National Institutes of Health

NIH HEAL Initiative Workshop on MYOFASCIAL PAIN

Quantitative Evaluation of Myofascial Tissues: Potential Impact for Musculoskeletal Pain Research

September 16-17, 2020

Co-organizers

NCCIH

NIBIB

NIH Partners

NIAMS

NICHD/NCMRR

NIDCR

NINDS

#nihHEALinitiative

Objective

Myofascial pain syndrome (MPS)—pain originating from muscles and/or associated soft tissues such as fascia—is estimated to affect 30 to 85 percent of patients with musculoskeletal pain. Compared to the skeletal (bones, joints, intervertebral discs) and central nervous system (CNS) contributions to musculoskeletal pain, the myofascial components, especially the fascia component, as well as the interactions between fascia and muscles, remain mostly unknown. Importantly, many chronic musculoskeletal pain patients don't respond to surgery (targeting the skeletal component) or develop significant side effects to opioids (targeting the CNS) or both. Therefore, there is a strong need to address the contributions of the myofascial tissues to chronic pain as they are among the last "unturned stones" of all the tissue types involved in musculoskeletal pain.

The NIH HEAL^{SM} Initiative is sponsoring this workshop to pursue research and technology opportunities addressing myofascial pain syndrome (MPS). This workshop will bring together clinical research experts in diagnosis and treatment of musculoskeletal painful conditions, imaging and biomechanics experts, and computational modelers to advance cutting-edge research related to the development or improvement of imaging technologies that would allow diagnosis and dynamic quantification of the pathophysiology as well as identification of biomarkers manifested in MPS. It also will present in-depth analyses of the state of science of myofascial pain, current usage of technologies (e.g., methodologies) and their limitations and challenges, potential current technologies to be adapted for myofascial pain biomarker imaging/recording, and potential emerging technologies and methodologies to be developed.

Acknowledgments

Co-Organizers

National Center for Complementary and Integrative Health (NCCIH)

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

NIH Partners

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Eunice K Shriver National Institute of Child Health and Human Development (NICHD)/National Center for Medical Rehabilitation Research (NCMRR)

National Institute of Dental and Craniofacial Research (NIDCR)

National Institute of Neurological Disorders and Stroke (NINDS)

Planning Committee

Helene Langevin, M.D., NCCIH
Wen Chen, Ph.D., NCCIH
Merav Sabri, Ph.D., NCCIH
Guoying Liu, Ph.D., NIBIB
Michael L. Oshinsky, Ph.D., NINDS
Alex Tuttle, Ph.D., NINDS
Brooks Gross, Ph.D., NINDS
Chuck Washabaugh, Ph.D., NIAMS
Leslie Derr, Ph.D., NIAMS
Gayle Lester, Ph.D., NIAMS
Theresa Hayes Cruz, Ph.D., NICHD/NCMRR
Yolanda F. Vallejo, Ph.D., NIDCR
Dena Fischer, D.D.S., NIDCR

Quantitative Evaluation of Myofascial Tissues: Potential Impact for Musculoskeletal Pain Research

September 16–17, 2020

An NIH HEAL Initiative Virtual Workshop

Co-organizers: NCCIH, NIBIB

NIH Partners: NIAMS, NICHD/NCMRR, NIDCR, NINDS

Day 1: September 16, 2020

8:45 a.m. Welcome and NIH HEAL Overview: Rebecca Baker, NIH HEAL Director

9:00 a.m. Opening Remarks: Helene Langevin, NCCIH Director
Historical Overview of Myofascial Pain Syndrome and Hypotheses

9:25 a.m. **Session One: State of Science of Myofascial Pain Syndrome: Clinical Presentation, Pathophysiological Hypotheses, and Challenges**

Chair: Michael L. Oshinsky, NINDS
Co-Chair: Leslie Derr, NIAMS

9:30 a.m. Carla Stecco, University of Padova
Fascial Anatomy, From Macro to Micro

9:42 a.m. Jay Shah, NIH /Clinical Center
Chronic Myofascial Pain: Myogenic Considerations in Its Pathogenesis and Clinical Manifestations

9:54 a.m. John Srbely, University of Guelph
The Role of Neurogenic Mechanisms in the Pathophysiology and Clinical Manifestation of Chronic Myofascial Pain

10:06 a.m. David Lesondak, University of Pittsburgh
A Clinician's Perspective on Treating Myofascial Pain: Overview and Challenges

10:18 a.m. Mary Barbe, Temple University
Basic Research/Animal Models Relevant to Myofascial Pain

10:30 a.m. BREAK

10:45 a.m. **Panelist Comments**
Lynn Gerber, George Mason University
Kendi Hensel, Texas College of Osteopathic Medicine
Eric Jacobson, Harvard Medical School
Jan Mundo, Mundo Lifework
Niki Munk, Indiana University
Kathleen Sluka, University of Iowa
Heather Tick, University of Washington

11:05 a.m. **Panel Discussion**

11:45 a.m. **Questions and Answers From the Zoom and Videocast Audiences**

12:00 Noon VIRTUAL LUNCH

1:00 p.m. **Session Two: Current Structural Imaging Approaches With Potential Application to Myofascial Pain Syndrome**

Chair: Guoying Liu, NIBIB
Co-Chair: Merav Sabri, NCCIH

1:05 p.m. Garry E. Gold, Stanford Schools of Engineering and Medicine
Current Magnetic Resonance Imaging Approaches With Potential Application to Myofascial Pain Syndrome

1:17 p.m. Bruce Damon, Vanderbilt University
Quantitative MRI Methods With Potential Application to Myofascial Pain Syndrome

1:29 p.m. Sandip Biswal, Stanford University
Use of Molecular Imaging and MR Neurography in the Identification of Peripheral Pain Generators

1:41 p.m. Siddhartha Sikdar, George Mason University
From Qualitative to Quantitative: Musculoskeletal Ultrasound Imaging for the Evaluation of Myofascial Tissues: Opportunities and Limitations

1:55 p.m. **Panelist Comments**
Christine Chung, University of California, San Diego
Bharti Khurana, Harvard Medical School
Levon Nazarian, Thomas Jefferson University
Antonio Stecco, New York University Langone Health

2:05 p.m. **Panel Discussion**

2:35 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

2:50 p.m. BREAK

3:05 p.m. **Session Three: Elastography Imaging Approaches with Potential Application to Myofascial Pain Syndrome**

Chair: Helene Langevin, NCCIH
Co-Chair: Merav Sabri, NCCIH

3:10 p.m. Kevin Parker, University of Rochester
Ultrasound Elastography for Evaluation of Tissue Mechanical Properties

3:22 p.m. Helene Langevin, NCCIH
Measurement of Shear Plane Tissue Mobility Using Ultrasound Elastography Techniques

3:34 p.m. Richard Ehman, Mayo Clinic College of Medicine and Science
MR Elastography: Quantitatively Characterizing the Mechanical Properties of Skeletal Muscle and Myofascial Interfaces

3:46 p.m. **Panelist Comments**
Shigao Chen, Mayo Clinic Rochester
Dieter Klatt, University of Illinois, Chicago
Neil Roberts, University of Edinburgh
Sergio Sanabria, Stanford University School of Medicine
Siddhartha Sikdar, George Mason University
Robert Vining, Palmer College of Chiropractic

4:00 p.m. **Panel Discussion**

4:30 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

4:45 p.m. **WRAP UP**

5:00 p.m. **ADJOURN**

Day 2: September 17, 2020

8:45 a.m. Welcome Back: Jill Heemskerk, NIBIB Deputy Director

9:00 a.m. **Session Four: Emerging Promising Technologies for Myofascial Pain Syndrome: Electrophysiology, MRI, and PET**

Chair: Alex Tuttle, NINDS
Co-Chair: Chuck Washabaugh, NIAMS

9:05 a.m. Abhijit J. Chaudhari, University of California, Davis
Innovations in PET for Future Applications in Myofascial Pain Syndrome

9:17 a.m. Espen Spangenburg, East Carolina University
Application of Techniques That Assess Physiological and Metabolic Parameters of Skeletal Muscle To Advance Our Understanding of Myofascial Pain Syndrome

9:29 a.m. Seward Rutkove, Beth Israel Deaconess Medical Center, Harvard
Electrophysiology Techniques and Potential Applications for Myofascial Tissues

9:41 a.m. Els Fieremans, New York University Langone Health
***In Vivo* Imaging of Tissue and Muscle Microstructure**

9:53 a.m. **Panelist Comments**
Vania Apkarian, Northwestern University
Mark D. Does, Vanderbilt University
Jordi Serra, King's College Hospital, London
Samuel R. Ward, University of California, San Diego

10:05 a.m. **Panel Discussion**

10:35 a.m. **Questions and Answers From the Zoom and Videocast Audiences**

10:50 a.m. BREAK

11:10 a.m. **Session Five: Emerging Promising Technologies for Myofascial Pain Syndrome: Tissue Engineering, Artificial Intelligence, and Computational Modeling**

Chair: Yolanda F. Vallejo, NIDCR
Co-Chair: Theresa Hayes Cruz, NICHD/NCMRR

11:15 a.m. Jeffrey Lotz, University of California, San Francisco
Quantifying Associations Between Paraspinal Muscle Quality, Spinal Pathologies, and Skeletal Biomechanics

11:27 a.m. Sharmila Majumdar, University of California, San Francisco
The Role of Machine Learning for Muscle Segmentation and Characterization of Muscle Properties

11:39 a.m. Silvia Blemker, University of Virginia
Multiscale Computational Modeling Integrates Biology and Mechanics To Prove New Insights Into Muscle Dysfunction

11:51 a.m. Hai Yao, Clemson University/Medical University of South Carolina
Integrating Multimodality Measurement and Multiscale Modeling To Assess TMDs

12:05 p.m. **Panelist Comments**
Lucia Cevidanes, University of Michigan
Adam Hantman, Janelia Research Campus
Lealem Mulugeta, *InSilico* Labs, LLC, and Medalist Performance
Thomas Myers, University of Rochester

12:15 p.m. **Panel Discussion**

12:45 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

1:00 p.m. VIRTUAL LUNCH

2:00 p.m. **Session Six: General Discussion**

Chair: Wen Chen, NCCIH
Co-Chair: Dena Fischer, NIDCR

2:05 p.m. **Panelist Comments**
Allan Basbaum, University of California, San Francisco
Christine Chung, University of California, San Diego
William Maixner, Duke University Medical Center
Julie Fritz, The University of Utah
Daniel K. Sodickson, New York University Langone Health

2:30 p.m. **Panel Discussion**

3:00 p.m. **Summary and Concluding Remarks**

Helene Langevin, NCCIH Director

3:30 p.m. **ADJOURN**

Agenda, Speaker Bios and Abstracts, and Panelist Bios

September 16, 2020

8:45 a.m. Welcome Remarks: Rebecca Baker, NIH HEAL Director

Rebecca Baker, Director, NIH HEAL

Dr. Baker is director of the Helping to End Addiction Long-term^{SM} Initiative, or NIH HEAL Initiative, in the Office of the Director (OD), NIH. Dr. Baker helped develop the Initiative and leads coordination of NIH HEAL Initiative programmatic activities between the NIH OD and relevant institutes and centers. She also provides expert advice to and represents the NIH Director on Initiative-related activities, including interagency efforts in pain and opioid research and policy. Prior to this position, Dr. Baker served as special assistant to the NIH Director and the Principal Deputy Director working directly with NIH leadership to analyze complex biomedical research policy issues and assist in the development of new science and policy initiatives. She earned her Ph.D. from the University of Pennsylvania and her bachelor's degree from Cornell University.

9:00 a.m. Opening Remarks: Helene Langevin, NCCIH Director

Historical Overview of Myofascial Pain Syndrome and Hypotheses

Helene Langevin, Director, National Center for Complementary and Integrative Health (NCCIH)

Dr. Langevin was sworn in as director of NCCIH on November 26, 2018. Prior to her arrival, she worked at the Osher Center for Integrative Medicine, jointly based at Brigham and Women's Hospital and Harvard Medical School, Boston. Dr. Langevin had served as director of the Osher Center and professor-in-residence of medicine at Harvard Medical School since 2012. She also has served as a visiting professor of neurological sciences at the University of Vermont Larner College of Medicine, Burlington.

As principal investigator of several NIH-funded studies, Dr. Langevin's research interests have centered on the role of connective tissue in chronic musculoskeletal pain and the mechanisms of acupuncture, manual, and movement-based therapies. Her recent work has focused on the effects of stretching on inflammation resolution mechanisms within connective tissue. She is author of more than 70 original scientific papers and a fellow of the American College of Physicians.

