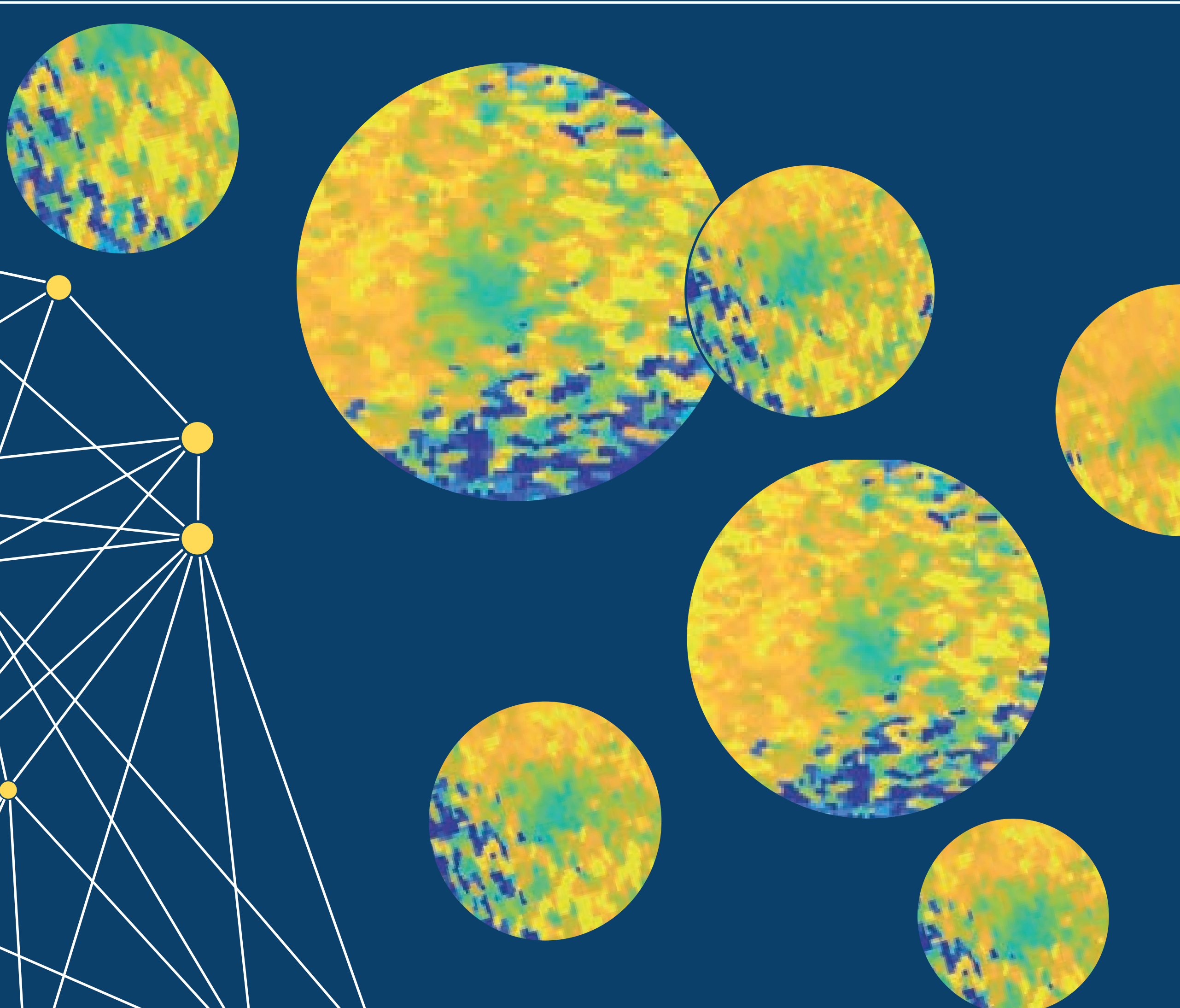
RCBU ANNUAL REPORT 2018

Rochester Center for Biomedical Ultrasound



UNIVERSITY of ROCHESTER

Pictured: Robert B. Goergen Hall, home to several RCBU research laboratories

RCBU Director
Diane Dalecki, Ph.D.
RCBU Associate Director
Deborah J. Rubens, M.D.
University of Rochester President
Richard Feldman, Ph.D.
University of Rochester Provost
Robert L. Clark, Ph.D.
Dean of the School of Medicine and Dentistry; CEO of the University of Rochester Medical Center
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Donald Hall, Ph.D.
Dean of the Hajim School of Engineering and Applied Sciences
Wendi Heinzelman, Ph.D.
Editing & Graphic Design
Courtney Rieder Nielsen

on the COVER

Images on the cover are elasticity maps of phantoms obtained using Hadamard-encoded, multi-element synthetic aperture beamforming and state-of-the-art compounded plane wave imaging. For more information on this work from the laboratory of Professor Marvin Doyley, please see pg. 24 of this report.

CONTENTS

Message from the Directors

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. Research in RCBU laboratories is advancing biomedical ultrasound for imaging and therapy. Included in this report are highlights of RCBU research across diverse topics in ultrasound, such as novel elastography techniques, contrast agents, nonlinear acoustics, ultrasound technologies for tissue engineering and regenerative medicine, quantitative ultrasound tissue characterization including the new H-scan technique, and therapeutic applications of ultrasound (pg. 21-31).

This year we established the annual RCBU Biomedical Ultrasound Symposium Day (pg. 6-11). The symposium is designed to showcase advances in biomedical ultrasound research and technology, foster collaborations, and provide a platform for trainees to present their research and network with other scientists, engineers, and clinicians. A highlight of this symposium is the *Distinguished Edwin L. Carstensen Lecture*. This year, the inaugural lecture was delivered by Frederick W. Kremkau, PhD and titled, "Your New Paradigm for Understanding and Applying Sonographic Principles." The symposium also featured the Distinguished RCBU Alumni Lecture presented by Theresa Tuthill, PhD. Dr. Tuthill is the Senior Director, Clinical and Translational Imaging at Pfizer, Inc, and her lecture discussed advances in ultrasound imaging for pharmaceutical development. The remainder of the full-day symposium included topical lectures, student presentations, a scientific poster session, and opportunities for networking. The RCBU Biomedical Ultrasound Symposium Day was inspired and enabled by the establishment of the Edwin and Pam Carstensen Family Endowment (pg. 9). This endowment honors the legacy of Ed Carstensen and ensures that his vision for the RCBU endures. The inaugural RCBU Biomedical Ultrasound Symposium Day was a resounding success!

This report also summarizes recent funding news, and awards and achievements of RCBU investigators (pg. 17-20). RCBU faculty have been very successful in garnering new funding to support their research in biomedical ultrasound. A list of selected patents by RCBU members in areas of biomedical ultrasound can be found on pg. 32-33, including descriptions of two new patents. Collaborative projects between RCBU clinicians, engineers, and scientists continue to fuel new discoveries in diagnostic and therapeutic applications of ultrasound.

Our student members are also a vital component of the RCBU. The RCBU provides exciting opportunities for education and research training in biomedical ultrasound. Included within this report are awards and fellowships garnered by RCBU student members, highlights of student research, updates on community outreach by RCBU students, and educational advances by RCBU members (pg. 12-16). This was an exciting year of research, education, and innovation at the RCBU!

Ultrasound continues to grow at the University of Rochester Medical Center; by the end of 2018 we were at 37,316 exams for the Imaging Sciences Department. Our clinical enterprise includes Strong West, and out-patient sites at Penfield, and at East River Road. 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 93,592 ultrasound examinations/year.

At the University of Rochester, Dr. Rubens participated in two national events: the inaugural RCBU Biomedical Ultrasound Symposium Day, and the Urology Festschrift honoring Dr. Edward Messing. 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, the Society of Emergency Radiology and the Radiologic Society of North America. Dr. Rubens continues in her faculty role for the American Institute of Radiologic Pathology, which offers a four-week course five times annually for radiology residents and practitioners from the United States, Canada and international attendees. She is also a program director for the Ultrasound Case Based Review course for the Radiologic Society of North America.

Internationally, Dr. Sidhu was an invited lecturer in India in both 2018 and 2019. Dr. Dogra was an invited speaker in Athens, Greece and in Indore, India and continues his efforts with Medical Imaging Partnership, delivering ultrasound equipment and training in underserved areas throughout the world. Dr. Avice O'Connell is a world-renowned speaker and is frequently solicited for her expert opinion in the media. This year she was invited to speak in Beijing, China, and India.

Dr. Dogra continues his investigations of photoacoustic imaging of the prostate and the thyroid. He is editor-in-chief of the Journal of Clinical Imaging Science and also of the newly launched American Journal of Sonography. Dr. Rubens and Dr. Ashwani Sharma have completed a grant with Professor Kevin Parker and Samsung on liver elasticity and steatosis with results published in the Journal of Ultrasound in Medicine and Biology. Dr. O'Connell is also collaborating with Samsung on developing ultrasound techniques for breast elastography. Dr. Thomas Marini and Dr. Kate Kaproth-Joslin are working with Professor Benjamin Castaneda in Peru, to deliver ultrasound diagnosis of pneumonia in rural settings.

Diane Dalecki, Ph.D.
RCBU Director

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 32 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.

Inaugural RCBU Biomedical Ultrasound Symposium Day

Tuesday, November 6, 2018
8:00am-6:00pm

agenda

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.

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
Your New Paradigm for Understanding and Applying Sonographic Principles
Frederick W. Kremkau, Ph.D., FACR, FAIMBE, FAIUM, FASA
Professor of Radiologic Sciences, Director, Program for Medical Ultrasound
Wake Forest University School of Medicine

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

Ultrasound and Artificial Intelligence
Ajay Anand, Ph.D.
Deputy Director of the Goergen Institute for Data Science
University of Rochester

Lunch, Scientific Poster Session, and Networking

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

Distinguished RCBU Alumni Lecture
Ultrasound in Drug Development
Theresa Tuthill, Ph.D.
Senior Director, Clinical and Translational Imaging, Pfizer, Inc.

Clinical Challenges
Deborah J. Rubens, M.D., Professor of Imaging Sciences
University of Rochester
Stefanie Hollenbach, M.D., M.S., Department of Obstetrics and Gynecology
University of Rochester
Moderator: Kevin J. Parker, Ph.D., William F. May Professor of Engineering, Professor of Electrical and Computer Engineering
University of Rochester

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

Concluding Remarks
Diane Dalecki, Ph.D.

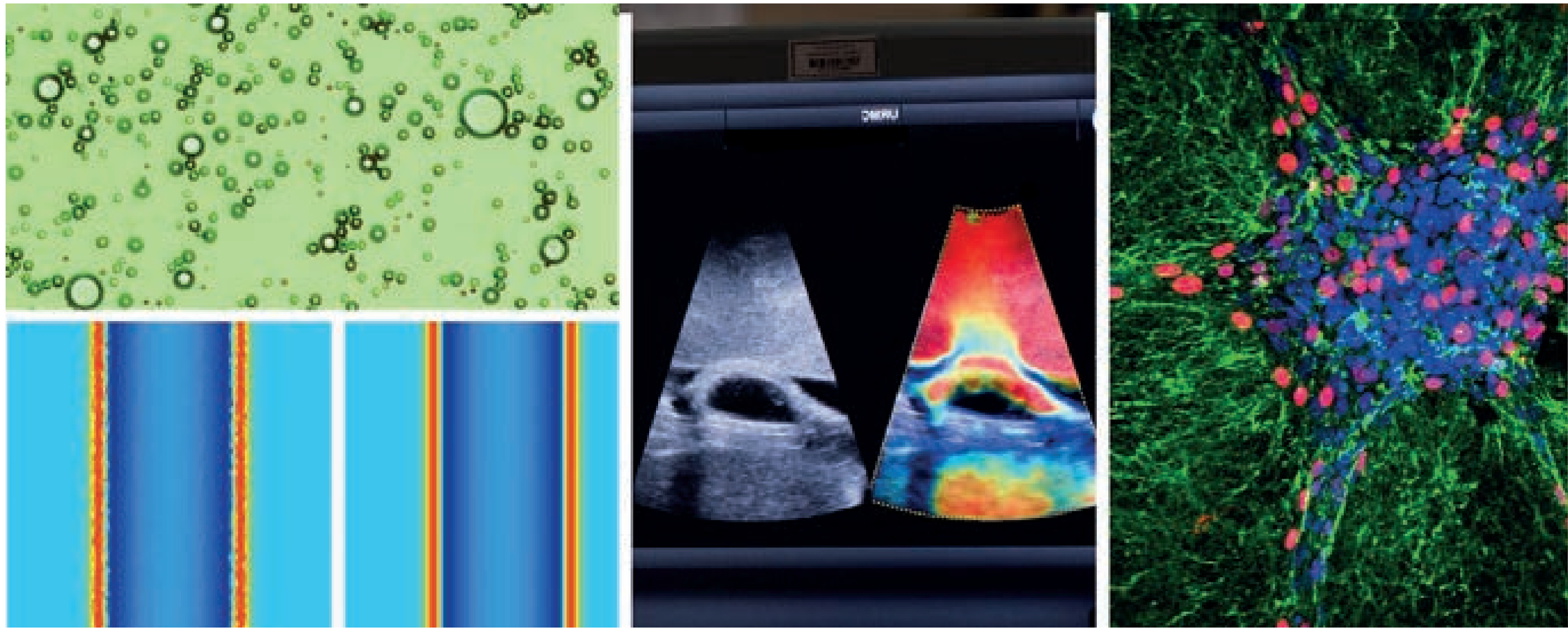
Networking Hour & Refreshments

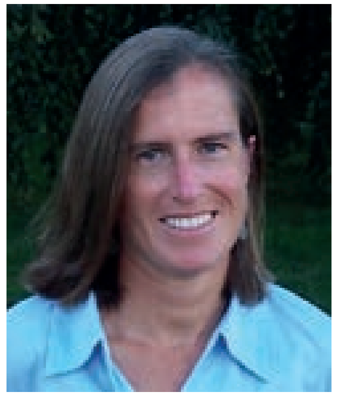
Distinguished Lectures

Distinguished Edwin L. Carstensen Lecture

Your New Paradigm for Understanding and Applying Sonographic Principles
Frederick W. Kremkau, Ph.D., FACR, FAIMBE, FAIUM, FASA
Professor of Radiologic Sciences, Director, Program for Medical Ultrasound
Wake Forest University School of Medicine

Dr. Kremkau is Professor of Radiologic Sciences at Wake Forest University School of Medicine. He holds degrees in Electrical Engineering from Cornell University and the University of Rochester. He is a Past President of the AIUM and holds fellowships in the AIUM, the ACR, the American Institute for Medical and Biological Engineering and the Acoustical Society of America. Dr. Kremkau co-directs the annual AIUM Advanced Ultrasound Seminar in Orlando and the annual Thomas Jefferson University Leading-Edge Diagnostic Ultrasound conference in Atlantic City. He authors the textbook, Sonography Principles and Instruments, which is in its 9th edition. He is currently in his 48th year in academic medicine and in his 14th year of half-time transition to retirement.





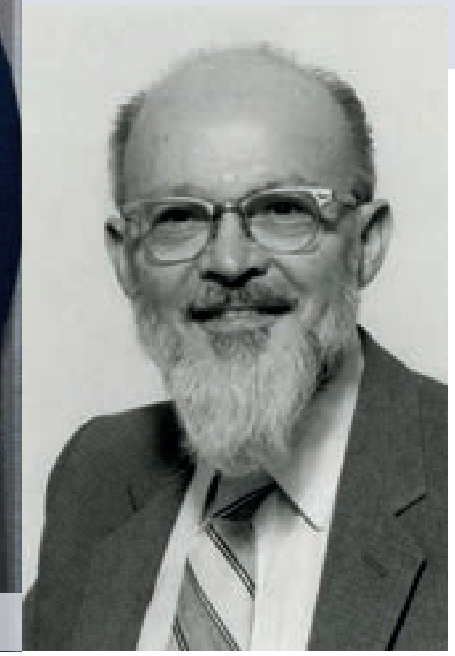
Distinguished RCBU Alumni Lecture

Ultrasound in Drug Development
Theresa Tuthill, Ph.D.
Senior Director, Clinical and Translational Imaging, Pfizer, Inc.

