MAYO CLINIC



# Division of Orthopedic Surgery Research

## 2023 Year in Review

# Table of Contents

# Message From the Chair of Research and Vice Chair of Orthopedic Surgery

Dear Colleagues and Friends,

The 2023 academic year marked a year of unprecedented growth, achievements, and success by our surgeons, clinicians, and career scientists regarding research and academic productivity. Looking back as I write this message in early 2024, our department has experienced tremendous growth, including onboarding a world-class career scientist, a search for an additional career scientist, and successfully recruiting numerous illustrious clinicians with strong interests in clinical and translational research. Our surgeons, clinicians, and scientists continue to excel in their fields and cultivate the Mayo Clinic vision of Cure, Connect, and Transform as we carry out our primary value: "The needs of the patient come first."

In partnership with our generous benefactors, all of whom have strong ties to the Department of Orthopedic Surgery, major contributions were allocated toward the new Proton Beam Therapy Building and the Kellen Research Building, both in Rochester, Minnesota. The transformative research being conducted by our industrious surgeons, clinicians, and scientists has been noticed by institutional leaders and benefactors, resulting in a 400% increase in annual department-awarded funds mobilized via RFPs during the past four years. In addition, our *de novo* Orthopedic Surgery Artificial Intelligence (AI) Laboratory (OSAIL) team has quickly become one of the preeminent AI teams in the nation, with the group encompassing consultant leads from various clinical divisions as well as several data scientists, analysts, and annotators.

In 2023, orthopedic surgery research ranked among the top of all surgical specialties at Mayo Clinic, being placed in the top tier in the per person metrics of publications and gross royalties. This was possible in part due to the expansion of research resources in support of our principal investigators, including substantial investment in clinical research coordinators, virtual clinical trials, biostatistics, and research temporary professionals' support. Expanding these research resources has allowed our dedicated investigators to remain intensely focused on their research as they drive departmental productivity.

Additionally, 2023 proved to be a successful and prolific year for the Division of Orthopedic Surgery Research as we achieved our 2023 goals and further developed our strategic priorities for 2030, the 2027 milestones to advance these priorities, and the 2024 specific tactics to support that mission. The team formalized four strategic priorities for 2030: discovery science, artificial intelligence, clinical trials, and regenerative medicine. In the near term, we look forward to enhancements in individualized medicine, regenerative biotherapeutics, virtual orthopedic clinical trials, expanded prospective data collection with whole-exome sequencing, and U.S. Food and Drug Administration (FDA)-approved clinical trials.

Looking to 2024, we remain fully committed to delivering impactful outcomes as we carry out our Mayo Clinic mission of inspiring hope and contributing to health and well-being by providing the best care to every patient through integrated clinical practice, research, and education. As we implement plans that will directly benefit our patients with a keen focus on addressing health inequities, we take a moment to reflect on gains realized during the past academic year.

To that end, this report offers a glimpse into a few of our department's research accomplishments during this past year, including clinical, translational, and basic science research. This time of reflection leaves us with not only significant pride in the dedication of our investigators and administrative team, but also a renewed sense of commitment to provide transformative musculoskeletal care that enhances the quality of life for each of our Mayo Clinic patients.

I eagerly await the opportunity to share our 2024 outcomes and progress toward our strategic goals with you next year!

Very best personal regards,

**Matthew P. Abdel, M.D.**
Chair, Mayo Clinic Surgical and Procedural Practice
Chair, Division of Orthopedic Surgery Research
Vice Chair, Department of Orthopedic Surgery
Andrew A. and Mary S. Sugg Professor of Orthopedic Surgery

## 2023 Volume and Quality Data

**72**
Consultants

**63**
Residents and Fellows

**460**
Research Publications

# Our Vision

### Cure
Musculoskeletal Disease With Innovative Diagnostics and Therapeutics.

### Connect
Patients to Optimal Care Through Predictive Analytics and Advanced Registry Technologies.

### Transform
Musculoskeletal Care Through Predictive Algorithms and AI.

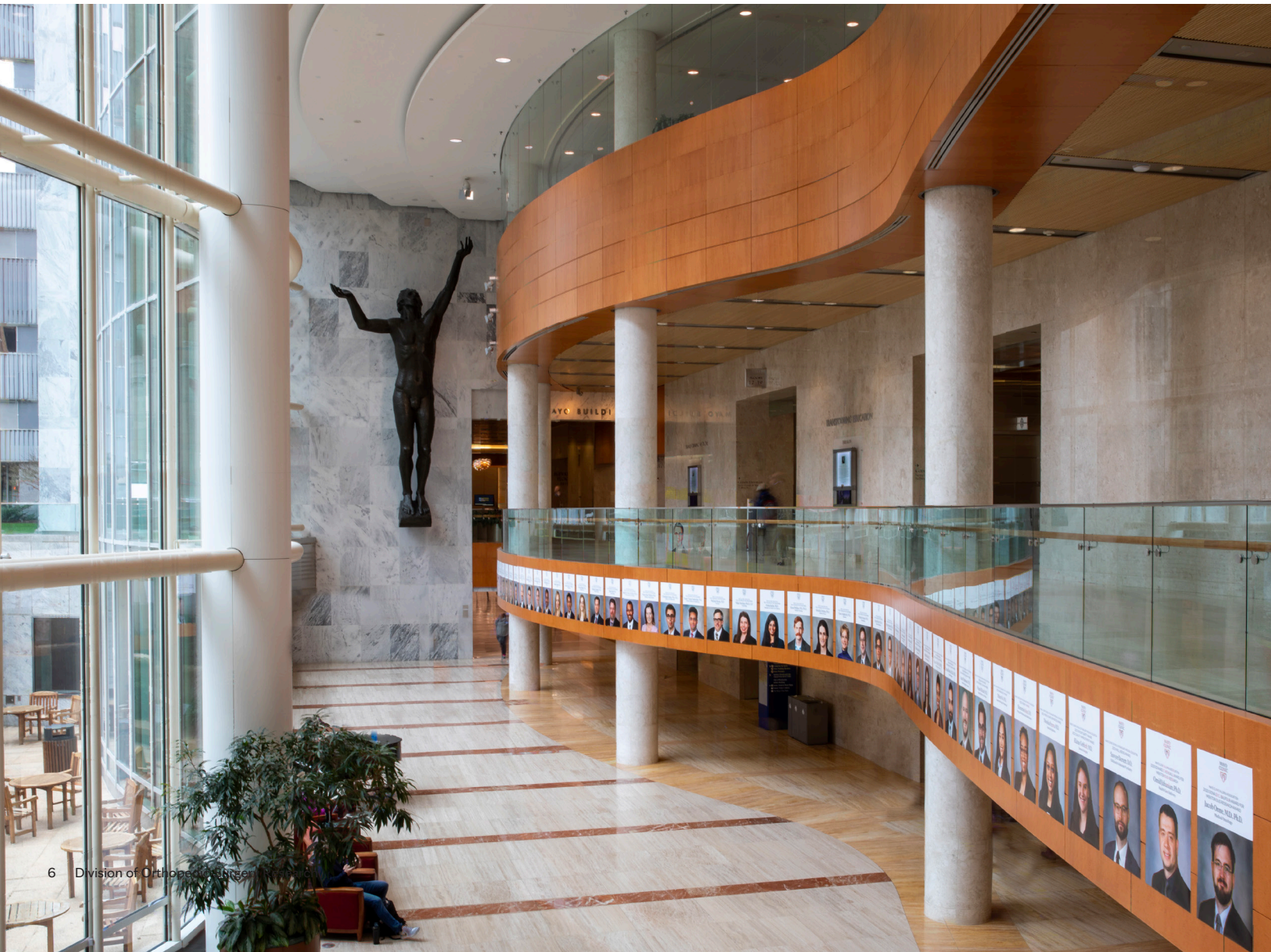
# Division of Orthopedic Surgery Leadership

**Aaron J. Krych, M.D.**
Department Chair

**Matthew P. Abdel, M.D.**
Department Vice Chair,
Chair of Research

**Jonathan D. Barlow, M.D.**
Chair of Education

**Peter C. Rhee, D.O., M.S.**
Chair of Practice



## Research Labs and Cores

**400%**

increase in annual department awarded funds since 2020

**12**

Research Labs

**1**

Core

"It is a great thing to make scientific discoveries of rare value, but it is even greater to be willing to share these discoveries and to encourage other workers in the same field of scientific research."

— William J. Mayo, Remark on the Romance of Medicine. *Proc. Staff Meet., Mayo Clin.*, 10:393-394 (June 19) 1935)

## ELBOW AND SHOULDER RESEARCH LABORATORY

**Principal Investigator: Shawn W. O'Driscoll, M.D., Ph.D.**

Despite scientific advances in orthopedic surgery, one area lags behind the others: the elbow. Elbow injuries and disorders can be debilitating. Overcoming the pain, loss of motion, and resulting loss of function can be a significant challenge for patients and the surgeons who treat them.

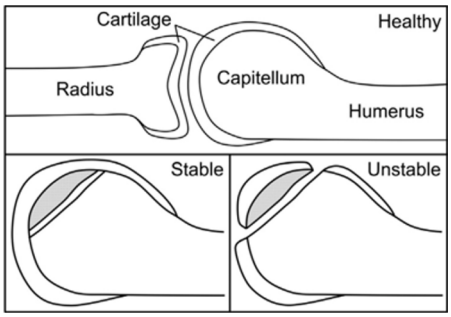
Led by Principal Investigator Shawn O'Driscoll, M.D. Ph.D., the Elbow and Shoulder Research Team works in Research and Education to develop and refine techniques to repair and reconstruct injured and impaired elbows and shoulders. They, along with a large network of physician-scientist collaborators, develop theoretical and anatomic models that permit them to study the biomechanics of joints when they are intact, when their function has been impaired, and to optimize methods to repair them and restore function. Dr. O'Driscoll's basic science research includes the biomechanics of implants (prosthetic and otherwise) used in elbow surgery, and his clinical research encompasses all aspects of elbow injury diagnosis and treatments.