Dr. Langevin received an M.D. degree from McGill University, Montreal. She completed a postdoctoral research fellowship in neurochemistry at the MRC Neurochemical Pharmacology Unit in Cambridge, England, and a residency in internal medicine and fellowship in endocrinology and metabolism at The Johns Hopkins Hospital in Baltimore.

As NCCIH director, Dr. Langevin oversees the Federal Government's lead agency for scientific research on diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. NCCIH funds and conducts research to help answer important scientific and public health questions about natural products, mind and body practices, and pain management.

9:25 a.m.–Noon **Session One: State of Science of Myofascial Pain Syndrome: Clinical Presentation, Pathophysiological Hypotheses, and Challenges**

Session Chairs

Chair: Michael L. Oshinsky, NINDS
Co-Chair: Leslie Derr, NIAMS

9:30–10:30 a.m. **Session Speakers**

Carla Stecco, University of Padova
Jay Shah, NIH Clinical Center
John Srbely, University of Guelph
David Lesondak, University of Pittsburgh
Mary Barbe, Temple University

10:30–10:45 a.m. BREAK

10:45–11:05 a.m. **Panelist Comments**

Lynn Gerber, George Mason University
Kendi Hensel, Texas College of Osteopathic Medicine
Eric Jacobson, Harvard Medical School
Jan Mundo, Mundo Lifework
Niki Munk, Indiana University
Kathleen Sluka, University of Iowa
Heather Tick, University of Washington

11:05–11:45 a.m. **Panel Discussion**

11:45–Noon **Questions and Answers From the Zoom and Videocast Audiences**

Noon–1:00 p.m. VIRTUAL LUNCH

9:25 a.m.–Noon **Session One: State of Science of Myofascial Pain Syndrome: Clinical Presentation, Pathophysiological Hypotheses, and Challenges**

Chair: Michael L. Oshinsky, NINDS
Co-Chair: Leslie Derr, NIAMS

Session Chair: Michael L. Oshinsky, National Institute of Neurological Disorders and Stroke (NINDS)

Dr. Oshinsky joined NINDS in 2014 as program director for Pain and Migraine Research, where he is responsible for research and administrative issues related to migraine, other headache disorders, neuropathic pain, peripheral and central mechanisms that mediate pain, central processing of pain, disease-related pain disorders, and therapeutic pain devices. Dr. Oshinsky received a bachelor's degree in biology with a concentration in neuroscience from Brandeis University and his Ph.D. in neurobiology and behavior from Cornell University. He received postdoctoral training as an NIH-sponsored postdoctoral fellow at the University of Pennsylvania. From 2001 through 2014, Dr. Oshinsky was an associate professor in the Department of Neurology at Thomas Jefferson University; during those years, he was director of preclinical research at the Jefferson Headache Center and led an NIH-funded research program aimed at developing and characterizing animal models of headache. In 2011, Dr. Oshinsky received the Harold G. Wolff Award for headache research.

Session Co-Chair: Leslie Derr, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Dr. Derr is currently program coordinator for the Back Pain Consortium Research Program administered by NIAMS as part of the NIH Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative. Dr. Derr has led a number of strategic initiatives, most recently as a program director for the NIH Common Fund, and earlier in her career for the National Cancer Institute (NCI) cancer Biomedical Informatics Grid and NCI "Areas of Extraordinary Opportunity." She also served as communities of practice coordinator for the Regional Extension Center Program in the Office of the National Coordinator for Health Information Technology, Office of the Secretary, Department of Health and Human Services. Dr. Derr received a Ph.D. in genetics from Duke University and, following postdoctoral work at the Frederick Cancer Research and Development Center, joined NIH as a principal investigator with the National Institute of Allergy and Infectious Diseases. Her lab used the yeast *Saccharomyces cerevisiae* and its retrotransposon, Ty, as a model to study RNA-mediated recombination and increase our understanding of the role of RNA in genome evolution.

Speaker: Carla Stecco, University of Padova

Dr. Stecco is an orthopedic surgeon and professor of human anatomy at the University of Padova and a founding member of the Fascial Manipulation Association and Fascial Research Society. She is a member of the Italian Society of Anatomy and Histology, the European Association of Clinical Anatomy, and the International Academy of Manual Musculoskeletal Medicine. Her scientific activity is devoted to the study of the anatomy of human fasciae from a macroscopic, histologic, and pathologic point of view. Dr. Stecco personally has made over 200 cadaver dissections for research. Since 2000, she has organized and personally held theoretical-practical courses about the fascial manipulation technique in Italy and in other countries.
Dr. Stecco is author of more than 100 *in extenso* papers about the fascial anatomy, two books about fascial manipulation that have been translated into 10 languages, and chapters about the fascial anatomy. She wrote the first photographic atlas about fasciae*, Functional Atlas of Human Fasciae*.

Fascial Anatomy, From Macro to Micro

For many years, the fasciae have been considered only as a "white envelope for the muscles," and little attention has been given to their macroscopic and histological anatomy. The presentation will illustrate the gross and microscopic anatomy of the superficial and deep fasciae, with particular attention to their structural organization, fiber content, and innervation. Based on the latest research, it is clear that many fasciae can be distinguished by specific features. The superficial fascia is rich in elastic fibers, adaptable, and strongly connected with the skin. It envelops and protects the superficial vessels and nerves and probably plays a key role in lymphatic drainage. The deep fasciae are distinguished in two large groups: the aponeurotic fasciae that work as a bridge connecting different muscles and the epimysial fasciae that are specific to each muscle. The deep fasciae are formed by collagen fibers organized in layers, and each layer is separated from its neighbor by loose connective tissue, rich in hyaluronan. The collagen fibers define the mechanical behavior of fasciae, and the hyaluronan defines the tissue hydration and ability to glide. The fasciae are also very well innervated. Finally, the presence of various receptors for hormones such as estrogen, relaxin, and the endocannabinoid system will be discussed, focusing on the ability of hormonal inputs to modify the microscopic aspects of the fasciae. This knowledge could contribute to understanding of the biomechanical behavior of the fasciae and their role in acute and chronic myofascial pain.

Speaker: Jay Shah, National Institutes of Health Clinical Center (NIH/CC)

Dr. Shah is a physiatrist and clinical investigator in the Rehabilitation Medicine Department at NIH. His interests include the symptoms and signs, pathogenesis, and pathophysiology of myofascial pain syndrome (MPS) associated with myofascial trigger points (MTrPs) and the integration of physical medicine techniques (e.g., dry needling) with promising integrative approaches in the management of neuro-musculoskeletal pain and dysfunction. Dr. Shah is intrigued by the dynamic roles that neurogenic inflammation, central sensitization, somato-visceral and viscero-somatic reflexes, spinal facilitation, and limbic system dysfunction play in MPS associated with MTrPs. For the last 20 years, Dr. Shah and his coinvestigators have been studying the clinical, biochemical, and imaging aspects of MPS associated with MTrPs. They have developed and successfully utilized novel microanalytical and ultrasound imaging techniques that have uncovered the unique biochemical milieu (e.g., inflammatory mediators, neuropeptides, cytokines, and catecholamines) and the viscoelastic and blood flow properties of MTrPs and surrounding soft tissue.

Chronic Myofascial Pain: Myogenic Considerations in Its Pathogenesis and Clinical Manifestations

Myofascial pain is a condition that can be acute or, more commonly, chronic that involves the muscle and its surrounding connective tissue. According to Travell and Simons, the myogenic component of myofascial pain is characterized by local contraction knots known as myofascial trigger points, which they believe to be central to the diagnosis of the condition.

MTrPs are hard, palpable, hyperirritable nodules in taut bands of skeletal muscle that can present as either active or latent. Active MTrPs are spontaneously painful at rest, with digital pressure reproducing the myofascial component of pain. Latent MTrPs exhibit all the physical characteristics of active MTrPs but are not painful at rest. In addition, latent MTrPs are commonly found in individuals with active MTrPs.

The current prevailing theory on the pathogenesis of MTrPs is Simons' Integrated Hypothesis. This considers the local milieu and electrical activity of the MTrP, taut band, endogenous muscle contracture, and release of sensitizing substances to explain local muscle tenderness and pain associated with chronic myofascial pain. Research offers support for this hypothesis by demonstrating a unique biochemical milieu within the active MTrP region, characterized by elevated levels of proinflammatory mediators, neuropeptides, catecholamines, and a more acidic pH.

This unique profile of biochemicals serves to increase levels of acetylcholine (ACh) at the neuromuscular junction, leading to the characteristic endplate noise and local contractures observed within affected muscles.

Speaker: John Srbely, University of Guelph

Dr. Srbely currently holds a tenured faculty position at the rank of associate professor in the Department of Human Health and Nutritional Science, College of Biological Sciences, University of Guelph (Guelph, Ontario, Canada). He has held a Canadian Chiropractic Research Foundation Research Chair in Spine Mechanics and Neurophysiology (2008–2013) and is director of the Neuromuscular Health and Chronic Pain Laboratory at the University of Guelph. His primary area of research interest encompasses the study of the physiologic mechanisms and management of chronic musculoskeletal (myofascial) pain. He employs both animal and human models to investigate the underlying role of central sensitization and neurogenic inflammation on the clinical manifestation of chronic inflammatory muscle disease. Dr. Srbely is a member of the editorial board of the *Journal of the Canadian Chiropractic Association* and associate chair of the Natural, Physical and Engineering Science Research Ethics Board at the University of Guelph.

The Role of Neurogenic Mechanisms in the Pathophysiology and Clinical Manifestation of Chronic Myofascial Pain

Chronic myofascial pain is one of the most common forms of chronic musculoskeletal pain encountered daily by rehabilitation specialists. Despite its prevalence, the underlying physiologic mechanisms are still poorly understood. The current prevailing thought in the field suggests that the clinical manifestation of chronic myofascial pain, and the formation of its characteristic extrafusal fiber contractions known as myofascial trigger points (MTrPs), is precipitated by a frank and/or chronic mechanical injury to the myotendinous unit. Clinical observation, however, challenges this theory, with emerging science suggesting neurogenic mechanisms may play a key role in the initiation and ongoing manifestation of chronic musculoskeletal pain. Two important such mechanisms include central sensitization and neurogenic inflammation. The recently proposed Neurogenic Hypothesis suggests that chronic musculoskeletal pain and MTrP formation are the physiologic expressions of central sensitization evoked by a primary pathology that is distinct, but neurologically linked, to the affected muscle(s). Central sensitization is also important in mediating the maladaptive sympathetic and motor responses commonly observed in the clinical presentation of chronic myofascial pain and can manifest without local mechanical injury within the affected muscle(s). This presentation will explore the emerging science characterizing the neurogenic mechanisms in both human and animal models, and their important implications to the clinical manifestation of chronic myofascial pain.

Speaker: David Lesondak, University of Pittsburgh

Dr. Lesondak is an allied health member in the Department of Family and Community Medicine at the University of Pittsburgh Medical Center (UPMC). He is the resident fascia specialist at UPMC's Center for Integrative Medicine, maintaining a practice in anatomy that trains structural integration, fascial stretch therapy, and other fascial modalities. He is the author of *Fascia: What It Is and Why It Matters* and editor of *Fascia, Function, and Medical Applications* and has contributed to other publications. Dr. Lesondak lectures on fascia science and teaches therapeutic approaches internationally.

A Clinician's Perspective on Treating Myofascial Pain: Overview and Challenges

Accidents, injuries, surgeries, repetitive motions, as well as a more sedentary lifestyle, can all contribute to chronic myofascial pain. Guarding, reduced range of motion, and unconscious patterns of compensation create stiff and hypomobile fascia that affect posture and create body-wide patterns of strain. These patterns and postural distortions are often directly implicated in pain complaints. Fascial therapeutics that combine the patient's subjective complaints with a more objective patho-anatomical analysis of postural and movement elements to determine the therapeutic points of intervention have the potential to better manage and even reverse conditions previously thought to be chronic. Challenges to greater understanding and acceptance of these interventions include the need for better methods for objectively measuring patient outcomes, better-designed trials and replication studies, and continued streamlining and standardization of education.