Theresa Tuthill is Head of the Imaging Methodologies, Biomarkers and Development line within Early Clinical Development at Pfizer. She oversees a small group dedicated to the development of imaging biomarkers for metabolic, cardiovascular, and safety applications. She holds a Ph.D. in Electrical Engineering from the University of Rochester where her research emphasis was on ultrasonic tissue characterization. Before joining Pfizer, she served as a Research Investigator for the Radiology Department at the University of Michigan Health Center where she led projects investigating blood flow and ultrasound contrast agents

Pictured above (from left to right): Theresa Tuthill, Ph.D., Professor Stephen McAleavey, Professor Kevin J. Parker, Professor Diane Dalecki, and Professor Frederick W. Kremkau

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.

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 or contact Derek Swanson at derek.swanson@rochester.edu or 585.273.1341

Pictured above: Professor Ajay Anand, Deputy Director of the Goergen Institute for Data Science, discusses ultrasound and artificial intelligence.

Pictured at left: Professor Frederick W. Kremkau delivers the Distinguished Edwin L. Carstensen Lecture titled, "Your New Paradigm for Understanding and Applying Sonographic Principles." Pictured at right: RCBU Director Diane Dalecki and Theresa Tuthill, Ph.D. at the RCBU Biomedical Ultrasound Symposium.

RCBU Symposium Poster Presentations

Poster Presentation Winners
(highlighted below)
1st Place: Emma Grygotis Norris
2nd Place: Hannah R. Goldring
3rd Place: Aldo Tecse

Acoustic Modification of Collagen Scaffolds Facilitates Cellular Remodeling
Emma Grygotis Norris, Diane Dalecki, Denise C. Hocking

Cerebrovascular Impulse Response to Tactile Somatosensory and Motor Stimulation Measured with fTCD
Dominique James, Benjamin Hage, Jake Greenwood, Steven Barlow, Greg Bashford

Elastographic Imaging of the Pancreatic Cancer Tumor Microenvironment
Hexuan Wang, Reem Mislati, Rifat Ahmed, Bradley Mills, Jason Gunn, Scott Gerber, Brian Pogue, Marvin Doyley

Estimates of Lossy Media Parameter in Normal and Steatotic Livers
Juvenal Ormachea, Zaegyoo Hah, Kevin J. Parker

Gaussian Shear Wave Propagation in Viscoelastic Media: Validation of an Approximate Forward Model
Fernando Zvietcovich, Natalie Baddour, Jannick P. Rolland, Kevin J. Parker

High-Frequency Quantitative Ultrasound for Characterizing Collagen Fiber Alignment in Tendon
Sarah Wayson, Maria Helguera, Denise C. Hocking, Diane Dalecki

Hybrid Force Velocity Control with Compliance Estimation via Strain Elastography for Robot Assisted Ultrasound Scanning
Michael E. Napoli, Christian Freitas, Soumya Goswami, Stephen McAleavey, Marvin Doyley, Thomas M. Howard

Low Complexity Compressed Ultrasound
Jovan Mitrovic, Zeljko Ignjatovic

Machine Learning Algorithm for Automated Diagnosis of Pneumonia in Children Using Ultrasound
Breno V. Munoz, Omar Zenteno, Benjamin Castaneda C., Gilberto Pena, Dante Ramos, Roberto Lavarello, Benjamin Castaneda

Mapping Compressive and Tensile Strains in the Patellar Tendons of Patients with Osgood-Schlatter Disease Using Ultrasound Elastography
Grace E. Weyand, Hannah R. Goldring, Catherine K. Kuo, Michael S. Richards, Mark R. Buckley, Katherine H. Rizzone

Mechanical Anisotropy in the Healthy and Pathological Achilles Tendon Assessed Using Shear Wave Elastography
Hannah R. Goldring, Crystal (Kyoung) Kim, Grace E. Weyand, Rifat Ahmed, Zachary Dejager, Soumya Goswami, Stephen A. McAleavey, Mark R. Buckley

Non-Invasive Ultrasound Imaging to Assess Tendon Healing
Jessica Ackerman, Valentina Studentsova, Marlin Myers, Michael Richards, Alayna Loiselle

Novel Real-Time Motion Sensitive Ultrasound Enables High Resolution Imaging of Tumor Stiffness and Microenvironment in Freely Breathing Mice
Rifat Ahmed, Bradley Mills, Scott Gerber, Marvin Doyley

Novel Sonographic Technologies for Innovation in Placental Assessment of Gestation: The NESTING Study
Stefanie J. Hollenbach, Richard Miller, Kevin J. Parker, Diane Dalecki, Stephen McAleavey

Quantitative Imaging of Nonlinear Shear Modulus with Bi-Axial Motion Registered Local Strain Distribution
Soumya Goswami, Rifat Ahmed, Marvin Doyley, Stephen McAleavey

Shear Wave Elastography to Investigate the Role of Interferon-Gamma on Treatment of Pancreatic Ductal Adenocarcinoma
Reem Mislati, Hexuan Wang, Rifat Ahmed, Jeremy Deniega, Bradley Mills, Marvin M. Doyley, Scott Greger

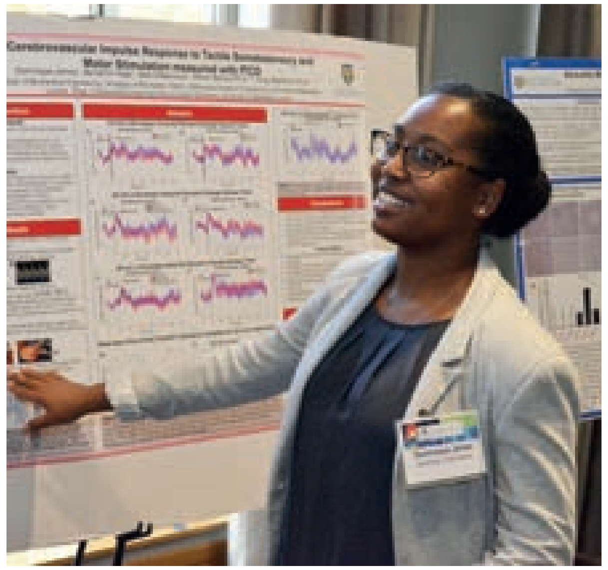
Size Manipulation of Ultrasound Contrast Agent and Its Impact on Nonlinear Emissions
Jeffrey Rowan, James McGrath, Marvin Doyley

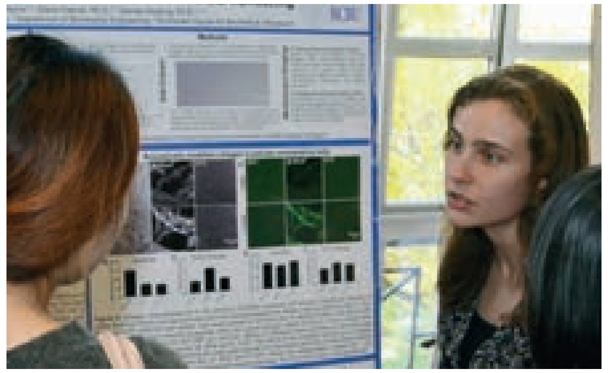
The Estimation of Viscoelastic Properties in Ex-Vivo Liver and Oil-in-Gelatin Phantoms Using Ultrasound and Mechanical Measurements
Sedigheh Sheykholeslami, Juvenal Ormachea, Kevin J. Parker

Therapeutic Ultrasound and Fibronectin in Dermal Wound Healing
Melinda A. Vander Horst, Carol H. Raeman, Denise C. Hocking, Diane Dalecki

Ultrasound Patterning for Tissue Engineering
Victoria Breza, Melinda A. Vander Horst, Sarah E. Wayson, Denise C. Hocking, Diane Dalecki

Validation of Quantitative Sonoelastography for Skin Characterization: Preliminary Results
Aldo Tecse, Ana Cecilia Saavedra, Benjamin Castaneda





RCBU Symposium Graduate Student Oral Presentations

Acoustic Modification of Collagen Scaffolds Facilitates Cellular Remodeling
Emma Grygotis Norris, Diane Dalecki, Denise C. Hocking

Elastographic Imaging of the Pancreatic Cancer Tumor Microenvironment
Hexuan Wang, Reem Mislati, Rifat Ahmed, Bradley Mills, Jason Gunn, Scott Gerber, Brian Pogue, Marvin Doyley

High-Frequency Quantitative Ultrasound for Characterizing Collagen Fiber Alignment in Tendon
Sarah Wayson, Maria Helguera, Denise C. Hocking, Diane Dalecki

Hybrid Force Velocity Control with Compliance Estimation via Strain Elastography for Robot Assisted Ultrasound Scanning
Michael E. Napoli, Christian Freitas, Soumya Goswami, Stephen McAleavey, Marvin Doyley, Thomas M. Howard

Low Complexity Compressed Ultrasound
Jovan Mitrovic, Zeljko Ignjatovic

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Jessica Ackerman, Valentina Studentsova, Marlin Myers, Michael Richards, Alayna Loiselle

Novel Real-Time Motion Sensitive Ultrasound Enables High Resolution Imaging of Tumor Stiffness and Microenvironment in Freely Breathing Mice
Rifat Ahmed, Bradley Mills, Scott Gerber, Marvin Doyley

Novel Sonographic Technologies for Innovation in Placental Assessment of Gestation: The NESTING Study
Stefanie J. Hollenbach, Richard Miller, Kevin J. Parker, Diane Dalecki, Stephen McAleavey

Reverberant 3D Optical Coherence Elastography (Rv3D-OCE): A Novel Method for Elasticity Mapping of Single Layers in Cornea
Fernando Zvietcovich, Pornthep Pongchalee, Jannick P. Rolland, Panomsak Meemon, Kevin J. Parker

Size Manipulation of Ultrasound Contrast Agent and Its Impact on Nonlinear Emissions
Jeffrey Rowan, James McGrath, Marvin Doyley

Therapeutic Ultrasound and Fibronectin in Dermal Wound Healing
Melinda A. Vander Horst, Carol H. Raeman, Denise C. Hocking, Diane Dalecki

2D Linear Dispersion Slope Images Using a Reverberant Shear Wave Field: Application of CIRS Phantoms and In Vivo Liver Tissue
Juvenal Ormachea, Kevin J. Parker

BME design teams focused on ultrasound projects

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.

Pictured: BME master's students (CMTI) Eric Ravinal (left) and Vladimir Tokarchuk (right), members of the Quick and Repeatable Ultrasound Imaging during CPR team, demonstrate their project at the Hajim School Design Day

Pictured: BME senior Kwasi Nimako, a member of the Guiding US IV team, explains their prototype

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

The 2017-2018 senior design experience also included a team focused on an ultrasound project. Students on this team were Kate Bushway, Anisha Khosla, Kwasi Nimako, and Veronica Valencerina. Their project focused on designing a device to aid in ultrasound guided IV insertion in an emergency room setting.

Graduate students in the BME Master's program in Medical Device Design also regularly tackle ultrasound-related engineering design problems. In 2018, one team of students (Eric Ravinal and Vladimir Tokarchuk) focused on an approach to reduce the time required to find an appropriate ultrasound image in cardiac arrest patients in order to minimize patient scan time.

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 reach out to Greg Gdowski (greg_gdowski@urmc.rochester.edu).

Professor Marvin Doyley discusses imaging research in UR CTSI massive open online course promoting translational research

Professor Marvin Doyley was a lecturer in a new massive open online course (MOOC) developed by the University of Rochester Clinical and Translational Science Institute (UR CTSI). The course, titled Introduction to Translational Science, is available for enrollment on Coursera. Through six modules, the course provides an understanding of clinical and translational science. Professor Doyley described his research on ultrasound imaging and its impact in the diagnosis and treatment of cancer. For more information on the course, visit https://www.urmc.rochester.edu/clinical-translational-science-institute/stories/september-2017/ur-ctsi-demystifies-translational-science-with-new.aspx.

RCBU ultrasound outreach propagates across New York

RCBU trainees are active members of the greater Rochester community, and regularly share their work with audiences of all ages. Through a series of demonstrations, RCBU students share the science of waves on a string, introducing how concepts like amplitude and frequency determine the sounds that we hear. A vibrating Chladni plate helps to visualize how standing waves can be used to move colorful sand into complex patterns. For a more hands-on demonstration, kids have the opportunity to make their own waves using giant Slinkys, and they always have a blast teaching graduate students their own lesson: just how tangled a Slinky can really get!

The team of RCBU student members (Emma Grygotis Norris, Melinda Vander Horst, Sarah Wayson) have featured these demonstrations at a variety of events including the IMAGINE fair hosted at Honeoye Falls Manor Intermediate School. Members of the Biomedical Engineering Graduate Student Council, including RCBU student member Melinda Vander Horst (BME doctoral student), organized the trip, which brought together graduate students from across the UR BME department to feature hands-on learning experiences in the fair's engineering wing. Hundreds of 2nd through 5th graders had the opportunity to explore concepts across physics, optics, robotics and acoustics through exciting and educational demonstrations that introduced them to new ideas and activities, inspiring them to explore the world beyond their classwork.

Pictured: Sarah Wayson (left) and Melinda Vander Horst (right) demonstrate waves on strings at the Rochester Science Expo.

Pictured: Emma Grygotis Norris, Haley Bertrand, and Dominique James (left to right) demonstrate standing wave fields for elementary school students at the IMAGINE Fair hosted at a local elementary school.

RCBU members also participated in both the first and second annual Rochester Science Expo, alongside presenters from area schools, local businesses, and educational organizations. In addition to standing wave field demonstrations, the events also featured Professor Denise Hocking, who prepared an interactive exhibit on the science of beer brewing and yeast biology, and Professor Diane Dalecki, who discussed the many ways advances in biomedical engineering benefit us all. The events were hosted by the Rochester NY March for Science, a non-profit educational and advocacy organization co-founded by RCBU student member Emma Grygotis Norris (Pharmacology and Physiology doctoral student), alongside fellow researchers, educators and parents from the Rochester area, all passionate about creating informal opportunities for scientists and creators of all ages to share their work.

For high school students, actively considering the many career options available to them, the path to becoming a scientist can seem a daunting one. RCBU student member Sarah Wayson (BME doctoral program) was invited to give an alumna lecture to high school seniors at Tioga Central High School's Leadership Week in Tioga Center, New York. Sarah introduced her motivation for pursuing a career in biomedical engineering, and her academic path to becoming a doctoral student. She shared her experiences studying engineering in college, and strategies for overcoming challenges along the way. She emphasized the importance of informational interviews, job shadowing, and creating a network for students interested in pursuing careers in science and engineering. Students ended with a conversation about effective leadership qualities.

These events are wonderful opportunities for RCBU members to step outside the lab and become better communicators. They are also a chance to share their enthusiasm for biomedical ultrasound and acoustics with science enthusiasts of all ages, and to inspire others to use the tools of science to solve problems big and small.

"It is wonderful to see RCBU student members sharing their knowledge, experience, and enthusiasm for ultrasound and acoustics with the broader community."
- Diane Dalecki, RCBU Director

TRAINING COMPLETED

MATTHEW ARCHIBALD

Matthew Archibald completed his M.S. training in Electrical and Computer Engineering at the University of Rochester. His thesis, titled, "Parallel 3D Harmonic Finite Element Analysis," was supervised by Professor Marvin Doyley.

