabe, and Jun Xia

Shear Wave Elasticity Imaging to Investigate the Role of Interferon Gamma on Treatment of Pancreatic Ductal Adenocarcinoma
Reem Mislati, HexuanWang, Rifat Ahmed, Bradley Mills, Scott Gerber, Marvin M. Doyley

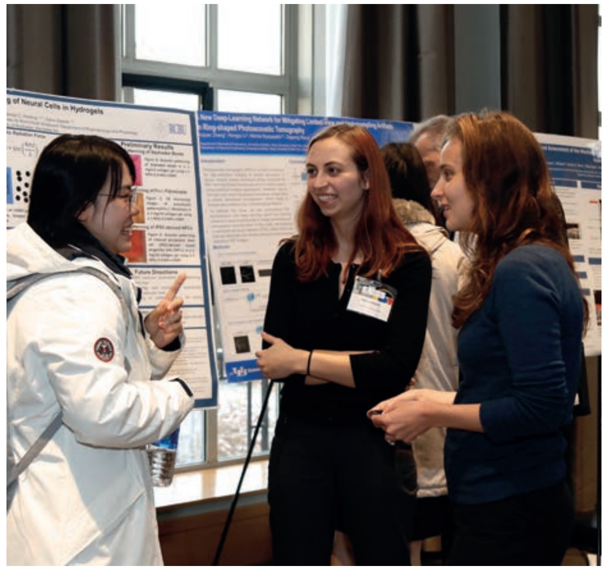
Quantitative High-Frequency Ultrasound for Characterizing Collagen Microstructure in Tendon
Sarah E. Wayson, María Helguera, Denise C. Hocking, Diane Dalecki

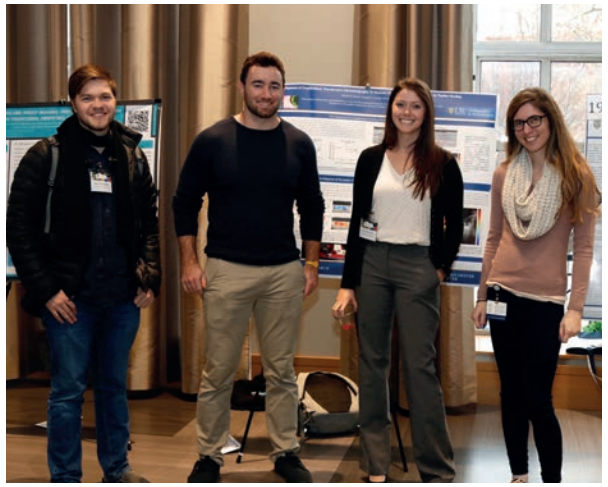
The Study of Speckle First-Order Statistics from the Fractal Branching Vasculature: Dependence on Number Density
Sedigheh S. Poul, Kevin J. Parker

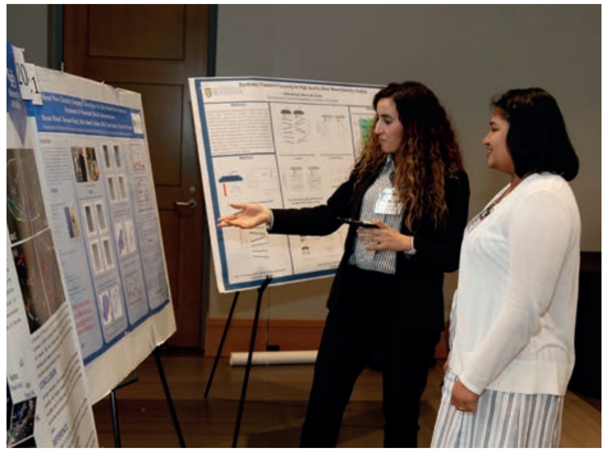
Investigating Novel Biomarkers for Ultrasound Breast Viscoelastography
Siladitya Khan, Soumya Goswami, Fang Fen, Stephen A. McAleavey

Placental Elasticity Imaging Demonstrates Feasibility of an Ultrasound-Based Method for Generation of a Placental Biomarker
Stefanie J. Hollenbach, Loralei Thornburg, Helen Feltovich, Richard K. Miller, Kevin Parker, Stephen McAleavey

Volume Sweep Imaging of the Lung: Rationale and Training Overview
Thomas Marini, Benjamin Castaneda, Timothy Baran, Rafael Ortega, Phoebe Huang, Alexander Yeo, Lorena Tamayo, Katherine Kaproth-Joslin







RCBU Symposium Graduate Student Oral Presentations

Characterizing Thyroid Tissue Using H-scan Ultrasound Imaging
Gary R. Ge, Rosa Laimes, Joseph Pinto, Jorge Guerrero, Himelda Chavez, Claudia Salazar, Roberto J. Lavarello, Kevin J. Parker

Deformation Independent Non-linear Elasticity Estimation: Studies and Implementation in Ultrasound Shear Wave Elastography
Soumya Goswami, Rifat Ahmed, Siladitya Khan, Marvin M. Doyley, Stephen A. McAleavey

Shear Wave Elasticity Imaging Can Measure Treatment Response of Pancreatic Tumors Treated with Stereotactic Body Radiation Therapy
Reem Mislati, Hexuan Wang, Bradley Mills, Rifat Ahmed, Scott Gerber, David Linehan, Marvin M. Doyley

2-D Shear Wave Dispersion Images Using the Reverberant Shear Wave Field Approach: Application in Tissues Exhibiting Power Law Response
Juvenal Ormachea, Richard G. Barr, Kevin J. Parker

Pulsed Ultrasound for the Treatment of Chronic Wounds
Melinda A. Vander Horst, Carol H. Raeman, Diane Dalecki, Denise C. Hocking

Elastic Characterization of Heterogeneous Tissues Using Longitudinal Shear Waves in Optical Coherence Elastography
Fernando Zvietcovich, Gary R. Ge, Humberto Mestre, Michael Giannetto, Maiken Nedergaard, Jannick P. Rolland, Kevin J. Parker

Monitoring the Chemotherapy Response in Metastatic Pancreatic Cancer Using Shear Wave Elastography
Rifat Ahmed, Jian Ye, Scott Gerber, Marvin Doyley

Quantitative High-Frequency Ultrasound for Characterizing Collagen Microstructure in Tendon
Sarah E. Wayson, María Helguera, Denise C. Hocking, Diane Dalecki

Elasticity Imaging of Placental Tissue Demonstrates Potential for Disease State Discrimination
Stefanie J. Hollenbach, Loralei Thornburg, Helen Feltovich, Richard K. Miller, Kevin Parker, Stephen McAleavey

"Holding a professorship that bears Kevin's name is an outstanding honor, and thoroughly humbling," said Dalecki, the newly installed Kevin J. Parker Distinguished Professor.

Pictured from left to right: Donald Hall, the Robert L. and Mary L. Sproull Dean of the Faculty of Arts, Sciences & Engineering, Diane Dalecki, the Kevin J. Parker Professor in Biomedical Engineering, Kevin J. Parker, the William F. May Professor of Engineering, and Sarah Mangelsdorf, University President

Diane Dalecki installed as Kevin J. Parker Distinguished Professor

"It's as if a number of threads are woven together today in this place, in a very wonderful way," said Parker, the William F. May Professor of Engineering and dean emeritus of engineering and applied sciences

Diane Dalecki was installed as the Kevin J. Parker Distinguished Professor in Biomedical Engineering in a ceremony that also honored the two mentors who most influenced her.

"(Edwin) Carstensen and (Kevin) Parker. Those names are simply giants in the field, and I have been so fortunate to have learned from and worked with them," Dalecki said.

The chair of biomedical engineering was praised as an outstanding researcher, educator and leader during the ceremony, which was presided over by University President Sarah Mangelsdorf and Donald Hall, the Robert L. and Mary L. Sproull Dean of the Faculty of Arts, Sciences & Engineering.

"As the department begins celebrating its 20th anniversary next year, we can have every confidence that Diane will continue to build the Department into a nationally prominent, internationally known BME program," Hall said. The ceremony was held as part of the Rochester Center for Biomedical Ultrasound Symposium Day. Carstensen, a pioneer in biomedical ultrasound, was founding director of the RCBU, followed by Parker and now Dalecki.

The endowed professorship is funded with royalties from blue noise mask, a novel half-tone imaging process that Parker co-invented with then PhD student Theophana Mitsa ("91). The royalties also provided seed money for establishing the Department of Biomedical Engineering.

'Rochester through and through'

Dalecki, who earned a BS in chemical engineering and master's and PhD degrees in electrical engineering from the University, is "Rochester through and through," Hall said.

Even before Biomedical Engineering became a department, Dalecki wrote the curriculum for what was then a fledgling interdepartmental program for undergraduates.

She was one of the department's first faculty members, oversaw its first ABET accreditation visit, and created an introductory biomedical engineering course that served as a model for similar courses now offered by all Hajim School departments.

In addition to running her own research lab, which develops novel diagnostic ultrasound techniques and new applications of ultrasound for therapy and tissue engineering, Dalecki leads a robust group of nearly 100 researchers as director of the RCBU. The center includes visiting scientists from across the country and is dedicated to advancing the use of ultrasound in diagnosis and discovering new therapeutic applications of ultrasound in medicine and biology.

On July 1, 2016 she became the second chairperson of biomedical engineering, replacing Richard Waugh.

Hall praised Dalecki's "very warm and welcoming leadership style. Her door is always open to faculty, staff and students."

"She is particularly passionate about promoting a mutually beneficial relationship with her department's 1,000 alumni – nearly all of whom she personally taught during their first year."

Dalecki described the department as "truly a home. I simply could not imagine better faculty and staff colleagues. I am proud of what we have accomplished together, and I am excited by what we will achieve together in the future."

Contributing author: Bob Marcotte

EDUCATION

High praise for Sally Child

Sally Child is not one to toot her own horn. But that's okay. Plenty of other people are more than willing to do it for her.

Drop by the annual Rochester Center for Biomedical Ultrasound (RCBU) Symposium, for example, and you will invariably hear former students, now pursuing successful careers in academia or industry, sing the praises of the senior lab associate who showed them how to do the experiments necessary for a master's or PhD thesis. Indeed, "if you talk to anyone around the world about biomedical ultrasound research, or the biological effects of ultrasound, they will know her name," says Diane Dalecki, director of the RCBU and chair of the Department of Biomedical Engineering.

And small wonder. Child's name appears on nearly 70 journal articles, including first authorship of "really seminal papers that are important for understanding how sounds interacts with tissues, and the safe use of ultrasound," Dalecki says. That's pretty impressive. Especially when you consider that Child began working at the University in 1965 without knowing "anything about engineering," she says.

Sally earned an associate degree in laboratory technology from SUNY Morrisville in June 1965. That same month she was hired to work in the lab of Edwin Carstensen, a young professor of electrical engineering who became a pioneer in the bioeffects of ultrasound and the founding director of the RCBU.

"He liked me because he could train me," Child says. "I didn't know anything about engineering, and his technician was leaving." Carstensen, she adds, "was wonderful. He was kind. He cared about you. He taught you the scientific method and anything you needed to know. And he never got mad. I almost tear up thinking about him." Women rarely worked in an engineering lab in those days. But it made no difference to Carstensen. He fully supported Child's decision to attend night classes at the University, where she received a BS in general science in 1973, and a master's degree in environmental science in 1979. "In the early years, being one of the only women in research in electrical engineering was a little intimidating," Child says. "However, Dr. Carstensen supported me in many ways and I will always be grateful."

Child's research partnership with Carstensen lasted for more than 30 years. In 2000, after Carstensen's retirement, Child became senior lab associate for Diane Dalecki, who at the time was an assistant professor in the newly-formed biomedical engineering department. During that 52-year span, Child engaged in a wide range of research. Her initial work with Carstensen, for example, included studying the dielectric properties of bacteria, erythrocytes and various solutions, and the effects of ultrasound on various other biological materials, such as plant roots, liver, and red blood cells. Later, she helped Carstensen's lab discover the effects of ultrasound and lithotripter fields on kidney and lung tissue. After joining Dalecki's lab, she contributed to a project sponsored by the Office of Naval Research to study the response of biological tissues to underwater sonar fields. More recent projects included using ultrasound to engineer microvessel networks in collagen gels, and patterning cells in 3D collagen hydrogels as part of the lab's interest in using ultrasound for tissue engineering and regenerative medicine.