Speaker: Mary Barbe, Temple University

Dr. Barbe is a full professor in the Department of Anatomy and Cell Biology at Lewis Katz School of Medicine, Temple University. She has a Ph.D. from Wake Forest University School of Medicine, where she was trained as a neuroscientist with a broad background in neuroanatomical and musculoskeletal biology. She completed postdoctoral training at the Medical College of Pennsylvania in Philadelphia. Dr. Barbe joined Temple University in 1990 as an assistant professor in the Department of Physical Therapy, College of Health Professions. She joined the Department of Anatomy and Cell Biology as a full professor in 2010. Dr. Barbe has an active research agenda examining underlying mechanisms and treatments for work-related musculoskeletal disorders and methods of reinnervation of the bladder after spinal injury. Since 2000, one key focus of her lab has been studying the effects of repetition and force on tissues as a consequence of upper extremity overuse injuries. Using a unique operant rat model developed in her laboratory, she has examined the effects of varying levels of repetitive and forceful work tasks on musculoskeletal and nervous system pathophysiology, initially focusing on injury and inflammation, and how these processes induce tissue degeneration and sensorimotor dysfunction. Dr. Barbe currently is exploring injury-induced inflammation and inducers of tissue fibrosis and degeneration occurring with overuse. Her work is currently funded by NCCIH, NIAMS, and NINDS.

Basic Research/Animal Models Relevant to Myofascial Pain

Three animal models relevant to myofascial pain will be presented. In one model, repeated contusion and eccentric exercise for 8 weeks induced myofascial trigger points in association with increased spontaneous electrical activity during electromyography testing and histological evidence of damage (myofiber knots, beading, atrophy, disorganization, and centronucleation). The next two models are related, with rats performing repetitive reaching and grasping tasks for extended periods (a food pellet retrieval task versus a lever-pulling task at high-repetition high-force loads). Both repetitive tasks induced motor weakness and discomfort-related behaviors that were associated with muscle, peripheral nerve, and/or central nervous system changes. Muscle changes included time-dependent histological evidence of damage (e.g., focal injury-repair, myofiber atrophy, and centronucleation), inflammation, and fibrosis, and biochemical alterations (increased inflammatory cytokines and stress proteins, altered Ca^{2+} regulation and altered production of sarcoplasmic reticulum proteins involved in Ca^{2+} homeostasis, and activation of autophagy systems). Peripheral nerve changes included injury (degraded myelin and axonal beading), inflammation (increased activated macrophage infiltration and inflammatory cytokines), extra- and intraneural fibrosis related to Substance P release because it could be blocked with a neurokin-1 receptor antagonist, heightened proportion of ongoing activity in nociceptor axons, and altered conduction velocities. Lastly, central nervous system changes related to prolonged reaching and grasping included increased nociceptor-related neuropeptide production in dorsal root ganglia and spinal cord dorsal horns, increased inflammatory cytokines in spinal cord glia and neurons, and degraded somatosensory cortical maps and increased electrical responsiveness of neurons in the somatosensory cortex.

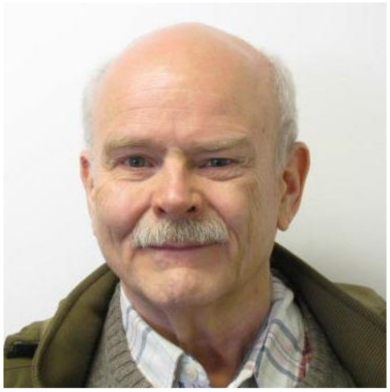
10:45–11:45 a.m. **Panelist Comments and Discussion**

Panelist: Lynn Gerber, George Mason University

Dr. Gerber is a professor at George Mason University, where she established the Center for the Study of Chronic Illness and Disability and the Laboratory for the Study and Simulation of Human Movement. She is Rheumatology section chief and director for Research, Medicine Service Line, for the Inova Health System. Dr. Gerber was chief of the Rehabilitation Medicine Department at the NIH Clinical Center from 1975 through 2005. A graduate of Tufts University School of Medicine, Dr. Gerber is a diplomate of the American Board of Internal Medicine (rheumatology subspecialty) and the American Board of Physical Medicine and Rehabilitation. She is a member of the National Academy of Medicine. Dr. Gerber's research has focused on human movement, its relationship to pain syndromes and mechanisms, and assessment of fatigue. Dr. Gerber has written 60 textbook chapters and authored 180 peer-reviewed manuscripts and has received grants from NIH; the National Science Foundation; the National Institute on Disability, Independent Living, and Rehabilitation Research; PNC Foundation; and Jackson Foundation.

Panelist: Kendi Hensel, Texas College of Osteopathic Medicine

Dr. Hensel is an associate professor in the Department of Family Medicine and Osteopathic Manipulative Medicine at the University of North Texas Health Science Center's Texas College of Osteopathic Medicine in Fort Worth. She is president of the American Academy of Osteopathy (AAO), having become an AAO fellow in 2018 for exemplary scholarship in osteopathic medicine. Dr. Hensel is a board-certified physician and conducts research on the efficacy and mechanism of action of osteopathic manipulative medicine (OMM) (e.g., in an NCCIH-funded study on the physiologic and clinical effects of OMM in pregnancy). She received her Doctor of Osteopathic Medicine degree from Oklahoma State University College of Osteopathic Medicine and her Ph.D. in OMM clinical research and education from the University of North Texas Health Science Center. She completed a combined residency in family practice and neuromusculoskeletal medicine at the University of New England College of Osteopathic Medicine in Maine.



Panelist: Eric Jacobson, Harvard Medical School

Dr. Jacobson is a research scientist who investigates alternative medicine at Harvard Medical School, where he conducted an NIH-funded pilot clinical trial of structural integration, a method of soft tissue manipulation, as an adjunct to outpatient rehabilitation for chronic low-back pain. He also has worked on studies of the placebo effect and diagnostic reasoning in acupuncture. Dr. Jacobson was trained in structural integration by its founder, the biochemist Ida Rolf, in 1974, and has been in private practice in the Boston area since then. He currently serves on the Research Committee of the Dr. Ida P. Rolf Institute and the Board of Directors of the Ida P. Rolf Research Foundation.

Panelist: Jan Mundo, Mundo Lifework

Ms. Mundo is a certified master somatic coach, body-centered therapist, massage therapist, and self-care educator with advanced training in somatics and trauma and multiple healing modalities. She specializes in headache, migraine, myofascial pain, stress, tension, and trauma. In 1970, she developed Mundo Method acute headache therapy—a focused touch and concentration protocol that works with the sensations of headache and migraine. In 1992, she created a holistic, hands-on somatic self-care program for headache and migraine relief and prevention and has held programs at medical centers, universities, corporations, and multiple conferences, including the New York Headache Center, Kaiser Permanente, University of California, Stanford University, RetreatMigraine, The Embodiment Conference, and the U.S. Association for Body Psychotherapy. The peer-reviewed medical journal, *Cephalalgia*, published a retrospective study of the program in May 2001. Ms. Mundo authored *The Headache Healer's Handbook*, and her work has been published in anthologies, magazines, and on line. She practices in the San Francisco Bay Area, Manhattan, and via webcam.

Panelist: Niki Munk, Indiana University

Dr. Munk is an associate professor of health sciences in Indiana University's School of Health and Human Sciences at Indiana University-Purdue University Indianapolis, a nonpracticing Kentucky-licensed massage therapist, and member of the Academic Collaborative for Integrative Health research work group. She is 1 of 13 international Fellows in the Australian Research Centre in Complementary and Alternative Medicine's International Complementary Medicine Research Leadership Program and coinvestigator on the Department of Veterans Affairs Trial Outcomes for Massage: Caregiver-Assisted vs. Therapist Treated (TOMCATT) study that examines therapist-applied and care-ally-assisted massage therapy for chronic neck pain in veterans. Dr. Munk earned her doctorate in gerontology from the University of Kentucky in 2013. Her research explores real-world massage therapy for chronic pain and associated factors, including emotional well-being, trigger point self-care, and accessibility challenges to massage. Prior to her academic career, Dr. Munk's clinical massage practice regularly incorporated trigger point therapy, with results and treatment adaptability inspiring her research interests.

Panelist: Kathleen Sluka, University of Iowa

Dr. Sluka is a professor in the Department of Physical Therapy and Rehabilitation Science at the University of Iowa. She received a physical therapy degree from Georgia State University and a Ph.D. in anatomy from the University of Texas Medical Branch in Galveston. After a postdoctoral fellowship with Dr. William D. Willis, she joined the faculty at the University of Iowa, where she has served for 24 years. Dr. Sluka's research focuses on the neurobiology of musculoskeletal pain as well as the mechanisms and effectiveness of nonpharmacologic pain treatments. She has published over 200 peer-reviewed manuscripts, numerous book chapters, and a textbook, *Pain Mechanisms and Management for the Physical Therapist*. Her numerous awards include the Marian Williams Award for Research in Physical Therapy, the Catherine Worthingham Fellowship from the American Physical Therapy Association, and the Frederick W.L. Kerr Basic Science Research Award from the American Pain Society. She is actively involved in the International Association for the Study of Pain, the American Pain Society, and the American Physical Therapy Association serving on committees, task forces, and society boards.

Panelist: Heather Tick, University of Washington

Dr. Tick has worked in pain management for 30 years, focusing on musculoskeletal injuries. She cofounded integrative pain centers in Toronto and the University of Arizona and now works in comprehensive pain management at the University of Washington Department of Anesthesia and Pain Medicine. Dr. Tick led the pain task force for the Academic Consortium for Integrative Medicine and Health and was first author on their 2016 "Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care" white paper. She has coauthored numerous refereed journal articles and book chapters and authored a book for consumers, *Holistic Pain Relief*, that has since been translated into several languages. Throughout her career, Dr. Tick has followed basic science research on underlying mechanisms of chronic musculoskeletal pain, which has led her to novel, holistic treatment approaches. She was trained by C.C. Gunn to assess and treat myofascial pain as a neuropathic condition, based on the work of Walter Cannon on supersensitivity.

11:45 a.m.–Noon	**Questions and Answers From the Zoom and Videocast**
Noon–1:00 p.m.	**Audiences** VIRTUAL LUNCH

1:00–2:50 p.m. **Session Two: Current Structural Imaging Approaches With Potential Application to Myofascial Pain Syndrome**

Session Chairs

Chair: Guoying Liu, NIBIB
Co-Chair: Merav Sabri, NCCIH

1:05–1:55 p.m. **Session Speakers**

Garry E. Gold, Stanford Schools of Engineering and Medicine
Bruce Damon, Vanderbilt University
Sandip Biswal, Stanford University
Siddhartha Sikdar, George Mason University

1:55–2:05 p.m. **Panelist Comments**

Christine Chung, University of California, San Diego
Bharti Khurana, Harvard Medical School
Levon Nazarian, Thomas Jefferson University
Antonio Stecco, New York University Langone Health

2:05–2:35 p.m. **Panel Discussion**

2:35–2:50 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

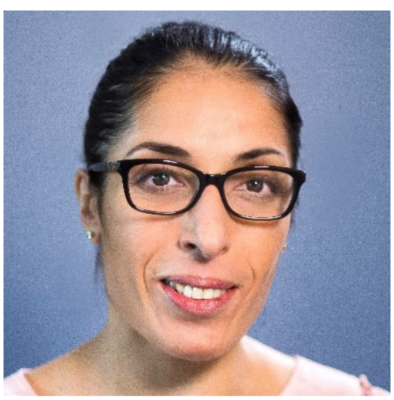
2:50–3:05 p.m. BREAK

1:00–2:50 p.m. **Session Two: Current Structural Imaging Approaches With Potential Application to Myofascial Pain Syndrome**

Chair: Guoying Liu, NIBIB
Co-Chair: Merav Sabri, NCCIH

Session Chair: Guoying Liu, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Dr. Liu is program director for magnetic resonance imaging (MRI) at NIBIB. After receiving her Ph.D. in physical chemistry and a postdoctoral fellowship in MRI, she was an assistant professor in radiology and neuroscience at Albert Einstein College of Medicine. Her work focused on development of MR techniques for imaging neuronal activity and connections. From 2001 until 2008, Dr. Liu was a program director in the National Cancer Institute Cancer Imaging Program. For nearly 20 years, she has been a strong advocate for the imaging community, seeking to fund the best science and facilitate technology development and clinical translation. Dr. Liu has served as one of the lead NIH staff for numerous trans-NIH initiatives, including the Human Connectome Project, the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, the Quantitative Imaging Biomarkers Alliance, the Human Placenta Project, and the recently announced Medical Imaging and Data Resource Center for Rapid Response to the COVID-19 Pandemic.