SHUJIE CHEN

Shujie Chen completed his Ph.D. in Electrical and Computer Engineering at the University of Rochester. His thesis, titled, "Enhanced Resolution in Pulse-Echo Imaging," was supervised by Professor Kevin Parker.

ERIC COMEAU

Eric Comeau completed his Ph.D. in Biomedical Engineering at the University of Rochester. His thesis, titled, "Ultrasound Standing Wave Field Technologies for Cell Patterning and Microvessel Network Formation in Vitro and In Situ," was supervised by Professor Diane Dalecki and Professor Denise Hocking.

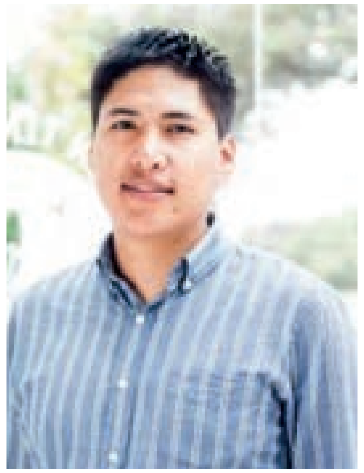
OSCAR OSAOPETRA

Oscar Osaopetra received his Ph.D. in Physics from the University of Rochester. His thesis, titled, "Quantitative Corneal Elastography Using High-frequency Ultrasound," was supervised by Professor Stephen McAleavey.

STUDENT AWARDS

Emma Grygotis Norris (Pharmacology and Physiology) was the recipient of the Outstanding Student Mentor Award from the University of Rochester School of Medicine and Dentistry. She received this award based on her contributions to mentoring, leadership, science advocacy, and community outreach. Emma also received First Place in the Best Poster Award competition at the 2018 RCBU Biomedical Ultrasound Symposium Day for her poster titled "Acoustic Modification of Collagen Scaffolds Facilitates Cellular Remodeling." Emma is a doctoral student working in the laboratory of Professor Denise Hocking.

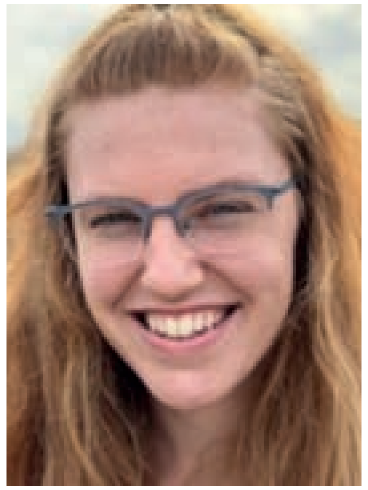
Fernando Zvietcovich (ECE) received First Place in the Best Student Oral Presentation category at the 2018 International Tissue Elasticity Conference for his presentation titled "Reverberant 3D Optical Coherence Elastography (REV3D-OCE): A Novel Method for the 3D Elastic Mapping of Layers in Cornea." He also received the Best Poster Award at the same conference for his poster titled "Gaussian Shear Wave Propagation in Viscoelastic Media: Validation of an Approximate Forward Model." Fernando's doctoral research is supervised by Professor Kevin Parker.



Juvenal Ormachea (ECE) received the New Investigator Honorable Mention award at the 2018 American Institute of Ultrasound in Medicine (AIUM) Annual Convention for his work titled "Reverberant Shear Wave Elastography: Implementation and Feasibility Studies." Juvenal is a doctoral student in Electrical and Computer Engineering and his research is supervised by Professor Kevin Parker.

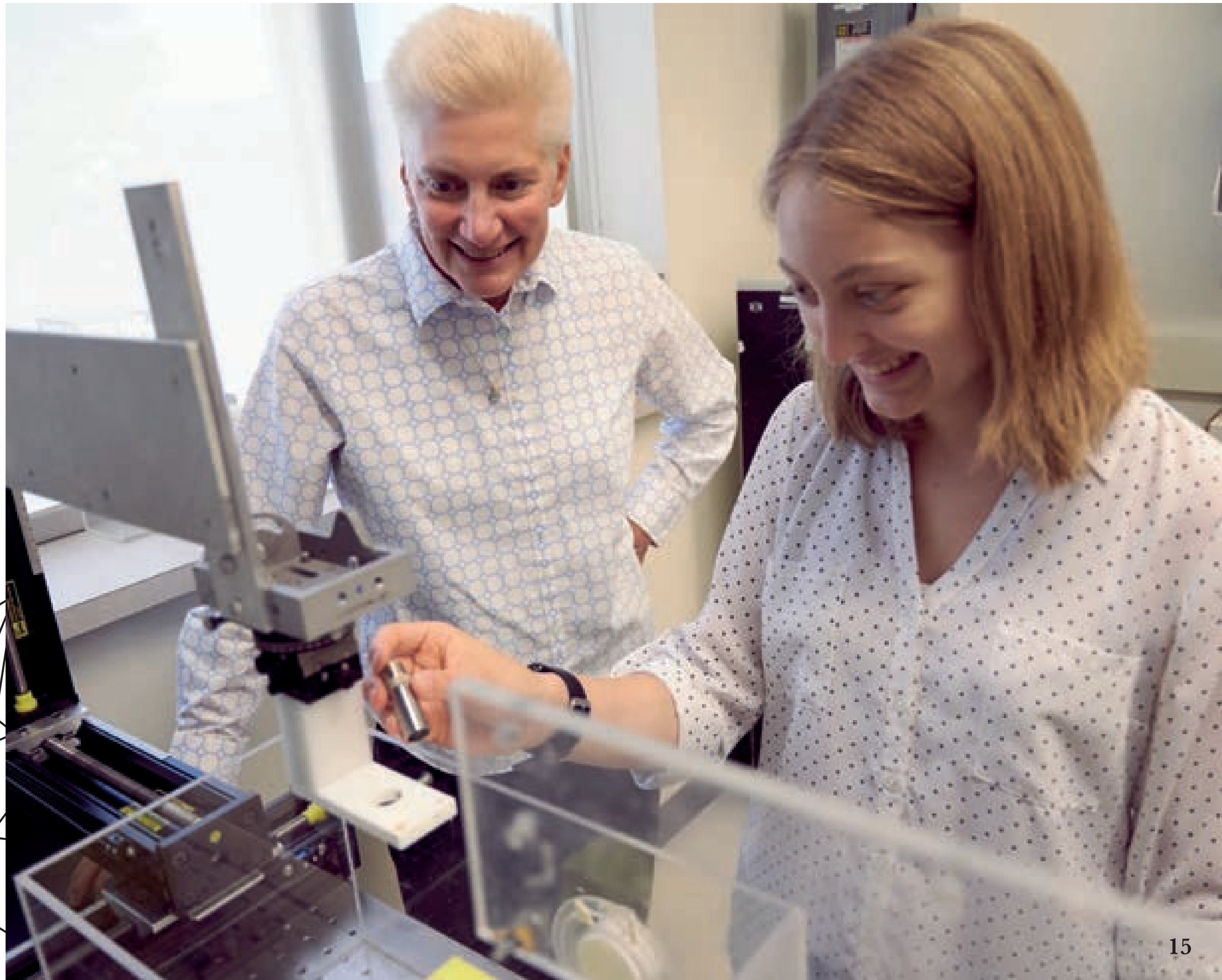
Pictured on opposite page: RCBU Director Diane Dalecki (left) mentors Holly Coleman (right), a student at Missouri University of Science and Technology, as part of the NSF-sponsored REU summer research program titled "Advancing Human Health, from Nano to Network" at the University of Rochester.

STUDENT FELLOWSHIPS



Victoria Breza was the recipient of a Xerox Undergraduate Research Fellowship. Victoria, a UR biomedical engineering student, worked with Professor Diane Dalecki and Professor Denise Hocking on a project to advance ultrasound patterning technologies for tissue engineering. The Xerox Undergraduate Fellowship is a highly selective program that provides research experience for undergraduates during the summer and continuing through the academic year.

Holly Coleman, a chemical engineering student from the Missouri University of Science & Technology, was a recipient of an National Science Foundation (NSF) REU Human Health from Nano to Network Applications Fellowship at the University of Rochester. This fellowship enabled Holly to spend the summer performing research on high-frequency ultrasound imaging of collagen in the laboratories of Professor Diane Dalecki and Professor Denise Hocking.



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.

Biomedical Optics

(BME 492) Introduces the major diagnostic methods in biomedical optics. The course emphasizes spectroscopy (absorption, fluorescence, Raman, elastic scattering), photon migration techniques (steady-state and time-resolved), and high-resolution subsurface imaging (confocal, multi-photon, optical coherence tomography). Essential methods of multivariate data analysis are taught in the context of spectroscopy.

Applied Vibration Analysis

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

Nonlinear Finite Element Analysis

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

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.

FACULTY AWARDS & HONORS

NEW APPOINTMENTS

Marvin Doyley

Marvin Doyley was promoted to full professor of Electrical and Computer Engineering. The promotion recognizes Professor Doyley's internationally-recognized achievements in biomedical ultrasound research, his teaching expertise, and his dedication to service within the university and across the broader scientific community.

Sheryl Gracewski

Sheryl Gracewski was recently appointed Emeritus Professor of Mechanical Engineering at the University of Rochester. Throughout her career, Professor Gracewski has been an internationally recognized scholar in biomedical ultrasound and an outstanding teacher and mentor. Her expertise and dedication continue to have impact in the research and teaching missions of the RCBU and the university.

Michael Richards

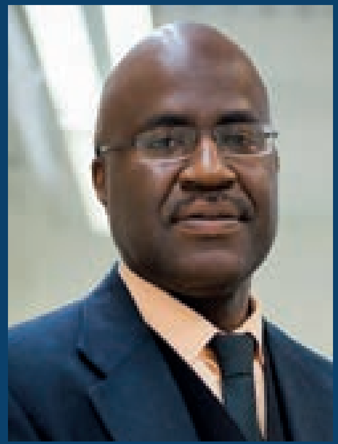
Michael Richards has been appointed an Assistant Professor in the Department of Biomedical Engineering at the Rochester Institute of Technology. Professor Richards' Biomechanical Imaging Lab focuses on the development of image processing techniques that make use of clinical imaging systems in novel ways to study the mechanical properties and mechanical interactions of biological tissues. Through cross-disciplinary collaboration and focus on translational science, the lab is able to bring techniques to the clinic for the diagnosis and treatment of a variety of human diseases.

Professor Sheryl Gracewski receives Lifetime Achievement Award

Pictured: Dean Wendi Heinzelman (right) presents Professor Gracewski (left) with Hajim School of Engineering & Applied Sciences Lifetime Achievement Award

Sheryl Gracewski was honored as the recipient of the Lifetime Achievement Award from the Hajim School of Engineering and Applied Sciences at the University of Rochester. The Lifetime Achievement Award recognizes Professor Gracewski's long-standing excellence in research, teaching, mentoring, and service to the university. Professor Gracewski joined the University of Rochester in 1984 as an assistant professor in the Department of Mechanical Engineering, and developed a research laboratory focused on wave propagation and vibration in biological and non-biological materials. She is internationally recognized for her expertise in modeling the interaction of ultrasound fields with biological tissue, with particular focus on computational modeling of the nonlinear dynamic responses of microbubbles exposed to acoustic fields (i.e., acoustic cavitation). She has a long history of research and seminal publications in biomedical ultrasound and lithotripsy. Her contributions to the field are internationally recognized, and she was elected a Fellow of the Acoustical Society of America in 2006. The Lifetime Achievement Award also recognized Professor Gracewski's breadth of expertise in engineering education and outstanding teaching acumen. Over the years, she has mentored nearly 20 graduate student thesis projects, included many undergraduate students in her research, and mentored and led the UR Mini Baja team for decades. In summary, the award honored Professor Gracewski's outstanding scholarly research and dedicated teaching and mentorship throughout her career. Congratulations!

Denise Hocking (Pharmacology and Physiology) received the Academic Mentoring Award for Basic Science Trainees at the University of Rochester School of Medicine and Dentistry. This award recognizes Professor Hocking's excellence in mentoring graduate students and graduate education. Professor Hocking was also appointed a regular member of the NIH Study Section on Biomaterials and Biointerfaces (BMBI) for a 4-year term spanning 2018-2022.



Marvin Doyley (ECE) was elected a Senior Member of the IEEE. He was also invited as a member of the IEEE Computational Imaging Research Group. Professor Doyley continued as a standing member of the NIH Biomedical Imaging Technology (BMIT-B) Study Section.

Professor Amy Lerner among winners of 2018 Presidential Diversity Award

Amy Lerner, co-chair of the Commission on Women and Gender Equity in Academia (CWGEA) was among those honored with the 2018 Presidential Diversity Award. Former President Joel Seligman established the awards in 2009 to recognize faculty, staff, students, units, departments, or teams that "demonstrate a commitment to diversity and inclusion through recruitment and retention efforts, teaching, research, multicultural programming, cultural competency, community outreach activities, or other initiatives." As co-chair of the CWGEA, Amy helped to lead the commission, which is comprised of students, faculty and trainee volunteers, in evaluating campus policies and procedures. Utilizing a combination of scientific literature review and community input, CWGEA released their preliminary report with recommendations in May 2018. They continue to research, listen, and advocate for diversity and inclusion throughout the University community. When accepting the award, Professor Lerner said, "This award is a tremendous honor for us and is really rewarding to validate the very hard work that we have done so far. Perhaps just as important, I think it also goes a long way to validate the importance of the goals we are trying to achieve – real equity for all members of the University community. There are many wheels still turning to address some of the concerns we raised and we are grateful to see that many of our recommendations are being implemented. Thank you very much for the honor."

"This award is a tremendous honor for us and is really rewarding to validate the very hard work that we have done so far. Perhaps just as important, I think it also goes a long way to validate the importance of the goals we are trying to achieve – real equity for all members of the University community."
-Amy Lerner

Pictured: Professor Amy Lerner (front left) pictured with the Commission on Women and Gender Equity in Academia (CWGEA)

NEW FUNDING

Diane Dalecki (BME) and Denise Hocking (Pharmacology and Physiology) were recipients of a new NIH grant titled "Fibronectin Mimetics and Synergistic Ultrasound Therapy for Wound Healing in Aging". This project will advance pre-clinical fibronectin matrix mimetics for treatment of chronic dermal ulcers that are associated with aging, and identify synergistic actions of fibronectin matrix mimetics and therapeutic ultrasound.

Alayna Loiselle (Orthopaedics) was the recipient of a UR University Research Award for her project titled "Non-Invasive Quantitative Assessment of Tendon Healing Using Ultrasound and Machine Learning". This project aims to use machine learning algorithms to automate image segmentation in the analysis of ultrasound images of tendon healing.

Kevin Parker (ECE) is principal investigator on a new NIH grant titled "The H-Scan Approach to Classifying Ultrasound Echoes." The H-scan framework enables a matching of different classes of echoes (from different cells and structures) to different colors, and has application in improving disease diagnosis. This project will optimize and test the H-scan analysis to make it reliable for use in different scanners and organs.

Marvin Doyley (ECE) received a UR Researcher Mobility Travel Grant to establish a new collaboration with Dr. Ingolf Sack at the Charité Universitätsmedizin Berlin in Germany for research in the area of brain magnetic resonance elastography (MRE). The goal of the collaboration is to establish a novel contrast mechanism for noninvasive functional brain imaging.

Kevin Parker (ECE) is an investigator on a new project sponsored by Samsung Medison Co. titled "Breast Ultrasound Image Review with Assistance of Deep Learning Algorithms." The objective of this study entails a second review of ultrasound images with suspicious breast lesions using an interactive "deep learning" (or artificial intelligence (AI)) program developed by Samsung Medison.

Diane Dalecki (BME) and Denise Hocking (Pharmacology and Physiology) were awarded a new NIH grant for their project titled "Developing Acoustic Patterning for Neuroengineering". This project focuses on developing ultrasound patterning technologies to engineer functional neural constructs.