The Elbow and Shoulder Team's research advances translate into new and better treatment options. Dr. O'Driscoll is passionate about educating others about these to help improve outcomes for patients with elbow and shoulder injuries and decrease long- term health care costs.

**Elbow instability:** Our lab leads a multidisciplinary team to investigate a complex problem: recurrent elbow instability. Since Dr. O'Driscoll's original study on posterolateral rotary instability was published in 1991, significant advances in understanding, diagnosing, and treating recurrent instability continue to be made. Recently, in a cadaver-based study, we developed a model to study the role of the lateral part of the distal triceps as a stabilizer in the lateral collateral ligament-deficient elbow. Our findings substantiate the role of the lateral part of the distal triceps as a dynamic constraint against elbow varus, independent of the anconeus, which has clinical implications for preventing and rehabilitating elbow instability. We used a cadaver model to study the potential for increasing elbow instability due to disruption of the lateral collateral ligament-capsule complex (LCL-cc) during arthroscopic extensor carpi radialis brevis (ECRB) release for lateral epicondylitis. The findings of this study demonstrate that iatrogenic injury to the LCL-cc, which could occur during ECRB release, is an important risk that surgeons should be aware of because of its potential deleterious impact on elbow stability.

**Osteochondritis dissecans**: Osteochondritis dissecans (OCD) of the capitellum results from a stress fracture that is common in youth baseball and gymnastics. Unfortunately, it can reliably be diagnosed only with CT scan or MRI. In an attempt to obviate the risk of ionizing radiation or costly imaging, we, in collaboration with Matthew Urban, Ph.D. and a team of research engineers in the Mayo Clinic Department of Radiology, developed and investigated using a novel ultrasound reconstruction algorithm for better visualizing OCD lesions using medical ultrasonography in a clinical setting. This novel reconstruction algorithm is called low-pass delay-multiply-and-sum (low-pass DMAS). This method improved the ability of medical ultrasound to detect OCD lesions of the capitellum when compared with traditional medical ultrasound techniques.

**Figure 1.**




Sagittal views of stable and unstable OCD lesions of the humeral capitellum in the elbow. Stable OCD lesions have overlying cartilage that stabilizes the bone fragment. Unstable OCD lesions have disrupted overlying cartilage, which can lead to the formation of loose bodies within the elbow. In this work, we found that ultrasound images of OCD lesions could be improved when reconstructed using DMAS compared with traditional ultrasound techniques. This was true in a bone-mimicking phantom OCD model, a cadaveric OCD model and in vivo OCD images.

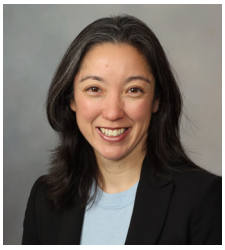

Ramazanian T, Muller-Lebschi JA, Merlet MH, Lee H, Vaichinger AM, Fitzsimmons JS, O'Driscoll SW. Effect of radiocapitellar joint over/under stuffing on elbow joint contact pressure. J Hand Surg Am 2023;48:403 e401-403 e409. 10.1016/j.jhsa.2021.11.006. Epub 2022 Oct 11. PMID: 36229309.

Kwak JM, Rotman D, Lievano JR, Xue M, O'Driscoll SW. The role of the lateral part of the distal triceps and the anconeus in varus stability of the elbow: a biomechanical study. J Shoulder Elbow Surg 2023;32:159-167. 10.1016/j.jse.2022.08.005. Epub 2022 Sep 24. PMID: 36167289.

Holmes PM, Chen K, Lee H, Fitzsimmons JS, O'Driscoll SW, Urban MW. Improving visualization of osteochondritis dissecans using delay-multiply-and-sum reconstruction. Ultrasound Med Biol 2023;49:1979-1995. 10.1016/j.ultrasmedbio.2023.05.001. Epub 2023 Jun 23. PMID: 37357080.

## LIMB REPAIR AND REGENERATION LABORATORY

**Principal Investigator: Mimi C. Sammarco, Ph.D.**

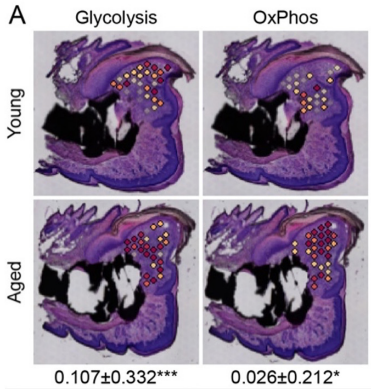


There are currently 1.6 million people currently living with limb loss in the United States. An additional 120,000 babies in the United States are born with limb reduction defects each year. While completely regenerating a limb is not yet possible, regenerative approaches that extend limbs or improve the integration of prosthetics can vastly improve quality of life. Understanding the mechanisms that drive tissue replacement and patterning and methods to accelerate this regenerative event are key steps in developing translational and clinical approaches to replace bone and soft tissue.

Our lab uses computer, animal, and cell models to target mechanisms that underpin high-fidelity musculoskeletal tissue replacement. Our long-term goal is to work with clinicians to develop bench-to-bedside strategies to build functioning, patterned, high-quality replacement tissue using therapeutic strategies and the body's own inherent regenerative capacity.

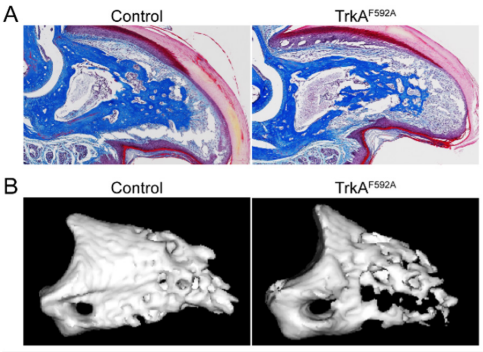
To this end our lab's research program encompasses several different regenerative approaches. The first approach focuses on cell metabolism, which drives almost every cell function. Cell metabolism has long been considered an optimal point of intervention for cancer therapies, where drugs are used to redirect cancerous cells by modulating cell metabolism. Our recent studies show that cells that make bone and soft tissue can be directed to do so by simple changes in their metabolic profile. This line of studies provides a therapeutic angle for promoting regeneration by using prior research in fields such as oncology. The cell metabolism process can also generate small molecular signals that tell surrounding regenerating tissue what pattern to take and when to stop. Our metabolic studies suggest these molecular signals play an integral role in directing tissue replacement after amputation. Regenerating tissue also takes direction from other cells, such as nerves and macrophages. Our studies have shown that sensory nerves play an integral role in limb regeneration and that they may be key in maintaining the stemness of cells. Similarly, macrophages are part of the injury response after amputation. These cells infiltrate during inflammation and direct the surrounding tissue to engage in either regeneration or undesirable scarring. Our data show that cell metabolism plays a key role in directing macrophage signaling during limb regeneration and can be exploited to promote tissue replacement. Finally, we are collaboratively working to develop a finite element model of bone regeneration. Our long-term goal is to identify and then predict where bone will form and what genes are expressed in this area. Further, since regenerated bone is often weaker than the original structure, we hope to spatially identify where we can enhance bone formation to generate higher-quality bone. Our team uses spatial transcriptomics as a key tool in identifying localized changes in gene expression and cell metabolism to refine therapeutic techniques.

**Figure 1.**




**Spatial transcriptomics can be used to identify localized gene expression and spatially restricted changes in cell metabolism.** Spatial plots of module scoring for cell metabolism pathways within young and aged amputated digits.

**Figure 2.**




**Sensory nerve disruption impairs digit regeneration.** Trichrome stained sections and micro-CT images of regenerated digits showing how removal of sensory nerves prevents bone formation (right).


Xiao X, Conan J, Drennon T, Uytingco C, Vishlaghi N, Xu L, Levi B, **Sammarco MC**, Tower RJ. Spatial transcriptomic interrogation of the murine bone marrow signaling landscape. Bone Res. 2023 Nov 6;11(1):59. doi: 10.1038/s41413-023-00298-1. PMID: 37926705; PMCID: PMC10625929.

Jaramillo J, Taylor C, McCarley R, Berger M, Busse E, **Sammarco MC**. Oxaloacetate enhances and accelerates regeneration in young mice by promoting proliferation and mineralization. Front Cell Dev Biol. 2023 Feb 24;11:1117836. doi: 10.3389/fcell.2023.1117836. PMID: 36910154; PMCID: PMC9999028.

Tower R, Busse E, Simkin J, Guntur A, Jaramillo J, Lacey M, Hoffseth K, **Sammarco MC**. Spatial transcriptomics reveals metabolic changes underly age-dependent declines in digit regeneration. eLife. 2022;11:e71542. doi: 10.7554/eLife.71542. PMID: 35616636; PMCID: PMC9135401.