Session Co-Chair: Merav Sabri, National Center for Complementary and Integrative Health (NCCIH)

Dr. Sabri is a program director in the NCCIH Basic and Mechanistic Research Branch. Her portfolio includes research and training programs on fundamental and translational science related to force-based manipulations/manual therapies, technology and methodology development for mind and body approaches, emotional well-being, addiction, science of behavioral change, and Small Business Innovation Research and Small Business Technology Transfer programs for mind and body approaches. Her areas of expertise include cognitive neuroscience as well as brain imaging technologies. Dr. Sabri has earned an M.A. (Bar-Ilan University, Israel) and a Ph.D. in experimental psychology (University of Ottawa, Ontario). She completed postdoctoral training in human neuroimaging at Indiana University School of Medicine, Indianapolis, and the Medical College of Wisconsin, Milwaukee. She was an assistant professor of neurology and otolaryngology at the Medical College of Wisconsin, where her research centered on the neural and cognitive bases of attention and perception.

Speaker: Garry E. Gold, Stanford Schools of Engineering and Medicine

Dr. Gold is professor and interim chair for the Department of Radiology at Stanford University and directs the Joint and Osteoarthritis Imaging with Novel Techniques laboratory. A professor (by courtesy) in bioengineering and orthopedic surgery, he received a B.S., M.S., and M.D. and completed a residency in radiology at Stanford University and a clinical musculoskeletal radiology fellowship at the University of California, San Diego.

Dr. Gold's research focuses on developing new methods for magnetic resonance imaging (MRI) that improve diagnosis and treatment of musculoskeletal disease. His contributions to the field include early applications of uTE imaging in musculoskeletal disease. His group has developed advanced methods for morphologic and physiologic imaging of articular cartilage, improved methods for imaging around metal, new approaches for dynamic MRI in muscle and joint motion, and application of positron emission tomography–magnetic resonance (PET-MR) in musculoskeletal disease. Dr. Gold is a fellow of the International Society for Magnetic Resonance in Medicine, the Society for Advanced Body Imaging, and the American Institute for Medical and Biological Engineering.

Current Magnetic Resonance Imaging Approaches With Potential Application to Myofascial Pain Syndrome

Myofascial pain syndrome (MPS) is characterized by excessive pain in focal regions and sensitivity to touch. Within these regions, there are structural changes that include inflammation, such as fascial thickening and enhancement, increased muscle water, fatty infiltration, and fibrosis with changes to muscle architecture. The focus of this presentation is on the potential application of several routine and advanced MRI methods for examining these anatomic changes seen in MPS. Methods such as T_1 and T_2-weighted images, 3D volumetric and rapid imaging, fat and water separation, and ultra-short echo time imaging will be discussed. Quantitative methods such as T_{1rho} mapping, T_2 mapping, and diffusion-weighted imaging of muscle will be shown. Application of MRI to MPS has been limited but offers potential to characterize basic features of this disease.

Speaker: Bruce Damon, Vanderbilt University

Dr. Damon is associate professor of radiology and radiological sciences at Vanderbilt University, with secondary appointments in biomedical engineering and molecular physiology and biophysics. A core faculty member of the Vanderbilt University Institute of Imaging Science, his research program uses *in vivo* imaging and spectroscopy methods to advance quantitative understanding of human physiology and pathophysiology. Dr. Damon has a longstanding interest in understanding the structure and function of skeletal muscle and other metabolically important organs, magnetic resonance imaging (MRI) contrast mechanisms in skeletal muscle, the function of human brown adipose tissue, and muscle structure-function relationships, as well as developing MRI biomarkers for muscle disease. Dr. Damon is director of Vanderbilt's Chemical and Physical Biology Ph.D. Program. He received the Distinguished Investigator Award from the Academy of Radiology and Biomedical Imaging Research and is a fellow of the American Institute of Medical and Biological Engineering and the American Association for the Advancement of Science.

Quantitative MRI Methods With Potential Application to Myofascial Pain

Myofascial pain syndrome is characterized by focal muscle regions of excessive pain and sensitivity to touch. Within these regions are structural and microstructural changes that include inflammation and a corresponding reorganization of tissue water, fibrosis, disrupted muscle architecture, and reduced glycosaminoglycan hydration. In addition, there are functional and mechanical changes that include increased stiffness and an altered metabolic state (i.e., intracellular acidosis, decreased perfusion, and mitochondrial dysfunction). The focus of this presentation is on the potential application of several advanced MRI methods for examining these functional and mechanical changes. Methods such as MR elastography, perfusion imaging, quantitative blood oxygenation level-dependent contrast, and amide proton transfer (APT) imaging are well-established methods for studying *in vivo* physiology and biomechanics. Although their application to MPS has been limited, they offer great potential as diagnostic, predictive, and mechanistic biomarkers.

Speaker: Sandip Biswal, Stanford University

Dr. Biswal is a musculoskeletal radiologist and associate professor at Stanford University. For the past couple of decades, he has been fascinated with how pain is managed. He felt the medical profession did a very poor job of diagnosing and treating pain syndromes, seeing the countless number of sufferers in the system. So, for more than 15 years, Dr. Biswal's goal and passion has been to develop translatable clinical imaging methods to identify the source of pain with the hope of improving the lives of pain sufferers. After developing and validating these methods preclinically, he has been conducting two ongoing clinical trials of imaging pain generators for the past 6 years using both Food and Drug Administration-approved (off-label) and new positron emission tomography (PET) radiotracers to "image" pain and inflammation. His group has imaged over 150 patients and "cured" or significantly decreased pain in a growing subset of patients. He looks forward to other sites adopting this approach and helping those who suffer from chronic pain.

Use of Molecular Imaging and Magnetic Resonance Neurography in the Identification of Peripheral Pain Generators

Pain—low-back pain, headache, myofascial pain syndrome, etc.—is collectively now the number one clinical problem in the world, yet current imaging methods for identifying pain generators remain woefully inaccurate. The lack of reliable diagnostic tools facilitates significant misdiagnosis, mismanagement, rampant use of opioids, unhelpful surgeries, and, ultimately, therapeutic failures. Recent developments in magnetic resonance neurography (MRN) and clinical molecular imaging (MI) afford opportunities to examine peripheral nerve pathology and pain generators with greater specificity and sensitivity than ever before. This presentation will cover how MRN enables visualization of peripheral nerve changes such as edema, swelling, enlargement, and impingement. Through advances in biomarker discovery, imaging technology, and radiotracer design, MI has the potential to pinpoint the site(s) of pain generation by identifying locally elaborated molecular or cellular changes in those suffering from chronic pain. Specifically, positron emission tomography, a translatable molecular imaging modality, offers a more accurate quantitative method to detect peripheral pain generators in human subjects. The ability to image increases in glucose metabolism, sigma-1 receptor density, bone turnover, and macrophage activation with specific PET radiotracers will be covered as well as how MRN and MI efforts are helping to improve outcomes in patients with chronic pain.

Speaker: Siddhartha Sikdar, George Mason University

Dr. Sikdar is a professor in the Department of Bioengineering at George Mason University. He is director of the Center for Adaptive Systems of Brain-Body Interactions (CASBBI), where Center faculty and students pursue transdisciplinary research on disability. Dr. Sikdar's research group at CASBBI conducts translational research using imaging to investigate brain-body interactions in a number of clinical conditions of major public health significance, such as chronic pain, stroke, spinal cord injury, and amputation. The group uses state-of-the-art ultrasound and laser instrumentation for developing new ultrasound, optical, and hybrid imaging techniques and assistive technologies. Dr. Sikdar obtained his Ph.D. in electrical engineering from the University of Washington, Seattle in 2005. He has received the National Science Foundation (NSF) CAREER Award, the Volgenau School of Engineering Rising Star Award, and Mason's Emerging Researcher/Scholar/Creator Award. Dr. Sikdar's current research is funded by the NSF, NIH, the Department of Defense, and the Department of Veterans Affairs.

From Qualitative to Quantitative: Musculoskeletal Ultrasound Imaging for the Evaluation of Myofascial Tissues: Opportunities and Limitations

Myofascial pain syndrome (MPS) is a highly prevalent clinical problem that has generated interest and confusion for decades. Although the pathophysiology of MPS still has not been elucidated and diagnostic criteria continue to be debated, there is agreement that some of the main clinical findings are in muscle, fascia, and associated tissues. Therefore, it is critically important to utilize imaging to better understand these findings and their role in the pain syndrome. Because of its wide availability and sensitivity to changes in neuromusculoskeletal tissues, ultrasound has emerged as a leading musculoskeletal imaging modality. It is used routinely to measure anatomical muscle dimensions (e.g., thickness, cross-sectional area), and subjective findings (e.g., abnormal echogenicity and echotexture) are often indicative of changes in musculoskeletal tissue structure and composition. A major drawback of ultrasound is its operator dependence, which often makes subjective findings difficult to reproduce; this problem is exacerbated by the highly anisotropic and heterogeneous nature of myofascial tissues. Therefore, there is a need to develop and evaluate objective ultrasound-based methods for quantifying muscle microarchitecture and composition. A number of approaches that have been described in the literature hold promise for understanding tissue changes in MPS. This talk will review the state of the art in quantitative ultrasound imaging of the structure and composition of muscle and related tissues and findings related to MPS.

1:55–2:35 p.m. **Panelist Comments and Discussion**

Panelist: Christine Chung, University of California, San Diego (UCSD)

Dr. Chung is a professor of radiology and executive vice chairperson at UCSD. A grant-funded clinical translational researcher and director of UCSD's Musculoskeletal (MSK) Imaging Research Group, she has more than 200 peer-reviewed manuscripts in scientific journals and has edited four MSK radiology textbooks. Dr. Chung's research interests lie in the application of novel magnetic resonance pulse sequences for the characterization of musculoskeletal tissues. Her laboratory group has done extensive evaluation of short and ultrashort T_2 tissues in the musculoskeletal system and currently is focused on quantitative magnetic resonance imaging (qMRI) biomarkers that may serve as noninvasive references to biochemical integrity and function of tissue. She has been recognized for her excellence in research with the President's Medal of the International Skeletal Society and the prestigious Distinguished Investigator Award from the Academy of Radiology & Biomedical Imaging Research. She has mentored undergraduate students, medical students, radiology residents, radiology fellows, postdoctoral candidates, and junior faculty.

Panelist: Bharti Khurana, Harvard Medical School

Dr. Khurana is director of the Trauma Imaging Research and Innovation Center at Brigham and Women's Hospital, Boston. She is an emergency and musculoskeletal radiologist and an assistant professor at Harvard Medical School. Dr. Khurana graduated from Maulana Azad Medical College, New Delhi, and completed a radiology residency and musculoskeletal radiology fellowship at Brigham and Women's Hospital. She is passionate about providing meaningful imaging interpretations by radiologists and developing machine learning algorithms for injury detection. Dr. Khurana has authored 94 peer-reviewed academic publications and the popular *Emergency Radiology COFFEE Case Book*. Her clinical and research efforts involve imaging and interpretation of trauma, acute musculoskeletal and back pain, intimate partner violence, automated body decomposition, sarcopenia and frailty in geriatric populations, and MRI optimization in the Emergency Department. Her research has received several prestigious awards from the Radiological Society of North America and was recognized among the Top 12 Artificial Innovations Disrupting Healthcare by Mass General Brigham in 2019.

Panelist: Levon Nazarian, Thomas Jefferson University

Dr. Nazarian is the William E. Conrady, M.D., Professor of Radiology and Vice-Chair for Education at the Sidney Kimmel Medical College of Thomas Jefferson University and director of the Jefferson Ultrasound and Radiology Education Institute. He has coauthored more than 100 peer-reviewed manuscripts and 100 abstracts on topics including the use of ultrasound to diagnose and guide innovative treatments for musculoskeletal conditions such as tennis elbow, carpal tunnel syndrome, and many others. Dr. Nazarian has given about 500 invited lectures and scientific presentations. He serves on the editorial board of numerous journals, and from 2011–2018 he was editor-in-chief of the *Journal of Ultrasound in Medicine*. In 2017, he was awarded the Joseph H. Holmes Clinical Pioneer Award by the American Institute of Ultrasound in Medicine, a society for which he is now president-elect.

Panelist: Antonio Stecco, New York University (NYU) Langone Health

Dr. Stecco is an assistant professor at Rusk Rehabilitation, NYU, and a physiatrist. He has served as president of the Fascial Manipulation Association since 2010 and as assistant to the president of the International Society of Physical Medicine and Rehabilitation from 2012 to 2014. Dr. Stecco's scientific activity is devoted to the study of the human fasciae from a macroscopical, histological, and physiopathological point of view. He personally has made over 100 cadaver dissections for research. He has organized and held theoretical-practical courses about the Fascial Manipulation method on five continents since 2007. Dr. Stecco is the author of more than 40 *in extensor* papers about the fascia and coauthor of five books and chapters of international books published by Elsevier.