Alayna Loiselle (Orthopaedics) is principal investigator on a new grant from the NIH titled "S100a4 Signaling in Fibrotic Diabetic Tendon Healing". Mark Buckley (BME) and Michael Richards (RIT BME) are co-investigators on this grant. This project will test the hypothesis that inhibition of the increased and sustained activation of pro-fibrotic S100a4-RAGE activity in diabetic tendons will promote mechanically superior, regenerative tendon healing.

Kevin Parker (ECE) received a University Research Award for the project titled "Brain Elastography with Optical Coherence Tomography." The goal of this project is to address key scientific questions on the sensitivity of brain elastography to regional differences within brain and to the progression of diseases. The project will employ the highest resolution brain elastography, using advanced optical coherence tomography techniques, on mouse models of normal and diseased brains.

Diane Dalecki (BME) and Denise Hocking (Pharmacology and Physiology) partnered with Imaginant Inc. on a project to develop and implement quantitative ultrasound systems for non-invasive, non-destructive characterization of engineered tissue constructs. The project was funded jointly by Imaginant, Inc. and the Center for Emerging and Innovative Sciences.

Alayna Loiselle (Orthopaedics) and Michael Richards (RIT BME) are multi-PIs on a new grant funded by the NIH titled "Ultrasound Elastography for Non-Invasive Assessment of Tendon Healing." The goal of this project is to develop longitudinal, non-invasive metrics of tendon healing by combining ultrasound elasticity imaging and novel image registration methods.

Diane Dalecki (BME) and Imaginant, Inc. received a grant from the Jeff Lawrence Innovation Fund for their collaborative project titled "Ultra-High-Frequency Ultrasound Transducer Manufacturing for Biomedical Markets." The overall goal of this project is to develop ultra-high-frequency ultrasound transducers, and novel manufacturing processes, for biomedical engineering and biotechnology markets.

RCBU Lab teams with Imaginant, Inc.

Pictured (from left to right): Jim Chwalek, Ph.D., Sarah Wayson, and Todd Jackson, Ph.D. during a project review at Imaginant's headquarters in Pittsford, NY.

The laboratory of Diane Dalecki at the University of Rochester has teamed with a local company, Imaginant Inc., to create high-frequency ultrasound systems for biomedical applications. Since its founding in 1986, Imaginant, located in Pittsford NY, has been an innovator in the design and manufacture of high-frequency ultrasound Pulser-Receivers and specialty non-destructive ultrasound test equipment. UR and Imaginant have established a productive collaboration with the goal of developing novel ultrasound instrumentation and quantitative imaging techniques for biomedical and biotechnology markets.

To date, this combined academia and industry team has received support for two projects.

- One project, funded by the Center for Emerging and Innovative Science, enabled the successful integration of Imaginant's state-of-the-art PureView™ family of Pulser-Receivers into the biomedical ultrasound research systems of the Dalecki lab, which improved the metrology capabilities within the lab.
- A second project has the goal of applying an innovative manufacturing process for the optimization of high-frequency ultrasound transducers that meet the demanding requirements of the Dalecki lab. This project is funded through the Jeff Lawrence Manufacturing Innovation Fund. Jim Chwalek, Imaginant's Chief Scientist and UR alum, states that this financial support was an important enabling factor for this research effort.

Sarah Wayson, a BME graduate student in the Dalecki lab, is employing the PureView™ instrumentation and optimized transducers for the development of quantitative ultrasound imaging techniques for characterizing collagen-based engineered tissues and native tissues.

Imaginant's CEO and UR alum, Todd Jackson, says that collaborating with UR was a natural fit to Imaginant's goal of expanding its role as an innovative leader in the design, manufacture, and application of high-frequency ultrasound instrumentation.

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 34-37.

2D linear dispersion slope images using a reverberant shear wave elastography field: Application in CIRS phantoms and in vivo liver tissue

Juvenal Ormachea, Benjamin Castaneda, Kevin J. Parker

Shear wave elastography estimates tissue stiffness by tracking shear wave propagation. However, many methods assume shear wave propagation is unidirectional and aligned with the lateral imaging direction. Recently, a new method was proposed to estimate tissue stiffness by creating a reverberant shear wave field propagating in all directions within the media. These reverberant conditions lead to simple solutions, facile implementation, and rapid viscoelasticity estimation of local tissue.

The aim of recent work from the Parker lab was to obtain 2D linear dispersion slope (LDS) images using the local estimated shear wave speed (SWS) at different frequencies in CIRS phantoms and in 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 multi-frequency (80-360 Hz) external sources. A Verasonics ultrasound system was used to track the induced displacements. The SWS was estimated using the method previously described, then the LDS was calculated from a chosen frequency range. A Samsung ultrasound system (model RS85, Samsung Medison) was used to measure the SWS for comparison purposes in the CIRS phantoms and it was considered as the reference method. 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 and the University of Rochester Institutional Review Board

Figure 1 shows 2D images of SWS and LDS for different cases: mean SWS of 2.49 m/s and 2.10 m/s (at 220 Hz), an accuracy error of 11.06% and 4.10% compared with Samsung system, and mean LDS of 0.25 m/s/100Hz and 0.69 m/s/100Hz 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/100Hz were estimated. In conclusion, it was possible to estimate the viscoelastic properties in phantom materials and in vivo human tissue using the R-SWE approach with consistent results in SWS and in LDS estimations. Moreover, results from the multi-frequency estimations indicate that it is not only feasible, but it can also more quickly assess frequency dependence than using single vibration frequencies which facilitates the use of the R-SWE approach for clinical applications.

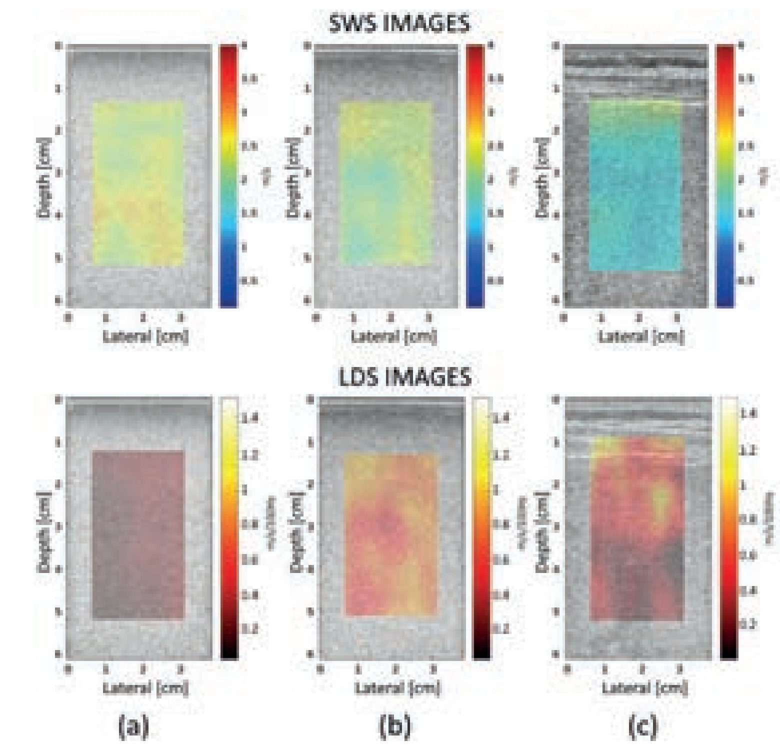


Figure1. SWS (top) and LDS (bottom) images using the R-SWE approach for (a) breast CIRS phantom, (b) viscoelastic CIRS phantom, and (c) in vivo human liver.

Mechanical anisotropy in the healthy and pathological Achilles tendon assessed using shear wave elastography

Hannah R. Goldring, Rifat Ahmed, Soumya Goswami, Zachary DeJager, Stephen A. McAleavey, Mark R. Buckley

The laboratories of Stephen McAleavey and Mark Buckley are working together to improve clinical monitoring of Achilles tendinopathy (AT), a common overuse pathology characterized by pain and swelling in the Achilles tendon. AT is known to impact the shear wave speed (SWS) – a parameter closely related to stiffness – in the Achilles tendon. However, other properties of the Achilles tendon are also altered by AT. In particular, a salient feature of AT is a loss of collagen organization that presumably impacts the relative stiffness of the Achilles tendon along its long and short axes. Thus, our objective was to test the hypothesis that AT is associated with an increase in "mechanical anisotropy", defined as the SWS along the long axis of the tendon (sagittal SWS) divided by the SWS along the short axis of the tendon (transverse SWS).

Four subjects (4 male; mean age 20) with AT (severity measured using a VISA-A survey determining pain levels with various activities) and four subjects (2 male, 2 female; mean age 25) with healthy Achilles tendons volunteered for the study. All subjects signed a consent form approved by the Institution's Research Subjects Review Board. Shear wave speed was determined with the subjects in four different positions: 1) sitting with the ankle plantarflexed to 30° (slack tendon) and the transducer in a sagittal orientation; 2) sitting with the ankle plantarflexed to 30° and the transducer in a transverse orientation; 3) standing (tendon tensed) with the transducer in a sagittal orientation; and 4) standing with the transducer in a transverse orientation. The transducer was held in place at either the insertion or the midportion of the Achilles tendon using a ring stand and clamp, with an ultrasound gel pad placed between the transducer and the subject. The midportion of the Achilles was identified as 4 cm above the middle of the lateral malleolus. Subjects were instructed to remain as still as possible for the duration of each test. Shear waves were propagated through the tissue and SWS recorded by tracking the echo.

Interestingly, assessment of SWS at the tendon insertion was not feasible due to acoustic reflection from the bone (Fig. 1). Assessment at the midportion demonstrated that anisotropy was more evident in tensed tendons as compared to slack tendons (Fig. 2). Surprisingly, anisotropy did not appear to be altered by pathology in these subjects.

The finding that anisotropy is higher in tensed tendon is consistent with previous studies in vitro and helps validate the anisotropy index (sagittal SWS divided by the transverse SWS) as a metric of collagen alignment. While AT did not impact this metric in the small cohort of subjects tested for this study, further investigation into the utility of this metric to quantify the response of pathological tendons to clinical interventions is warranted.

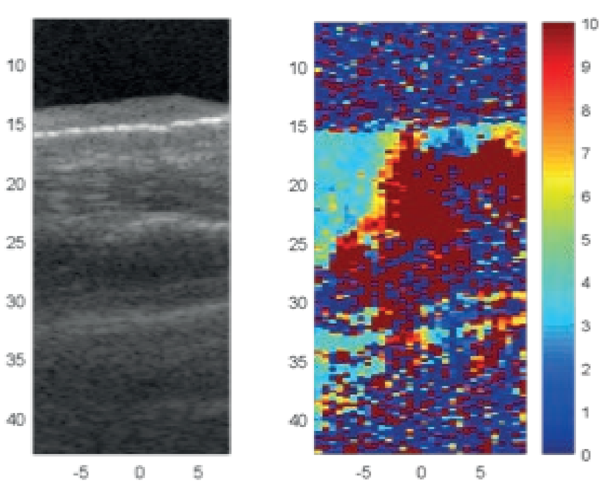


Figure 1. Saturation occurs when using SWE to measure the insertion into the calcaneus.

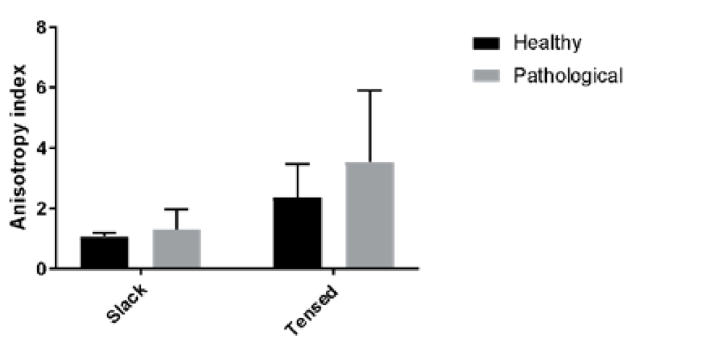


Figure 2. Anisotropy index for slack and tensed tendon, healthy vs. pathological. Anisotropy index=(sagittal SWS)/(transverse SWS).

The H-scan sensitivity to scatterer diameter

Kevin J. Parker

The H-scan analysis links the mathematics of Gaussian weighted Hermite (GWH) functions to the physics of scattering and reflections from different objects within a standard convolution model of pulse echo systems. Specific integer orders, termed GH_n, are related to the nth derivative of a Gaussian function. Matched filters employing specific orders of GH_n functions are used to analyze the content of echoes and to colorize the display, providing visual discrimination between scattering and reflecting types. Previous works have studied phantoms and tissues where resulting H-scan colors could be linked to scattering types and sizes. An important related issue is the sensitivity of H-scan analysis to small changes in scattering sizes, down to cellular level diameters such as 8–10 microns for red blood cells. Cell sizes and vascular diameters can vary in tissue in response to a number of factors including inflammation, edema, injury, and various pathological processes. In these cases, the detection of small changes in scattering sizes and visualization of the resulting changes in scattering properties is a longstanding goal in medical ultrasound. The H-scan analysis represents a distinct approach tied to the properties of the GWH functions, and the sensitivities of these are analyzed theoretically using the theory of scattering from spherical inhomogeneities. Experimental confirmations in phantoms and in beef liver sections exposed to hypotonic solution were demonstrated. With a 6 MHz center frequency broadband transducer it is possible to visualize changes in scattering size on the order of 10 to 15 microns in phantoms and also changes in ex vivo bovine liver tissue due to edema caused by hypotonic perfusion.

Acoustic modification of collagen biomaterials facilitates cell-mediated remodeling

Emma Grygotis Norris, Diane Dalecki, Denise C. Hocking

Chronic and hard to heal wounds are a major public health burden affecting 6.5 million adults in the United States alone, with healthcare costs upwards of $25 billion annually. Regenerative medicine approaches, including the use of tissue-engineered biomaterials, are a promising strategy to reinitiate healing in these patients. Engineered biomaterials rely on scaffolding structures, often extracellular matrix (ECM) glycoproteins, either alone or in combination with other components. Of these, type I collagen has proved a valuable starting material due to its ability to self-assemble into three-dimensional structures in vitro, as well its high abundance in a variety of tissues including skin, tendon, and bone. Collagen achieves this versatility through a cell-mediated hierarchical assembly process that imparts tissue-specific characteristics including collagen fibril conformation, fiber density and alignment, and binding affinities to other ECM components such as fibronectin. Therefore, strategies to control collagen structure and organization in vitro are essential for the development of improved biomaterials that can direct the behavior of cells within engineered constructs. Ongoing work in the Hocking and Dalecki labs seeks to develop therapeutic ultrasound as a novel strategy for the manipulation of collagen structure and function in vitro for regenerative medicine applications.

Wound healing is a complex process requiring cells to repair and rebuild tissue through a series of coordinated ECM remodeling behaviors. Therefore, the ability of an engineered scaffold to support cell-mediated ECM remodeling is essential for the design of therapeutic biomaterials that support tissue healing and integration. In a series of recent studies, we asked whether ultrasound-induced changes in collagen structure and organization altered ECM remodeling by fibronectin-null mouse embryonic fibroblasts (FN-null MEFs). In these experiments, aliquots of soluble collagen were exposed to ultrasound (8.8 MHz, 8 W/cm^2) or unexposed sham conditions for 15 minutes to manufacture acoustically modified collagen hydrogels. Collagen hydrogel samples were then cultured for 24 hours in the presence or absence of cells and then stained with collagen-hybridizing peptides (CHPs) to label areas of conformationally-altered collagen. Multiphoton imaging revealed several characteristics indicative of cell mediated remodeling in ultrasound-exposed samples, including cell accumulation, fiber bundle contraction, and increased CHP staining, which were not present in non-exposed sham control samples (Figure 1). These results are a promising step forward in harnessing the ability of ultrasound to improve collagen functionality within engineered tissue constructs.