## MOTION ANALYSIS LABORATORY

**Principal Investigator: Kenton R. Kaufman, Ph.D., P.E.**

The Motion Analysis Laboratory, directed by Kenton R. Kaufman, Ph.D., P.E., offers state-of-the-art treatment planning for patients with movement difficulties, documents results of therapeutic procedures, and conducts research on clinical applications of human movement. The laboratory uses motion capture and other human performance measurement modalities to provide clinical care for patients across the institution; performs extensive and varied research; and educates learners including medical students, predoctoral students, and postdoctoral fellows. Research focus areas include preventing falls in combat veterans with lower-extremity trauma and other populations with balance concerns, improving quality of life in patients with knee and hip arthroplasty, managing spinal deformities, optimizing functional outcomes for pediatric patients with scoliosis, and improving function after brachial plexus reconstruction. Dr. Kaufman also leads an effort to develop the Limb Loss and Preservation Registry, the first national registry of its kind for people who have lost limbs or have had limb preservation procedures. The goal of the registry, supported by the National Institutes of Health (NIH) and the U.S. Department of Defense (DoD), is to generate knowledge about what treatments and prosthetic/orthotic advances will improve functional outcomes for individuals with limb loss and limb difference.

The laboratory's work received the Julian M. Bruner Award for Outstanding Poster at the 2023 American Society for Surgery of the Hand meeting. The poster was titled "Voluntary Neuromuscular Control of Gracilis Free Functioning Muscle Transfer for Elbow Flexion: Spinal Accessory Nerve vs Intercostal Nerve" by Sandesh Bhat, Alexander Shin, and Kenton Kaufman.

Our research collaborator, Benjamin I. Binder-Markey P.T., D.P.T., Ph.D., Assistant Professor, Drexel University, won the 2023 Orthopaedic Research Society Young Investigator Award for work conducted in the laboratory.

The Motion Analysis Laboratory had the pleasure of hosting State Department sponsored Ukraine delegates.


Kaufman KR, Miller EJ, Deml CM, Sheehan RC, Grabiner MD, Wyatt M, Zai CZ, Kingsbury T, Tullos ML, Acasio JC, Mahon CE, Hendershot BD, Dearth CL. Fall prevention training for service members with an amputation or limb salvage following lower extremity trauma. Mil Med. 2023 Feb 16::usad005 doi: 10.1093/milmed/usad005. Epub ahead of print. PMID: 36794799.

Binder-Markey BI, Persad LS, Shin AY, Litchy WJ, Kaufman KR, Lieber RL. Direct intraoperative measurement of isometric contractile properties in living human muscle. J Physiol. 2023 May;601(10):1817-1830. doi: 10.1113/JP284092. Epub 2023 Apr 25. PMID: 36905200.

Persad LS, Binder-Markey BI, Shin AY, Lieber RL, Kaufman KR. American Society of Biomechanics Journal of Biomechanics Award 2022: Computer models do not accurately predict human muscle passive muscle force and fiber length: evaluating subject-specific modeling impact on musculoskeletal model predictions. J Biomech. 2023 Oct;159:111798. doi: 10.1016/j.jbiomech.2023.111798. Epub 2023 Sep 9. PMID: 37713970.

## MUSCULOSKELETAL BIOLOGY AND IMMUNOLOGY LABORATORY

**Principal Investigator: Anne Gingery, Ph.D.**

The Musculoskeletal Biology and Immunology Laboratory focuses on an integrated systems approach to pathologies found in the musculoskeletal system to drive mechanistic understanding and develop preventatives and therapeutics to improve health span, the time patients remain relatively disease free. Research in our laboratory encompasses multiple tissues in the musculoskeletal system including tendon, connective tissue, tendon-to-bone conjunction, muscle, nerves, bone, and the immune system.

One focus area of our laboratory is the role of senescent cell accumulation in musculoskeletal tissues. Aging is a major risk factor for musculoskeletal disorders and is hallmarked by low- grade sterile inflammation called inflammaging, matrix damage, organelle dysfunction, stem/progenitor cell exhaustion, and increased senescent cell burden in tissues. Cellular senescence is a programmed response that limits proliferation of damaged or aged cells and results in an essentially irreversible growth arrest. Failure to clear senescent cells over time can promote pathology. (Figure 4).

An example is the increased accumulation of senescent cells found in the subsynovial connective tissue in patients with carpal tunnel syndrome (CTS). Figure 5 shows increased senescent cell marker p15 in CTS patient connective tissue. These senescent cells are resistant to apoptosis, or programmed cell death. Given this increased burden of senescent cells and that apoptosis can be targeted, we have begun a phase 2 clinical trial using senolytic drugs that specifically target the apoptosis resistant senescent cells for removal in CTS patients. Additional work in the Musculoskeletal Biology and Immunology Laboratory explores the role of cellular senescence in tendon disorders, as well as the role of metabolic and immune system dysfunction on musculoskeletal pathology, injuries, aging and tissue regeneration.

**Figure 1. Senescent Cell Accumulation in Normal and Pathologic Conditions.**

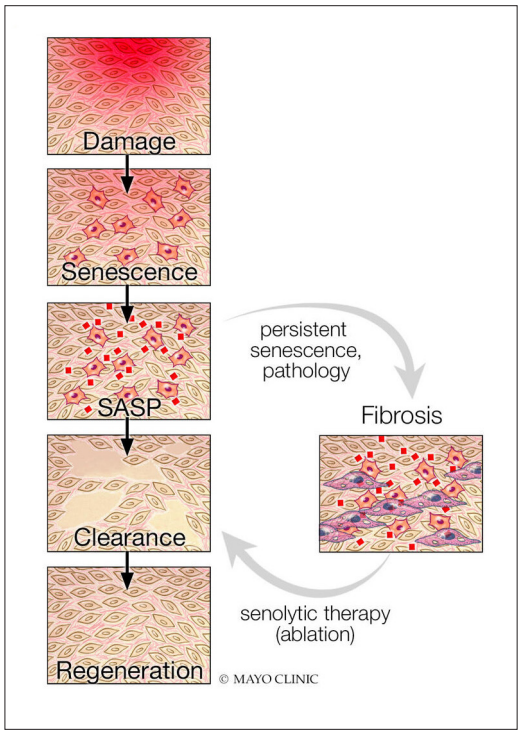
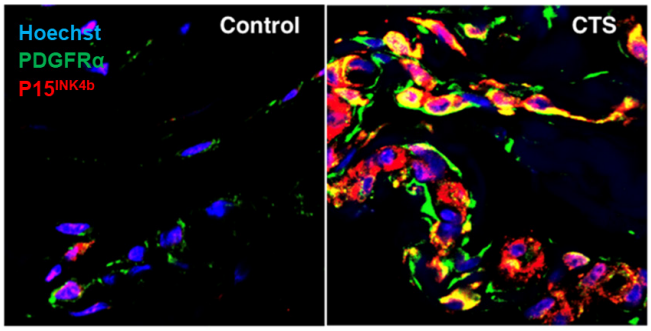



**Figure 2. Senescent cell marker p15 is highly expressed in patient connective tissue.**





Cellular senescence in human skin aging: leveraging senotherapeutics. Wyles SP, Carruthers JD, Dashti P, Yu G, Yap JQ, Gingery A, Tchkonia T, Kirkland J. Gerontology. 2024;70(1):7-14. PMID: 37879300.

Gene expression of Postn and FGF7 in canine chordae tendineae and their effects on flexor tenocyte biology. Ren Y, Wan R, Zhao G, Kuroiwa T, Moran SL, Gingery A, Zhao C.J Orthop Res. 2023 Nov 22. PMID: 37990927.

Impact of aging on tendon homeostasis, tendinopathy development, and impaired healing. Korcari A, Przybelski SJ, Gingery A, Loiselle AE. Connect Tissue Res. 2023 Jan;64(1):1-13. PMID: 35903886.

## NEURAL REGENERATIVE RESEARCH LABORATORY

**Principal Investigators: Alexander Shin, M.D. and Nicholas Pulos, M.D.**

Peripheral nerve injuries occur in adults, children, and babies due to multiple mechanism. In adults and children, injuries can occur secondary to high-energy trauma, lacerations, gunshot wounds, or iatrogenic injuries. In babies, birth injuries can cause tearing the nerves in the neck, resulting in paralyzed and insensate arms. The incidence of peripheral nerve injuries in adults is estimated to be 13-23 per 100,000 people, or in the United States between 4.3 and 7.6 million peripheral nerve injuries, of which 5%-30% may require surgical reconstruction. Birth injuries occur with an incidence of 1.5 per 1,000 live births, of which approximately 5% require nerve surgery. Surgical reconstruction often focuses on restoring motor function and requires large quantities of nerve grafts, which are often harvested from a patient's expendable sensory nerve. Unfortunately, there is a limited supply, and harvest results in permanent sensory deficits. Because of the limited supply, optimal surgical reconstructions are not feasible.

Our surgical practice has benefited from advances in research and provides fertile ground for translational research. Since 2001, our multidisciplinary Peripheral Nerve Clinic providers have evaluated over 8,500 patients (adults, children, and babies) and surgically reconstructed over 3,000 patients, and the need to improve nerve regeneration is evident daily in our clinics and in surgery.