2:35–2:50 p.m. **Questions and Answers From the Zoom and Videocast**

2:50–3:05 p.m. **Audiences** BREAK

3:05–4:45 p.m. **Session Three: Elastography Imaging Approaches With Potential Application to Myofascial Pain Syndrome**

Session Chairs

Chair: Helene Langevin, NCCIH
Co-Chair: Merav Sabri, NCCIH

3:10–3:46 p.m. **Session Speakers**

Kevin Parker, University of Rochester
Helene Langevin, NCCIH
Richard Ehman, Mayo Clinic College of Medicine and Science

3:46–4:00 p.m. **Panelist Comments**

Shigao Chen, Mayo Clinic Rochester
Dieter Klatt, University of Illinois, Chicago
Neil Roberts, University of Edinburgh
Sergio Sanabria, Stanford University School of Medicine
Siddhartha Sikdar, George Mason University
Robert Vining, Palmer College of Chiropractic

4:00–4:30 p.m. **Panel Discussion**

4:30–4:45 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

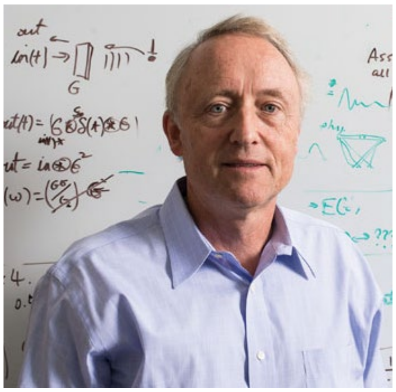
4:45–5:00 p.m. **WRAP UP**

5:00 p.m. **ADJOURN**

3:05–4:45 p.m. **Session Three: Elastography Imaging Approaches With Potential Application to Myofascial Pain Syndrome**

Chair: Helene Langevin, NCCIH
See bio on page 9.

Co-Chair: Merav Sabri, NCCIH
See bio on page 22.



Speaker: Kevin Parker, University of Rochester

Dr. Parker earned his graduate degrees from the Massachusetts Institute of Technology and has served at the University of Rochester as department chair, director of the Rochester Center for Biomedical Ultrasound, and dean of the Hajim School of Engineering and Applied Sciences. His research is in image processing and medical imaging.
Dr. Parker is an inventor/pioneer in a number of enterprises, including the field of sonoelastography and the Blue Noise Mask. Founder of VirtualScopics, Inc., he holds 26 U.S. patents and 13 international patents. A fellow of the Institute of Electrical and Electronics Engineers, the American Institute of Ultrasound in Medicine (AIUM), the Acoustical Society of America, the American Institute for Medical and Biological Engineering, and the National Academy of Inventors, Dr. Parker has published 230 journal articles and numerous book chapters. He has received the Eastman Medal, the AIUM Joseph Holmes Pioneer Award for Contributions to Medical Ultrasound, the Eastman Kodak Outstanding Innovation Award, and the Ultrasound in Medicine and Biology World Federation Prize.

Ultrasound Elastography for Evaluation of Tissue Mechanical Properties

Elastography developed over the past 30 years as imaging systems have been adapted to study tissue motion, including shear waves propagating through tissue. The results are a merging of imaging and biomechanics, leading to better understanding of the viscoelastic properties of tissues *in vivo*. Particular applications of ultrasound elastography to musculoskeletal studies will be reviewed.

Speaker: Helene Langevin, NCCIH

See bio on page 9.

Measurement of Shear Plane Tissue Mobility Using Ultrasound Elastography Techniques

Shearing forces are unaligned forces pushing one part of a material body in one direction and another part in the opposite direction, and shear strains are the deformations that occur as a result. Shear strains play an important physiological role in the body. This is especially true in myofascial tissues because of their layered organization that creates multiple interfaces where shear deformations naturally occur when the tissues are passively moved due to an external force or actively moved by muscle contractions.

The diagnosis of myofascial pain syndrome currently is made by palpation of tender indurated nodules. During palpation, a combination of pressure and shear forces are applied manually to detect local variations in both tissue stiffness (resistance to applied pressure) and/or shear plane mobility (sensation that tissues are "stuck" and not moving freely).

Elastography techniques are potentially useful in quantifying pathophysiological phenotypes associated with myofascial pain syndrome because: 1) they can allow detailed mapping of local tissue stiffness; and 2) they can be adapted to measure the amount of shear plane movement between specific anatomical layers in response to a standardized mechanical input.

This presentation will show measurements of shear strain between the connective tissue layers of the thoracolumbar fascia in human subjects undergoing passive trunk flexion while lying supine on a motorized table. Strengths and limitations of this technique will be discussed, focusing on its potential application to research on myofascial pain syndrome.

Speaker: Richard Ehman, Mayo Clinic College of Medicine and Science

Dr. Ehman is a professor of radiology and Blanche and Richard Erlanger Professor of Medical Research at Mayo Clinic. His research is focused on developing advanced medical imaging technology. The holder of more than 100 U.S. and foreign patents for his inventions, he and his team invented and translated magnetic resonance elastography, a technology now widely used in clinical practice. He has chaired the NIH Radiology and Nuclear Medicine Study Section; served as president of the International Society for Magnetic Resonance in Medicine (ISMRM), the Academy of Radiology Research, the Society for Advanced Body Imaging, and the Radiological Society of North America; and served on the National Advisory Council of the National Institute of Biomedical Imaging and Bioengineering. Dr. Ehman is a fellow of the National Academy of Inventors and an elected member of the National Academy of Medicine. He received the Gold Medal from ISMRM.

MR Elastography: Quantitatively Characterizing the Mechanical Properties of Skeletal Muscle and Myofascial Interfaces

Tissue mechanical properties and tension distribution in skeletal muscle, ligaments, and myofascial surfaces are highly relevant to the pathophysiology, treatment, and natural history of myofascial pain syndrome. Conventional imaging modalities such as computed tomography, ultrasonography, and magnetic resonance can provide anatomic information but do not depict mechanical properties. Magnetic resonance elastography (MRE) is a magnetic resonance imaging (MRI)-based technology that was developed to quantitatively image tissue properties such as stiffness, viscosity, attenuation, and anisotropic behavior—providing noninvasive access to a range of tissue biomarkers relevant in diagnostic medicine, biomechanics, and mechanobiology.

Currently, the main clinical application of MRE has been as an alternative to liver biopsy for detection of hepatic fibrosis. More than 1,500 MRI systems globally have been equipped to use MRE. Since MRE of skeletal muscle was first demonstrated in 1996, over 50 publications have reported on the use of this technology to assess the mechanical properties of normal and myopathic subjects, explore identification of taut bands, and assess loading behavior and tension distribution for biomechanics studies.

This presentation will provide a survey of demonstrated and potential applications of MRE as a tool for exploring the pathophysiology of myofascial pain syndrome, such as assessment of complex shear modulus of skeletal muscle over a range of conditions, the spatial distribution of tension, and the potential to use MRE-based measurements of microscopic local shear strain to characterize adhesion at myofascial slip interfaces.

3:46–4:30 p.m. **Panelist Comments and Discussion**

Panelist: Shigao Chen, Mayo Clinic Rochester

Dr. Chen is professor of radiology at Mayo Clinic. He is an elected Fellow and a member of the Board of Governors of the American Institute of Ultrasound in Medicine (AIUM) and has served as chair of the AIUM Technical Standards Committee and chair of the AIUM Elastography Community. Dr. Chen has pioneered the development of a novel ultrasound elastography technology that is licensed by several companies and widely used in clinical care around the world. He is a member of the Quantitative Imaging Biomarkers Alliance Ultrasound Shear Wave Speed Technical Committee.

Panelist: Dieter Klatt, University of Illinois, Chicago

Dr. Klatt is associate professor in the Richard and Loan Hill Department of Bioengineering and director of the Motion-Encoding MRI Lab at the University of Illinois at Chicago. A geophysicist by training (Diploma 2002, Ruhr-University, Bochum, Germany), he obtained his Ph.D. in physics (2010, Humboldt University, Berlin, Germany) with a thesis project in magnetic resonance elastography (MRE) methodology development. Dr. Klatt's research interests include the development of rapid motion-encoding magnetic resonance imaging acquisition approaches, fusion of MRE and diffusion tensor imaging, development of noninvasive tools for assessing muscle structure and function, and relating tissue mechanics to pathology (e.g., neurodegenerative brain, prostate cancer, liver fibrosis). He is a member of the governing committee of the MRE Study Group within the International Society for Magnetic Resonance in Medicine and has authored and coauthored 40 archival journal publications with a current h-index of 20.

Panelist: Neil Roberts, University of Edinburgh

After graduating in physics from the University of Liverpool, Dr. Roberts was awarded a personal fellowship from the Natural Environment Research Council and subsequently moved to the United States, where he was a research associate at the University of California, Santa Barbara. He was appointed lecturer at, and subsequently became director of, the University of Liverpool Magnetic Resonance and Image Analysis Research Centre, built to house the United Kingdom's first commercial magnetic resonance imaging system. In 2009, Dr. Roberts moved to the University of Edinburgh, where he is chair of Medical Physics and Imaging Science at the Queen's Medical Research Institute and leads research in the application of magnetic resonance elastography for noninvasive measurement of muscle mechanical properties in collaboration with Dr. Richard Ehman at Mayo Clinic, Minnesota. Dr. Roberts has been a teacher of the Alexander Technique since 2007.

Panelist: Sergio Sanabria, Stanford University School of Medicine

Dr. Sanabria received his doctoral degree from ETH Zurich, Switzerland in 2012, with a dissertation about nondestructive testing of wood with air-coupled ultrasound. After a postdoc in neutron and synchrotron tomography, he joined the Computer Vision Laboratory of ETH as senior assistant, where he was responsible for ultrasound elastography research. From 2017 to 2018, Dr. Sanabria led an entrepreneurial project about ultrasound breast cancer diagnostics. Since 2018, he has been a principal investigator (www.zurt.ch) at the University of Zurich. Since October 2019, he has been a visiting scholar at the Stanford University Department of Radiology. His current research revolves around ultrasound quantification based on the measurement of acoustic properties and machine learning techniques. Dr. Sanabria is developing imaging biomarkers to quantify muscular adipose tissue fraction and investigating confounding variables in musculoskeletal ultrasound elastography. Recently, he submitted a patent for objectivizing ultrasound-guided injections for the treatment of idiopathic masticatory myalgia.

Panelist: Siddhartha Sikdar, George Mason University

See bio on page 26.

Panelist: Robert Vining, Palmer College of Chiropractic

Dr. Vining is a professor and associate dean of clinical research at Palmer College of Chiropractic in Davenport, Iowa. He is a graduate of Logan University (Doctor of Chiropractic) and Jefferson College of Health Sciences (Doctor of Health Science). Dr. Vining is an experienced practitioner, educator, and clinical researcher. He has served on 11 Federally funded clinical studies, including those conducted within the Departments of Veterans Affairs and Defense health systems. His research program includes spine-related musculoskeletal diagnosis, clinical decisionmaking, and integration of chiropractic into multidisciplinary settings. Currently, Dr. Vining's research involves assessing fascial mobility in persons receiving chiropractic care. An author on over 45 peer-reviewed articles and 2 book chapters, he is also the 2019 recipient of the American Chiropractic Association Academician of the Year award.

4:30–4:45 p.m.	**Questions and Answers From the Zoom and Videocast**
4:45–5:00 p.m.	**Audiences WRAP UP**
5:00 p.m.	**ADJOURN**

September 17, 2020

8:45–9:00 a.m. Welcome Back

Jill Heemskerk, Deputy Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Dr. Heemskerk has an 18-year record of distinguished service at NIH. She joined NIBIB as associate director for research administration and subsequently was appointed NIBIB Deputy Director. Previously, she was deputy director for the Division of Adult Translational Research at the National Institute of Mental Health and acting director of the Office of Translational Research at the National Institute of Neurological Disorders and Stroke (NINDS). At NINDS, she built a large program in preclinical therapeutics development for neurological diseases, emphasizing drug discovery chemistry and translation of basic research findings to the clinic. Dr. Heemskerk has served on scientific advisory boards for the ALS Association, the Spinal Muscular Atrophy Foundation, and the Huntington's Disease Society of America. She earned her Ph.D. in biochemistry and biophysics from the University of California, San Francisco, and conducted research in developmental molecular genetics at Columbia University.