Equally important has been Child's role as a mentor for dozens upon dozens of students -- an increasing number of them women -- who have worked with her in the labs. "She's a great listener," Dalecki says. "But she really wants to teach students the rigorous scientific method and how to be a good scientist. And that's important whether you're coming into a lab for the first time, or a postdoc who needs to learn new skills that the lab can offer."

Child officially "retired" two years ago. However, much as an emeritus professor might do, she still attends Dalecki's lab meetings with collaborator Denise Hocking, professor of pharmacology and physiology, and biomedical engineering. "I miss it," she says. "All in all, these past 50 or so years were great. I couldn't have asked for better PI's or better people to work with. It's been like a family." Child, as much as anyone, has helped make it so. "She has been a contributor to the department in every way-going to senior design events, pitching in to help with special events, and welcoming people who are new to the department. She's an important part of our community."

Senior design teams focus on ultrasound

Pictured from left to right: Shafieul Alam, Tiffany Nicholas, and Dominique James

Through either the BME senior design sequence or through the BME master's program in Medical Device Design, BME students partner with companies, institutions, clinicians, and/or research laboratories to solve biomedical engineering design problems. BME seniors gain real-world experiences through the two-semester Senior Design course taught by RCBU member Amy Lerner and Scott Seidman. Graduate students in the BME CMTI Master's in Medical Device Design program, led by Greg Gdowski and Amy Lerner, learn how to apply engineering principles to translate unmet clinical needs into a proven concept and prototype design.

In the 2019-2020 academic year, one team of senior BME students worked to improve ultrasound imaging. This team, with members Charles Patterson, Ananya Goyal, and Mariel Sackman, designed an ultrasound probe mounting and stabilization device for anastomosis monitoring. The faculty supervisor for this team was Professor Stephen McAleavey. The company customer for this design team was Sonavex with CEO David Narrow, a UR BME alumunus.

In the 2018-2019 academic year, three teams of BME seniors worked on ultrasound-related projects. The EchoMount Team, with members Shafieul Alam, Dominique James, Bill MacCuaig, and Tiffany Nicholas, worked on developing an ultrasound probe mounting system to enable long-term, repeatable ultrasound imaging. This team was supervised by Professor Diane Dalecki. A second team, with members Manikanta Nori, Kimberly Richards, Conor Shanahan, and Lincoln Zhao, worked to design a benchtop ultrasound phantom to mimic physiological flow in arteriovenous fistulae. This team was supervised by Professor Steve McAleavey. The company customer for both of these design teams was Sonavex.

If you are interested in becoming an industry partner or customer for the senior design program, please contact Amy Lerner (amy.lerner@rochester.edu).
To learn more about the BME Master's program in Medical Device Design, please contact Greg Gdowski (greg_gdowski@urmc.rochester.edu).

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 453) Investigates the imaging techniques applied in state-of-the-art ultrasound imaging and their theoretical bases. Topics include linear acoustic systems, spatial impulse responses, the k-space formulation, methods of acoustic field calculation, dynamic focusing and apodization, scattering, the statistics of acoustic speckle, speckle correlation, compounding techniques, phase aberration, 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.

Advanced Biomedical Optics

(BME 472) 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

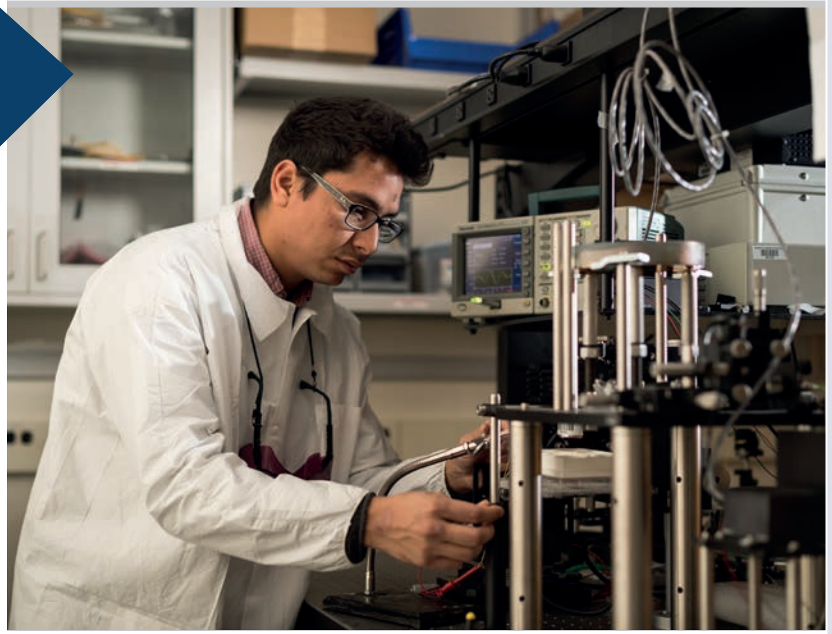
(BME 487) The theory and application of nonlinear FE methods in solid and structural mechanics, and biomechanics. Topics: review and generalization of linear FE concepts, review of solid mechanics, nonlinear incremental analysis, FE formulations for large displacements and large strains, nonlinear constitutive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

Physiological Control Systems

(BME 428) Focuses on the application of control theory to physiological systems. Presents modern control theory in the context of physiological systems that use feedback mechanisms. Begins with an overview of linear systems analysis, including Laplace transforms and transfer functions. Discusses the response dynamics of open- and closed-loop systems such as the regulation of cardiac output and level of glucose, stability analysis, and identification of physiological control systems.

Student News

Fellowships



Fernando Zvietcovich (ECE) was the recipient of the prestigious SPIE-Franz Hillenkamp Postdoctoral Fellowship in Problem-Driven Biomedical Optics and Analytics. This annual award of $75,000, supports interdisciplinary problem-driven research and provides opportunities for translating new technologies into clinical practice for improving human health. Fernando, who was co-advised by Professor Kevin Parker (ECE) and Professor Jannick Rolland (Institute of Optics), will work on translating a novel biophotonics-based optical coherence elastography (OCE) method, developed and designed for the non-invasive quantification of corneal spatial biomechanical properties in 3D, into in vivo clinical use for diagnosing and monitoring the treatment for human ocular disease. Congratulations to Fernando for receiving this prestigious award!

Sophie Mackenzie

Xerox Summer Scholarship

Supervising Professor: Mark Buckley

Project: Investigating the effects of viscoelastic heating on collagen denaturation

Alyssa Garvin

REU Health

Supervising Professor: Diane Dalecki

Project: Testing the feasibility of acoustic patterning in the near-field for tissue engineering

Kelly Lannigan

REU Health

Supervising Professors: Diane Dalecki & Denise Hocking

Project: Detecting full length and engineered fragments of fibronectin using immunocytochemistry

Mazid Muhit

Ronald E. McNair Program

Supervising Professor: Marvin Doyley

Project: Investigating the impact of acoustic scattering on the performance of shear wave elasticity imaging (SWEI)

Ananyal Goyal

Xerox Fellows Program

Supervising Professor: Mark Buckley

Project: Effect of underlying bone on tendon shear wave elastography

Kelly Merrell

NSF REU in Physical Sciences

Supervising Professor: Cristian Linte

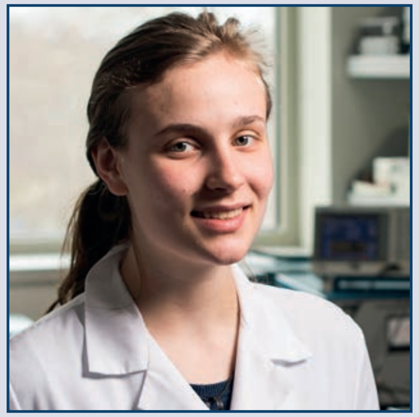
Project: Image segmentation, modeling and 3D printing for orthopedic applications

CONGRATULATIONS TO OUR RCBU STUDENTS WHO RECENTLY GRADUATED

Training Completed

Alexander Kotelsky

Alexander Kotelsky completed his Ph.D. training in Biomedical Engineering at the University of Rochester. His thesis, titled "Elucidating the Factors that Govern Vulnerability of In Situ Articular Chondrocytes to Mechanical Loading," was supervised by Professor Mark Buckley.



Emma Grygotis Norris

Emma Grygotis Norris completed her Ph.D. training in Biomedical Engineering at the University of Rochester. Her thesis, titled "Development of Acoustically-Modified Collagen-Based Biomaterials for Regenerative Medicine Applications," was supervised by Professor Denise Hocking.

Juvenal Ormachea

Juvenal Ormachea completed his Ph.D. training in Electrical and Computer Engineering at the University of Rochester. His thesis, titled "Viscoelastic Tissue Characterization Based on Harmonic and Transient Shear Wave Elastography," was supervised by Professor Kevin Parker.

Shusil Dangi

Shusil Dangi completed his Ph.D. training in Imaging Science at the Rochester Institute of Technology. His thesis, titled, "Computational Methods for Segmentation of Multi-Modal Multi-Dimensional Cardiac Images," was supervised by Professor Cristian Linte.

April Wang

April Wang completed her Ph.D. training in Electrical and Computer Engineering at the University of Rochester. Her thesis, titled "Elastographic Imaging of Pancreatic Cancer Tumor Microenvironment," was supervised by Professor Marvin Doyley.

Fernando Zvietcovich

Fernando Zvietcovich completed his Ph.D. training in Electrical and Computer Engineering at the University of Rochester. His thesis, titled "Dynamic Optical Coherence Elastography," was supervised by Professor Kevin Parker and Professor Jannick Rolland.

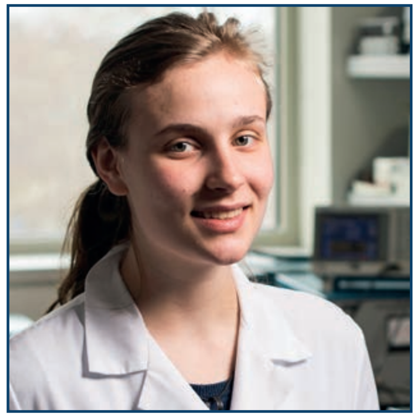
Student awards & honors

Ream Mislati

Ream Mislati (ECE) was the recipient of the President's Choice Award in Engineering and Mathematics for outstanding poster presentation at the 2019 UR Undergraduate Research Expo. Reem presented a poster of her work, titled "Shear Wave Elastography to Investigate the Role of Interferon Gamma on Treatment of Pancreatic Ductal Adenocarcinoma." Reem's research was supervised by Professor Marvin Doyley.

Anna Olsen

Anna Olsen (BME) received a Travel Award from the Knights Templar Eye Foundation.



Emma Grygotis Norris

Emma Grygotis Norris (Pharmacology & Physiology) was a participant at the National ComSciCon Workshop. Emma was one of 50 students (out of 750 applicants) selected to attend this national Communicating Science Conference hosted by the University of California, San Diego in July 2019.

Jeffrey Rowan

Jeffrey Rowan (ECE) received a travel grant from the AS&E Graduate Student Association to support his travel to attend and present at the 178th Meeting of the Acoustical Society of America in San Diego, CA in December, 2019.

Alexander Kotelsky

Alexander Kotelsky (BME) was the recipient of the 2019 UR BME Graduate Teaching Award. He also received a Travel Award to attend the Biomechanics, Bioengineering, and Biotransport Conference.

Yehuda Kfir Ban-Zikri

Yehuda Kfir Ban-Zikri (RIT BME) received a Best Student Paper Award at the Visualization & Image Processing (VIPImage) Conference in Porto Portugal in October of 2019. His project was titled, "Toward an Affine Feature-Based Registration Method for Ground Glass Lung Nodule Tracking."

Faculty News

NEW APPOINTMENTS

Deborah Rubens

Deborah Rubens was appointed Vice-Chair of Faculty and Professional Development for Imaging Sciences at the University of Rochester Medical Center. In this role, Dr. Rubens will lead faculty career development initiatives, research and education seminars, faculty on-boarding, and scholarship activities for trainees in the Department of Imaging Sciences.