Our team: Dr. Nicholas Pulos, Dr. Rachida Liebrand, Dr. Alexander Y. Shin

**Figure 1.**

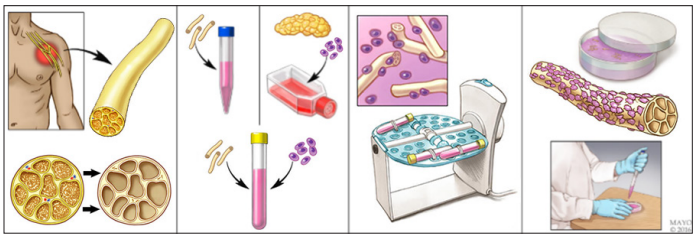
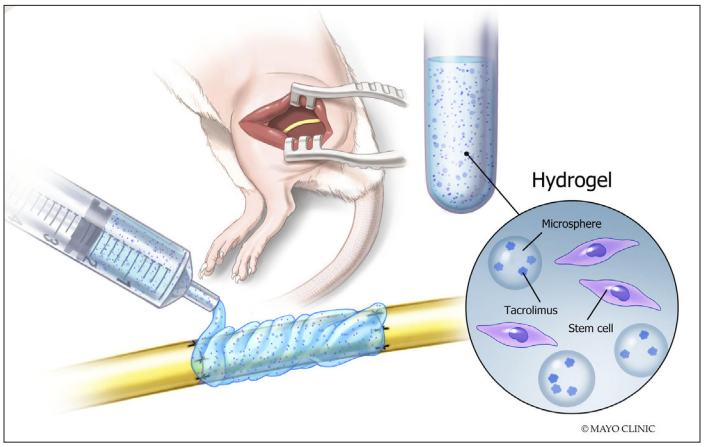


**Figure 2.**




**The goal of our lab is threefold:**

1 To enhance the function of cadaver nerves by decellularization and addition of cellular elements (stem cells) to provide an unlimited supply of nerve grafts that are as effective as a patient's own donor nerves

2 Create in surgery addition of microenvironment-enhancing suspension for nerve regeneration (allograft and autograft nerves) by adding extracellular vesicles (exosomes), stem cells and/or locally delivered FK506 in a hydrogel suspension.

3 Develop animal models of brachial plexus birth palsy to evaluate the effect of humeral growth plate inhibition secondary to nerve injury.

We are blessed with an outstanding team and collaborators and are confident we can translate of our research to our patients within the next two to five years.

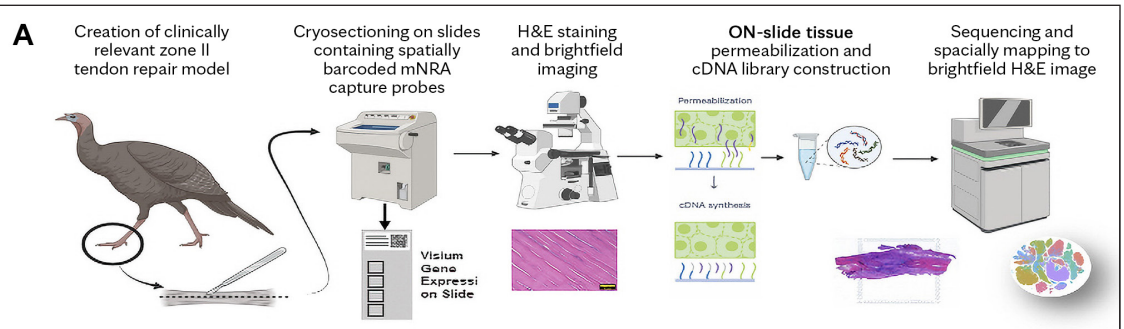
## ORTHOPEDIC BIOMECHANICS RESEARCH LABORATORY

**Principal Investigator: Chunfeng Zhao, M.D.**

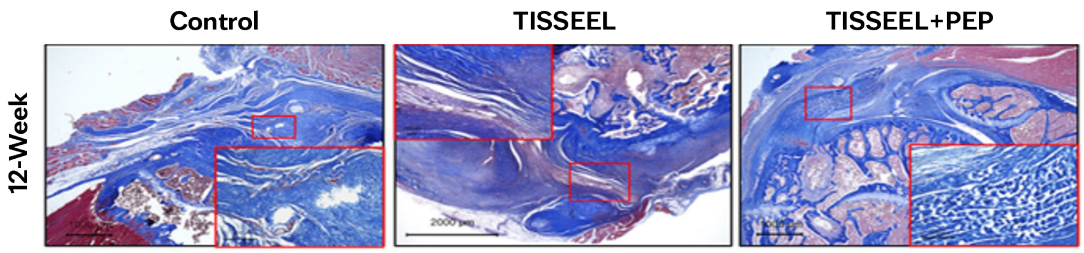
The laboratory, under the leadership of Dr. Zhao, is a leading multidisciplinary research facility dedicated to advancing clinical translation research particularly focusing on musculoskeletal soft tissues. In 2023, our team embarked on several pivotal research projects, the highlights of which are outlined below.

Looking ahead to 2024, we will continue to advance our research through multiple federally (NIH and DoD) funded projects, including flexor tendon, rotator cuff, and compartment syndrome projects. We will also focus on innovative projects such as exosome for OA treatment in large animal models, PEP for wound healing, and periostin in tendinopathy. These endeavors not only underscore our commitment to excellence in orthopedic biomechanics research but also pave the way for future federal grant applications.

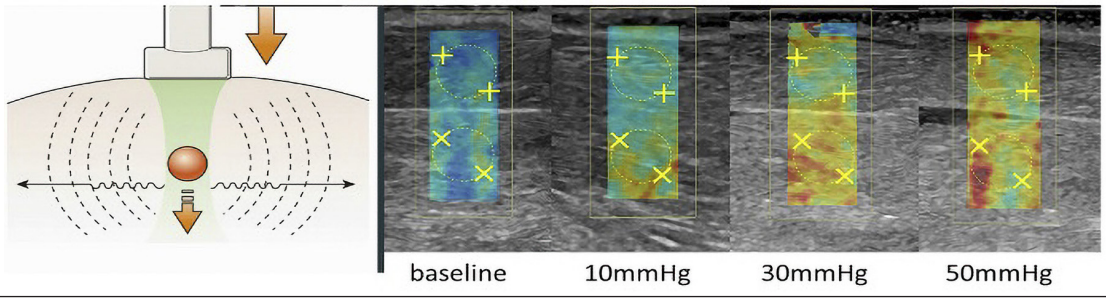
**Flexor tendon intrinsic healing:** We explored the key elements of intrinsic healing following flexor tendon injuries, including tenocytes, vinculum, and synovium, using a novel turkey digit model. This research is crucial for improving clinical outcomes in tendon repair.




**Rotator cuff repair and regeneration:** Our laboratory pioneered tendon-fibrocartilage-bone composite approach for enhancing rotator cuff repair. Additionally, we investigated exosomes in rotator cuff regeneration across rat and canine models, yielding promising results.




**Ultrasound elastography for compartment syndrome:** We developed a groundbreaking noninvasive ultrasound technology aimed at diagnosing, prognosticating, and monitoring acute compartment syndrome, setting a new standard in patient care.





H Li, L Berglund, S Lin, Z Wang, AJ Krych, C Zhao. Biomechanical comparisons of bone-patellar tendon-bone graft with or without suture tape for anterior cruciate ligament reconstruction. Orthop J Sports Med. 5 (2023): 428-436.

Y Ren, R Wan, G Zhao, T Kuroiwa, SL Moran, A Gingery, C Zhao. Gene expression of Postn and FGF7 in canine chordae tendineae and their possible relations to tenogenesis in chordae tendineae and potential effects on flexor tenocyte biology. J Orthop Res. 37990927 doi: 10.1002/jor.25745

RL Reisdorf, H Liu, C Bi, AM Vrieze, SL Moran, PC Amadio, C Zhao. Carbodiimide derivatized synovial fluid for tendon graft coating improves long-term functional outcomes of flexor tendon reconstruction. Plast Reconstr Surg. 2023 Nov 1;152(5):840e-849e. doi: 10.1097/PRS.0000000-000010390. Epub 2023 Mar 14. PMID: 36912937.

## ORTHOPEDIC CARTILAGE AND BIOLOGICS TRANSLATIONAL LAB

**Principal Investigator: Daniel B. F. Saris, M.D., Ph.D.**

Our laboratory studies injuries to the articular cartilage and meniscus structures within synovial joints, which are common among young, active individuals participating in sports-related activities. These injuries are debilitating, and because these tissues do not have the intrinsic capacity to heal, they can cause degenerative changes in the joint and eventual osteoarthritis (OA). Our research group is focused on developing regenerative, cell-based therapies and biologics to improve healing and restore native joint function. Our aim is to innovate and translate research from the laboratory to clinical practice to improve healing and get our patients back to activity.

One of the regenerative cell-based projects in the laboratory was to develop RECLAIM, a one-step cartilage repair procedure for the knee (Figure 1A) and hip (Figure 1B). This treatment uses autologous cartilage cells isolated from the rim of the cartilage defect and combines them with allogeneic mesenchymal stromal cells (MSCs) from a donor bank. Our phase 1 clinical trial on the safety and viability of regenerative therapy for knee cartilage defects included 25 patients. Our two-year follow-up is currently ongoing. We have also just enrolled the first few patients in a phase 1 study using this same RECLAIM procedure for hip cartilage defects.

We are also investigating the potential of using this technique for treating meniscus and tendon injuries. We have isolated and characterized meniscus and tendon cells surrounded by the pericellular matrix that we refer to as “meniscons” and “tenons.” Future work will focus on evaluating the therapeutic potential of these cell types. We have developed an in vitro model to study meniscus healing using human tissue from patients undergoing knee replacement surgery. Using this model, we can study histological changes and biomechanics of the repair tissue. Furthermore, we have optimized a robotic testing protocol to study meniscus tear formation under physiological and supraphysiological loads.

Other studies in the laboratory include enhancing sutures by using a functionalization technique to bind growth factors and cytokines to their surfaces to promote tissue repair. In addition, growth plate defects caused by trauma or cancer can lead to abnormal growth patterns or bone deformities. We have demonstrated that excised growth plates maintain their viability and can be transplanted in a representative pig model with a growth plate defect **(Figure 2)**.