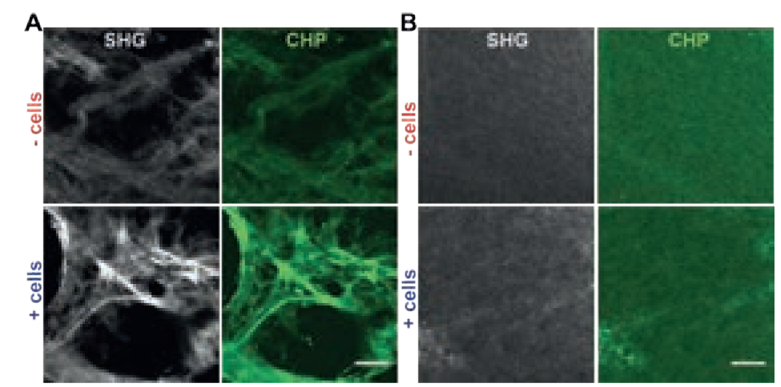


Figure 1. Cell-mediated collagen fibril remodeling is enhanced in acoustically modified hydrogels. Collagen gels were polymerized for 15 min during exposure to 8.8 MHz ultrasound (8 W/cm^2, A), or under sham conditions (B). Gels were cultured for 24 h in cell culture media containing either no cells, or fibronectin-null mouse embryonic fibroblasts before decellularization and staining with collagen hybridizing peptides (CHP, 4 μM). Images are maximum intensity z-projections through a depth of 20 μm. Scale bars = 100 μm.

Development of longitudinal, non-invasive ultrasonography to assess scar formation during flexor tendon healing

Jessica E. Ackerman, Alayna E. Loiselle

Following injury, tendons heal through a scar-mediated process that results in compromised mechanical properties and impaired gliding function. Currently, tendon healing in pre-clinical models is typically assessed via endpoint analyses of biomechanical properties and gliding function. While these endpoint metrics have provided valuable insights into the healing process, there are limitations including an inability to track healing in a single animal over time. To that end, the Loiselle lab has developed an ultrasound-based metric to quantify scar tissue volume (STV), that allows rapid, longitudinal, and non-invasive in vivo characterization of tendon healing. In work described below, the Loiselle lab demonstrated that segmentation of ultrasound images reliably identifies scar tissue, that STV strongly correlates with traditional end-point metrics of gliding function, and has the sensitivity to detect differences in STV between strains of mice that heal with restricted gliding function and those that heal with improved gliding function.

C57Bl/6J mice were used to longitudinally quantify STV via ultrasound imaging, and for correlation analyses to end-point metrics of gliding function. To determine the sensitivity of STV to non-invasively identify differences in healing between mice that heal via scar-mediated healing versus more regenerative healing, we utilized S100a4GFP/+ and wild type (WT) littermates. The Loiselle lab has previously shown that S100a4GFP/+ mice heal with significant improvements in gliding function. At 10-12 weeks of age mice underwent complete transection and surgical repair of the flexor digitorum longus tendon. C57Bl/6J mice underwent longitudinal imaging at 7, 14, 20, and 28 days post-surgery (n=7), an additional cohort of specimens was harvested for correlation analyses at 14 and 28 days post-surgery (n=9). S100a4GFP/+ and WT mice underwent imaging and endpoint analyses at 14 days post-surgery (n=7-11).

A high-frequency (70-MHz) ultrasound scanner (Vevo® 3100) was used for imaging of the healing tendon in vivo. 105 frames of B-mode images in the sagittal plane were taken with 0.04-mm steps to capture the entire width of the tendon. All system settings, including gain (96%), monitor dynamic range (70 dB), and depth (2 cm), were kept constant throughout the study. 3D scans were loaded into Amira (Hillsboro OR) and processed for segmentation and 3D reconstruction to quantify scar tissue volume (STV). Scar formation was quantified by measuring metatarsophalangeal (MTP) joint angle upon incremental loading from 0-19 g of the proximal flexor tendon. Two parameters were determined from these measurements: MTP flexion angle, the change in flexion angle from 0-19g loading, and gliding resistance, a constant derived from the flexion angle over the range of applied loads. A lower gliding resistance and higher MTP flexion angle indicate decreased scar/adhesion formation and better gliding function. Data were analyzed using either a t-test or a one-way analysis of variance (ANOVA) as appropriate followed by Bonferroni's multiple comparisons with a significance level of p=0.05.

Segmentation performed in Amira demonstrated that different tissues can be identified, segmented and reconstructed in 3D (Fig.1), allowing subsequent quantification of tissue volumes. STV was significantly increased relative to un-injured control tendons at all time-points, and progressively increased during healing, peaking at day 20 post-surgery, followed by a significant decline at day 28 (Fig. 2). To confirm appropriate segmentation of scar tissue, serial histological sections were reconstructed and segmented to quantify STV. No significant differences in STV were observed between ultrasound-based and histology-based segmentation approaches. Ultrasound-based measures of STV correlated well (r2=0.74) with measures of gliding resistance (Fig. 3). STV was also significantly decreased in S100a4GFP/+ repairs (1.003 ± 0.08mm^3), relative to WT at day 14 (0.8 ± 0.04mm^3).

This work has developed a novel ultrasound imaging method that permits repeated quantification of scar tissue volume in the mouse flexor tendon. The study demonstrated feasibility of segmenting different tissues in the mouse hindpaw and quantifying STV and demonstrated strong correlations between STV and endpoint metrics of gliding function. Taken together, these data suggest that ultrasound may be able to replace endpoint analyses, allowing longitudinal characterization of the healing process.

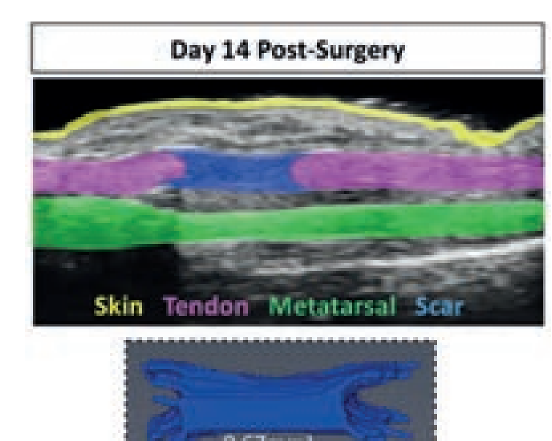


Figure 1. 2D ultrasound slice through the sagittal plane of the foot with skin (yellow), metatarsal bone (green), tendon (pink), and scar (blue). Scar tissue reconstructed in 3D.

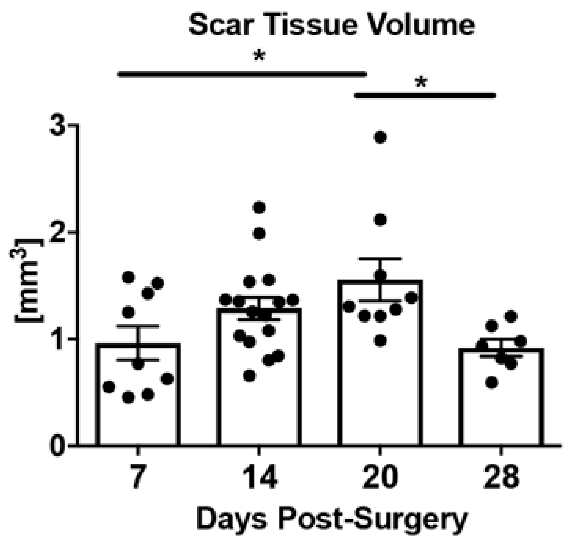


Figure 2. Ultrasound-based quantification of scar tissue volume.

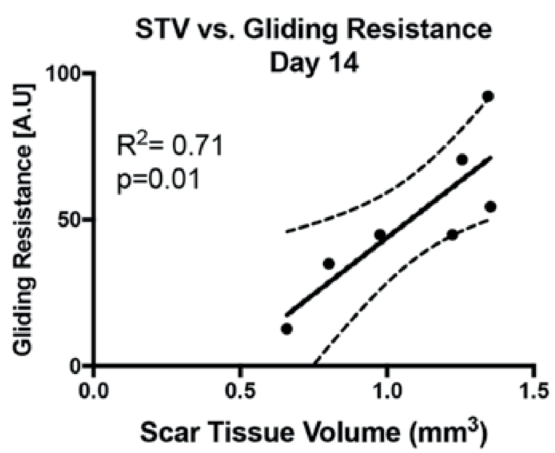


Figure 3. Correlation of scar tissue volume and gliding resistance.

Hadamard encoded multi-element synthetic aperture imaging (H-MSA) for high quality tracking of shear waves

Rifat Ahmed, Marvin M. Doyley

In shear wave elasticity imaging (SWEI), high frame rate tracking of transient shear waves is usually performed using plane or diverging beams. Imaging with these wide beams results in wider point spread functions (PSFs) that reduce image contrast which can be improved by coherently compounding multiple steered beams. However, such wide beam imaging and beam steering with conventional lambda-pitch transducers result in grating lobe artifacts. This condition is exacerbated at large steering angles. Recent work from the Doyley lab proposed the use of multielement synthetic aperture imaging (MSA) which uses multiple laterally-shifted virtual sources to reduce PSF width without performing beam steering. Hadamard encoded transmission (H-MSA) was used to improve the transmit power of MSA. Novel techniques were developed to optimally distribute a large number of encoded virtual sources over multiple push-detect events to achieve high-quality shear wave speed maps.

Virtual sources (VSs) with 15-element sub-apertures were transmitted at multiple lateral sites following the transmission of push pulses. Four configurations were tested where 4, 8, 16, and 32 unique VSs were transmitted over 1, 2, 4, and 8 push-detect events, respectively. Each set of 8 consecutive transmissions spanning over 2 push-detect events were encoded with Hadamard codes to achieve high transmit power. Performance of H-MSA methods was evaluated on attenuating homogeneous and inclusion phantoms, and compared against plane wave imaging for equivalent numbers of push-detect events and transmissions. Feasibility of chirp coded transmission will be evaluated to further enhance the transmit power. The beam sequence for H-MSA with 16 encoded VSs was distributed over 2 push-detect events. The elastographic SNR of H-MSA was 200% higher than compounded plane wave (CPW) based SWEI. H-MSA achieves better lesion visualization than CPW-based SWEI (Fig. 1).

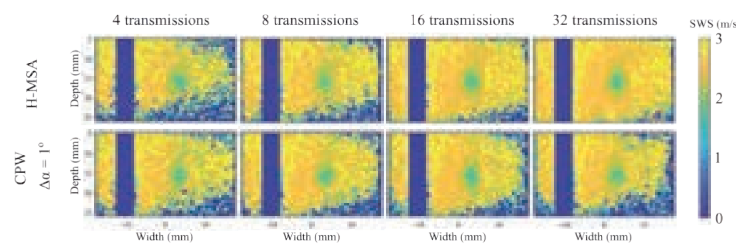


Figure 1. Elasticity map of a soft inclusion phantom obtained using proposed Hadamard-encoded multi-element synthetic aperture (H-MSA) beamforming (1st row) and state-of-the-art compounded plane wave (CPW) imaging (2nd row). Results show that, by using a large number of synthetically focused and encoded sub-apertures, H-MSA can significantly outperform the conventional CPW based elastography.

Visualizing angle-independent principal strains in the longitudinal view of the carotid artery: phantom and in vivo evaluation

Rohit Nayak, Giovanni Schifitto, Marvin M. Doyley

Non-invasive vascular elastography can evaluate the stiffness of the carotid artery by visualizing the vascular strain distribution. Axial strain estimates of the longitudinal cross-section of the carotid artery are sensitive to the angle between the artery and the transducer. Anatomical variations in branching and arching of the carotid artery can affect the assessment of arterial stiffness. In a recent study (UMB 44:1379-1391; 2018), a team from the Doyley lab hypothesized that principal strain elastograms computed using compounded plane wave imaging can reliably visualize the strain distribution in the carotid artery, independent of the transducer angle. This hypothesis was corroborated by conducting phantom and in vivo studies using a commercial ultrasound scanner (Sonix RP, Ultrasonix Medical Corp., Richmond, BC, Canada). Phantom studies were conducted using a homogeneous cryogel vessel phantom. The goal was to assess the feasibility of visualizing the radial deformation in the longitudinal plane of the vessel phantom, independent of transducer angle (±30°, ±20°, ±10° and 0°). In vivo studies were conducted on 20 healthy human volunteers in the age group 50–60 y. All echo imaging was performed at a transmit frequency of 5 MHz and sampling frequency of 40 MHz. Elastograms obtained from the phantom study revealed that for straight vessels, that had their lumen parallel to the transducer, principal strains were similar to axial strains. At non-parallel configurations (angles ±30°, ±20° and ±10°), magnitudes of mean principal strains were within 2.5% of the parallel configuration (0° angle) estimates and, thus, were observed to be relatively unaffected by change in angle. However, in comparison, the magnitude of the axial strain decreased with increase in angle because of coordinate dependency. Further, the pilot in vivo study indicated that principal and and axial strain elastograms were similar for subjects with relatively straight arteries. However, for arteries with arched geometry, axial strains were significantly lower ($p < 0.01$) than the corresponding principal vascular strains, consistent with results obtained from the phantom study. In conclusion, results of phantom and in vivo studies revealed that principal strain elastograms computed using CPW imaging could reliably visualize angle-independent vascular strains in the longitudinal plane of the carotid artery.

Pulsed ultrasound for the treatment of chronic wounds

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

Chronic wounds are a prominent societal concern; they afflict over 6.5 million Americans, cost over $10 billion worldwide annually, and reduce quality of life. The current standard of care for these injuries primarily involves supportive strategies, including antimicrobial bandages and surgical debridement. Current studies in the laboratories of Diane Dalecki and Denise Hocking are investigating an ultrasound-based method for treating chronic, cutaneous wounds that holds potential to accelerate healing noninvasively.

Preliminary results demonstrate that a pulsed, 1-MHz, ultrasound treatment administered to full-thickness dermal wounds in a diabetic mouse model can facilitate healing over two weeks. Daily ultrasound treatments were administered to the periphery of 6-mm, punch biopsy wounds. Wound areas were exposed to 1-MHz pulsed ultrasound (2 ms pulse, 100 Hz PRF) for 8 min/day for 10 days over a 2-week period. Pressure amplitudes of 0 (sham), 0.1, 0.2, and 0.4 MPa were investigated. After two weeks, wounds were excised, sectioned and histologically analyzed with hematoxylin and eosin staining (Figure 1). To evaluate the extent of wound healing, the thickness of newly formed granulation tissue was measured at the center of the wound space. Results showed significantly increased granulation tissue deposition in wounds that were exposed to 0.4 MPa ultrasound. In contrast, granulation tissue of wounds exposed at 0.1 or 0.2 MPa was not significantly different from sham.

The results of this study suggest that ultrasound may be an effective tool for facilitating chronic wound healing by stimulating new matrix deposition. Histological analyses of excised tissue will be used to gain greater insight into the mechanism of ultrasound-induced healing in biological tissues. The Dalecki and Hocking laboratories are currently investigating the hypothesis that mechanical forces associated with ultrasound exposure use a mechanosensitive, fibronectin-dependent pathway to facilitate healing.