Diane Dalecki

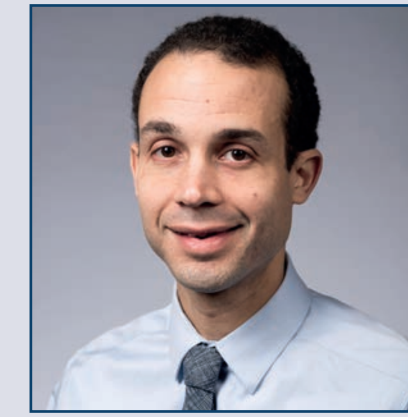
Diane Dalecki was named the Kevin J. Parker Distinguished Professor in Biomedical Engineering (see full story on pages 12 and 13 of this report).

Cristian Linte

Cristian Linte was promoted to Associate Professor in the Department of Biomedical Engineering at the Rochester institute of Technology.

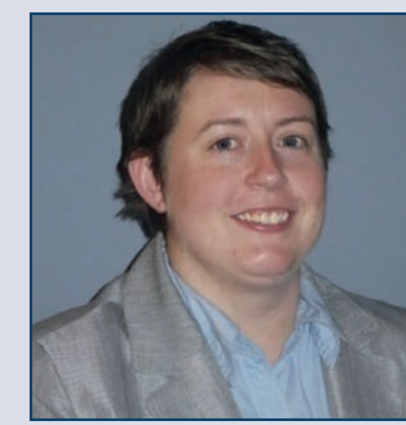
Marvin Doyley

Marvin Doyley was promoted to Full Professor of Electrical and Computer Engineering, and Imaging Sciences. Professor Doyley's was also named Associate Chair of Electrical and Computer Engineering at the University of Rochester.



Mark Buckley

Mark Buckley was promoted to tenured Associate Professor of Biomedical Engineering. Professor Buckley's research laboratory is dedicated to understanding soft tissue biomechanics in order to improve treatments for diseases and injuries.



Alayna Loiselle

Alayna Loiselle was promoted to Associate Professor in the Department of Orthopaedics. Professor Loiselle's laboratory is dedicated to identifying novel strategies to improve post-operative tendon healing.

FACULTY AWARDS & HONORS

Amy Lerner was inducted as a fellow in the American Institute for Medical and Biological Engineering (AIMBE) in recognition of her outstanding contributions to orthopaedic biomechanics, engineering design education, and diversity in engineering and academia.

Marvin Doyley became a member of the AIUM Technical Standards Committee.

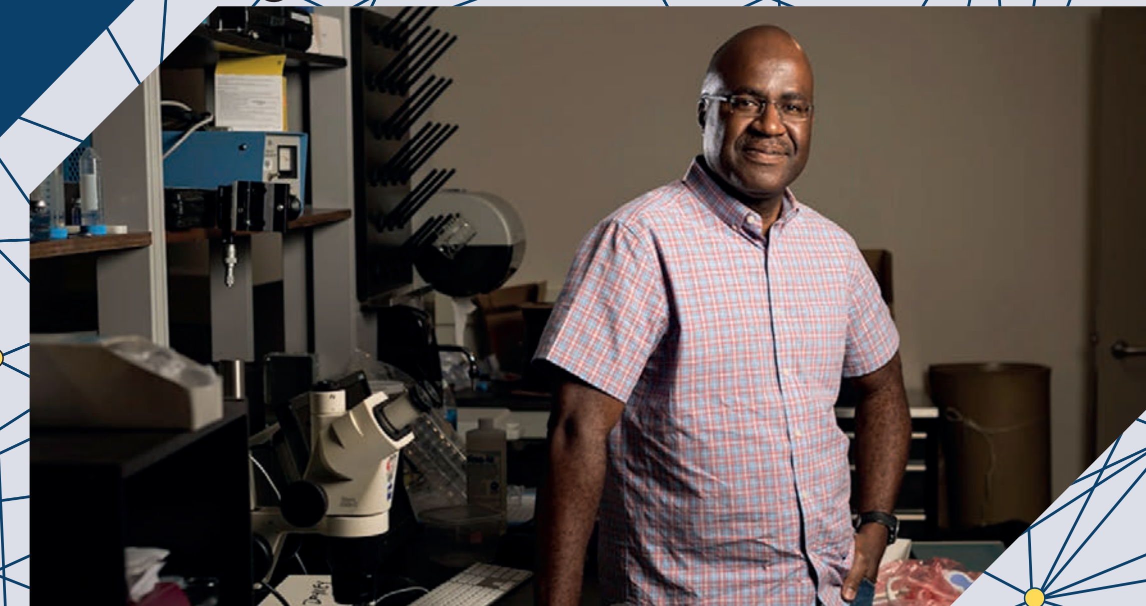
Diane Dalecki was appointed a member of the AIUM FUTURE Fund Council, which directs and guides planning and distribution of philanthropic funds for the American Institute of Ultrasound in Medicine. She was also appointed a member of the external advisory group for the NIH-sponsored Lithotripsy Program Project at the University of Washington. This program project, led by Michael Bailey, entered its 25th year of funding.

Mark Buckley was honored with the David T. Kearns Faculty Mentoring and Teaching Award that recognizes outstanding faculty members who excel at mentoring and teaching low-income, first-generation, and/or underrepresented students. Professor Buckley began working with the University of Rochester's Kearns Center in 2014 and was the first faculty member to host a high school "STEMtern" – Upward Bound Math/Science students who complete six-week mentored research projects. Buckley has mentored seven Upward Bound students in research positions. Two of the students later enrolled at the University as undergraduates and another two presented their research at the National Society of Black Engineers annual convention. He is also an active mentor with the McNair, REU, and Xerox programs for undergraduates.

Stephen McAleavey was elevated to Senior Member of IEEE.

Cristian Linte, associate professor of biomedical engineering at the Rochester Institute of Technology (RIT), was inducted into a new class of RIT's PI Millionaires, a designation given to RIT researchers who have achieved funding of $1 million or more since 2000. The celebration event, in RIT's University Gallery, was hosted by Sponsored Research Services, which has recognized 139 PI Millionaire researchers since 2001. "The principal investigators we are celebrating today are making critical contributions to the advancement of knowledge in many of the most significant interdisciplinary challenges faced by society today," said Ryne Raffaelle, vice president for research and associate provost. "The growth in sponsored research reflects the commitment, dedication, and talent of our researchers in all areas and is a tremendous source of pride for RIT." In 2019, Cristian Linte was also a guest editor for a special issue of the IET Journal Healthcare Technology Letters (HTL) dedicated to augmented environments for computer-assisted interventions and computer-assisted robotic endoscopy.

Kevin J. Parker (ECE) was selected for Life Membership by the Institute of Electrical and Electronics Engineers (IEEE). From the selection letter: "This honor is reserved for individuals who have truly distinguished themselves through their lasting contributions to IEEE. Your Life Member status speaks to both your professional achievements in technology as well as the significant impact you have made to the growth and development of the IEEE."



Marvin Doyley selected for first cohort of national STEM leadership program

When Marvin Doyley attends the next major conference for electrical engineers, he will likely be one of nearly 5,000 delegates.

"But there won't be many who look like me," says the University of Rochester professor of electrical and computer engineering. He estimates only about 10 of the participants at the IEEE conference will be black.

"It doesn't bother me now as much as it did before," Doyley says. "Now, I am a senior member, I have worked my way up, people know me, we have common experiences to talk about. But I'll be looking at someone else who is a minority just starting to come up, who will be hesitant to speak or ask questions."

Doyley is embarking on a mission to help address the glaring underrepresentation of minorities and women in STEM fields. He has been selected for the first cohort of the IAspire Leadership Academy, a program aimed at helping STEM faculty from underrepresented backgrounds ascend to leadership roles at colleges and universities.

"Marvin is a great faculty colleague and over the years he has contributed tremendously to ECE's research profile and teaching mission," says Mark Bocko, chair of the Department Electrical and Computer Engineering. "He clearly already possesses the skills and energy to be a wonderful leader for our department and the University, and the IAspire program is an excellent opportunity for him to hone those skills and prepare to take on new challenges in academic leadership."

Doyley hopes his participation in the academy will connect him with other participants, especially those from historically black colleges without graduate programs of their own, who could recommend top students from their institutions to participate in the REU and NIH training programs Doyley hopes to establish in his department.

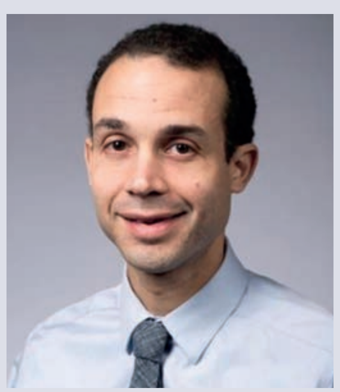
"It's a slow process; it's not a quick fix," Doyley acknowledges.

But it's a start.

Professor Doyley's research was featured on the cover of the April 2019 issue of the journal Clinical Cancer Research. The feature was titled "Elastography can map the local inverse relationship between shear modulus and drug delivery within the pancreatic ductal adenocarcinoma microenvironment," with authors Hexuan Wang, Reem Mislati, Rifat Ahmed, Phuong Vincent, Solumtochukwu Nwabunwanne, Jason Gunn, Brian Pogue, and Marvin Doyley.

FUNDING

Marvin Doyley (ECE) and Giovanni Schifitto (Neurology) are principal investigators on a new NIH grant titled "HIV neuroinflammation alters brain microstructure and viscoelastic properties." The goal of this project is to use a combination of imaging modalities (MR elastography (MRE) and neurite-orientation-dispersion density imaging (NODDI)) and peripheral blood biomarkers to understand how immune activation affects neurites morphology (NODDI) and associated changes in tissue viscoelastic properties (MRE).



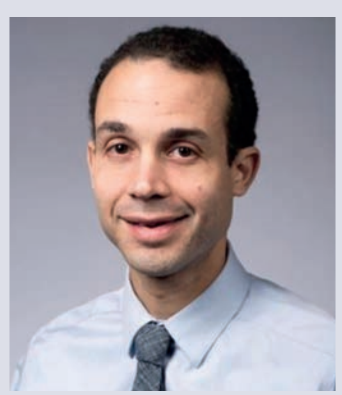
Mark Buckley (BME) received a UR PumpPrimer Award for his project titled "Recurring rupture and repair as a potential mechanism of osteoarthritis progression." This project tests the hypothesis that progression of osteoarthritis is driven by the ability of cartilage to repeatedly tear and repair their membranes when exposed to periodic extreme mechanical forces.

Cristian Linte is a co-investigator on a grant from the National Science Foundation's Office of Advanced Cyberinfrastructure titled, "CDS&E: Collaborative Research: A Computational Framework for Reconstructing and Visualizing Myocardial Active Stress."

Amy Lerner (BME) is a co-investigator on a grant from the NIH titled "How partial meniscectomy effects contact mechanics and tissue response." The goal of this project is to identify which knee forces are predictors for the development of osteoarthritis after partial meniscectomy procedure.

Denise Hocking (Pharmacology and Physiology) received a University Research Award for her project titled "Bacterial pathogens, fibronectin mimicry and intestinal permeability." This project will determine whether fibronectin, a principal component of the extracellular matrix of the intestinal wall, contributes to barrier function.

Marvin Doyley (ECE) is a co-investigator on a new grant from the NIH titled "Development of a new strategy to treat locally advanced pancreatic cancer." The goal of this project is to develop an innovative and feasible strategy to treat pancreatic cancer. Studies will be conducted to confirm that localized stereotactic body radiotherapy plus interleukin-12 encapsulated in microspheres therapy modulates the hepatic micro-environment so that it is capable of destroying mestastases.



Mark Buckley (BME) received support from IanTech/Carl Zeiss Meditec for his project titled "Comparison of the effects of miPORT and traditional phacoemulsification on the viability and vulnerability of corneal endothelial cells." This study's objective is to compare how traditional ultrasonic phacoemulsification and a novel cataract removal technique impact corneal endothelial cell viability and vulnerability to mechanical forces.