**Figure 1. Single-step cartilage transplantation.**

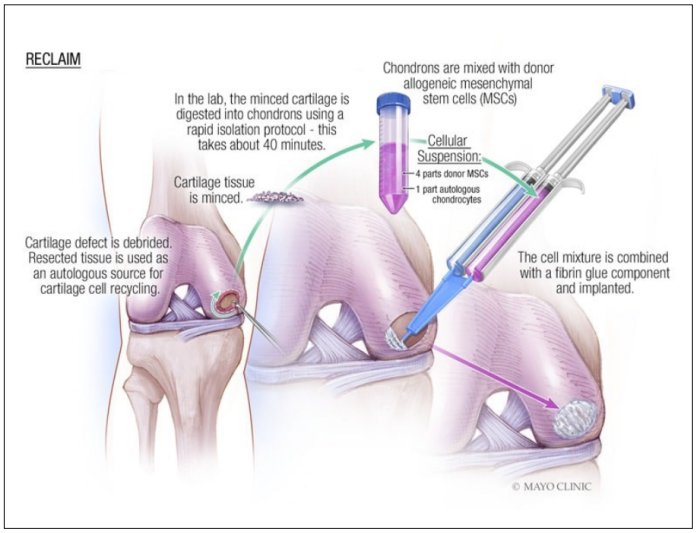
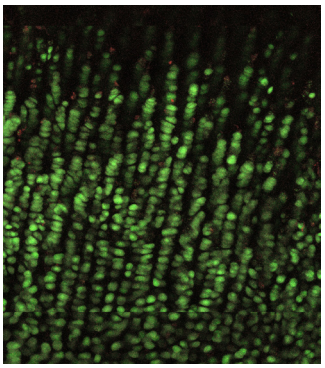
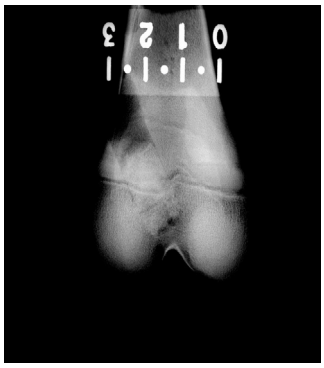



**Figure 2. Growth plate transplantation.**



Live/Dead staining growth plate.



Radiographic image of transplanted.

## ORTHOPEDIC GENETIC HOST VARIATION LABORATORY

**Principal Investigator: Matthew P. Abdel, M.D.**

Total knee arthroplasty (TKA) is one of the most common surgical procedures, with about 1 million procedures performed annually. Unfortunately, a subset of patients will require revision TKA, and that number is also increasing. One failure mode of particular interest to our lab is arthrofibrosis.

Arthrofibrosis is a debilitating complication with limited surgical and nonsurgical treatment options. It affects 5% of patients who undergo TKA surgery and despite advancements in surgical techniques and implant devices, there are no preventative or therapeutic options for arthrofibrosis.

Our lab pursues mechanistic studies on arthrofibrosis by acquiring patient-derived samples, primary cell culture studies, and animal models. Our goal is to transform the practice of arthroplasty by developing theragnostic approaches that permit genetic diagnosis and implementation of pharmacotherapies aimed at preventing and treating arthrofibrosis.

We are conducting several research projects to learn more about arthrofibrosis and improve treatment options for patients. In particular, we are i) investigating the demographic, imaging, and surgical characteristics of patients affected by arthrofibrosis; ii) defining the pathophysiology of arthrofibrosis; iii) evaluating genetic predispositions to arthrofibrosis; iv) assessing molecular characterization of arthrofibrotic pathways; v) developing and employing arthrofibrosis animal models to evaluate therapeutic options for arthrofibrosis; and vi) using artificial intelligence to identify patients at risk of developing arthrofibrosis.

Our recent studies suggest that knee arthrofibrosis may be caused by a molecular imbalance within the knee joint. For example, molecular analysis showed a reduction in the expression of adiponectin (ADIPOQ) within arthrofibrotic knee tissues when compared to control tissues. Together, this evidence suggests that normal soft tissue healing following TKA requires a balance between scar tissue generating fibroblasts and other cell populations within the knee. Thus, we are now testing the hypothesis that an imbalance of different cell types may cause arthrofibrosis development in the knee. Our present studies are focused on the role of adiponectin in the development of knee arthrofibrosis **(Figure 1)**.

We have shown that AdipoRon, an adiponectin mimetic, reduces the arthrofibrotic phenotype (i.e., reduction in collagen) of primary knee fibroblasts undergoing TGFβ1-mediated myofibroblasts differentiation (Figure 2). Our current studies are focused on defining the mechanisms by which adiponectin-related signaling impairs the fibrotic process, and evaluating the protective potential of AdipoRon in our mouse and rabbit animal models of arthrofibrosis.

**Figure 1. Adiponectin signaling and the (arthro)fibrotic TGFβ1 cascade.**

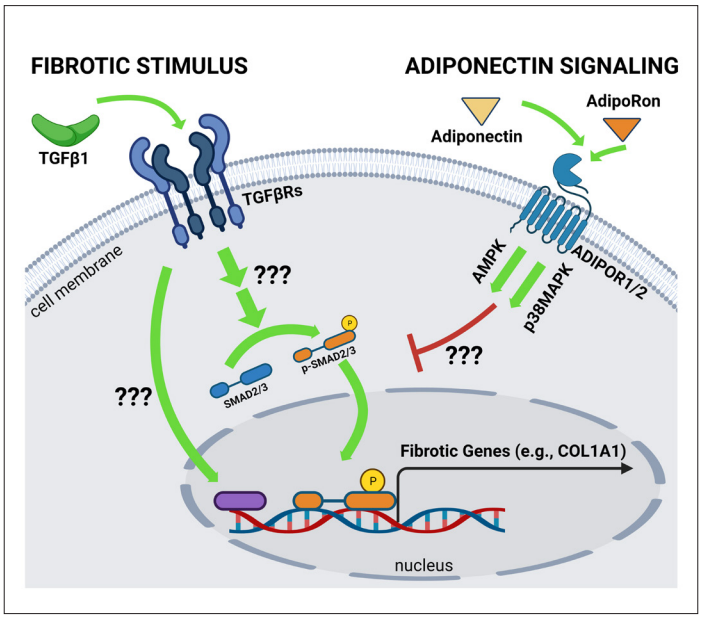
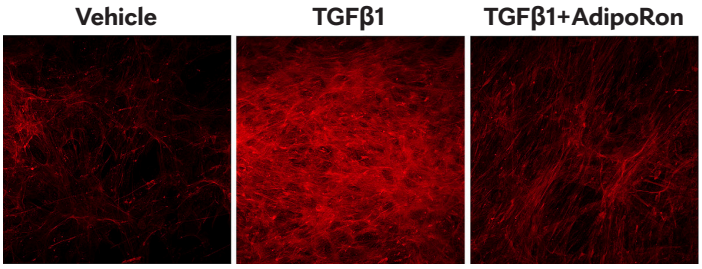



**Figure 2. Picrosirius Red Staining (Collagen Levels)**





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## ORTHOPEDIC SURGERY ARTIFICIAL INTELLIGENCE LABORATORY

**Principal Investigators: Michael J. Taunton, M.D., and Cody C. Wyles, M.D.**

The Orthopedic Surgery Artificial Intelligence Laboratory (OSAIL), led by Principal Investigators Michael J. Taunton, M.D., (left) and Cody C. Wyles, M.D. (right) is based at Mayo Clinic in Rochester, Minnesota. OSAIL is pursuing state-of-the-art tools and analytics to design novel solutions for treating patients with a wide variety of orthopedic problems.

The team has multidisciplinary expertise in orthopedics, radiology, epidemiology, biostatistics, and medical imaging informatics. OSAIL is innovating the practice of orthopedics by leveraging cutting-edge AI techniques including machine learning, deep learning, and large language models (LLMs). OSAIL supports active investigation in all anatomic areas of orthopedic surgery through leadership from world experts in each subdiscipline.

Over the last year, OSAIL has published 25 peer-reviewed articles in top orthopedic surgery, radiology, and informatics journals. Additionally, OSAIL has presented works at several national conferences, including American Academy of Orthopedic Surgeons, American Association of Hip and Knee Surgeons, Radiological Society of North America, Conference on Machine Intelligence in Medical Imaging, and Society for Imaging Informatics in Medicine and received three awards at conferences for Best Paper, Best Poster, and Best Project by a Trainee.

Last year OSAIL successfully translated four of their algorithms into clinical practice at Mayo Clinic, including tools that yield patient-specific risks and recommendations for mitigating dislocation and periprosthetic fracture as well as tools that automatically annotate measurements of acetabular component position and femoral component subsidence on post total hip arthroplasty radiographs.

Over the coming year, OSAIL will focus on using generative artificial intelligence (AI) for both imaging and LLM applications. The lab has a strong track record with generative imaging, including tools that can take preoperative hip radiographs and generate ideal target postoperative radiographs in an application known as THA-Net. There is potential to further the use cases of generative imaging to create novel image transformations including view correction. LLMs are being used to build clinical registries, phenotype patients, and solve rate-limiting clinical workflow problems.