9:00–10:50 a.m. **Session Four: Emerging Promising Technologies for Myofascial Pain Syndrome: Electrophysiology, MRI, and PET**

Session Chairs

Chair: Alex Tuttle, NINDS
Co-Chair: Chuck Washabaugh, NIAMS

9:05–9:53 a.m. **Session Speakers**

Abhijit J. Chaudhari, University of California, Davis
Espen Spangenburg, East Carolina University
Seward Rutkove, Beth Israel Deaconess Medical Center, Harvard
Els Fieremans, New York University Langone Health

9:53–10:05 a.m. **Panelist Comments**

Vania Apkarian, Northwestern University
Mark D. Does, Vanderbilt University
Jordi Serra, King's College Hospital, London
Samuel R. Ward, University of California, San Diego

10:05–10:35 a.m. **Panel Discussion**

10:35–10:50 a.m. **Questions and Answers From the Zoom and Videocast Audiences**

10:50–11:10 a.m. BREAK

9:00–10:05 a.m. **Session Four: Emerging Promising Technologies for Myofascial Pain Syndrome: Electrophysiology, MRI, and PET**

Chair: Alex Tuttle, NINDS
Co-Chair:- Chuck Washabaugh, NIAMS

Session Chair: Alex Tuttle, National Institute of Neurological Disorders and Stroke (NINDS)

Dr. Tuttle is a health program specialist for the Systems and Cognitive Neuroscience Cluster in the Division of Neuroscience at NINDS. He completed a postdoctoral fellowship at the University of North Carolina in Dr. Mark Zylka's lab, where he worked on developing deep learning platforms to promote novel pain drug discoveries. Dr. Tuttle received his Ph.D. in psychology from McGill University, where he worked with Dr. Jeffrey Mogil to better understand the social effects of acute and chronic pain. He received the Richard H. Tomlinson Doctoral Fellowship for his work at McGill.

Dr. Tuttle provides key coordination and support for the NIH Helping to End Addiction Long-term[SM] Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. He is proud to serve as part of NIH's effort to enhance pain management strategies and improve treatment for opioid misuse and addiction.

Session Co-Chair: Chuck Washabaugh, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Dr. Washabaugh is a program director for the NIAMS Orthopaedic Research Program. He joined NIAMS in 2006, bringing with him over 17 years of basic research experience in academia. Dr. Washabaugh earned a B.S. in biology and molecular biology/biotechnology from Westminster College and later obtained his M.S. and Ph.D. in molecular biology/developmental biology from the University of Dayton, with a concentration in cellular and molecular aspects of limb regeneration in urodele amphibians. As a research assistant professor at the University of Pittsburgh School of Medicine, Department of Cell Biology & Physiology, his research focused on molecular biology of muscle development and regeneration with an emphasis on neuromuscular interactions, the expression of myogenic regulatory factors in knockout mice, and development of the neuromuscular junction.

9:05–9:53 a.m. **Session Speakers**

Speaker: Abhijit J. Chaudhari, University of California, Davis

Dr. Chaudhari is an associate professor of radiology and director of the Center for Molecular and Genomic Imaging at the University of California, Davis and a core scientist at the California National Primate Research Center. Dr. Chaudhari's laboratory focuses on developing novel *in vivo* medical imaging techniques, with emphasis on the applications of positron emission tomography (PET) and magnetic resonance imaging (MRI) in disorders of the musculoskeletal and neurological systems. His research is supported by NIH, the National Science Foundation, and the National Psoriasis Foundation. Dr. Chaudhari was the recipient of the 2011 Institute of Electrical and Electronics Engineers' Bruce Hasegawa Medical Imaging Science Award and an NIH Building Interdisciplinary Research Careers in Women's Health Scholar between 2013 and 2018. He received his bachelor's degree (electronics engineering) from the University of Pune, India, and his master's (applied mathematics) and Ph.D. (electrical engineering) degrees from the University of Southern California.

Innovations in PET for Future Applications in Myofascial Pain Syndrome

Positron emission tomography is a noninvasive molecular imaging modality that in the past few decades has had an increasingly important role in the clinical management of oncologic, cardiovascular, and neurologic conditions. Yet, its application in assessing acute or chronic myofascial dysfunction and pain has been limited. In this talk, recent advances in PET technology of relevance to characterizing myofascial and musculoskeletal tissues will be presented, with emphasis on: 1) novel PET instrumentation that is enabling tissue evaluation across the entire human body at a significantly reduced dose and at a high spatial resolution; 2) new radiotracers that have improved specificity for evaluating key pathologies of interest; and 3) advances in mathematical modeling of radiotracer kinetics and PET image reconstruction that lead to enhanced quantification accuracy of the imaging modality and its sensitivity to changes in pathology. Finally, given that these PET advances can be employed in an analogous manner across species (e.g., small animals, nonhuman primates, companion animals, and humans), a framework for the future design, validation, and translation of PET-based imaging biomarkers of myofascial pain syndrome will be discussed.

Speaker: Espen Spangenburg, East Carolina University

Dr. Spangenburg is an associate professor of physiology in the Brody School of Medicine and a member of the East Carolina Diabetes and Obesity Institute at East Carolina University. He received his Ph.D. in 2000 with a research focus on skeletal muscle physiology and then completed an NIH-funded postdoctoral fellowship at the University of Missouri.

Dr. Spangenburg's lab has been funded by NIH since 2005 and has published more than 100 papers in the area of skeletal muscle biology with a focus on defining novel regulators of physiological and metabolic function of skeletal muscle. His lab employs an integrative experimental approach that uses cell culture and animal models to define mechanisms that his team works to translate to the human. Dr. Spangenburg employs techniques that enable quantitative assessment of muscle force production and/or image microstructure coupled with assessment of mitochondrial bioenergetics across a variety of biochemical and imaging platforms.

Application of Techniques That Assess Physiological and Metabolic Parameters of Skeletal Muscle To Advance Our Understanding of Myofascial Pain Syndrome

This presentation will describe and discuss techniques employed in skeletal muscle research that could contribute to an improved understanding of myofascial pain in basic science and clinical settings. One theme of the talk will be techniques that can be used in preclinical models where the results can be translated to human patients. Many of the methods considered have analogous techniques that can be utilized in a noninvasive manner in human patients. Methodology to be discussed will include approaches that assess muscle function, muscle mass, mitochondrial bioenergetics, skeletal muscle perfusion, and oxygen tension, with a focus on muscle weakness, muscle ischemia, and metabolic dysfunction. Application of discovery-based approaches also will be considered as a means to advance the field. Finally, sex as a biological variable will be discussed, with emphasis on study design. The presentation objective is to discuss possible methods that can be employed across a variety of models and approaches that would help advance our understanding of myofascial pain syndrome.

Speaker: Seward Rutkove, Beth Israel Deaconess Medical Center, Harvard

Dr. Rutkove is a professor of neurology at Harvard Medical School and serves as chief of the Division of Neuromuscular Disease in the Department of Neurology at Beth Israel Deaconess Medical Center. With support from NIH, Dr. Rutkove's medical research focuses on the application of innovative techniques for the assessment of neuromuscular disorders and muscle dysfunction, with an emphasis on electrical impedance and ultrasound methodologies. His research efforts also have included the study of partial gravity analogue models in rodents with past and ongoing support from the National Aeronautics and Space Administration. An investigator with over 200 publications, he is currently serving as an associate editor for *Annals of Neurology.* In 2011, Dr. Rutkove was awarded the Biomarker Challenge Prize from the nonprofit foundation Prize4Life, Inc., for his work demonstrating that electrical impedance measurements of muscle could speed clinical therapeutic studies in amyotrophic lateral sclerosis (ALS). In 2019, he received the Herman P. Schwan International Award in Electrical Bioimpedance.

Electrophysiology Techniques and Potential Applications for Myofascial Tissues

To date, peripheral electrophysiological techniques have been applied only in limited ways to the assessment of myofascial pain. This is in part because standard approaches, including needle electromyography and nerve conduction studies, are relatively insensitive to the presumed pathological abnormalities associated with myofascial pain. Nevertheless, surface electromyography techniques have demonstrated a variety of different patterns of muscle dysfunction. Similarly, some nerve conduction techniques, including silent period assessment and H-reflex activity, have been applied, but these provide mainly information on central nervous system function. However, localized electrical impedance myography or tomography techniques could offer additional electrophysiological approaches for assessing myofascial pain, as they are sensitive to myofiber structural alterations, including atrophy and the deposition of fat or connective tissue. These technologies also could evaluate potential alterations in muscle structure, including abnormal muscle contraction/relaxation or the presence of edema. Combined electromyography needle/impedance methodology may have the potential to provide additional insights into myofascial disorders. In summary, work in both animal models and humans suggests that electrophysiological procedures, as a whole, are worthy of further exploration in the assessment of myofascial pain.

Speaker: Els Fieremans, New York University (NYU) Langone Health

Dr. Fieremans is an assistant professor and codirector of the MRI Biophysics Group at the Center for Biomedical Imaging in the Department of Radiology at the NYU Grossman School of Medicine. She received her master's degree in physics and Ph.D. in biomedical engineering from Ghent University, Belgium. The goal of her research is to leverage quantitative magnetic resonance imaging (MRI) methods, including diffusion toward specificity on the cellular scale through biophysical modeling and validation using numerical and physical phantoms, in order to find the earliest and most sensitive markers of disease in brain and body. Dr. Fieremans is active in the International Society of Magnetic Resonance in Medicine, where she serves on several committees. She is author of over 70 manuscripts (h-index 28). Her research is funded through the National Institute of Biomedical Imaging and Bioengineering and National Institute of Neurological Disorders and Stroke. She recently received the Irma T. Hirschl Career Scientist Award for academic excellence.

***In Vivo* Imaging of Tissue and Muscle Microstructure**

Human MRI is limited to millimeter voxels, yet diseases develop at the cellular scale. Diffusion MRI offers a direct probe to understanding the relationship between microstructure and function, whereby the time dependence of the diffusion coefficient is a hallmark of tissue complexity at the micrometer level. In skeletal muscle, we recently demonstrated how biophysical modeling, combined with a specifically tailored diffusion MRI acquisition performing diffusion tensor imaging (DTI) for varying diffusion times, can be used to determine myofiber size and sarcolemma membrane permeability *in vivo*. In this talk, I will present the random permeable barrier model (RPBM) for biophysical specificity, its underlying assumptions, and validation using simulations and comparison against histology in skeletal muscle growth and the Duchenne muscular dystrophy model in mice. In humans, several pilot studies suggest that the RPBM is sensitive to microstructural changes as shown by the increase in myofiber size with development and with exercise over time. In normal volunteer muscles, the RPBM method detects the expected myofiber dilation with exercise, while this dilation is notably absent in patients with chronic exertional compartment syndrome, along with changes in free diffusivity and permeability, pointing to increased interfiber fluid accumulation. The RPBM may be useful for clinical assessment of muscular pathologies (e.g., underlying myofascial pain) that require distinction between myofiber morphology and integrity, and may help translate some key diagnostic insights from the realm of histopathology to the noninvasive and broadly visualized area of MRI.

9:53–10:35 a.m. **Panelist Comments and Discussion**

Panelist: Vania Apkarian, Northwestern University

Dr. Apkarian is director of the Center for Translational Pain Research and a professor of physiology, anesthesiology, and physical medicine and rehabilitation at the Northwestern University Feinberg School of Medicine, Chicago. He earned his Ph.D. in neuroscience from the State University of New York Health Science Center and received postdoctoral training at the University of Wurzburg, Germany. His work is devoted to unraveling brain mechanisms that underlie acute and chronic pain and how the brain dynamically processes information that gives rise to perception. He has used brain imaging technology to delineate brain biomarkers of chronic pain, particularly back pain. Dr. Apkarian's work has produced many significant advances, including first identification of gray matter atrophy related to chronic pain, first account of brain activity unique to spontaneous fluctuations of chronic pain, first characterization of resting-state brain network abnormalities in chronic pain populations, first determination of mesocorticolimbic biomarkers predicting future pain chronification, first parallel human-rodent neuroimaging of the transition to chronic pain, first demonstration that hippocampal synaptic plasticity and neurogenesis are critical for neuropathic pain, and early identification of brain biomarkers for placebo response propensity.

Panelist: Mark D. Does, Vanderbilt University

Dr. Does is a professor of biomedical engineering and founding member of the Vanderbilt University Institute of Imaging Science. His research interests include developing and applying magnetic resonance imaging methods and technologies to quantitatively characterize various properties and/or compositions of tissue. He is a former National Science Foundation CAREER Awardee, a Fellow of the American Institute of Medical and Biological Engineers, and a Fellow of the International Society of Magnetic Resonance in Medicine.