Cristian Linte is the principal investigator on a Maximizing Investigator Research Award for Early-stage Investigators (MIRA-ESI R35) from the NIH's National Institute of General Medical Sciences. The title of this project is "Biomedical computing and visualization tools for computer-integrated diagnostic and therapeutic data science."

Marvin Doyley (ECE) is a principal investigator of a subaward on the new NIH grant titled "Validation of cranial neurosurgery simulator and assessment of minimally invasive techniques." The goal of this project is to develop an inanimate cranial neurosurgery model utilizing novel concepts in 3D printing technology.

RESEARCH

Research laboratories of RCBU members are advancing the use of ultrasound for diagnosis and therapy. The following pages highlight recent research accomplishments. Selected publications and presentations can be found on pages 36-41.

Reverberant 3D optical coherence elastography maps the elasticity of individual corneal layers

Fernando Zvietcovich, Pornthep Pongchalee, Panomsak Meemon, Jannick P. Rolland, Kevin J. Parker

The elasticity mapping of individual layers in the cornea using non-destructive elastography techniques advances diagnosis and monitoring of ocular diseases and treatments in ophthalmology. However, transient Lamb waves, currently used in most dynamic optical coherence and ultrasound elastography techniques, diminish the translation of wave speed into shear/Young's modulus. Recent work from the labs of Professor Kevin Parker and Professor Jannick Rolland employed reverberant 3D optical coherence elastography (Rev3D-OCE) as a novel approach leveraging the physical properties of diffuse fields in detecting elasticity gradients not only in the lateral direction, but also along the depth axis of the cornea. A Monte Carlo analysis, finite element simulations, and experiments in layered phantoms were conducted to validate the technique and to characterize the axial elastography resolution. Experiments in ex vivo porcine cornea at different intraocular pressures revealed that Rev3D-OCE enables the elastic characterization of single layers that matches the anatomical description of corneal layers with unprecedented contrast in the dynamic OCE field.

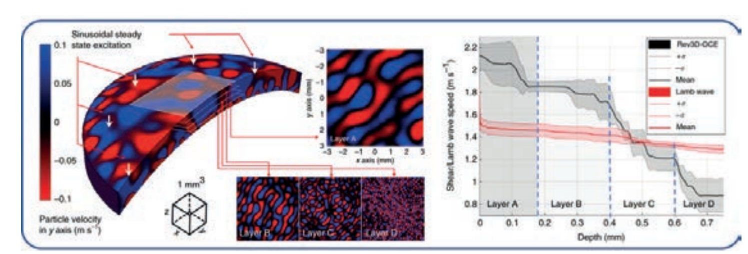


Figure 1. Comparative analysis of reverberant 3D optical coherence elastography (Rev3D-OCE) and the Lamb wave method using numerical simulations

Non-invasive ultrasound quantification of scar tissue volume identifies early functional changes during tendon healing

Jessica E. Ackerman, Valentina Studentsova, Marlin Myers, Mark R. Buckley, Michael S. Richards, Alayna E. Loiselle

Tendon injuries are very common and disrupt the transmission of forces from muscle to bone, leading to impaired function and quality of life. Successful restoration of tendon function after injury is a challenging clinical problem due to the pathological, scar-mediated manner in which tendons heal. Currently, there are no standard treatments to modulate scar tissue formation and improve tendon healing. A major limitation to the identification of therapeutic candidates has been the reliance on terminal endpoint metrics of healing in pre-clinical studies, which require a large number of animals and result in destruction of the tissue. To address this limitation, a team of RCBU investigators (Alayna Loiselle, Mike Richards, Mark Buckley) and their labs have identified quantification of scar tissue volume (STV) from ultrasound imaging as a longitudinal, non-invasive metric of tendon healing. STV was strongly correlated with established endpoint metrics of gliding function including gliding resistance and metatarsophalangeal (MTP) flexion angle. However, no associations were observed between STV and structural or material properties. To define the sensitivity of STV to identify differences between functionally discrete tendon healing phenotypes, the team utilized S100a4 haploinsufficient mice (S100a4GFP/+), which heal with improved gliding function relative to wild-type (WT) littermates. A significant decrease in STV was observed in S100a4GFP/+ repairs, relative to WT at day 14. Taken together, these data suggest ultrasound quantification of STV as a means to facilitate the rapid screening of biological and pharmacological interventions to improve tendon healing, and identify promising therapeutic targets, in an efficient, cost-effective manner.

Microfibril assembly is a critical window for the induction of ultrasound bioeffects during acoustically-modified collagen hydrogel fabrication

Emma G. Norris, Joseph Majeski, Sarah E. Wayson, Holly Coleman, Regine Choe, Diane Dalecki, and Denise C. Hocking

Biocompatible scaffolds that support the endogenous regenerative capacity of native cells are a promising avenue to restore healing in the over 6.5 million American adults affected by chronic and hard-to-heal wounds. Such materials are frequently constructed from extracellular matrix (ECM) glycoproteins. Of these, type I collagen is an ECM protein with high abundance, low antigenicity, and robust self-assembly capacity, making it a versatile material for diverse tissue engineering applications, including the treatment of non-healing cutaneous wounds. Ultrasound-based techniques to manipulate the structural organization and biological activities of these acellular, ECM-based hydrogels further offer a promising strategy for engineering biomaterials with enhanced regenerative properties.

Previous studies from the Dalecki and Hocking labs have established a paradigm in which neutralized soluble collagen (0.8 mg/mL) is polymerized in the presence of continuous wave ultrasound (7.8-8.8 MHz, 0-10 W/cm^2) for 15 minutes. The resulting collagen hydrogels exhibit multiple distinct structural features, including radial collagen fiber alignment and interconnected porosity. Acoustically-modified collagen hydrogels in turn support enhanced cellular migration and ECM remodeling, behaviors essential for regeneration in response to cutaneous tissue injury. In the present study, the team investigated the temporal dependence of ultrasound bioeffects with respect to the progression of collagen assembly. Actively polymerizing collagen solutions were exposed to ultrasound for five-minute windows corresponding to one of three distinct stages of collagen self-assembly. Collagen assembly rate was manipulated by adjusting the solution pH and the temperature at which acoustic exposures were performed, and was monitored via both temperature and optical turbidity measurements.

Results indicated that during collagen polymerization, the lateral association of precursor nanofibrils into larger microfiber bundles served as a critical window during which the pro-migratory effects of ultrasound exposure were induced. Together with previous results, the current studies indicate that ultrasound exposure can influence collagen fiber microstructure via thermal and non-thermal acoustic mechanisms at different stages of the collagen assembly process. These findings raise the possibility that the timing of acoustic exposure with respect to biomaterial assembly is an important modulator of the mechanisms of ultrasound bioeffects on collagen. As therapeutic applications of ultrasound continue to expand, this parameter may be exploited in a point-of-care clinical setting to enhance the efficacy of therapeutic ultrasound for regenerative medicine applications.

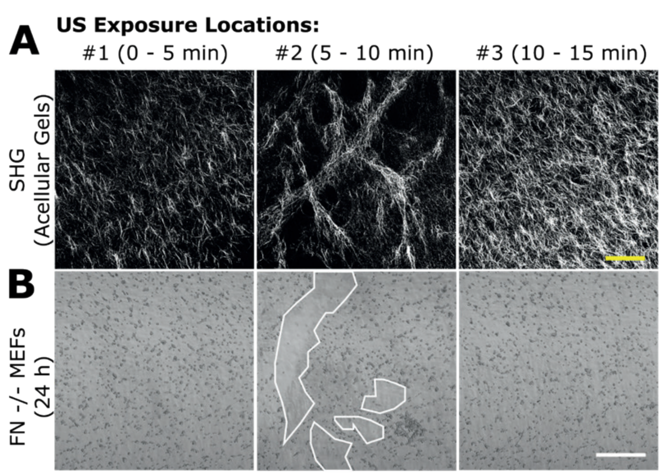


Figure 1. Mechanical bioeffects of ultrasound are selectively induced during a critical window of collagen self-assembly. Aliquots of neutralized soluble collagen (0.8 mg/mL) were exposed to 8.8-MHz ultrasound (7.9 W/cm^2) or sham-exposed at 3 spatially independent locations for 5 min each over the course of 15 min. Exposure windows were selected such that they corresponded to time periods before (0-5 min), during (5-10 min), or after (10-15 min) lateral association of collagen nanofibers. A) Fiber structure of acellular, acoustically modified collagen gels visualized using second harmonic generation (SHG) imaging, scale bar = 100 µm. B) Distribution of cells (fibronectin-null mouse embryonic fibroblasts) after 24-h migration period on the surface of acoustically modified collagen visualized by phase-contrast microscopy, scale bar = 500 µm.

Tissue dispersion using a reverberant shear wave elastography field

Juvenal Ormachea, Kevin J. Parker

Recently, a new method was proposed to estimate tissue stiffness by creating a reverberant shear-wave field within tissues. These reverberant conditions lead to simple solutions, facile implementation, and rapid viscoelasticity estimation of local tissue. From these, the investigators obtained 2D linear dispersion slope (LDS) images using the local estimated shear wave speed (SWS) at different frequencies in CIRS phantoms and in an in vivo human liver by applying a reverberant shear wave elastography (R-SWE) field. Continuous harmonic reverberant shear waves were generated in a breast and a viscoelastic CIRS phantom by applying vibrations using multifrequency (80-360 Hz) external sources. A Verasonics ultrasound system was used to track the induced displacements. A Samsung ultrasound system (model RS85) was used to measure the SWS for comparison purposes in the CIRS phantoms. Finally, the clinical feasibility of this technique was analyzed by assessing the SWS and LDS in an in vivo human liver under the requirements of informed consent.

2D images of SWS and LDS for different cases demonstrated a mean SWS of 2.49 m/s and 2.10 m/s (at 220 Hz), a difference of 11.06% and 4.10% compared with the Samsung system, and mean LDS of 0.25 m/s/100 Hz and 0.69 m/s/100 Hz were estimated using multifrequency excitations for the breast and viscoelastic phantoms, respectively. For the in vivo liver, a SWS of 1.43 m/s at 200 Hz and a LDS of 0.61 m/s/100 Hz were estimated. In conclusion, it is possible to estimate the viscoelastic properties in phantom materials and human tissue in vivo using the R-SWE approach with consistent results in SWS and in LDS estimations. Results from the multifrequency estimations indicated that it was not only feasible, but also, faster to assess frequency dependence than using single vibration frequencies, thus facilitating the use of the R-SWE approach for clinical applications.

Shear wave elasticity imaging can measure treatment response of pancreatic tumors treated with stereotactic body radiation therapy

Hexuan Wang, Brady Mills, Reem Mislati, Rifat Ahmed, Scott Gerber, Marvin M. Doyley

Pancreatic adenocarcinoma (PDAC) is the 4th leading cause of cancer related death in the United States with a 5-year survival rate less than 8%. Stereotactic body radiation therapy (SBRT) is an emerging treatment plan that delivers high radiation doses in shorter therapeutic courses to patients with tolerable toxicity. Studies have shown that SBRT causes cell apoptosis, reduces interstitial fluid pressure, and changes the collagen matrix stiffness. Investigators from the Doyley lab hypothesized that shear moduli of pancreatic cancer tumors decrease in response to stereotactic body radiation as a result of reduced texture energy and collagen density. KCKO (n = 30) and PAN02 (n = 30) murine pancreatic tumors were implanted in 60 female C56BL/6 mice by injecting 105 tumor cells in Matrigel (BD Biosciences, San Jose, California, USA) orthotopically into the pancreas. Starting from day 6 to day 9 post injection, the SBRT treated mice (n = 15, KCKO; n = 15, PAN02) were targeted with daily 6 Gy radiation in 4 fractions using the small animal radiation research platform (SARRP, XStrahl) with a 5-mm collimator. Upon animal sacrifice at day 29 post injection, excised tumors were embedded in a gelatinous solution consisting of 10% gelatin, 1% corn starch, and water. Single tracking location shear wave elasticity imaging (STL-SWEI) was implemented on a Verasonics Vantage 256 scanner with a 5-MHz L7-4 transducer. After STL-SWEI, each tissue sample was sectioned and stained with Masson's trichrome to investigate necrosis area, collagen density, and collagen texture features. SWEI elastography indicated that the average shear modulus for untreated PAN02 tumors was 32.4% softer than untreated KCKO tumors, and were insensitive to SBRT, as the average shear modulus decreased marginally. On the other hand, the mean shear modulus for the KCKO tumors was reduced by 37.7% when subject to radiation therapy. Results demonstrated that shear modulus measured with SWEI can estimate the positive response to SBRT treatment in KCKO tumors and the negative response in PAN02 tumors, potentially establishing the usage of SWEI to optimize radiation dosage and fractions of the stereotactic body radiation therapy for pancreatic cancer patients.