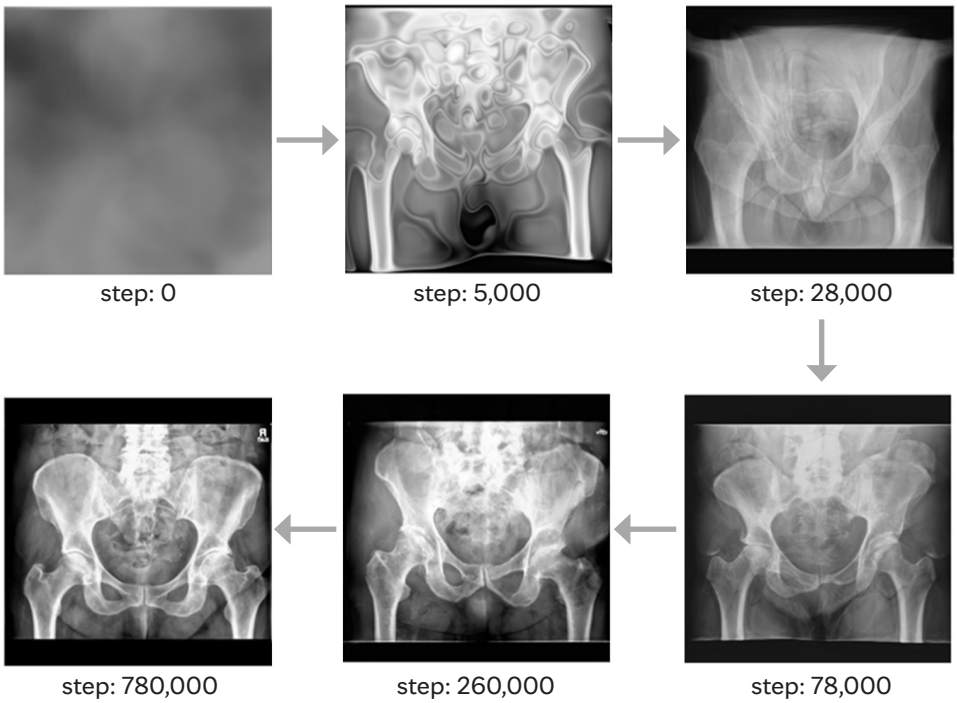



**Figure 1.** Fully synthetic pelvis radiograph constructed from a generative adversarial network. Evolution of the model's output quality during training steps from 0 to 780,000 after being trained on 25 million images.

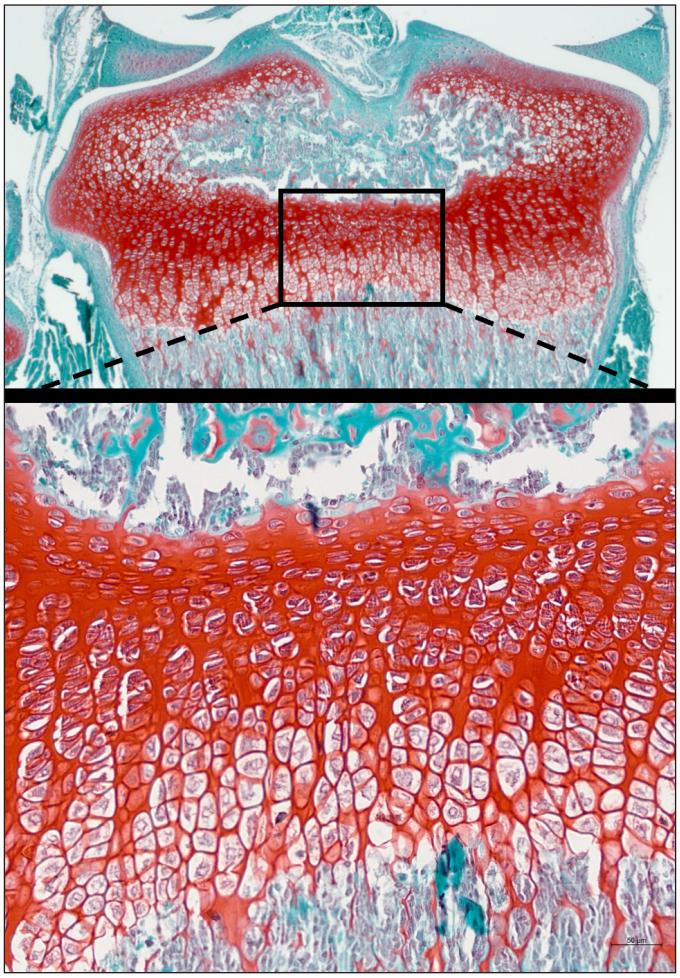
## SKELETAL DEVELOPMENT AND REGENERATION RESEARCH LABORATORY

**Principal Investigator: Jennifer J. Westendorf, Ph.D.**

The Skeletal Development and Regeneration Research Laboratory directed by Jennifer J. Westendorf, Ph.D., studies the molecular underpinnings of musculoskeletal diseases like OA, osteoporosis, and cancer-associated bone disease. Research in the lab focuses on the cellular, molecular, and epigenetic bases for skeletal formation, bone and cartilage regeneration, and primary and metastatic bone tumors. Our research aims to identify cellular events and molecules whose activities could be modified to improve bone and joint health.

Current projects in the lab focus on the role of phosphatases Phlpp1/2, the potassium channel Girk3, and the histone deacetylase Hdac3 in bone and cartilage development and repair. We have found that Phlpp1 deletion stunts skeletal growth and prevents injury-induced OA, as measured by cartilage structure and stiffness and functional behavior. The lab received new grants to fund reasearch to determine how Phlpp1 and Phlpp2 contribute to temporary and permanent cartilage development, mechanical integrity, and regeneration, as well as pain-related behaviors and sensory neuron innervation in OA models. We are also developing novel OA therapeutics based on PHLPP inhibitors. A second line of research identified the potassium channel subunit Girk3 as a regulator of bone mass. Its deletion induces bone mass accrual after skeletal maturity. We are currently identifying the mechanisms for this increased bone mass and determining if Girk3 deletion prevents ovariectomy-induced bone loss. A third line of research in the lab focuses on Hdac3 and the mechanisms by which it regulates bone density, bone marrow adiposity, and cellular senescence in the skeleton.

**Figure 1.**

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## TENDON AND SOFT TISSUE BIOLOGY LABORATORY

**Principal Investigator: Peter C. Amadio, M.D.**

Dr. Amadio's research interest is the role of tendon injury and degeneration in the hand. This has led to a series of investigations over the years, starting with ways to improve repair and rehabilitation of tendon injuries in the fingers; tissue engineering to speed tendon healing and reduce scarring around tendons after injury and repair; the role of fibrosis around tendons in the cause and progression of carpal tunnel syndrome (CTS); and, most recently, ultrasound imaging of tendon function in the hand and the potential to use ultrasound images of tendon and nerve motion, size, and shape as imaging biomarkers to predict outcomes and guide treatment for patients with CTS and other hand problems. While Dr. Amadio continues to serve as a collaborator, major work initiated in the Tendon and Soft Tissue Biology Laboratory (TSTB) lab is currently being carried out primarily by former students who are now themselves Mayo faculty and funded investigators: Chunfeng Zhao, M.D. (tendon reconstruction) and Anne Gingery, Ph.D. (cellular senescence and its effect on CTS and tendinopathy). As the nature of the work in the TSTB lab has changed, attention is now concentrated on new, more clinically focused areas:

1 A project to prepare a **bioengineered tendon lubricant**, initially developed with NIH funding for clinical use, for example to prevent adhesion formation after tendon repair, reconstruction, or tenolysis. This is being done in collaboration with Mayo's **Center for Regenerative Biotherapeutics**, which will initially manufacture the clinical-grade product. The short-term goal is an Investigational Device Exemption submission to the U.S. Food and Drug Administration (FDA) in early 2024, with hopefully a phase 1 clinical trial to follow. **(Figure 1)**

2 A clinical trial of **fisetin**, a senolytic supplement to treat CTS, based on the hypothesis that senescent cells in the tenosynovium within the carpal tunnel cause and drive the progression of CTS.

3 The use of **ultrasound shearwave elastography** to evaluate the function of the thenar muscles in patients with CTS and other hand disorders, and potentially to serve as a biomarker that might distinguish neuropathy and myopathy from disuse atrophy. (Figure 2) This would allow for a noninvasive and inexpensive tool—ultrasound—to diagnose and monitor a variety of common hand problems in the office setting.

4 The use of **dynamic 3D and 4D ultrasound** to monitor nerve function in patients with CTS, again using an office-based noninvasive modality to avoid or minimize the need for invasive, expensive, and painful electrophysiological monitoring.

5 Development of a new comprehensive **multimodality 3D atlas of hand anatomy**, updating the Visible Human Project with new high-resolution (10.5T) magnetic resonance imaging, 2D and 3D ultrasound, and high-resolution computerized tomography (CT) imaging to complement updated thin section visible imaging of the hand and wrist.

Investigation of a novel yet apparently ubiquitous anatomic finding of **fatty degeneration of the oponens pollicis muscle in patients with thumb base arthritis**.

TSTB funding comes from various sources, including DoD and NIH grants; grant support from the **Mayo Kogod Center for Aging Research, the Mayo Ultrasound Research Center**, and generous support from Mayo benefactors.