Panelist: Jordi Serra, King's College Hospital, London

Dr. Serra has been a consultant in clinical neurophysiology at King's College Hospital, London, since 2014. He completed his neurology specialty in 1992 at the Hospital de Bellvitge, Barcelona, Spain, and spent the next three years as a Fellow at the neuromuscular unit of Good Samaritan Hospital and Oregon Health Sciences University in Portland, Oregon, where he specialized in the study, diagnosis, and treatment of neuropathic pain patients. During this period, Dr. Serra was trained in the technique of microneurography, which can record objective evidence of the abnormal nerve impulse activity responsible for paresthesia and spontaneous pain. This is the only available technique to detect and quantify positive sensory phenomena of peripheral nerve origin in humans by recording individual action potentials from single sensory fibers. Dr. Serra produced pioneering work on the recording of abnormal spontaneous activity in C-nociceptors from patients and animal models of neuropathic pain.

Panelist: Samuel R. Ward, University of California, San Diego (UCSD)

Dr. Ward is a professor in the Departments of Orthopaedic Surgery, Radiology, and Bioengineering; vice-chair of research in orthopaedic surgery; director of the Device Acceleration Center; and director of the Muscle Physiology Laboratory at UCSD. He is a clinician-scientist, and his research program focuses on musculoskeletal design and plasticity. His scientific accomplishments include defining the structural features of human skeletal muscle that predict function in the extremeties and spine. This work has been extended to understand normal and pathological muscle biology and physiology in the presence of joint disease. His current focus is on understanding chronic muscle atrophy and cell death in mature adults, with an emphasis on the use of stem cells and regenerative medicine approaches to treat these disease processes. Related to imaging, Dr. Ward and his team focus on simulation and *in vivo* methods comparing diffusion magnetic resonance imaging to normal and pathological muscle histology and microstructural measurements.

10:35–10:50 a.m. **Questions and Answers From the Zoom and Videocast Audiences**

10:50–11:10 a.m. BREAK

11:10 a.m.–1:00 p.m. **Session Five: Emerging Promising Technologies for Myofascial Pain Syndrome: Tissue Engineering, Artificial Intelligence, and Computational Modeling**

Session Chairs

Chair: Yolanda F. Vallejo, NIDCR
Co-Chair: Theresa Hayes Cruz, NICHD/NCMRR

11:15 a.m.–12:05 p.m. **Session Speakers**

Jeffrey Lotz, University of California, San Francisco
Sharmila Majumdar, University of California, San Francisco
Sylvia Blemker, University of Virginia
Hai Yao, Clemson University/Medical University of South Carolina

12:05–12:45 p.m. **Panelist Comments and Discussion**

Lucia Cevidanes, University of Michigan
Adam Hantman, Janelia Research Campus
Lealem Mulugeta, *InSilico* Labs, LLC, and Medalist Performance
Thomas Myers, University of Rochester

12:45–1:00 p.m. **Questions and Answers From the Zoom and Videocast Audiences**

1:00–2:00 p.m. VIRTUAL LUNCH

11:10 a.m.–1:00 p.m. **Session Five: Emerging Promising Technologies for Myofascial Pain Syndrome: Tissue Engineering, Artificial Intelligence, and Computational Modeling**

Chair: Yolanda F. Vallejo, NIDCR
Co-Chair: Theresa Hayes Cruz, NICHD/NCMRR

Session Chair: Yolanda F. Vallejo, National Institute of Dental and Craniofacial Research (NIDCR)

Dr. Vallejo is director of the Neuroscience of Orofacial Pain and Temporomandibular Disorders Program at NIDCR. She manages a diverse portfolio of basic, translational, and clinical research focused on orofacial pain, neuropathies, and temporomandibular disorders. Prior to joining NIDCR, Dr. Vallejo was a program director at the National Cancer Institute's Center to Reduce Cancer Health Disparities and served as a program analyst at the National Institute of Neurological Disorders and Stroke. She also held the position of research scientist at Pierce Biotechnology, Inc., where she conducted protein function research and product development. She received a Ph.D. in neurobiology, pharmacology, and physiology from the University of Chicago.

Session Co-Chair: Theresa Hayes Cruz, National Center for Medical Rehabilitation Research (NCMRR)

Dr. Cruz became Acting Director of NCMRR in September 2019. As a health scientist administrator at NCMRR, Dr. Cruz manages grants in the Devices and Technology Development and Rehabilitation Diagnostics and Interventions Programs. She also manages Small Business Innovation Research and Small Business Technology Transfer Research awards in medical rehabilitation. Dr. Cruz leads a team in the NIH Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, where she comanages a grant portfolio in neurotechnology development, validation, and translation for applications in neuroscience, neurophysiology, movement disorders, pain, neuromodulation, and other interfaces with the nervous system. In 2015, Dr. Cruz performed a research detail at the Functional and Applied Biomechanics Laboratory in Rehabilitation Medicine. She received her bachelor's degree in biomedical engineering with highest honors from the School of Engineering at Rutgers, the State University of New Jersey, and her master's and doctoral degrees in biomedical engineering from Northwestern University.

11:15 a.m.–12:05 p.m. **Session Speakers**

Speaker: Jeffrey Lotz, University of California, San Francisco (UCSF)

Dr. Lotz is the David S. Bradford M.D. Endowed Chair in Orthopaedic Surgery and vice chair of orthopaedic research at UCSF. He has led the Orthopaedic Tissue Engineering Laboratory at UCSF since 1992 and is principal investigator of one of the three Mechanistic Research Centers funded through the NIH Back Pain Consortium Research Program (under the NIH Helping End Addiction Long-term [HEAL] Initiative). Dr. Lotz directs three other research centers, including the National Institute of Dental and Craniofacial Research-funded Center for Dental, Oral and Craniofacial Tissue and Organ Regeneration; the NIH-funded Core Center for Musculoskeletal Biology in Medicine; and the National Science Foundation-funded Industry/University Cooperative Research Center. Dr. Lotz has expertise in spine biomechanics, intervertebral disc biology, and tissue engineering, and his laboratory work focuses on identifying mechanisms of disc degeneration, developing novel diagnostics and therapies for low-back pain, and the biomechanics of spinal instrumentation.

Quantifying Associations Between Paraspinal Muscle Quality, Spinal Pathologies, and Skeletal Biomechanics

The paraspinal muscles (PSM) work synergistically with passive spinal structures (discs, vertebra, ligaments) to stabilize posture and movement. Biomechanical and biological crosstalk between the active and passive spinal stabilizers can potentiate degenerative changes that often underlie pain and disability. A longitudinal study in astronauts demonstrated that PSM atrophy significantly alters spinal posture and motion and that pain from pathology in the passive tissues can be amplified by PSM atrophy. Additionally, poor posture and movement of the spine necessitate compensation by the lower extremities to enable stable total-body biomechanics. Studies of spine surgery patients demonstrate unique movement signatures associated with disability and surgical outcomes. In addition, coordinated movement of the entire kinetic chain can be influenced by psychological factors such as fear of movement and pain catastrophizing.

Investigation of hypothesized behavioral and biophysical relationships in myofascial pain patients requires methods that can be deployed easily in the clinical setting. Fat fraction magnetic resonance imaging can measure PSM quality that associates with patient outcomes; that PSM quality may compensate for disc pathology and mitigate symptoms. In clinical measurements of biomechanical function, a depth-camera-informed biomechanical model can quantify total-body patient movement and joint loading. In clinical tests of spine surgery, patients have demonstrated unique biophysical signatures that associate with disability and surgical outcomes. Combined with measures of patient distress and fear avoidance, anatomic and biomechanical measurements may be useful to disentangle complex relationships between muscle dysfunction, joint degeneration, and psychological status. In doing so, therapies may be better matched to individual patients.

Speaker: Sharmila Majumdar, University of California, San Francisco (UCSF)

Dr. Majumdar is a UCSF professor and vice chair for research and Margaret Hart Surbeck Distinguished Professor in Advanced Imaging in the Departments of Bioengineering and Therapeutic Sciences and Orthopedic Surgery; director of the Musculoskeletal Research Interest Group at UCSF, an interdisciplinary group comprising faculty, postdoctoral scholars, and students; and scientific and executive director of the Center for Intelligent Imaging.

Dr. Majumdar's research on imaging, particularly magnetic resonance and microcomputed tomography, development of image processing and analysis tools, and machine and deep learning, has focused on osteoporosis, osteoarthritis, and lower back pain. Supported by NIH grants and corporate entities, her research ranges from technical development to clinical trials. She is principal investigator of a technology development grant in the NIH Back Pain Consortium, serves as a reviewer, serves on the editorial board of scientific journals, and is a recognized expert in the area of imaging.

The Role of Machine Learning for Muscle Segmentation and Characterization of Muscle Properties

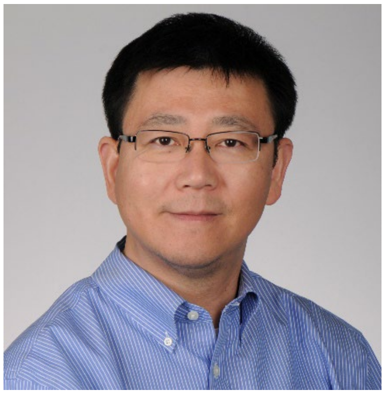
Myofascial pain is a debilitating joint disease that affects millions of American adults. Muscle atrophy, fatty infiltration, and muscle weakness have been implicated. Magnetic resonance imaging (MRI) provides excellent soft tissue contrast and can characterize different aspects of muscle degeneration. For example, T_2 values reflect fatty infiltration and, often, blood flow effects in muscle. In such analyses, identification of different muscle groups (i.e., image segmentation) is essential. Muscle centroid locations are important to constructing biomechanical models. The segmentation of muscle groups is time-intensive, with variability of interreader agreement. We present two specific goals: 1) develop machine-learning-based automatic segmentation and quantification pipelines to estimate the volume and fat fraction in thigh muscle and 2) for paraspinal muscles. The comparison between manual segmentations in terms of cross-sectional area and time taken will be presented, as well as associations with patient characteristics and other adjoining tissue characteristics such as $T_{1\rho}$ and T_2.

Speaker: Silvia Blemker, University of Virginia (UVA)

Dr. Blemker is a professor of biomedical engineering, with joint appointments in Mechanical & Aerospace Engineering, Ophthalmology, and Orthopaedic Surgery, at UVA. She obtained B.S. and M.S. degrees in biomedical engineering from Northwestern University and a Ph.D. in mechanical engineering from Stanford University. Before joining the faculty at UVA in 2006, Dr. Blemker worked as a postdoctoral research associate at Stanford University's National Center for Biomedical Computation. At UVA, she leads the Multi-Scale Muscle Mechanophysiology Lab (M3 Lab), which develops advanced multiscale computational and experimental techniques to study skeletal muscle biomechanics and physiology. The M3 Lab is applying these techniques to a variety of areas, including speech disorders, movement disorders, vision impairments, muscle atrophy, aging, and muscular dystrophies. While the work is grounded in biomechanics, it draws strongly from many other fields, including biology, muscle physiology, biomedical computation, imaging, and a variety of clinical fields.

Multiscale Computational Modeling Integrates Biology and Mechanics To Prove New Insights into Muscle Dysfunction

Skeletal muscles are extraordinarily adapted motors that enable us to perform many important functions, from walking to sight to speech. Thus, muscle dysfunction arising from muscle atrophy, degeneration, fatty infiltration, and fibrosis presents major healthcare problems. From a basic science perspective, we have a sophisticated understanding of the fundamental biology and mechanics of skeletal muscle. However, how these fundamentals relate to *in vivo* function and whole-muscle adaptation is complex and remains poorly understood, which limits the translation of basic biological understanding to the development of effective treatments for muscle dysfunction. The goal of the Multi-Scale Muscle Mechanophysiology Lab's research is to develop and experimentally validate multiscale computational models of skeletal muscle that allow us to relate structure, biology, and function across a range of scales. We aim to apply these models to answering questions related to the role of complex muscle biology and mechanics in a variety of clinical problems, including muscular dystrophy, disuse-induced atrophy, and volumetric muscle loss injury. In this presentation, I will describe these approaches and present some recent examples of how computational models of muscle have led to new ideas and insights.