Intraocular pressure–dependent corneal elasticity measurement using high-frequency ultrasound

L. Oscar Osapoetra, Daniel M. Watson, Stephen A. McAleavey

Measurement of corneal biomechanical properties can aid in predicting corneal responses to diseases and surgeries. For delineation of spatially resolved distribution of corneal elasticity, a high-resolution elastography system is required. In a recent study, the McAleavey lab demonstrated a high-resolution elastography system using high-frequency ultrasound for ex vivo measurement of intraocular pressure (IOP)-dependent corneal wave speed. Tone bursts of 500-Hz vibrations were generated on the corneal surface using an electromagnetic shaker. A 35-MHz single-element transducer was used to track the resulting anti-symmetrical Lamb wave in the cornea. The team acquired spatially resolved wave speed images of the cornea at IOPs of 7, 11, 15, 18, 22, and 29 mmHg. The IOP dependence of corneal wave speed was apparent from these images. Statistical analysis of measured wave speed as a function of IOP revealed a linear relation between wave speed and IOP, cs = 0.37 + 0.22IOP, with the coefficient of determination R^2 = 0.86. Depth-dependent variations of wave speed in the cornea were also observed, decreasing from anterior toward posterior. This depth dependence was more pronounced at higher IOP values. This study demonstrated the potential of high-frequency ultrasound elastography in the characterization of spatially resolved corneal biomechanical properties.

Using a murine metastatic liver model to investigate the relationship between shear wave speed and survival during chemotherapy

Rifat Ahmed, Jian Ye, Scott A. Gerber, Marvin M. Doyley

Gemcitabine is the standard therapy used to treat patients with locally advanced or metastatic pancreatic cancer. There is a strong correlation between low tissue pressure and patient survival in many cancers, but this has never been demonstrated for pancreatic cancers with liver metastasis. Although tissue pressure is difficult to measure with current in vivo techniques, the Doyley lab has previously demonstrated that shear modulus is a surrogate. In recent work from the Doyley lab, a metastatic liver murine model and plane wave single track location shear wave elasticity imaging (pSTL-SWEI) was used to investigate the relationship between shear wave speed and survival of rodents undergoing chemotherapy.

Injecting KCKO-luc cells into the hemispleen produced liver metastases in mice (n = 22), which were divided into two groups: untreated and treated by Gemcitabine. Mice were imaged under anesthesia with pSTL-SWEI and optical bioluminescence imaging (BLI) two times per week for 7 weeks. For pSTL-SWEI, which was implemented on a Vantage 256 scanner (Verasonics, Inc.) with L11-5v probe (10 MHz), a total of 41 laterally-spaced push beams, each with 4 rapid multi-focal zones, were transmitted followed by compounded plane wave tracking. To suppress respiration motion, novel automated gating, using real-time cross-correlation of plane wave images, was used to achieve one push-detect ensemble per respiration beat. Liver stiffness was consistently high (>3 m/s) before demise. Scatterplots of data (12 mice at 14 timepoints) showed that SWEI and BLI measurements have a good (R^2=0.39) correlation. However, the correlation was stronger (R^2=0.54) in more established tumors, indicating that SWEI measurements are more sensitive to macro-scale structural changes than cell growth.

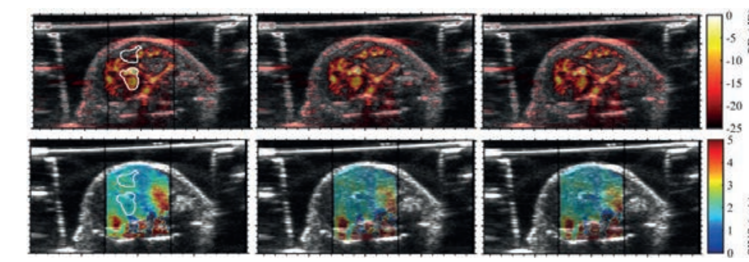


Figure 1. Functional and mechanical imaging of a mouse liver in vivo. Microvascular network (top row) and stiffness map (bottom row) of a mouse liver produced by non-contrast plane wave power Doppler imaging and shear wave elastography imaging, respectively.

Attenuation of shear waves in normal and steatotic livers

Ashwani K. Sharma, Joseph Reis, Daniel C. Oppenheimer, Deborah J. Rubens, Juvenal Ormachea, Zaegoo Hah, Kevin J. Parker

Shear wave propagation in the liver has been a robust subject of research, with shear wave speed receiving the most attention. The correlation between increased shear wave speed and increased fibrosis in the liver has been established as a useful diagnostic tool. In comparison, the precise mechanisms of shear wave attenuation, and its relation to diseased states of the liver, are less well-established. This study focused on the hypothesis that steatosis adds a viscous (lossy) component to the liver, which increases shear wave attenuation. Livers of twenty patients were scanned with ultrasound and with induced shear wave propagation. Resulting displacement profiles were analyzed using recently developed estimators to derive both the speed and attenuation of the shear waves within 6-cm^2 regions of interest. The results were compared with pathology scores obtained from liver biopsies taken under ultrasound guidance. Across these cases, increases in shear wave attenuation were linked to increased steatosis score. This preliminary study supports the hypothesis and indicates the possible utility of the measurements for non-invasive and quantitative assessment of steatosis.

Therapeutic effects of ultrasound on dermal wound healing in diabetic mice

Melinda Vander Horst, Carol H. Raeman, Diane Dalecki, Denise C. Hocking

Chronic wounds, including diabetic, leg, and pressure ulcers, impose a significant health care burden worldwide. The current standard of care for these injuries primarily involves supportive strategies, such as antimicrobial bandages, and surgical debridement. Some evidence indicates low intensity, pulsed ultrasound can be a non-invasive method for enhancing soft tissue regeneration in both animal models and humans. However, the effectiveness of therapeutic ultrasound can vary among populations.

Current studies in the laboratories of Diane Dalecki and Denise Hocking are investigating the effects of ultrasound on dermal wound healing using a murine model of chronic, diabetic wounds. Full thickness, punch biopsy wounds were made on the dorsal skin of genetically diabetic, male mice. Daily, 1-MHz, pulsed ultrasound treatments were administered to the periphery of the wounds for 8 min per day, for either 2 or 3 weeks. After treatment, wounds were excised and processed for histology. After 2 weeks, the average granulation tissue thickness at the center of wounds exposed to ultrasound at 0.4 MPa was significantly increased compared to sham-exposed wounds (Fig. 1A). Interestingly, the mean granulation tissue thickness of one subpopulation of mice exposed to 0.4 MPa ultrasound was statistically different than that of a second subpopulation (594 ± 41 µm, n=9 versus 62 ± 25 µm, n=10). Increasing the treatment time to 3 weeks (Fig. 1B) increased the percentage of mice that responded to ultrasound treatment from 47% at 2-weeks to 86% (Fig. 1C). Similar increases in the percent of responders from 2 to 3 weeks were also observed for 0.1 and 0.2 MPa ultrasound treated mice.

Results of this study suggest that ultrasound may be an effective tool for facilitating chronic wound healing by encouraging new extracellular matrix deposition. Furthermore, data demonstrate a dose- and time- dependent difference in the responsiveness of young, male diabetic mice to pulsed ultrasound treatment protocols. Further histological analysis of excised tissue is currently being used to gain greater insight into the mechanism of ultrasound induced healing in biological tissues.

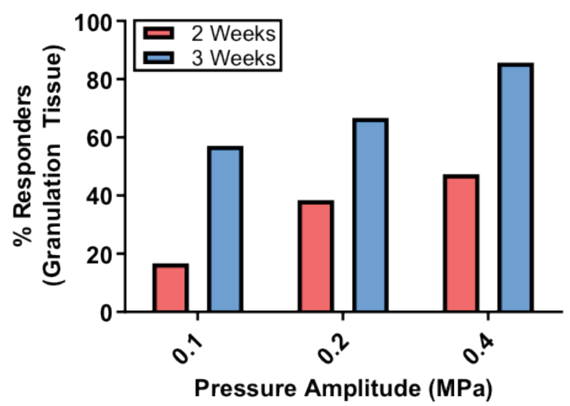


Figure 1. Granulation tissue thickness was measured at the wound center of mice exposed to daily, 1-MHz pulsed ultrasound, or sham exposed, for either 2 or 3 weeks. A 99% confidence interval (CI) of sham data was determined for both 2- and 3-week exposures. Granulation tissue thickness values greater than the 99% CI were considered statistically different from sham controls and categorized as "responders". Percentages of mice that responded to ultrasound treatment after 2 (red) and 3 (blue) weeks of treatment are shown as a function of pressure amplitude.

Shear wave elasticity imaging to investigate the role of interferon gamma on the treatment of murine pancreatic ductal adenocarcinoma

Reem Mislati, Hexuan Wang, Brady Mills, Rifat Ahmed, Scott Gerber, Marvin M. Doyley

Pancreatic cancer is a lethal disease that can be targeted with radiotherapy. Studies on the effectiveness of radiotherapy on cancer treatment suggest dependency on the immune system. Interferon-gamma (IFN-G) is a key cytokine responsible for regulating immigration of T-cells to tumor tissue. In recent work from Professor Doyley's lab, the team hypothesized that depletion of IFN-G will not modify biomechanics. To test this hypothesis, shear wave elasticity imaging (SWEI) was used to investigate how depletion of IFN-G combined with radiotherapy impacts tumor stiffness.

Orthotropic KCKO pancreatic tumors were implanted in 27 IFN-G knockout mice that were divided into 2 groups: 15 mice in the control group and 12 mice treated with (5Gy) stereotactic body radiation over 5 days. Another 2 groups of orthotropic KCKO pancreatic tumors were implanted in 36 wild-type mice: 19 mice in the control group and 17 treated with the same treatment regime. Tumors were removed and implanted in a gelatin matrix consisting of 10% gelatin, 1% cornstarch, and 89 % water. SWEI was performed using a Vantage 256 scanner (Verasonics, Inc.) with a 5-MHz L7-4 transducer in order to obtain shear modulus. Quantitative histological analysis was also performed to assess how collagen density varied between the 2 groups during treatment.

The average Young's moduli measured were 62.30 ± 17.68 kPa and 48.28 ± 12.77 kPa for the control and treated IFN-G knockout groups, respectively. The stiffness results showed there was a statistical difference between the control and treated IFN-G knockout groups. Young's moduli of the treated IFN-G knockout and wild-type groups have no statistical difference. The stiffness results showed that IFN-G did not impact the stiffness of pancreatic cancer.

Tendon thickness and impingement in insertional Achilles tendinopathy

Anthony Aggouras, Mark R. Buckley, Michael S. Richards

Insertional Achilles tendinopathy (IAT) is often characterized by tendon degradation and thickening near where the tendon inserts on the calcaneus bone. Impingement of the calcaneus on the Achilles tendon is believed to contribute to pathogenesis of IAT. However, it is unclear how increased tendon thickness in individuals with IAT influences risk of impingement. Through a collaboration of the labs of Michael Richards and Mark Buckley, the team reanalyzed data collected from a prior study to determine the ankle flexion angle at which the Achilles tendon is impinged on by the calcaneus bone in individuals with and without IAT. The hypothesis was that the thicker Achilles in individuals with IAT would be associated with calcaneal impingement at wider angles of ankle flexion, potentially exacerbating and sustaining the disease. Co-op trainee, Anthony Aggouras, found that the angle of impingement and thickness of the Achilles tendon insertion were both significantly greater in subjects with symptomatic IAT (P= 0.0036, P= 0.0012). It was also found that angle of impingement and thickness had a moderate correlation, suggesting increased tendon thickness raises the range of ankle angles over which the tendon becomes impinged.