**Figure 1.**

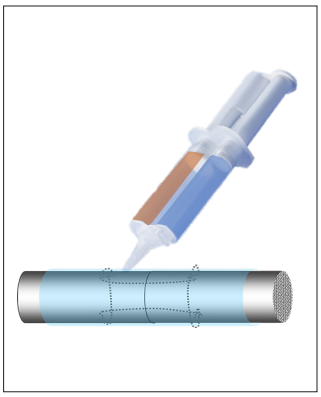
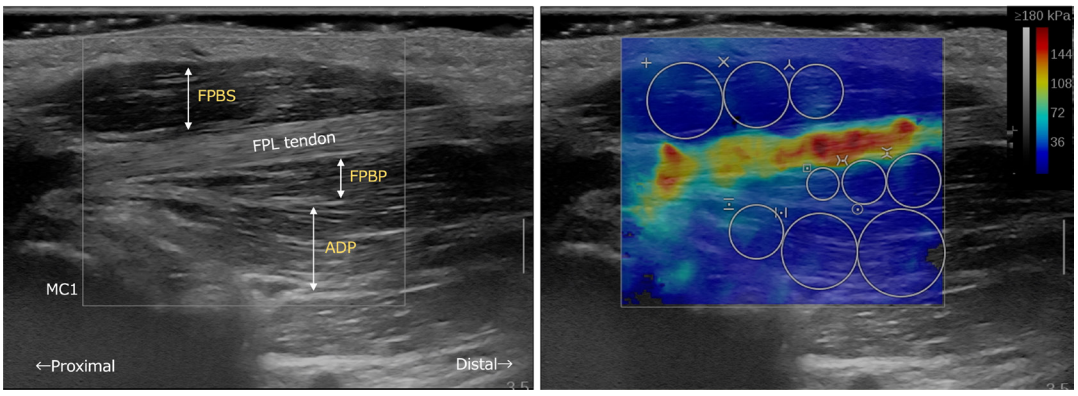


**Figure 2.**



## BIOMECHANICS CORE LABORATORY

**Director: Chunfeng Zhao, M.D.**

The Mayo Clinic Biomechanics Core Facility provides a biomechanics platform and service to support and promote innovations in clinical practice, research, and technological development for all investigators within and outside Mayo Clinic. This Core Facility offers a complete range of services to suit the biomechanics testing needs of its research and clinical collaborators and clients, including study design and protocol development, mechanical testing, and data analysis.

The experience and expertise of the Biomechanics Core include work with cadaveric, animal, and other biological tissues as well as synthetic materials such as arthroplasty devices and tissue scaffolds. This diverse skill and knowledge set enables us to conduct research ranging from microscale analysis, such as histological measurements of decalcified bone, to complex macroscale work, such as bio-robotic investigations of joint function following surgical intervention. Our innovative capabilities include strength and compliance testing of biological materials and implants, structural deformation testing quantified using 3D digital image correlation and optical metrology, microscale characterization using reference point indentation and nanoindentation, FDA-recognized implant wear testing, and hard tissue and metal implant histology. In 2023, the core's work included collaborations with 12 orthopedic surgeons on projects funded by the NIH, DoD, the Mayo Clinic Department of Orthopedic Surgery, and external industry. Projects in 2023 included studies of the spine, hip, knee, elbow, and shoulder as well as biomaterials and implants. Looking forward to 2024, the Biomechanics Core plans to continue to grow its capacity for rapidly translating biomechanical function into clinical practice as well as its ability to better match its soft and hard tissue microscale testing to the demands of current investigators.

**Figure 1.**



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## AMERICAN JOINT REPLACEMENT RESEARCH COLLABORATIVE (AJRR-C)

**Investigators: Daniel Berry, M.D., David Lewallen, M.D., Hilal Maradit Kremers, M.D.**



The American Joint Replacement Research-Collaborative (AJRR-C) is a NIAMS-funded (P30AR076312) Core Center for Clinical Research (CCCR) in total joint arthroplasty (TJA). AJRR-C is led by Directors Dr. Daniel Berry (left), Dr. David Lewallen (center), and Dr. Hilal Maradit Kremers (right), in partnership with the American Academy of Orthopaedic Surgeons (AAOS) and the American Joint Replacement Registry (AJRR). AJRR-C facilitates innovative, methodologically rigorous, and interdisciplinary clinical research that will directly improve the outcomes for TJA patients. The AJRR-C is exclusively focused on TJA research and provides methodological expertise, education, and data resources for developing future TJA clinical projects and improving translation of effective practices into patient care.

The AJRR-C Mayo team provides methodological support and consultation services to the analytics staff at AJRR, through the AAOS Registry Analytics Institute® (RAI) and preparation of the AJRR annual reports. Our team participates in the review of the AJRR studies to ensure application of state-of-the-art analytical methodologies for success of each study.

AJRR-C team members at Mayo Clinic and the AAOS collaborate in creation of the infrastructure for registry-nested prospective studies. Our recent efforts focused on establishing the infrastructure for a nested RCT for extended antibiotic prophylaxis in high-risk TJA patients (PI: Dr. Nicholas Bedard). The infrastructure efforts consisted of optimization the dataflow pathways between institutions and AJRR to accommodate prospective data collection, modifications to AJRR data storage, and development of standardized clinical trial agreements and statements of work to be utilized not only for the initial nested trial but for all future nested studies within the AJRR network of hospitals. Our team also worked in partnership to create a preliminary plan for a multi-center data validation of AJRR data.

AJRR-C Mayo team provides numerous education opportunities for the nationwide TJA research community. A series of statistical methodology papers are published in the Journal of Arthroplasty and the web-based educational videos are hosted on the AJRR-C YouTube channel. These educational modules include 18 videos that cover the topics of survivorship analysis, observational study designs and data collection, common biases in TJA research, PROMs, artificial intelligence, machine learning, natural language processing and computer vision. These videos are being used at Mayo Clinic for clinical research training of residents and fellows.

AJRR-C established a Registry Research Fellowship program in collaboration with the AJRR and provided funding for the first fellowship year begin in August 2023 with Josh Rozell, M.D. as the inaugural Fellow. AJRR-C also funded 4 pilot grants to date to internal and external TJA researchers.

As we move into 2024, AJRR-C team looks forward to the successful renewal of the grant. We continue to disseminate educational materials to other institutions and develop additional educational material on advanced clinical research methods. We aim to sponsor two Research Fellowships at the AJRR and fund two pilot and feasibility studies each year. Our AJRR-C partners at AJRR focus on linkage with additional private payor and Medicaid databases, standardization and validation of TJA-specific data elements and analytical tools, disparities research, increasing the network of collaborators focused on EHR data sources, and initiation of additional registry-nested clinical trials in collaboration with major orthopedic societies (AAOS, AAHKS, Hip Society, Knee Society, OREF).

**Website:** American Joint Replacement Research-Collaborative (AJRR-C) (americanjointreplacementresearchcollaborative.org)

## Clinical Research Programs

Ranked among the top surgical specialties at Mayo Clinic.

"There are two objects of medical education: To heal the sick and to advance the science."

— Charles H. Mayo, M.D.

## DIVISION OF FOOT AND ANKLE SURGERY

**Division Chair and Division Research Director: Daniel B. Ryssman, M.D.**

The Division of Foot and Ankle Surgery at Mayo Clinic Rochester focuses on comprehensive, collaborative, and fully integrated patient care for both nonsurgical and surgical treatment of foot and ankle problems. The division integrates both research and cutting-edge technologies to address our patients' needs.

Elizabeth Bondi, D.P.M., is the newest addition to the division and focuses on various nonsurgical treatment modalities for the foot and ankle. Her research direction involves forensic gait analysis, electromagnetic transduction therapy (EMTT), and shockwave therapy.

She is currently studying the various applications and outcomes on EMTT and shockwave therapy for numerous foot and ankle problems, including plantar fasciitis, Achilles tendinopathy, and sports injuries. In a short time, Dr. Bondi has proven to be a valuable team member for our patients and research involving nonsurgical foot and ankle care.

The division's orthopedic foot and ankle surgeons have a history of studying various clinical outcomes following surgery. They will continue to apply up-to-date surgical techniques for patients and study meaningful outcomes. Moving forward, the division is studying the outcomes of surgical treatments for ankle arthritis (ankle fusion and ankle replacement) and of complex deformity correction, as well as the efficacy of a collaborative approach to sports injuries (such as chronic exertional compartment syndrome and talus osteochondral defects).