Speaker: Hai Yao, Clemson University and Medical

Dr. Yao is the Ernest R. Norville Endowed Chair and Professor of Bioengineering at Clemson University and Professor of Oral Health Sciences at MUSC. He serves as associate chair for the Clemson-MUSC Joint Bioengineering Program and is director of the NIH Center of Biomedical Research Excellence for Translational Research Improving Musculoskeletal Health at Clemson and the NIH Dental T32 Research Training Program at MUSC. His research focuses on the biomechanical function, degeneration, and regeneration of musculoskeletal systems; specifically, the temporomandibular joint (TMJ). His lab has established multiscale TMJ models, which integrate joint morphology and kinematics, tissue mechanics, cell metabolism, and genetics, to facilitate earlier diagnosis and management of temporomandibular disorders (TMDs). He served on the committee for the most recent TMD study report from the National Academies of Sciences, Engineering, and Medicine.

Integrating Multimodality Measurement and Multiscale Modeling To Assess TMDs

Musculoskeletal systems feature intimate relationships between form and function, with a gracefully efficient physical order that manifests itself on the organ, tissue, cell, and molecular levels. The existence of such a hierarchy of structural and functional harmony is closely regulated by mechanical forces. Breakdown of this harmony leads to pathological changes, eventually resulting in pain. To elucidate the underlying mechanobiological mechanisms, research thus is conducted at multiscale levels: imaging-based morphology and kinematics (body level), tissue characterization and constitutive modeling (tissue level), single-cell mechanics and mechanobiology (cell level), and molecular transport and assembly (molecular level). This multiscale approach of integrating principles of biomechanics and biology provides new perspectives for studying musculoskeletal system pathophysiology. Due to the challenges of direct measurement *in vivo*, a combination of multimodality direct measurement and multiscale computational modeling presents a powerful means to systematically and quantitatively determine complex physicochemical signals within musculoskeletal tissues induced by mechanical loading. In this seminar, we will introduce our work on integrating magnetic resonance imaging/computed tomography/ultrasound-based craniofacial morphology, optical-motion-tracking-based jaw kinematics, electromyography-based masticatory muscle function, nondestructive assessment of tissue properties, multibody musculoskeletal modeling, and a multiphasic finite element tissue model to determine sex-specific temporomandibular joint pathophysiology in humans. The results have facilitated early diagnosis and management of temporomandibular disorders, a major source of orofacial pain. This new approach of integrating multimodality direct measurement and multiscale computational modeling may be applied to other musculoskeletal systems for better understanding and managing myofascial pain.

12:05–12:45 p.m. **Panelist Comments and Discussion**

Panelist: Lucia Cevidanes, University of Michigan

Dr. Cevidanes is the Thomas and Doris Graber Professor of Dentistry and an associate professor in the Department of Orthodontics at the University of Michigan and a Diplomate of the American Board of Orthodontics. Her interests include artificial intelligence and 3D imaging to solve difficult clinical problems in dentistry and application of data science approaches to study current and new therapies and understand treatment outcomes for temporomandibular disorders, craniofacial anomalies, and dentofacial deformities. She is a practicing clinician who has published over 150 manuscripts and has received research grants from the American Association of Orthodontics Foundation and the National Institute of Dental and Craniofacial Research. Her work has been recognized by the American Association of Orthodontists Thomas M. Graber Award, the B.F. Dewel Award, the Milo Hellman Award, and the Wuehrmann Award from the American Academy of Oral and Maxillofacial Radiology.

Panelist: Adam Hantman, Janelia Research Campus

Dr. Hantman is a group leader at the Howard Hughes Medical Institute's Janelia Research Campus, where his research team seeks to understand the neural basis of dexterous movements. Considering the range of possible actions and the complexity of musculoskeletal arrangements, control of the hand is an amazing achievement of the nervous system. Dexterous behavior involves understanding objects in the world, developing appropriate plans, converting those plans into appropriate motor commands, and adaptively reacting to feedback. By combining anatomy, physiology, and specific (genetic and temporal) manipulations, Dr. Hantman's group is identifying the neural elements responsible for dexterous motor control. Dr. Hantman received a bachelor's degree in biology from Providence College and a doctorate degree in cell and molecular physiology from the University of North Carolina at Chapel Hill, where he was mentored by Dr. Edward Perl. He then completed a postdoctoral fellowship in Dr. Tom Jessell's lab at Columbia University.

Panelist: Lealem Mulugeta, *InSilico* Labs, LLC, and Medalist Performance

Mr. Mulugeta was the Project Scientist on the National Aeronautics and Space Administration's (NASA) Digital stronaut Project (DAP), where he was responsible for scientific content for implementing well-validated computational models to help predict and assess spaceflight health and performance risks and enhance therapeutics development. He also helped NASA spin off DAP's work to healthcare applications by actively engaging with NIH, the U.S. Food and Drug Administration, the Department of Defense, and other leading organizations.

Mr. Mulugeta founded *InSilico* Labs and Medalist Performance to translate his expertise in biomedical computational modeling, engineering, and competitive sports to health care and human performance applications. This includes understanding the influence of the myofascial network on musculoskeletal health and implications on physical and mental performance. He has been translating this work to help athletes, tactical personnel (e.g., Special Weapons and Tactics and special operations), and executives significantly enhance their performance in a compressed timeframe. It also has shown promise to help people with significant musculoskeletal injuries such as paralysis.

Panelist: Thomas Myers, University of Rochester

Dr. Myers graduated from Duquesne University (M.P.T.) and Temple University (M.D.). He then spent a year at the University of Virginia working on a vaccine against Methicillin-Resistant (MRSA) in a total joint arthroplasty rabbit model. He then completed an orthopaedic residency at the University of Pittsburgh Medical Center and a fellowship year at the Cleveland Clinic in total joint replacement. Dr. Myers worked in private practice in Indiana for 4 years before returning to academics in 2016 at the University of Rochester, where he is an assistant professor. Dr. Myers is a high-volume total joint replacement surgeon interested in topics surrounding value-based care, predictive analytics involving artificial intelligence, orthopaedic rehabilitation, competency-based medical education, and simulation training in orthopaedics.

12:45–1:00 p.m.	**Questions and Answers From the Zoom and Videocast Audiences**
1:00–2:00 p.m.	VIRTUAL LUNCH

2:00–3:00 p.m. **Session Six: General Discussion**

Session Chairs

Chair: Wen Chen, NCCIH
Co-Chair: Dena Fischer, NIDCR

2:05–3:00 p.m. **Panelist Comments and Discussion**

Allan Basbaum, University of California, San Francisco
Christine Chung, University of California, San Diego
William Maixner, Duke University Medical Center
Julie Fritz, The University of Utah
Daniel K. Sodickson, New York University Langone Health

3:00–3:30 p.m. **Summary and Concluding Remarks**

Helene Langevin, NCCIH Director

3:30 p.m. **ADJOURN**

2:00–3:00 p.m. **Session Six: General Discussion**

Chair: Wen Chen, NCCIH
Co-Chair: Dena Fischer, NIDCR

Chair: Wen Chen, National Center for Complementary and Integrative Health (NCCIH)

Dr. Chen is chief of NCCIH's Basic and Mechanistic Research Branch in the Division of Extramural Research. Her portfolio includes research and training programs related to fundamental and translational science research on acupuncture, meditation, and music and art interventions. Dr. Chen is involved in the trans-NIH Helping to End Addiction Long-term℠ Initiative. She is NCCIH's program representative on the NIH Pain Consortium, a working group member for the NIH Common Fund initiative on Stimulating Peripheral Activity to Relieve Conditions, and a member of the trans-NIH Music and Health Working Group, Collaborative Research in Computational Neuroscience, and NIH Blueprint BRAIN Initiative Marmoset Working Group. Leader of the NIH Blueprint Interoception Working Group, Dr. Chen's areas of expertise include neurobiology, molecular biology, biochemistry, pain, sensory and motor systems, and epigenetics. She earned a Ph.D. in biological chemistry and molecular pharmacology from Harvard University and a master's degree in medical sciences through the Harvard-Markey Medical Scientist training program at Harvard Medical School. Dr. Chen did postdoctoral training in proteomics at the Massachusetts Institute of Technology.

Co-Chair: Dena Fischer, National Institute of Dental and Craniofacial Research (NIDCR)

Dr. Fischer is director of the Center for Clinical Research (CCR) and director of the Clinical Trials and Practice-Based Research Program at NIDCR. She provides leadership and guidance toward the planning, development, implementation, and evaluation of the CCR grant programs and broad clinical research portfolio, encompassing the National Dental Practice-Based Research Network, Oral Health Disparities and Inequities Program, clinical trials program, clinical technologies development and validation, and research to improve oral health outcomes in medically complex individuals, including those with HIV/AIDS. She joined NIDCR in 2011. Dr. Fischer also represents NIDCR on trans-NIH working groups related to women's health, management of acute pain, new craniofacial imaging/surgical planning techniques, and clinical research/trials operations and policies.

The CCR research program focuses on patient-oriented and population-based studies of oral and craniofacial diseases and disorders and clinical trials designed to test interventions to improve dental, oral, and craniofacial health.

2:05–3:00 p.m. **Panelist Comments and Discussion**

Panelist: Allan Basbaum, University of California, San Francisco

Dr. Basbaum completed undergraduate studies at McGill University in Montreal, his Ph.D. at the University of Pennsylvania, and postdoctoral research at University College London. Presently, he is professor and chair of the Department of Anatomy at the University of California, San Francisco. His research focuses on primary sensory and spinal cord circuits that process pain and itch messages, including the molecular mechanisms that contribute to persistent pain after tissue or nerve injury. Recently, he turned his attention to cortical mechanisms that process these messages. His laboratory also investigates novel approaches to pain management, including transplantation of embryonic cortical inhibitory precursor cells into the spinal cord. He has served as editor-in-chief of *PAIN*, the journal of the International Association for the Study of Pain; is a member of the American Academy of Arts and Sciences, the National Academy of Medicine, and the National Academy of Sciences; and is a fellow of the Royal Society in the United Kingdom.

Panelist: Christine Chung, University of California, San Diego

See bio on page 27.

Panelist: William Maixner, Duke University Medical Center

Dr. Maixner is codirector of the Center for Translational Pain Medicine at Duke University. He obtained his B.A., Ph.D., and D.D.S. at the University of Iowa, and was a research fellow at the National Institute of Dental Research. He held faculty and administrative positions at the University of North Carolina, Chapel Hill. Dr. Maixner received the Wilbert E. Fordyce Clinical Investigator Award from the American Pain Society, the 2018 Distinguished Scientist Award from the American Association for Dental Research, and the Senior Investigator Neuroscience Research Award from the International Association of Dental Research, and was appointed a member of the Foundation for Anesthesia Education and Research Academy in Anesthesiology. He served as president of the American Pain Society, provided expert opinion to the U.S. Senate's HELP Committee on the 2011 Institute of Medicine report, *Relieving Pain in America*, and recently completed service on the Department of Health and Human Services' Interagency Pain Research Coordinating Committee.

Panelist: Julie Fritz, The University of Utah

Dr. Fritz is a Distinguished Professor in the Department of Physical Therapy and Athletic Training, and associate dean for Research in the College of Health at The University of Utah, Salt Lake City, Utah. She is a licensed physical therapist and received her Ph.D. in rehabilitation sciences from the University of Pittsburgh. Her research has focused on examining treatments for spinal pain. This research has included clinical trials and the development of predictive models to identify which patients are most likely to respond to particular interventions, including mind-body therapies. She also has led research exploring physiologic mechanisms underlying the therapeutic effects of manipulative therapy, including the role of changes in spinal stiffness and trunk muscle activation.

Panelist: Daniel K. Sodickson, New York University (NYU) Langone Health

Dr. Sodickson is vice-chair for research in the Department of Radiology at NYU Langone Health; professor of radiology and physiology & neuroscience at NYU Grossman School of Medicine; and professor of biomedical engineering at NYU Tandon School of Engineering. He directs the Center for Advanced Imaging Innovation and Research (CAI^2R), a National Center for Biomedical Imaging and Bioengineering. Dr. Sodickson's research aims at seeing what previously has been invisible in order to improve human health. He is credited with founding the field of parallel imaging, in which distributed arrays of detectors are used to gather magnetic resonance images at previously inaccessible speeds. Dr. Sodickson was awarded the Gold Medal of the International Society for Magnetic Resonance in Medicine (ISMRM), and he recently completed a term as ISMRM president. A new institute he codirects—Tech4Health—aims to bring emerging technologies such as continuous sensing and artificial intelligence to biomedicine.

3:00–3:30 p.m.	**Summary and Concluding Remarks**
	Helene Langevin, NCCIH Director
3:30 p.m.	**ADJOURN**