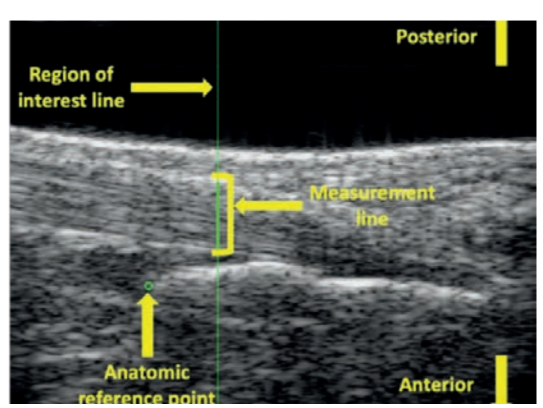


Figure 1. Representative ultrasound image thickness measurement of the Achilles insertion. Anterior-posterior thickness of the Achilles was measured 5 mm distal to the most superior point of the visible calcaneus.

A preliminary study on using reverberant shear wave fields in optical coherence elastography to examine mice brain ex vivo

Gary R. Ge, Fernando Zvietcovich, Jannick P. Rolland, Humberto Mestre, Michael Giannetto, Maiken Nedergaard, Kevin J. Parker

A number of approaches employ optical coherence tomography (OCT) to obtain the mechanical properties of biological tissue. These are generally referred to as optical coherence elastography (OCE), and have demonstrated promising applications with studies in cornea, breast, muscle, skin, and other soft tissues. A particular application of interest is the brain, in which changes in local and global elastic properties may correlate with the onset and progression of degenerative brain diseases. In this preliminary study, mouse brains were studied ex vivo and in situ with preservation of the brain/skull anatomical architecture. A small 6-mm diameter portion of the skull was replaced with a glass cap to allow for OCT imaging. Various permutations of source placement for generating shear waves and modes of excitation were evaluated to optimize the experimental setup. The use of reverberant shear wave fields, which takes advantage of inevitable reflections from boundaries and tissue inhomogeneities, allowed for estimation of the shear wave speed, which is directly related to the elastic modulus of soft tissues. Preliminary estimates for the shear wave speed in brains of recently deceased mice were obtained, demonstrating potential applications of OCE in brain.

The first order statistics of backscatter from the fractal branching vasculature

Kevin J. Parker

The issue of speckle statistics from ultrasound images of soft tissues such as the liver has a long and rich history. A number of theoretical distributions, some related to random scatterers or fades in optics and radar, have been formulated for pulse-echo interference patterns. Recent work from Professor Kevin Parker proposes an alternative framework in which the dominant echoes are presumed to result from Born scattering from fluid-filled vessels that permeate the tissue parenchyma. These are modeled as a branching, fractal, self-similar, multiscale collection of cylindrical scatterers governed by a power law distribution relating to the number of branches at each radius. A deterministic accounting of the echo envelopes across the scales from small to large was undertaken, leading to a closed form theoretical formula for the histogram of the envelope of the echoes. The normalized histogram was found to be related to the classical Burr distribution, with the key power law parameter directly related to that of the number density of vessels vs. diameter, frequently reported in the range of 2 to 4. Liver scans were studied to demonstrate the applicability of the theory.

Increased resonant frequency of microslit filtered contrast agents

Jeffrey S. Rowan, James McGrath, Marvin M. Doyley

Imaging using ultrasound contrast agents is highly dependent on the resonant frequency of the bubble population. According to the Marmottant model, modern lipid coated agents have three regimes of bubble dynamics, the buckled, elastic, and ruptured states. The transition from buckled to elastic regime corresponds to the largest change in resonant frequency due to the addition of a second term inversely proportional to bubbles' radii. For a 1.75 µm bubble, this corresponds to a change from approximately 1.7 MHz to approximately 5 MHz, leading to higher image resolution, and better separation between the fundamental and subharmonic components. Recent work from the Doyley lab used a novel ultrathin silicon nitride membrane for this purpose. The membrane itself contains thousands of 1.75 × 50 µm slits and is housed in a centrifuge device. While the exact mechanism is unknown, bubbles that are forced across the membrane during centrifugation show a higher resonant frequency than their strictly size isolated counterparts. In addition, the centrifuged agent also had a lower subharmonic threshold compared to native and size isolated agents, independent of concentration. The possibility of tuning the device to precise frequencies for optimized imaging was also studied.

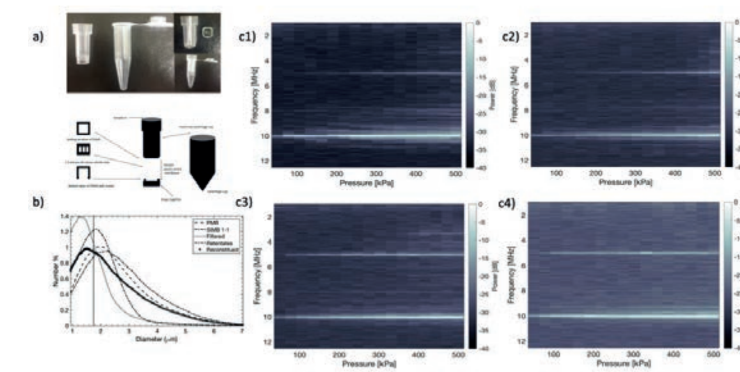


Figure 1. Ultrasound contrast agents and size isolation and subharmonic emissions. a) Schematic and photos of microchip device for centrifugation. b) Size distributions of poly-disperse bubbles, size isolated 1-2 micron, chip filtered, and retentate as recorded by Coulter counter. c1) through c4) are the frequency response of the poly-disperse, size isolated 1-2 micron, chip filtered and retentate respectively. Of interest is the lower threshold for subharmonic activation for 5-MHz and 3-MHz signal that is believed to correspond with shell rupture.

High-frequency quantitative ultrasound imaging for characterizing collagen microstructure in murine tendon

Sarah E. Wayson, María Helguera, Denise C. Hocking, Diane Dalecki

There is a need to design imaging systems to monitor tendon structure throughout rehabilitation protocols to optimize restoration of range of motion and mechanical properties in human and murine tendon. The Dalecki and Hocking labs, in collaboration with Imaginant, Inc., are developing high-frequency quantitative ultrasound as a non-destructive imaging modality to non-invasively characterize tendon microstructure. B-mode image appearance and interpretation is influenced by acoustic attenuation, receive system properties, and sonographer technique. Thus, this group is developing quantitative ultrasound systems and methods that estimate tendon structural properties from backscattered echoes, and characterize collagen fiber alignment in murine tendon.

The integrated backscatter coefficient (IBC) is a quantitative ultrasound spectral parameter that estimates how strongly scatterers within a tissue reflect the interrogating pulse back to the transducer. The group is testing the hypothesis that the IBC will exhibit anisotropy in murine tendon with aligned structure, and isotropy in murine liver with inhomogeneous structure. Backscattered echoes from murine tail tendon and liver were acquired at varying insonification angles using a 38-MHz single-element transducer. Results indicated the IBC was angular-dependent in tendon and isotropic in liver. These data suggest that the IBC can be used to detect collagen fiber alignment in murine tendon, and help establish the foundation for a device to non-invasively monitor collagen remodeling during tendon healing.

The Dalecki and Hocking laboratory has partnered with Imaginant, Inc. to design and manufacture a novel high-frequency ultrasound system for quantitative imaging of tendon. This system incorporates Imaginant's state-of-the-art PureViewTM H pulser-receiver with a specialty 55-MHz single-element focused immersion transducer (Figure 1). This system enhances the team's image acquisition capabilities and will allow for future higher resolution quantitative analysis of tendon microstructure.

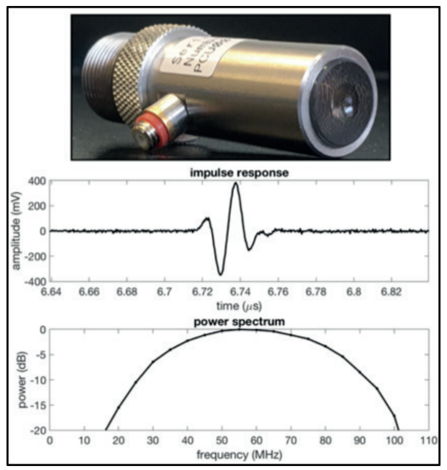


Figure 1. (A) Imaginant's single-element 55-MHz focused immersion transducer. (B) Impulse response and power spectra measured using a steel reflector at the focal distance.

A new platform for assessing phacoemulsification-associated corneal health

Mark R. Buckley

The Buckley lab has developed a new in vitro experimental platform facilitating measurement of phacoemulsification-associated corneal endothelial cell (CEC) loss and CEC health across large regions of the endothelium. A key advantage of this platform compared with other in vivo and in vitro methods is that CEC density is evaluated in intact eyes both before and after simulated surgery without dissecting the eye (a process that could induce additional CEC loss and confound findings). Moreover, the method enables visualization of CECs and quantification of CEC density and health across regions several times larger than previous studies (~16 mm^2 compared with < 0.5 mm^2 in most previous studies). Finally, the method employs fluorescent dyes that can be used to evaluate not only numbers of CECs, but also CEC health (e.g., intracellular oxidative stress and the presence of reactive oxygen species).

Shear wave propagation in viscoelastic media: Validation of an approximate forward model

Fernando Zvietcovich, N. Baddour, Jannick P. Rolland, Kevin J. Parker

Many approaches to elastography incorporate shear waves; in some systems these are produced by acoustic radiation force (ARF) push pulses. Understanding the shape and decay of propagating shear waves in lossy tissues is key to obtaining accurate estimates of tissue properties, thus analytical models have been proposed. In recent work from the Parker lab, the investigators reconsidered a previous analytical model with the goal of obtaining a computationally straightforward and efficient equation for the propagation of shear waves from a focal push pulse. This model was compared with an experimental optical coherence tomography (OCT) system and with finite element models, using two viscoelastic materials that mimic tissue. The team found that the three different cases—analytical model, finite element model, and experimental results—demonstrated reasonable agreement within the subtle differences present in their respective conditions. These results support the use of an efficient form of the Hankel transform for both lossless (elastic) and lossy (viscoelastic) media, and for both short (impulsive) and longer (extended) push pulses that can model a range of experimental conditions.

Deformation independent non-linearity estimation: Studies and implementation in ultrasound shear wave elastography

Soumya Goswami, Siladitya Khan, Rifat Ahmed, Marvin M. Doyley, Stephen A. McAleavey

Nonlinear elasticity imaging provides additional information about tissue behavior that is potentially diagnostic and may lead to better tissue characterization. Nonlinear elastic properties of tissue become apparent upon application of large deformation to the medium. The majority of nonlinear elasticity estimation techniques rely on uniaxial compression. Investigators from the McAleavey and Doyley labs studied the change in shear wave speed with the medium subjected to simple shear stress and also pure uniaxial compressive stress. Axial and lateral deformation of the tissue were tracked using quasi-static strain elastography. The local stress map was computed from the cumulative sum of apparent shear modulus (measured by shear wave elastography) times the estimated differential strain. By fitting the change in local stress obtained to the estimated strain, nonlinear shear modulus was mapped. The rate of change in local stress distribution in the medium differed with different deformations applied. However, the absolute value of nonlinear shear modulus obtained for different deformations applied were similar, thereby demonstrating the ability to give a quantitative measure of material non-linearity irrespective of subjected deformations.

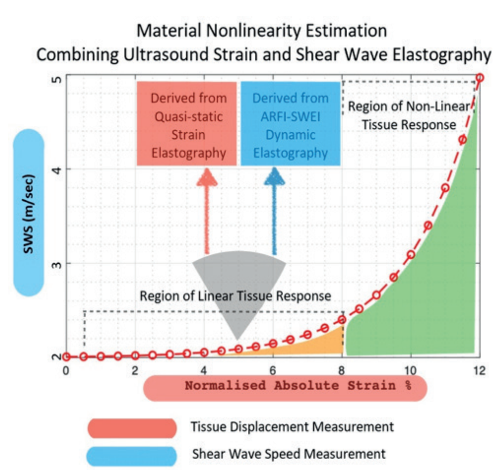


Figure 1. Material nonlinearity estimation combining ultrasound strain and shear wave elastography.