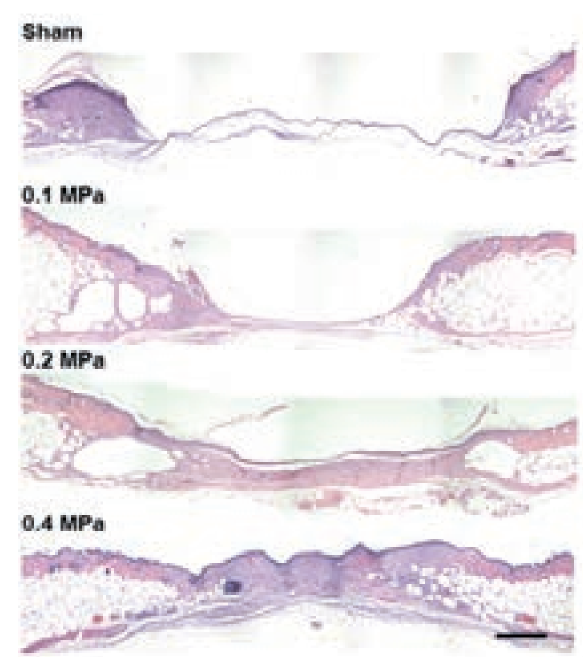


Figure 1. Representative images of granulation tissue deposition in murine wounds treated with ultrasound after two weeks. Full-thickness cutaneous wounds in diabetic male mice were exposed to 1-MHz ultrasound at 0, 0.1, 0.2, 0.4 MPa (from top to bottom). On day 14, the skin surrounding and including the wound was excised and stained with hematoxylin and eosin. Scale bar = 500 µm.

Reverberant 3D optical coherence elastography (RE-V3D-OCE): A novel method for the 3D elastic mapping of layers in cornea

Fernando Zvietcovich, Jannick P. Rolland, P. Meemon, Kevin J. Parker

Measuring the elasticity of layers in cornea is fundamental to better understanding, diagnosing, and monitoring degenerative ocular diseases. Current methods in optical coherence tomography (OCT) use air-puff or acoustic radiation force (ARF) systems to produce the propagation of Lamb waves. However, Lamb wave speed values (1) are dispersive, (2) are dependent on the boundary conditions (cornea thickness), and (3) do not provide high contrast in depth layer mapping. Therefore, the estimation of shear modulus of each corneal layer remains a challenge. Previous work from this team on reverberant shear wave (RevSW) fields demonstrated its application for lesion detection in breast models using ultrasound. Current simulations of RevSW performed in finite element models of the cornea suggest its potential for the elastic characterization of layers.

The aim of recent work was to demonstrate the capabilities of RevSW fields applied to OCT for the 3D elastic characterization of depth-dependent corneal layers in experiments using animal models and numerical simulations. This novel method is called reverberant 3D optical coherence elastography: Rev3D-OCE. RevSW fields were generated in an ex vivo cornea by the sinusoidal, steady-state excitation (2 kHz) of a 3D printed ring actuator with eight heads touching the corneal epithelium (Fig. 1a top). The motion was detected by Doppler phase shift detection using a custom-made, spectral-domain OCT system with 1307-nm central wavelength and about 100 nm spectral width. 3D volumes of 8×8×2 mm of cornea were acquired at a line rate of 25 kHz using the MB-mode acquisition protocol. Subsequently, complex-valued cross correlation maps extracted from reverberant volumes (Fig. 1a bottom) were used to estimate local wave number. Experiments in fresh porcine corneas at controlled intraocular pressure were conducted. Regular tone burst (Lamb wave propagation) experiments were also conducted in the same samples for further comparison. Numerical simulation in Abaqus/CAE (6.14-1, Dassault Systems) were also generated to corroborate results.

Experiments with porcine cornea revealed differentiated layers as shown in the 2D and 3D shear wave speed maps (Fig. 1b). Moreover, it was found that the speed contrast of the approach was much superior than the regular Lamb wave method when a vertical depth profile was analyzed (Fig. 1c). The Rev3D-OCE speed values ranged from 3.4 m/s to 4.2 m/s, while Lamb wave results ranged from 3.73 m/s to 3.81 m/s. Numerical simulations confirmed the detection of independent layers in cornea for a four-layer model. In conclusion, this work demonstrated that Rev3D-OCE is successful in the identification of differentiated layers in ex vivo cornea using OCT. In addition, speed profiles (Fig. 1c) have the same tendency as results provided by Brillouin Scattering, and they enable the direct calculation of shear modulus.

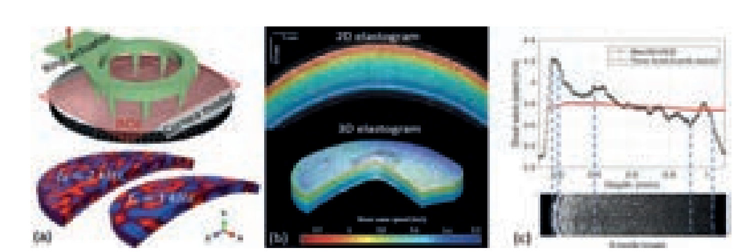


Figure 1. (a) Ring actuator and RevSW motion volumes from numerical simulations. (b) 2D and 3D elastography of porcine cornea. (c) Depth-resolved shear wave speed profile depicting differentiated corneal layers versus regular Lamb wave method.

Size manipulation of ultrasound contrast agent and its impact on subharmonic emissions and delayed onset

Jeffrey Rowan, James McGrath, Marvin M. Doyley

Ultrasound contrast agents have a growing number of applications in medical diagnostics and theranostics. Of particular interest have been super resolution techniques and sonoporation. While current research has shown promising results within these applications, they are still limited by the properties of microbubble agents, in particular, their size distribution. Previous efforts at modifying contrast agent distributions have relied either on single bubble generation from microfluidics or post-production filtration. The former suffers from concentration issues, while the latter is not suitable for clinical applications in the case of centrifugation, or throughput issues in the case of cloth filters. The current work presents a solid silicon-based ports chip for filtration of contrast agent, and shows the change in subharmonic properties that results.

Modified centrifuge cups were used to hold microchip filters with 1.5-micron slits. The agents were centrifuged at 500 g for 1 minute in order to filter out larger bubbles. Following filtration, the contrast agent was imaged using two orthogonally-aligned transducers, with 10 MHz transmit and 5 MHz receive, to maximize subharmonic response. Filtered populations saw an overall increase in subharmonic amplitude. In addition, the delayed onset phenomena were completely eliminated, going from a two-hour delay to instantaneous emission. The threshold for acoustic emission was also decreased in the filtered population by over 100 kPa. In conclusion, a high throughput, highly-reproducible filter for ultrasound contrast agents has been developed. In addition to improved SNR, the proposed method also eliminates delayed onset and lowers the acoustic threshold for subharmonic emission, making low coherence methods, super resolution, and sonoporation much more feasible.

Viscoelastic characterization of dispersive media by inversion of a general wave propagation model in optical coherence elastography

Fernando Zvietcovich, Jannick P. Rolland, Emma Grygotis, Sarah Wayson, Maria Helguera, Diane Dalecki, Kevin J. Parker

Determining the mechanical properties of tissue such as elasticity and viscosity is fundamental for better understanding and assessment of pathological and physiological processes. Dynamic optical coherence elastography uses shear/surface wave propagation to estimate frequency-dependent wave speed and Young's modulus. However, for dispersive tissues, the displacement pulse is highly damped and distorted during propagation, diminishing the effectiveness of peak tracking approaches. The majority of methods used to determine mechanical properties assume a rheological model of tissue for the calculation of viscoelastic parameters. Further, plane wave propagation is sometimes assumed which contributes to estimation errors. To overcome these limitations, we invert a general wave propagation model that incorporates (1) the initial force shape of the excitation pulse in the space-time field, (2) wave speed dispersion, (3) wave attenuation caused by the material properties of the sample, (4) wave spreading caused by the outward cylindrical propagation of the wavefronts, and (5) the rheological-independent estimation of the dispersive medium. Experiments were conducted in elastic and viscous tissue-mimicking phantoms by producing a Gaussian push using acoustic radiation force excitation, and measuring the wave propagation using a swept-source frequency domain optical coherence tomography system. Results confirm the effectiveness of the inversion method in estimating viscoelasticity in both the viscous and elastic phantoms when compared to mechanical measurements. Finally, the viscoelastic characterization of collagen hydrogels was conducted. Preliminary results indicate a relationship between collagen concentration and viscoelastic parameters which is important for tissue engineering applications.

Hybrid force/velocity control with compliance estimation via strain elastography for robot assisted ultrasound screening

Michael E. Napoli, Christian Freitas, Soumya Goswami, Stephen A. McAleavey, Marvin M. Doyley, Thomas M. Howard

Ultrasound scanning provides a noninvasive solution for additional screening in breast cancer detection and could potentially be improved by utilizing a human-robot collaborative system. Alternative ultrasound modalities, such as elastography, offer promising improvements over current sonography cancer detection rates but require stability and knowledge of applied force. A human-robot scanning system could leverage the sonographer's capabilities to select transducer placement while the robot maintains stability during scanning. Recent work from this team of RCBU investigators developed a novel hybrid force velocity controller for ultrasound scanning which utilizes elastography to provide compliance feedback and improve controller performance. Investigations explored the sensitivity of the elastography algorithm to initial elasticity assumptions and analyzed the performance gains of compliance feedback. The results of the study show that the proposed controller provides a performance improvement when poor initial tissue compliance estimates are used.

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

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

In elastography using dynamic optical coherence tomography (OCT), shear/surface waves are tracked in order to estimate speed and Young's modulus. However, for dispersive tissues, the displacement pulse is damped and distorted, reducing its propagation to the near field and diminishing the effectiveness of peak tracking models with asymptotic assumptions of attenuation. Therefore, the use of a rheological model-independent approach that contemplates the initial shape of the force excitation source in space and time is needed. In that regard, propagation models have been previously proposed at the cost of high complexity, intensive computation, and satisfying strict boundary conditions. A simplified model incorporating the general viscoelastic parameters of the media, and the initial source shape which does not require assumptions of the tissue mechanical behavior is desired. The aim of recent work from this team of investigators, was to validate a first-order approximate forward model of near field wave propagation of a Gaussian force push in viscoelastic media using numerical simulations and experiments in phantoms.

An axisymmetric Gaussian shear wave propagation model, in radial space r and time t is proposed for a viscoelastic medium of density ρ complex shear modulus $\hat{\mu} = \omega^2 \rho / k^2$ temporal frequency ω, spatial frequency ε and complex first order approximation of wave number $k = \omega^2 / c_0 - i|\omega|\alpha_1$ where c_0 (m/s) is the wave speed and α_1 (Np/m/rad) is the attenuation:

$$v_z(r,t) = \frac{A_0}{2}\int_0^\infty \varepsilon \cdot e^{-\sigma^2\varepsilon^2} \cdot J_0(\varepsilon r)\cos(c_0 \varepsilon t) e^{-|\varepsilon| \alpha_1 c_0 t} d\varepsilon.$$

An acoustic radiation force (ARF) transducer (5 MHz, 5.01 cm focal length) was used to generate an axisymmetric Gaussian-shape ($\sigma = 0.34$ mm) force during 0.1 ms and 1 ms push durations in two viscoelastic phantoms M1 and M2, respectively. Particle velocity $v_z(r,t)$ was acquired using a phase-sensitive OCT system implemented with a swept source laser (HSL-2100-WR, Santec, Japan) of 1318-nm wavelength. Results were compared against numerical simulations (Abaqus/CAE 6.14-1) and the numerical integration of the proposed model.

Figure 1 shows the comparison of spatio-temporal profiles of particle velocity calculated from numerical integration of the proposed model, numerical simulations using finite elements, and real experiments in the two phantom materials M1 and M2 was made. c_0 (m/s) and α_1 (Np/m/rad) parameters are consistent with the mechanical testing of both phantoms. This work demonstrated the effectiveness of the proposed axisymmetric Gaussian shear wave propagation model in the near field for the viscoelastic characterization of dispersive media. Further research will concentrate on evaluating this approach in real tissue such as skin and cornea.

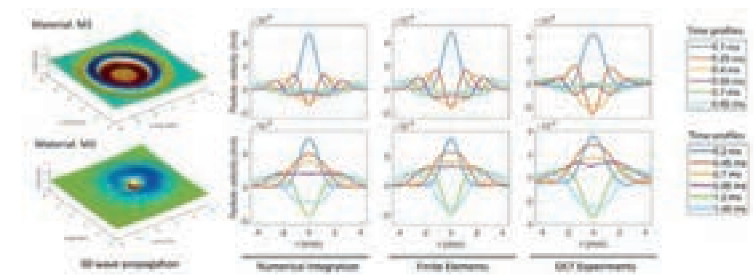


Figure 1. Comparison of wave propagation profiles during numerical integration, finite element analysis, and OCT experiments.

High-frequency quantitative ultrasound for characterizing collagen microstructure in tendon

Sarah Wayson, Denise C. Hocking, Diane Dalecki

Tendon injuries are debilitating, and two major complications following surgical repair are adhesion formation and tendon re-rupture. Tendon immobilization following surgical repair can increase adhesion formation between the tendon and its surrounding sheath, limiting patient range of motion. Therefore, it is recommended that patients perform exercises following surgical repair to reduce adhesion formation. However, the tendon may re-rupture if the repair site is over-stressed. Consequently, there is a need to establish personalized rehabilitation protocols following surgical repair.

Developing an imaging system for longitudinal monitoring of tendon healing will help assess changes in tendon structure throughout a rehabilitation protocol, and enable exercises to be tailored to optimize tendon functional capabilities. Ultrasound is an imaging modality that provides non-invasive, non-destructive, longitudinal monitoring of tissues. However, B-mode images are qualitative, and their appearance is impacted by receive system settings and acoustic attenuation. Therefore, there is a need to develop quantitative ultrasound imaging approaches that estimate tendon structural properties from backscattered echoes.

The objective of this project is to develop high-frequency quantitative ultrasound imaging techniques to characterize collagen microstructure in tendon. The integrated backscatter coefficient (IBC) is a quantitative ultrasound spectral parameter that estimates how strongly scatterers within a tissue reflect the interrogating ultrasonic pulse back to the transducer. The IBC is the ratio of backscattered to incident intensity, per unit volume of tissue, integrated across frequencies within the transducer's detectable bandwidth. Representative B-mode and IBC parametric images of a rat tail tendon fascicle ex vivo imaged at 38 MHz are shown in Figure 1. This project tests the hypothesis that the IBC can be used to characterize collagen microstructure in tendon. Successful completion of this project will establish the foundation for a dedicated, point-of-care clinical device to non-invasively monitor collagen remodeling during tendon healing, guiding physical therapy clinical practice and engineering innovations in tendon repair.

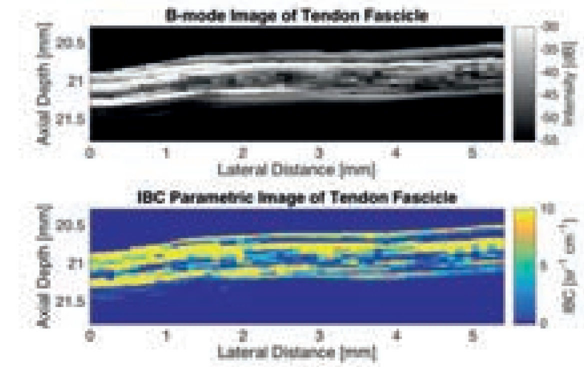


Figure 1. B-mode (top) and IBC parametric (bottom) images of a rat tail tendon fascicle ex vivo representing a cross section along the collagen fiber axis.