Nonlinear shear modulus estimation with bi-axial motion registered local strain

Soumya Goswami, Rifat Ahmed, Marvin M. Doyley, Stephen A. McAleavey

Nonlinear elasticity imaging provides additional information about tissue behavior that is potentially diagnostic and avoids errors inherent in applying a linear elastic model to tissue under large strains. Nonlinear elasticity imaging is challenging to perform due to the large deformations required to obtain sufficient tissue strain to elicit nonlinear behavior. Work from the labs of Professor Steve McAleavey and Professor Marvin Doyley uses a method of axial and lateral displacement tracking to estimate local axial strain with simultaneous measurement of shear modulus at multiple compression levels. By following the change in apparent shear modulus and the stress deduced from the strain maps, the team is able to accurately quantify nonlinear shear modulus (NLSM). They have validated their technique with a mechanical NLSM measurement system. Results demonstrated that 2-D tracking provided more consistent NLSM estimates than those obtained by 1-D (axial) tracking alone, especially where lateral motion was significant. The elastographic contrast-to-noise ratio in heterogeneous phantoms was 12.5%-60% higher using this method than that of 1-D tracking. The method is less susceptible to mechanical variations, with deviations in mean elastic values of 2-4% versus 5-37% for 1-D tracking.

Distributing synthetic focusing over multiple push-detect events enhances shear wave elasticity imaging performance

Rifat Ahmed, Marvin M. Doyley

Plane wave (PW) imaging is a commonly used method for tracking waves during shear wave elasticity imaging (SWEI), but its unfocused transmission beam reduces tracking accuracy and precision. Coherent compounding minimizes this problem, but SWEI's stringent frame rate requirement and the coarse pitch of most clinical transducers limit its effectiveness. Synthetic aperture imaging (SAI) is an alternate ultrasound imaging approach with a much tighter focus than PW imaging, but its lower transmission power has deterred researchers from using SAI in SWEI. Hadamard-encoded multielement SAI can overcome this limitation. However, only a limited number of subapertures (3-5) can be transmitted in a single push-detect event. Recently, Professor Doyley's lab developed methods to distribute more subapertures or more compounding angles over multiple push-detect events. Experiments were conducted on phantoms to assess SWEI's performance when using Hadamard-encoded distributed-multielement synthetic aperture (HDMSA) imaging or distributed plane wave compounding (DPWC) to track shear waves. Tracking shear waves with HDMSA improved the elastographic signal-to-noise ratio (SNRe) by 61.6%-89.5% depending on the phantom employed. Similarly, DPWC tracking improved SNRe by 56.2%-93.3% for the same group of phantoms. Compared to focused ultrasound tracking (at the focus), SNRe improved by 28.6% and 32.5% when tracking shear waves with HDMSA and DPWC, respectively. Long acquisitions could introduce decoding errors that decrease the performance when performing HDMSA tracking within the clinical setting. Nevertheless, results of studies performed on the bicep muscle of three healthy volunteers demonstrates that for stationary organs, tracking shear waves with HDMSA yielded repeatable elastograms that offer better elastographic performance than those produced with current tracking methods.

Real-time visualization and analysis of chondrocyte injury due to mechanical loading in fully intact murine cartilage explants

Alexander Kotelsky, Joseph S. Carrier, Mark R. Buckley

Homeostasis of articular cartilage depends on the viability of resident cells (chondrocytes). Unfortunately, mechanical trauma can induce widespread chondrocyte death, potentially leading to irreversible breakdown of the joint and the onset of osteoarthritis. Additionally, maintenance of chondrocyte viability is important in osteochondral graft procedures for optimal surgical outcomes. The Buckley lab has developed a method to assess the spatial extent of cell injury/death on the articular surface of intact murine synovial joints after application of controlled mechanical loads or impacts. This method can be used in comparative studies to investigate the effects of different mechanical loading regimens, different environmental conditions or genetic manipulations, as well as different stages of cartilage degeneration on short- and/or long-term vulnerability of in situ articular chondrocytes. The goal of the protocol is to assess the spatial extent of cell injury/death on the articular surface of murine synovial joints. Importantly, this method enables testing on fully intact cartilage without compromising native boundary conditions. Moreover, it allows for real-time visualization of vitally stained articular chondrocytes and single image-based analysis of cell injury induced by application of controlled static and impact loading regimens. Representative results demonstrate that in healthy cartilage explants, the spatial extent of cell injury depends sensitively on load magnitude and impact intensity. This method can be easily adapted to investigate the effects of different mechanical loading regimens, different environmental conditions or different genetic manipulations on the mechanical vulnerability of in situ articular chondrocytes.

Mechanical and functional validation of a perfused, robot-assisted partial nephrectomy simulation platform using a combination of 3D printing and hydrogel casting

Rachel Melnyk, Bahie Ezzat, Elizabeth Belfast, Patrick Saba, Shamroz Farooq, Timothy Campbell, Stephen McAleavey, Mark Buckley, Ahmed Ghazi

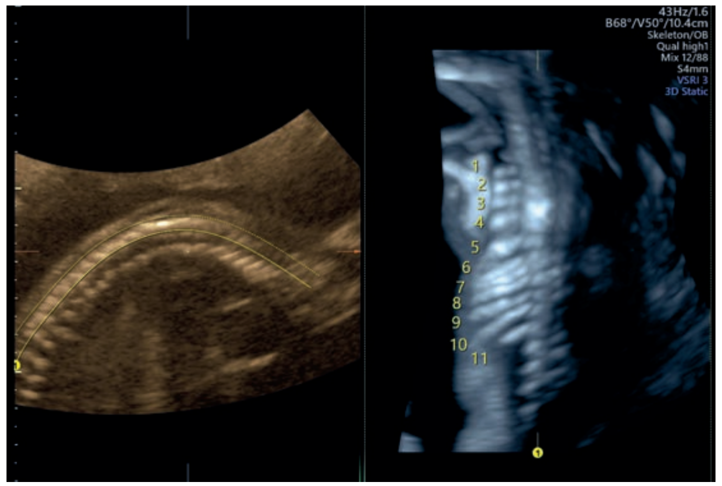
There is a scarcity of high-fidelity, life-like, standardized and anatomically correct polymer- based kidney models for robot-assisted partial nephrectomy (RAPN) simulation training. In recent work, mechanical and functional testing was performed on a perfused hydrogel kidney model created utilizing 3D printed injection casts for RAPN simulation and training. Anatomically correct, tumor-laden kidney models were created from 3D-printed casts designed from a patient's CT scan and injected with poly-vinyl alcohol (PVA). A variety of testing methods, including elastography, quantified Young's modulus in addition to comparing the functional effects of bleeding and suturing among fresh porcine kidneys and various formulations of PVA kidneys.

Fabrication at 7% PVA at three freeze–thaw cycles (7%-3FT) was found to be the formula that best replicates the mechanical properties of fresh porcine kidney tissue, where mean (± SD) values of Young's modulus of porcine tissue vs 7%-3FT samples were calculated to be 85.97 (± 35) kPa vs 80.97 (± 9.05) kPa, 15.7 (± 1.6) kPa vs 74.56 (± 10) kPa, and 87.46 (± 2.97) kPa vs 83.4 (± 0.7) kPa for unconfined compression, indentation, and elastography testing, respectively.

No significant difference was seen in mean suture tension during renorrhaphy necessary to achieve observable hemostasis and capsular violation during a simulated perfusion at 120 mmHg. This is the first study to utilize extensive material testing analyses to determine the mechanical and functional properties of a perfused, inanimate simulation platform for RAPN, fabricated using a combination of image segmentation, 3D printing and PVA casting.

Obstetrics & Gynecology Ultrasound Unit

Kathryn Drennan, MD and Kam Szlachetka RDMS



The University of Rochester OB/GYN Ultrasound Unit provides advanced obstetric and gynecologic imaging at multiple sites through the Strong system and the region. Advanced obstetric and gynecologic ultrasound services are providers in three locations locally, including Lattimore Road, Highland Hospital, and our facility at Red Creek Drive. The volume of patients seen for OB/Gyn ultrasound at the URMC locations (Lattimore and Red Creek) remains high and stable, with again over 15,000 studies on over 9000 patients. The sites have on-site genetic counseling and MFM services, with immediate consultation and testing available, and serve as the regional referral for diagnosis, evaluation and management of complex fetal disease from around the region. The MFM division also provides Level II ultrasound at FF Thompson, including 2 days/month of onsite services, with over 3000 studies performed last year, and our number of ultrasounds continues to grow year on year.

We have a stable fellowship with 6 fellows (2 in each year) and have continued to produce well trained MFM physicians, with a high rate of academic retention. Our ultrasound unit helps to train them in the foundational skills of maternal-fetal medicine. We also train our residences at the University of Rochester in basic ultrasound skills to help provide all women access to the care needed to have great pregnancy outcomes. The unit has 21 ultrasound machines within the SMH & HH hospitals, all with 3D and 4D capability, plus additional portable scanners. There are 35 sonographers at HH and SMH, all 31 of whom are NT certified, 17 of whom are CLEAR certified, and 11 of whom are fetal echocardiography certified.

The MFM Division performs ultrasound and consultation at many locations throughout the region. We provide onsite services to St. Joseph's Hospital and Associates for Women's Medicine in Syracuse for perinatal consultations and ultrasound services locally in Syracuse twice a month, and over the last academic year again saw nearly 200 patients in consultation. This has expanded in 2019 to a weekly service and now includes ultrasound services at St. Joseph's Hospital. We also cover ultrasound remotely at Noyes Hospital, Ob/gyn Associates of the Finger Lakes in Dansville, St. James in Hornell, Auburn Community Hospital in Auburn and Comprehensive Women's Health Services in Watertown. These locations together had over 2,800 ultrasounds last year. We have continued to cover at Catholic Health's Mercy Hospital in Buffalo 3 days/week by remote reading with almost 2,300 ultrasounds last year, and our Buffalo presence has expanded to include remote reads at Sisters' Hospital with ~50-100 ultrasounds per week. We have also grown our telemedicine consultative services in Elmira at Twin Tiers Women's Health, at Guthrie Corning Ob/GYN in Corning, at Ob-Gyn and Midwifery Associates of Ithaca and in Buffalo at Mercy Hospital, and have started an in-person consultative service in Elmira.

With the introduction of noninvasive testing options in pregnancy, reproductive genetic counseling services and confirmatory testing procedures are more needed than ever. The number of invasive diagnostic procedures continues to be lower than in the historical past with the new availability of non-invasive testing but remained approximately stable from last year. We performed nearly 300 fetal echocardiograms, more than 110 amniocenteses, 62 chorionic villi samplings, ~30 advanced fetal procedures (including fetal blood sampling and transfusion, vesicocentesis, thoracentesis and other procedures).

Research activities within the Maternal-Fetal Medicine Division continue to expand. Sarah Caveglia, our new full-time research coordinator, has fueled the growth of our research program. Ultrasound and the Maternal Fetal Medicine division remains an active part of the North American Fetal Therapy Network (NAFNET), and through this group we are participating in several database studies, as well as planning to start enrollment for several multi-site clinical trials. We continue to have a highly productive fellowship, and last year,faculty and fellows presented 24 abstracts at national and international meetings. Third-year fellow, Stephanie Hollenbach, is completing course work for a PhD in biomedical engineering, and her thesis is titled, "Novel Sonographic Technologies for Innovation in Placental Assessment Across Gestation: The NESTING Study." This work is nearing completion under the guidance of Professor Stephen McAleavey from the Department of Biomedical Engineering. Fellows, faculty, and sonographers also organize teaching and outreach sonographer education days related to both didactic and hands-on skills in ultrasound and procedural skills. Examples of recent research projects are provided below.

Does transvaginal ultrasound at 13-15 weeks improve anatomic survey completion rates in obese gravidas?