Mapping multiaxial strains in patellar tendons of individuals with and without Osgood-Schlatter disease using ultrasound elastography

Grace E. Weyand, Mark R. Buckley, Hannah R. Goldring, Catherine K. Kuo, Michael S. Richards, Katherine H. Rizzone

Osgood-Schlatter disease (OSD), also known as apophysitis of the tibial tuberosity, causes pain in the anterior knee that is exacerbated by running, jumping and other physical activities. OSD occurs during periods of growth and is estimated to affect 10% of adolescents involved in sports. Moreover, pain associated with this disease continues into adulthood in up to 10% of cases. While it has been theorized that OSD stems from excessive tensile strain on the patellar tendon due to muscle tightness during growth spurts and repetitive traction during activity, the etiology of OSD remains unclear. To elucidate the cause of OSD and the potential role of excessive tensile strain, the objective of a recent study from the Buckley lab was to establish the baseline multiaxial strains that occur in the adolescent patellar tendon during exercise in individuals with and without OSD. The hypothesis was that OSD increases axial tension in the patellar tendon, but does not alter transverse compression.

Ten adolescents without symptomatic OSD and 8 adolescents with symptomatic OSD participated in this study. All subjects signed a consent form approved by the institute's Research Subjects Review Board. Each participant was fit with a knee brace that held an ultrasound transducer (Ultrasonix) and ultrasound gel pad above the insertion of the patellar tendon to the tibia. With the ultrasound probe in place, the participant performed two exercises: (1) leg outstretched on bench, bench removed, participant lowers leg and bends knee to flexion angle of (60°±0.2), participant raises leg back to bench starting position; (2) participant performs a squat to a knee flexion angle of (60°±0.3) and then returns to starting standing position. Measurements were taken from both knees with two trials per exercise, for a total of 8 trials per subject. Tendon deformation was measured using a custom non-rigid image registration-based algorithm, and minimum and maximum principal strains (taken to reflect transverse compressive strain and axial tensile strain, respectively) were quantified as described previously. Knee flexion angle was tracked using a custom

MATLAB code that analyzed video image sequences of the participant performing exercise. Subjects with and without OSD were compared using a two-tailed t-test with $\alpha = 0.05$.

The magnitude of transverse compressive strain was found to be significantly lower in the patellar tendon of symptomatic participants during both the squat and bench exercises (Fig. 1). In contrast, axial tensile strain was not significantly different between groups during both the squat and bench exercises. Contrary to the hypothesis, during both types of exercises, OSD decreased transverse compression in the patellar tendon without affecting axial tension. The finding that axial tensile strain was equivalent in control and OSD subjects challenges the widely held belief that muscle tension is the root cause of this pathology. On the other hand, the finding that OSD tendons are more resistant to transverse compressive strain (i.e., appear to be stiffer under compression) suggests that OSD may be an adaptation to repetitive transverse compressive stresses. These compressive stresses (presumably due to impingement from the tibia) could lead to increased fibrocartilage formation and increased neo-vessel invasion, leading to tissue stiffening and increased pain sensation. Thus, the potential causal link between transverse compressive stress near the patellar tendon insertion and structural/mechanical changes associated with OSD warrants further investigation.

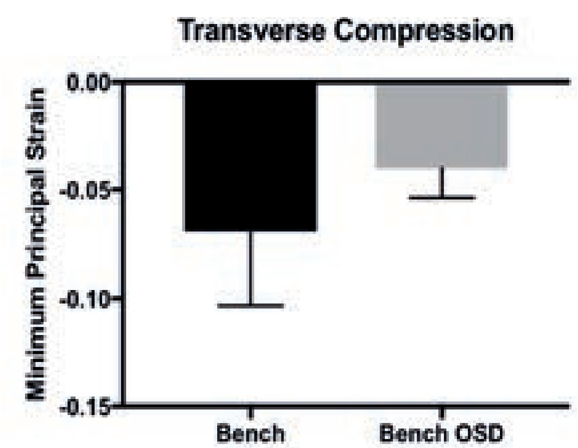


Figure 1. Ultrasound elastography was used to measure minimum principal strain (indicative of transverse compressive strain) during bench exercise (60°±0.2). Data are presented as mean+SD.

Elastography can map the local inverse relationship between shear modulus and drug delivery within the pancreatic ductal adenocarcinoma microenvironment

Hexuan Wang, Reem Mislati, Rifat Ahmed, Phoung Vincent, Solumtochukwu Nwabunwanne, Jason R. Gunn, Brian W. Pogue, Marvin M. Doyley

High tissue pressure prevents chemotherapeutics from reaching the core of pancreatic tumors. Therefore, targeted therapies have been developed to reduce this pressure. While point probes have shown the effectiveness of these pressure-reducing therapies via single location estimates, ultrasound elastography is now widely available as an imaging technique to provide real-time spatial maps of shear modulus (tissue stiffness). However, the relationship between shear modulus and underlying tumor microenvironmental causes has not been investigated. In recent work from the Doyley Lab, elastography was used to investigate how shear modulus influences drug delivery in situ, and how it correlates with collagen density, hyaluronic acid content, and patent vessel density, features of the tumor microenvironment known to influence tissue pressure.

Intravenous injection of verteporfin, an approved human fluorescent drug, was used in two pancreatic cancer xenograft models (AsPC1 (n=25) and BxPC3 (n=25)). Fluorescence intensity was higher in AsPC-1 tumors than in BxPC-3 tumors ($p < 0.0001$). Comparing drug uptake images and shear wave elastographic images with histological images revealed that: (1) drug delivery and shear modulus were inversely related, (2) shear modulus increased linearly with increasing collagen density, and (3) shear modulus was marginally correlated with the local assessment of hyaluronic acid content. These results demonstrate that elastography could guide targeted therapy and/or identify patients with highly elevated tissue pressure.

The nonlinear ultrasound needle pulse

P. Ted Christopher, Kevin J. Parker

Recent work has established an analytical formulation of broadband fields which extend in the axial direction and converge to a narrow, concentrated line. Those unique (needle) fields have their origins in an angular spectrum configuration in which the forward propagating wavenumber of the field (kz) is constant across any z plane for all of the propagated frequencies. In recent work from this team (JASA 144:861-871; 2018), a 3 MHz-based, finite amplitude distorted simulation of such a field was considered in a water path scenario relevant to medical imaging. That nonlinear simulation had its focal features compared to those of a comparable Gaussian beam. The results suggest that the unique convergence of the needle pulse to a narrow but extended axial line in linear propagation is also inherited by higher harmonics in nonlinear propagation. Furthermore, the linear needle field's relatively short duration focal pulses, and the asymptotic declines of its radial profiles, also hold for the associated higher harmonics. Comparisons with the Gaussian field highlight some unique and potentially productive features of needle fields.

Development of machine learning algorithms to automate non-invasive detection and quantification of scar volume during tendon healing

Jack Teitel, Tejas Bawaskar, Valentina Studentsova, Jessica E. Ackerman, Alayna E. Loiselle

Injuries to flexor tendons of the hand are very common and represent one of the most challenging orthopaedic procedures. Following injury and surgical repair, tendons heal with a scar tissue response rather than regeneration of native tendon morphology. Excessive scar formation restricts tendon range of motion due to both an increase in tendon size and formation of scar tissue adhesions between the tendon and surrounding tissue. Currently there are no automated, quantitative, non-invasive modalities to assess tendon healing pre-clinically or clinically. The Loiselle lab is developing novel ultrasound-based approaches to non-invasively and longitudinally image tendon healing. Their work has demonstrated that quantification of scar tissue volume (STV) from ultrasound images is strongly correlated with impairments in range of motion, thus identifying STV as a biomarker of tendon healing. Currently, image segmentation and quantification of STV requires highly-trained operators to manually segment images. While the STV metric holds immense promise as a means to facilitate more rapid and cost-effective identification of therapeutic targets, the high-throughput potential of this approach is limited by reliance on manual segmentation. Thus, development of machine learning algorithms is a key step in the clinical application of ultrasound-based metrics of healing as automated quantification of STV can provide real-time feed-back on patient progress that may enhance and facilitate clinical decision making.

In recent work, the Loiselle lab and collaborators have utilized and adapted 2D and 3D machine learning algorithms to determine the feasibility of automated segmentation and quantification of scar tissue during tendon healing. The study employed a pre-clinical mouse model of tendon healing that heals with abundant scar formation and restricted tendon range of motion. A high-frequency, ultrasound platform (Vevo® 3100) was used for imaging tendon healing in vivo. A 70-MHz transducer was placed in line with the mid-point of the tendon on the plantar aspect of the mouse hindpaw. 105 frames of B-mode images in the sagittal plane were taken with 0.04-mm steps to capture the entire width of the tendon. 3D scans were loaded into Amira (FEI v.6.1.1, Hillsboro OR) and segmented (Fig. 1). Histological analyses were used to validate segmentation of scar tissue in ultrasound images.

Both 2D and 3D machine learning algorithms were developed and tested. Samples were randomly divided into three sets: i) training set, ii) validation set, iii) testing set. The dice metric, which quantifies the overlap between manual and machine segmented images, was used to define the fidelity of automated, machine segmented masks relative to manually segmented scar tissue masks. For the 2D model, the training image set was used to train on an FCN-8 based model to perform automated segmentation. To develop a model of 3D image segmentation, the team used the same training data set as in the 2D model but used v-net as a model. To refine this initial 3D model, they then manually identified a 3D bounding box surrounding the scar tissue, and v-net was trained to specifically identify scar tissue voxels within this bounding box.

For the 2D segmentation model, a dice metric goal of 70% was set based on the 70% overlap in scar masks between two independent expert observers. Using 2D machine learning algorithms a dice metric of 55% was achieved, supporting the feasibility of using artificial intelligence/ machine learning to automate this process, but suggesting alternative algorithms are needed. In the first stage of 3D segmentation model development, training was done directly from v-net, however, this approach achieved only a 35% dice metric. A 3D bounding box was then used to eliminate much of the image surrounding scar tissue. This approach allows an initial coarse identification of scar tissue, followed by a fine identification of those voxels that are scar tissue. Application of a 3D bounding box resulted in a dramatic improvement, with the dice metric reaching 75%. In summary, adaptation of 3D segmentation machine learning approaches has the potential to rapidly and specifically identify scar tissue from ultrasound images. This approach allows for a more high-throughput analysis and screening of therapeutic candidates in pre-clinical models.

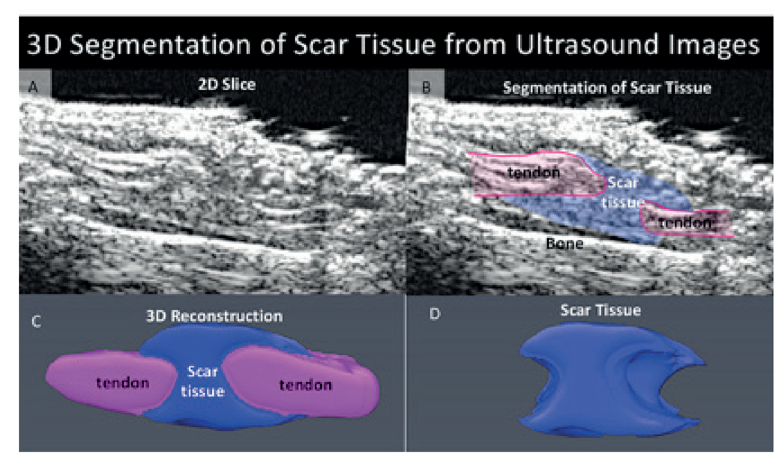


Figure 1. Segmentation and reconstruction of scar tissue from ultrasound images. A) Individual 2D ultrasound image through sagittal plane. B) Tendon and scar tissue are segmented on 20 images. C&D) Tendon and scar tissue masks are reconstructed in 3D.

Plane-wave imaging improves single-track location shear wave elasticity imaging

Rifat Ahmed, SA Gerber, Stephen A. McAleavey, Giovanni Schifitto, Marvin M. Doyley

Single-track location shear wave elasticity imaging (STL-SWEI) is immune to speckle bias, but the quality of the images is depth dependent. In this study (IEEE UFFC, 65:1402-1414; 2018), Professor Doyley and collaborators hypothesized that plane-wave imaging can reduce the depth dependence of STL-SWEI. To test this hypothesis, the team developed a novel technique known as planewave STL-SWEI (pSTL-SWEI). To evaluate the pSTL-SWEI's potential, studies were performed with phantoms and excised murine pancreatic tumors. Mean shear wave speeds measured with STL-SWEI and pSTL-SWEI were similar. However, the elastographic signal-to-noise ratio (SNRe) of pSTL-SWEI elastograms was noticeably higher than that produced with STL-SWEI. Specifically, an improvement in SNRe ranging from 39.9%–55.1% was observed, depending on tissue stiffness. The spatial resolution of pSTL-SWEI elastograms was 2.7%–12.1% lower than that produced with STL-SWEI. pSTL-SWEI elastograms displayed higher contrast-to-noise ratio (CNRe) than those produced with STL-SWEI, especially when imaging was performed with low push pulse intensities and low pulse durations.

Group vs. phase velocity of shear waves

Kevin J. Parker, Juvenal Ormachea, Zaegoo Hah

Across the varieties of waves that have been studied in physics, it is well established that group velocities can be significantly greater than or less than phase velocities measured within comparable frequency bands, depending on the particular mechanisms involved. The distinction between group and phase velocities is important in elastography, because diagnoses are made based on shear wave speed estimations from a variety of techniques. A recent paper (Ultrasonic Imaging 40:861-871; 2018) from this team reviewed the general definitions of group and phase velocity and examined their specific relations within an important general class of rheological models. For the class of tissues and materials exhibiting power law dispersion, group velocity is significantly greater than phase velocity, and simple expressions are shown to interrelate the commonly measured parameters. Examples are given from phantoms and tissues.

The influence of shear modulus on drug uptake in pancreatic ductal adenocarcinoma: an in vitro study

Hexuan Wang, Rifat Ahmed, Phoung Vincent, Reem Mislati, Solumtochukwo Nwabunwanne, Jason Gunn, Kayla Marra, Brian Pogue, Marvin M. Doyley

Pancreatic ductal adenocarcinoma (PDAC) is a prevalent form of pancreatic cancer with the 5-year survival rate less than 5% and a median survival of 4-6 months. The dense stroma is speculated to be a main factor in impairing delivery of both the existing chemotherapy agents and novel cancer-killing nanoparticle. This team of investigators tested the hypothesis that shear modulus measured with shear wave elasticity imaging influences drug delivery to pancreatic cancer tumors. AsPC-1 and BxPC-3 human pancreatic tumors were implanted in 50 immunodeficient Athymic Nude mice nu/nu by injecting 106 tumor cells in Matrigel (BD Biosciences) orthotopically into the pancreas. Drug verteporfin and perfused vessel marker lectin were

were injected 1 hour and 1 minute before animal sacrifice, respectively. Upon animal sacrifice, excised tumors were embedded in a gelatinous solution consisting of 10% gelatin, 1% corn starch, and water. A single tracking location shear wave elasticity imaging (STL-SWEI) method was implemented on a Verasonics Vantage 256 scanner with a 5 MHz L7-4 transducer. After STL-SWEI, each tissue sample was imaged for verteporfin uptake on a GE Typhoon 9410 flatbed scanner. Additional tissue samples were stained with Masson's Trichrome and lectin to investigate stromal density and vessel perfusion. SWEI elastography results reported an inverse relationship between tumor shear modulus distribution and verteporfin drug uptake (Figs. 1, 2). Linear regression test in (Fig. 2) showed a strong inverse correlation for both the AsPC-1 tumors (R2 = 0.507) and the BxPC-3 tumors (R2 = 0.520). Between the two tumor lines, the average fluorescence intensity (FI) of the drug uptake was measured to be higher in the AsPC-1 tumors (FI = 2.95, n = 16) in comparison to that in the BxPC-3 tumors (FI = 1.314, n = 17). These results demonstrated that shear modulus measured with SWEI affects verteporfin delivery to pancreatic cancer tumor, potentially establishing the usage of in vivo SWEI to evaluate the drug delivery efficiency in relevant studies.