Toscano M, Grace D, Pressman EK, Thornburg LL

Obesity increases the difficulty of completing the fetal anatomic survey. This is of added concern in obese gravidas who are at higher risk of congenital fetal anomalies. We hypothesized that incorporation of an early transvaginal assessment could improve the completion rate of the fetal anatomic survey in obese women.

We performed a prospective, longitudinal, blinded study of obese gravidas (BMI ≥ 35 kg/m^2) comparing the use of a single early second trimester transvaginal ultrasound in addition to mid-trimester transabdominal ultrasound versus traditional serial mid-trimester ultrasound alone for completion of the anatomic survey. Transvaginal ultrasound for anatomy was performed between 13 0/7 and 15 6/7 week followed by mid-trimester anatomic ultrasound, with each patient serving as her own control. Structures were marked as optimally or suboptimally viewed after each ultrasound. Sonographers and reviewers were blinded to images from the transvaginal ultrasound. Completion rates and gestational age at completion were compared between groups.

Fifty subjects were included. Fetal anatomic survey was completed in 62% using standard mid-trimester assessment versus 78% with the addition of early transvaginal assessment (p = .04). The survey was completed at an earlier gestational age utilizing the transvaginal approach (22 0/7 ± 6 3/7) compared to traditional mid-trimester transabdominal ultrasound approach (25 2/7 ± 5 3/7) p < .0005. In conclusion, incorporation of an early transvaginal assessment of anatomy in obese women improved the rate of completion and led to earlier gestational age at completion of the fetal anatomic survey. Consideration should be given to including an early transvaginal sonogram as part of routine assessment of women with a BMI ≥ 35.

The influence of intrauterine growth restriction and brain-sparing effect on neonatal lactate

Marinescu P, Toscano M, Gray L, Glantz C, Meyers J, Olson-Chen C, Thornburg LL, Drennan KJ

The objective of this study was to compare post-delivery lactate levels in infants with intrauterine growth restriction and brain sparing (IUGR-BS) to gestational age (GA) matched controls. Retrospective cohort study of non-anomalous singleton infants delivered between 23w0d-31w6d at an academic medical center between 2010-2018. Subjects were fetuses with IUGR and Doppler evidence of BS (n=42) compared with gestational age matched comparison group without IUGR (n=328). Primary outcome was first serum lactate level drawn within 24 hours of life, with lactate >2 designated as being clinically significant. Univariate analyses were performed with p<0.05 considered significant.

Median lactate levels in IUGR-BS cohort and control group were 5.4 (IQR 3.9) and 3.7 (IQR 2.2), respectively. IUGR-BS cohort had a statistically significant elevation of postnatal lactate levels compared to control group (P<4.73x10-8), in addition to risk elevation for being born with lactate >2 (RR:1.6, 95% CI 1.4-1.8; p<000.1). Demographic assessment showed similar GA age at delivery (28 weeks, P=0.4) for both groups. Percentages of maternal diabetes and placental abruption were comparable, while premature rupture of membranes and chorioamnionitis were higher in the control group. Among neonatal outcomes, no difference was seen in the 5-minute APGAR <7, immediate ventilation, assisted ventilation > 6 hours (H), and sepsis categories. Neonatal demise was higher in the IUGR-BS cohort. In conclusion, elevated postnatal lactate levels in infants identified as IUGR-BS is a novel finding. BS physiology appears to identify a group of infants who may be at higher risk of elevated lactate post-delivery and associated adverse outcomes not explained by variations in obstetric influences.

Posterior uterocervical angle for predicting spontaneous preterm birth

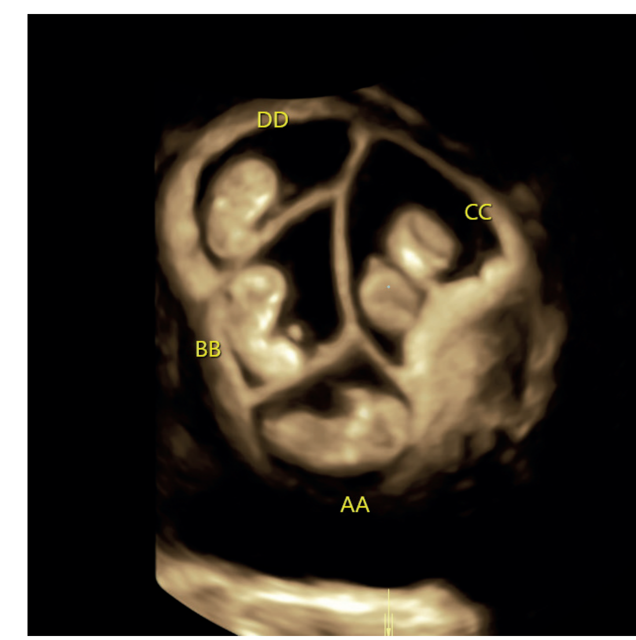
Lynch TA, Nicasio E, Szlachetka K, Seligman NS

Anterior uterocervical angle (aUCA), an alternative to cervical length (CL) screening, involves measurement of the angle between the anterior lower uterine segment (LUS) and cervix. However, studies have not consistently shown this to be a reliable predictor of spontaneous preterm birth (sPTB). Posterior uterocervical angle (pUCA), an alternative to the aUCA, measures the angle at the posterior LUS. pUCAhas been evaluated in third trimester prediction of labor induction success. To date, there are no studies of pUCA in the second trimester. Our objective is to evaluate if second trimester pUCA is predictive of sPTB <37w.

Retrospective cohort study of singletons with CL screening from 2014-2016. Post-hoc pUCA was measured on the shortest, best CL between 16-24w. pUCA was evaluated as a continuous variable and using thresholds of >95° and >105° (based on previous aUCA data). The primary outcome was sPTB <37w. Secondary outcomes were sPTB<32w and performance metrics. ROC curves were generated for pUCA, aUCA, and CL.

The study included 240 women: 10.8% with sPTB<37w and 2.5% with sPTB<32w. There was no difference in mean pUCA in women with or without sPTB<37w (p=0.14). Neither pUCA >95° or >105° were associated with sPTB<37w. For sPTB <32w, mean pUCA was significantly larger (155.0° [SD 25.1°] vs 115.8° [SD 33.4°]; p=0.005), and remained significant after adjusting for prior sPTB, tobacco use, and CL (p=0.007). Only pUCA >105° was associated with sPTB<32w (p=0.04). There was no difference in mean aUCA or aUCA >95° and >105° for sPTB <37 or <32w. Overall, pUCA >105° had a sensitivity of 100% and specificity of 43.5% for sPTB<32w. Based on the ROC for sPTB<32, a pUCA angle >135° had a sensitivity of 83.3% and specificity of 70.3%. Both pUCA and CL were predictive of sPTB<32w and were superior to aUCA (pUCA: ROC AUC 0.83, p<0.001; CL: ROC AUC 0.78, p=0.002; aUCA: ROC AUC 0.53, p=0.82).

In singletons, pUCA was not associated with sPTB <37w. pUCA>105° was associated with sPTB<32w but our analysis suggests that an angle of >135° may be a better cut off. Overall, pUCA is superior to aUCA in the prediction of sPTB<32w, however, use as an alternative, or in addition, to CL requires further study.



In this image, 3D rendering is used to image the uterus in 3 dimensional space and correctly define the number of fetuses.

INNOVATION

UR: A Leader in Technology Commercialization

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

The University of Rochester has a long-standing tradition of being at the forefront of innovation and scientific research. In 2019, 122 invention disclosures were received from 193 inventors from 40 University departments and divisions. Forty-one external collaborators from 28 institutions, agencies, and corporations were also named as inventors. Six copyright registrations and 115 patent applications were filed in FY 2019. Of the patent filings, 60 were new matter filings, while 55 were continuations of applications filed in previous years. In FY 2019, the UR was granted 32 U.S. patents and 46 foreign patents. These 78 patents cover 41 different technologies. In FY 2019, the UR also executed 34 new license and options agreements and monitored 187 active agreements.

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.

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Superresolution Imaging of Scatterers in Pulse-Echo Imaging, U.S. Patent No. 9,453,908	Kevin J. Parker September 27, 2016
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Photodynamic Therapy with Spatially Resolved Dual Spectroscopic Monitoring, U.S. Patent No. 9,044,140	Thomas H. Foster, et al. June 2, 2015
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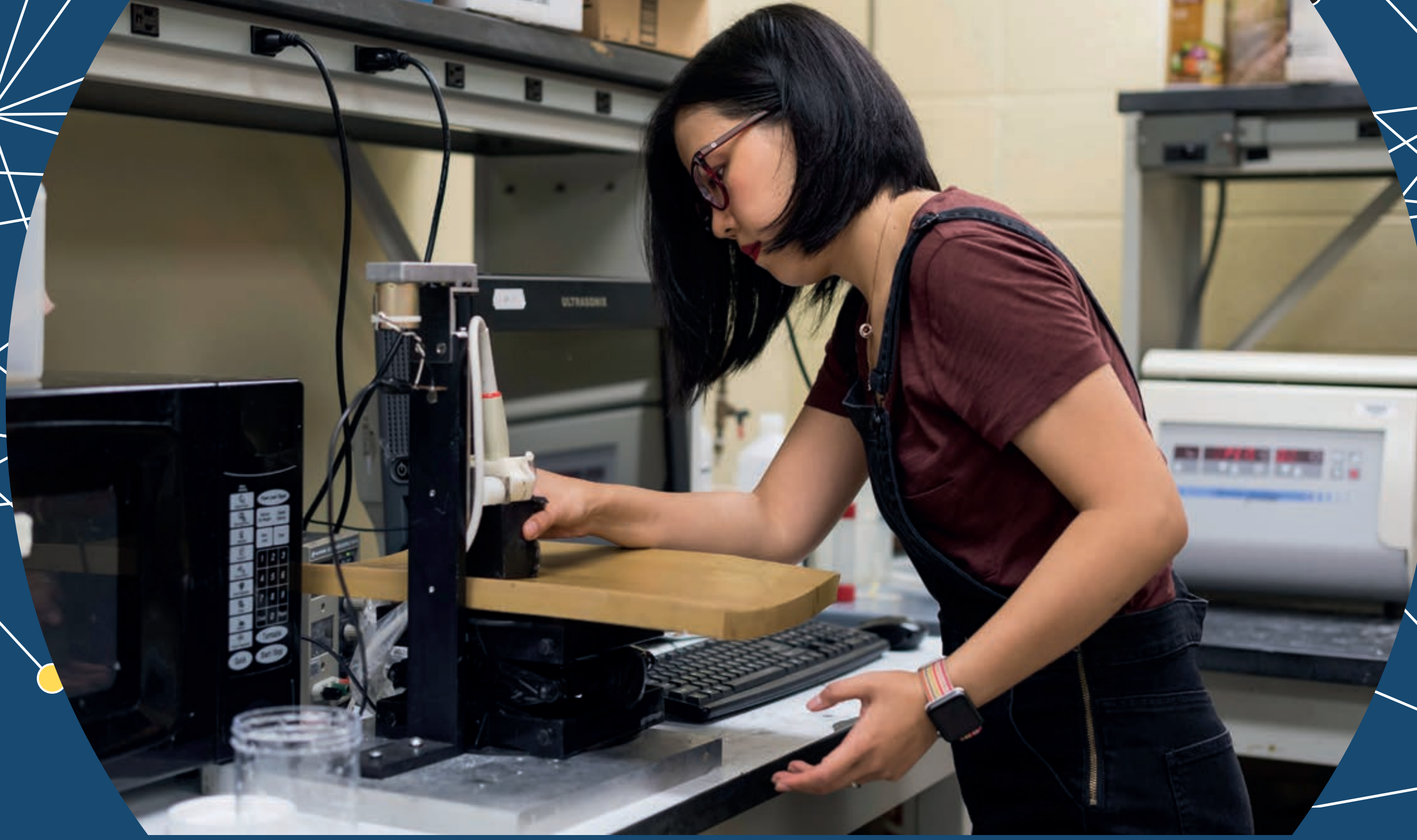

GRADUATE TRAINING OPPORTUNITIES at the RCBU

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 dalecki@bme.rochester.edu.

research areas

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

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