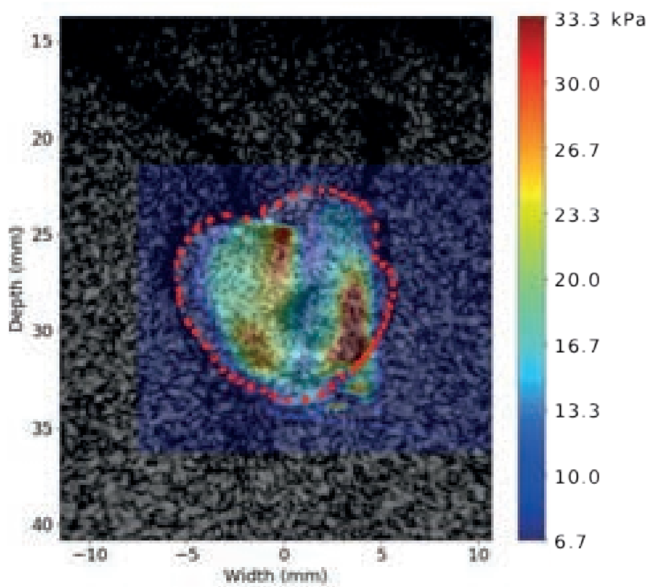


Figure 1. Shear modulus elastogram of a pancreatic BxPC-3 xenograft tumor overlaid over ultrasound B-mode image.

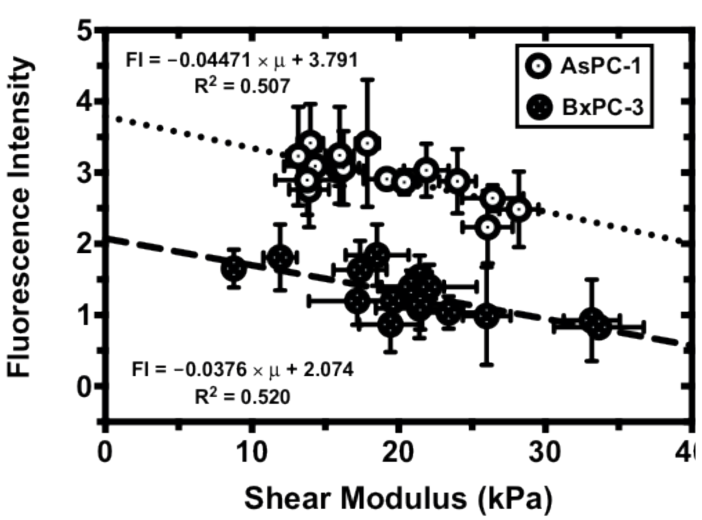


Figure 2. Plot of fluorescence intensity of drug uptake as a function of shear modulus for both the AxPC-1 and BxPC-3 xenograft tumors.

Obstetrics & Gynecology Ultrasound Unit

Kathryn Drennan, MD and Kam Szlachetka RDMS

The UR OB/GYN Ultrasound Unit provides clinical services at multiple sites through the University of Rochester Medical Center (URMC) and the region. Level II ultrasound services are providers in three locations locally, including Lattimore Road, Highland Hospital, and the 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.

The MFM Division also performs ultrasound and consultation at a number of locations throughout the region. Starting in 2009, we began to provide onsite services to St. Joseph's Hospital and Associates for Women's Medicine in Syracuse to provide 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 will likely expand in early 2019 to a weekly service and include ultrasound services at St. Joseph's Hospital.

We now 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. Additionally, last year we began to cover at Catholic Health's Mercy Hospital in Buffalo 3 days/week by remote reading with almost 2,300 ultrasounds last year. We have also begun to provide telemedicine consultative services at several additional hospitals.

The unit has 21 ultrasound machines within Strong Memorial Hospital (SMH)l and Highland Hospital (HH), all with 3D and 4D capability, plus additional portable scanners. There are 26 sonographers at HH and SMH, 25 of whom are NT certified, 16 of whom are CLEAR certified, and 11 of whom are fetal echocardiography certified. SMH remains an active member of NAFNET (North American Fetal Therapy Network). Examples of recent research projects are provided below.

Pre-conception exposure to gadolinium: An analysis of maternal and neonatal outcomes

Miller LA, Thornburg LL, Katzman P, Darrah T, Miller RK.

It is increasingly recognized that many metals, including Gadolinium (Gd), can be incorporated into human bone. The calcium requirements of pregnancy favor a state of bone resorption, during which metals, such as lead, are released into the maternal circulation. This study aimed to determine if pre-conception exposure to Gd-contrast agents is associated with adverse pregnancy or neonatal events.

This was a retrospective chart review identifying women ages 18-55 with an obstetric admission resulting in a live born singleton between 2007-2016. Women having an MRI within 10 years of their estimated date of conception were included in the study. Cohorts were defined by MRI type: Non-Gd-MRI vs. Gd-Contrast MRI (Gd-MRI). Two time points were examined: MRI within 10 years of conception and MRI within 2 years of conception. Pregnancy outcomes included gestational diabetes, chorioamnionitis and a composite outcome of placental morbidity (pre-eclampsia, abruption, IUGR). Neonatal outcomes included gestational age, birth weight and a composite outcome of newborn morbidity (NICU admission, APGAR <7 at 5 minutes, surfactant administration, need for respiratory support and neonatal death). Analysis by Chi-square, Fisher's exact, T-tests and T-test with bootstrapping. Logistic regression and generalized linear models were used to control for confounding.

The average interval between MRI and conception was slightly shorter in the Gd-MRI cohort at 2 years, but not at 10 years. Exposure to Gd-MRI within 10 years of conception was associated with decreased odds of having a newborn with a low 5-minute APGAR. No other significant differences were found between Non-Gd MRI and Gd-MRI exposed subjects when MRIs were within 2 years of conception, or within 10 years of conception. In conclusion, pre-conception exposure to gadolinium was not associated with obvious adverse maternal or neonatal outcomes during pregnancy or in the immediate newborn period.

The association between 3D cervical volume and spontaneous preterm birth

Olson-Chen C, Gilmandyar D, Szlachetka K, Faske E, Fountaine E, Ozcan T

Cervical length measurement is used to predict spontaneous preterm birth (sPTB), but it only evaluates the cervix in 2 dimensions and has a low sensitivity. Advances in 3D ultrasound allow imaging of the cervical volume. This investigation sought to investigate the relationship between cervical volume and sPTB. A prospective cohort study was conducted of singleton gestations between 16 0/7-23 6/7 weeks from February 2016 to March 2017. The cervical length was measured in 2D according to the CLEAR protocol, and a 3D volume of the cervix was obtained during routine cervical length screening. The cervical volume was later measured by two separate examiners using VOCAL software with 30 degree rotations of the cervix. The primary outcome was sPTB<37 wks. Multivariable regression was performed to account for potential confounding by maternal age, race, ethnicity, body mass index (BMI), history of sPTB and parity.

A total of 345 subjects underwent 3D imaging of the cervix. Two minutes of post-processing time were required for cervical volume measurement. The median cervical volume was 40 cm^3 (range 14.4-108.9 cm^3). Cervical volume measurements by the separate examiners were highly correlated (correlation coefficient 0.86, p<0.001). The rate of sPTB <37 wks in this cohort was 7.1%. There was a positive correlation between cervical volume measurement and gestational age at delivery (p=0.047). On average, subjects with sPTB had a significantly lower cervical volume compared to those without sPTB (36.4 cm^3 vs 43.1 cm^3, p=0.04). Lower cervical volume was associated with nulliparity (p=0.02), history of sPTB (p<0.001), lower BMI (p=0.02) but there were no differences in cervical volume by maternal age, race or ethnicity. The primary outcome remained significant after adjustment for parity, history of sPTB and BMI (p<0.001).

In conclusion, this prospective study found that 3D cervical volume is associated with gestational age at delivery and sPTB. Cervical volume measurement was reproducible across examiners. Further prospective studies are needed to determine if this measurement adds value to routine cervical length screening.

Ultrasonographic measurement of uterocervical angle in twins: predicting spontaneous preterm birth

Lynch TA, Szlachetka K, Seligman NS

Uterocervical angle (UCA) is the angle between the lower uterine segment and cervical canal. UCA angles >95° and >105° have been shown to correlate with an increased risk for spontaneous preterm birth (sPTB) in singletons. However, there is no data on the use of UCA for the prediction of sPTB in twins. Our objective was to determine the relationship between UCA and risk of sPTB <37wks in twins.

We performed a retrospective study from 2014-2017 of twins who underwent CL screening at a major urban university hospital. Women who had at least one CL between 14 to 24 6/7 wks were included. Monochorionic monoamniotic twins were excluded. Post-hoc UCA measurements were obtained using methods described by Dziadosz et al. Wide UCA was defined as an angle >95° and >105°. The primary outcome was the risk of sPTB at <37wks. Secondary outcomes were sPTB<32wks and performance metrics.

137 women were studied (118 (86.1%) dichorionic diamniotic and 19 (13.9%) monochorionic diamniotic). Median gestational age was 18.0 wks (IQR 17.0-19.0 wks) and median CL was 3.7 cm (IQR 3.2-4.2 cm). 7.3% of women had a CL<2.5 cm. 52.6% of women had a sPTB <37 wks and 19.0% <32 wks. The median UCA was 124.0° (IQR 104.5-142.5°). UCA > 95° and >105° were both associated with an increased risk of sPTB<37wks (55.9% vs 31.6%, p=0.05 and 58.3% vs 35.3%, p=0.02, respectively). There was a trend between UCA >95° and >105° and increased risk of sPTB<32 wks. In the subgroup of women with dichorionic twins, UCA > 95° and >105° was associated with a trend towards an increased risk of sPTB<37 wks, although this did not reach statistical significance. Evaluating performance metrics, UCA was a better screening test and was not improved with the addition of CL<2.5 cm. In conclusion, a UCA >95° and >105° was associated with an increased risk of sPTB <37 wks in twins. These findings enhance our understanding of the cervical changes associated with sPTB. As a screening tool in twins, second trimester UCA outperformed CL for the prediction of sPTB <37 wks.

Pictured: University of Rochester fellows and residents doing ultrasound simulation for invasive pregnancy procedures

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

INNOVATION

UR: A Leader in Technology Commercialization

The University of Rochester has a long-standing tradition of being at the forefront of innovation and scientific research. In 2018, 141 invention disclosures were received from 206 inventors from 47 University departments and divisions. Fifty external collaborators from 31 institutions, agencies, and corporations were also named as inventors. Four copyright registrations, 2 trademark registrations, and 100 patent applications were filed in FY 2018. Of the patent filings, 40 were new matter filings, while 60 were continuations of applications filed in previous years. In FY 2018, the UR was granted 45 U.S. patents and 32 foreign patents. These 77 patents cover 50 different technologies. In FY 2018, the UR also executed 36 new license and options agreements and monitored 166 active agreements.

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

U.S. PATENTS

New Patents Issued for RCBU Member Inventions

The patent titled "Superresolution Imaging of Scatterers in Pulse-Echo Imaging with Symmetric Stabilized Pulses" (US 10,073,176) was issued September 11, 2018. The patent has been assigned to the University of Rochester with inventors Kevin J. Parker and Shujie Chen. The patent describes systems and methods related to stabilized symmetric pulses for applications to pulse-echo imaging. The systems and methods extend the usefulness of super-resolution imaging.

The patent titled "Ultrasound Technology to Control the Spatial Distribution of Cells and Proteins in Engineered Tissues" (US 9,688,962) has been assigned to the University of Rochester with Inventors Diane Dalecki, Denise C. Hocking, and Kelley Garvin. The patent describes novel technology that uses acoustic forces within ultrasound standing wave fields to pattern cells volumetrically and engineer three-dimensional blood vessel networks within hydrogels. Primary applications of this technology include engineering vascularized tissue models for drug testing, tissue engineering, and regenerative medicine.

Superresolution Imaging of Scatterers in Pulse-Echo Imaging with Symmetric Stabilized Pulses, U.S. Patent No. 10,073,176	Kevin J. Parker and Shujie Chen September 11, 2018
Ultrasound Technology to Control the Spatial Distribution of Cells and Proteins in Engineered Tissues, U.S. Patent No. 9,688,962	Diane Dalecki, Denise C. Hocking, Kelley Garvin June 27, 2017
Chimeric Fibronectin Matrix Mimetics and Uses Thereof U.S. Patent No. 9,072,706	Denise C. Hocking and Daniel Roy July 7, 2015
Photodynamic Therapy with Spatially Resolved Dual Spectroscopic Monitoring, U.S. Patent No. 9,044,140	Thomas H. Foster, et al. June 2, 2015
Methods and Systems for Spatially Modulated Ultrasound Radiation Force Imaging, U.S. Patent No. 8,753,277	Stephen McAleavey June 17, 2014
Low-cost Device for C-scan Acoustic Wave Imaging, U.S. Patent Nos. 8,870,770 (2014) and 8,353,833 (2013)	Vikram S. Dogra and Navalgund Rao 2013
Sonoelastographic Shear Velocity Imaging using Crawling Wave Excitation, U.S. Patent No. 8,267,865	Kenneth Hoyt and Kevin J. Parker September 18, 2012
Statistical Estimation of Ultrasonic Propagation Parameters for Aberration Correction, U.S. Patent No. 7,867,166	Robert C. Waag and Jeffrey P. Astheimer January 11, 2011
Ultrasound Imaging of Tissue Stiffness by Spatially Modulated Acoustic Radiation Force Impulse (SM-ARFI), U.S. Patent No. 8,225,666	Stephen McAleavey May 9, 2008
Real Time Visualization of Shear Wave Propagation in Soft Materials with Sonoelastography, U.S. Patent No. 7,444,875	Zhe Wu and Kevin J. Parker November 4, 2008
Method of Treating Neurodegenerative Disease Using Ultrasound, U.S. Patent No. 7,211,054	Charles W. Francis and Valentina Suchkova May 1, 2007
Finite Amplitude Distortion-Based Inhomogeneous Pulse Echo Ultrasonic Imaging, U.S. Patent No. 7,104,956	Ted Christopher September 12, 2006
Ultrasound Distortion Compensation using Blind System Identification, U.S. Patent No. 6,699,189	Feng Lin and Robert C. Waag March 2, 2004
System and Method for 4D Reconstruction and Visualization, U.S. Patent No. 6,169,817	Kevin J. Parker, Saara Totterman, Jose Tamez-Pena January 2, 2001
System for Model-Based Compression of Speckle Images, U.S. Patent No. 5,734,754	Kevin J. Parker March 31, 1998
Thin-Film Phantoms and Phantom Systems, U.S. Patent No. 5,756,875	Daniel B. Phillips and Kevin J. Parker May 26, 1998
Smart Endotracheal Tube, U.S. Patent No. 5,785,051	Jack Mottley and Randy Lipscher July 29, 1998
Blue Noise Mask, U.S. Patent Nos. 5,111,310 (1992); 5,477,305 (1995); 5,543,941 (1996); 5,708,518 (1998); and 5,726,772 (1998)	Kevin J. Parker and Theophano Mitsa
Ultrasmall Porous Particles for Enhancing Ultrasound Backscatter, U.S. Patent No. 5,741,522	Michael R. Violante and Kevin J. Parker
Multiple Function Infant Monitor, U.S. Patent No. 5,479, 932	Joseph Higgins, E. Carr Everbach, Kevin J. Parker January 2, 1996
Butterfly Search Technique, U.S. Patent No. 5,419,331	S. Kaisar Alam and Kevin J. Parker May 30, 1995

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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 frequemcy imaging
- Ultrasound contrast agents
- 3D and 4D ultrasound imaging
- Acoustic radiation force imaging
- Novel therapeutic applications
- Multi-modal imaging techniques
- Biological effects of ultrasound fields
- Sonoelastography and elasticity imaging
- Acoustic scattering and wave propagation in tissue
- High intensity focused ultrasound (HIFU) techniques

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