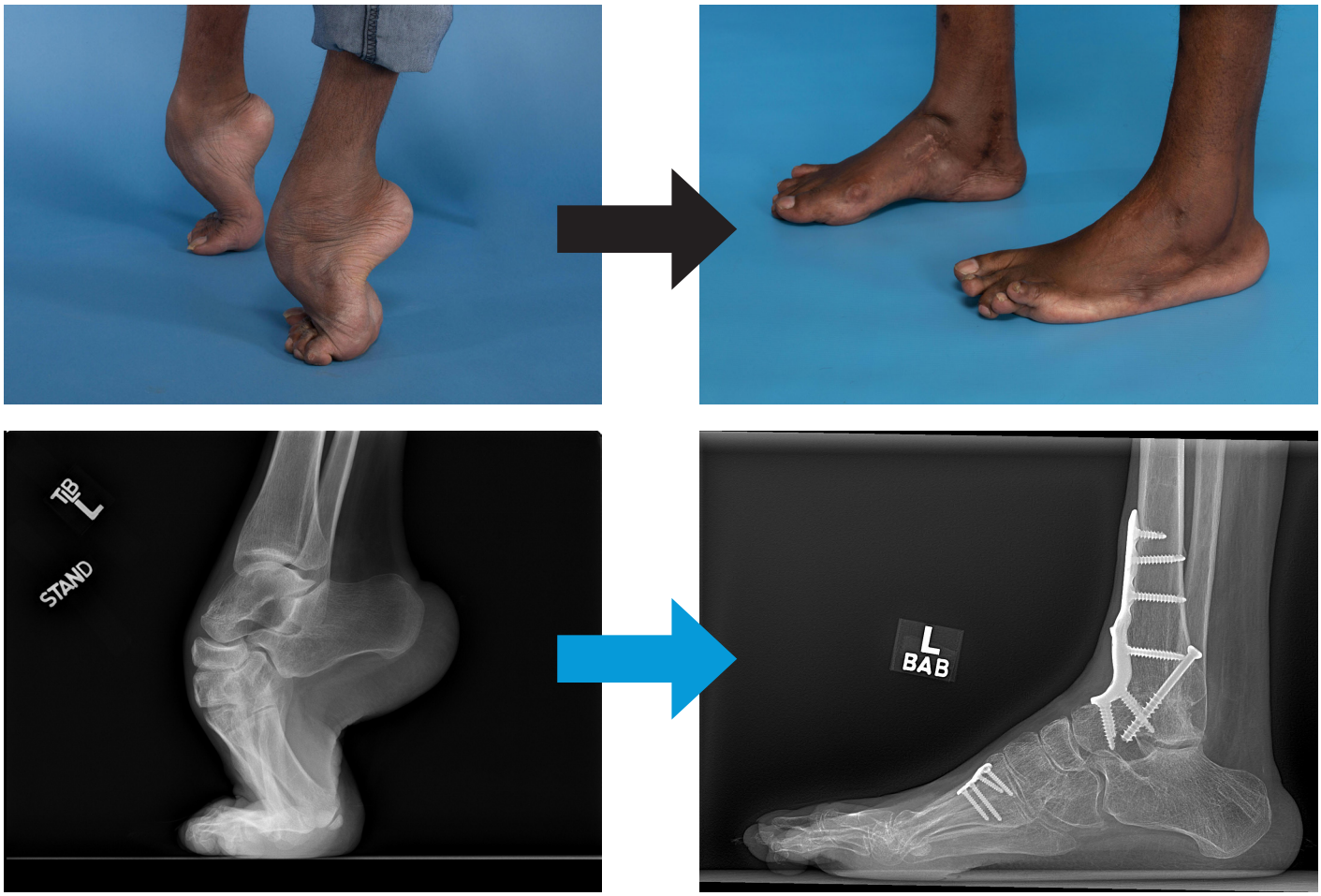



**Figure 1. Patient before and after a complex deformity correction.**

## DIVISION OF HAND SURGERY

**Division Chair: Marco Rizzo, M.D.**

**Division Research Director: Nicholas Pulos, M.D.**

The Division of Hand Surgery is a multidisciplinary group of orthopedic, plastic, and neurosurgeons as well as physical medicine and rehab physicians. There are currently 10 full-time hand surgeons in Rochester specializing in rheumatoid and degenerative arthritis, athletic injuries of the hand and wrist, congenital differences, spasticity, and peripheral nerve. The division remains a leader in more common hand and wrist pathology, with active clinical trials in the treatment of trigger fingers, CTS, flexor tendon repair, and basilar thumb arthritis. The division's mission is to advance the science of hand surgery care through innovative and ethical state-of-the-art research, helping us to provide the best possible care for our patients.

### Rethinking injections in the hand

The thumb carpometacarpal joint Is the most common site for degenerative arthritis in the hand. Surgical treatment varies widely, even among the cohort of surgeons practicing in Rochester. Nonsurgical treatment, however, is more standard with splinting and injections playing a role in the initial treatment of these patients. To avoid the side effects of corticosteroids, there has been interest in using intra-articular nonsteroidal anti-inflammatory injections for OA in other joints such as the hip, knee, and shoulder. Drs. Marco Rizzo, Kitty Wu, and the team are currently enrolling patients in a double-blind, randomized, controlled trial comparing ketorolac and triamcinolone to improve thumb base arthritis symptoms.

### Two Approaches to Spasticity

Injuries to the brain and spinal cord can result in both muscle weakness and spasticity. Dr. Peter Rhee is one of only a few hand surgeons in the country who treats patients suffering from the sequela of these types of injuries. Through hyperselective neurectomy, Dr. Rhee alters the underlying mechanism of spasticity by dividing most of the nerves that send impulses to the muscles, thus decreasing spasticity while maintaining strength. Dr. Rhee is currently performing an innovative prospective trial to better understand the changes to the architecture and gene expression of spastic muscles. Additionally, he is comparing the outcomes of hyperselective neurectomy and more traditional muscle-based procedures to determine the most effective procedure to improve patients' quality of life and function.

### Adult manifestation of congenital hand differences

Mayo Clinic remains a leader in the treatment of children with hand injuries and congenital hand differences both in Rochester and through outreach at Shriner's Hospital and Gillette Children's Hospital in the Twin Cities. Madelung deformity, which is caused by asymmetric growth of the distal radial physis, can be treated in young children with ligament release and removal of physial bars, but also through a corrective osteotomy in skeletally mature individuals. Drs. Steven Moran and Nicholas Pulos are uniquely able to follow these children into adulthood. They are currently surveying patients to understand how early surgical treatment for Madelung deformity affect these individuals later in life.

**Figure 1.**

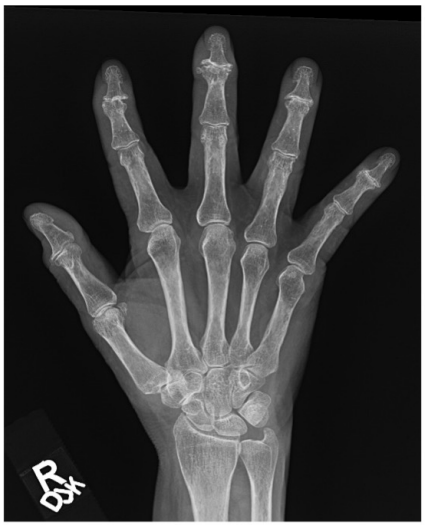
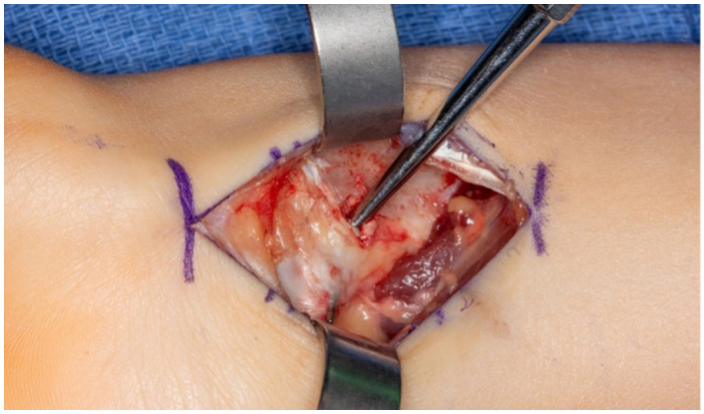


**Figure 2.**



## DIVISION OF HIP AND KNEE SURGERY

**Division Chair: Rafael J. Sierra, M.D.**

**Division Research Director: Matthew P. Abdel, M.D.**

The Division of Hip and Knee Surgery was again extremely successful academically, with a major presence in regional, national, and international meetings. The division published 191 peer-reviewed publications with a mean of 15 articles per consultant. The division continues to have members who are principal investigators on a NIH R01, a NIH P30 and projects within the NIH P30, co-principal investigators in NIAMS and DoD-funded grants, and investigators in multiple other industry and foundation grants. In 2023, Hip and Knee division members received awards from The Hip Society and The K nee Society.

The 2023 Annual Meeting of the American Academy of Orthopedic Surgeons was extraordinarily successful for the division. Division members had 11 podium presentations, 18 poster presentations, 11 traditional instructional course lectures, four case-based instructional course lectures, five symposia, one orthopedic showdown session, 17 specialty day sessions, and one OrthoDome presentation amongst a variety of other academic, research, leadership, and industry obligations.

The 2023 Annual Meeting of the AAHKS was equally successful for the group. Matthew Abdel, M.D., was elected as third vice President of AAHKS, and the group gave five podium presentations and 16 poster presentations, participated in all pre-courses and ask the experts sessions, and moderated five AAHKS symposia. In addition, many members of the division participated in other academic, research, leadership, and industry functions.

Research worth highlighting includes The Knee Society's Chitranjan S. Ranawat Award for the paper "Manipulation Under Anesthesia (MUA) to Treat Postoperative Stiffness after Total Knee Arthroplasty: A Multicenter Randomized Clinical Trial." This paper XX. In addition, researchers from the Hip and Knee Division were awarded The Hip Society's 2024 Frank Stinchfield Award for the paper "Assembly and Dissociation Forces Differ Between Commonly Used Dual Mobility Implants: A Biomechanical Study," which reported on the dissociation forces needed to disassemble modern highly cross-linked and vitamin E doped, dual mobility implants.

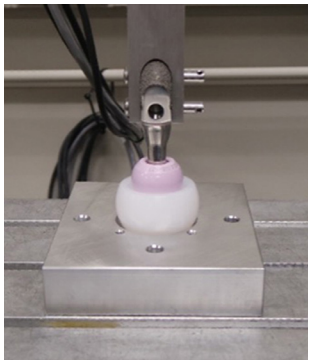
OSAIL, led by Cody C. Wyles, M.D., and Michael J. Taunton, M.D, had an extremely busy and successful year. Over the last year, OSAIL published 25 peer-reviewed articles in top orthopedic surgery, radiology, and informatics journals. Additionally, OSAIL presented works at several top national conferences and received three awards at conferences for Best Paper, Best Poster, and Best Project by a Trainee.

Nicholas A. Bedard, M.D., in collaboration with Robin Patel, M.D., from the Division of Infectious Disease at Mayo Clinic, has studied in a murine model of knee arthroplasty the impact of prophylactic antibiotic duration on PJI prevention and are exploring the role of phage therapy for treatment of biofilms that develop in their PJI murine model. This murine model will allow for the study of multiple facets of PJI with the hopes of translating these to clinical practice.

Charles P Hannon, M.D., recently collaborated with AAHKS and the American College of Rheumatology to publish the Optimal Timing of Total Hip and Knee Arthroplasty Clinical practice guideline for patients for whom nonoperative management is ineffective.

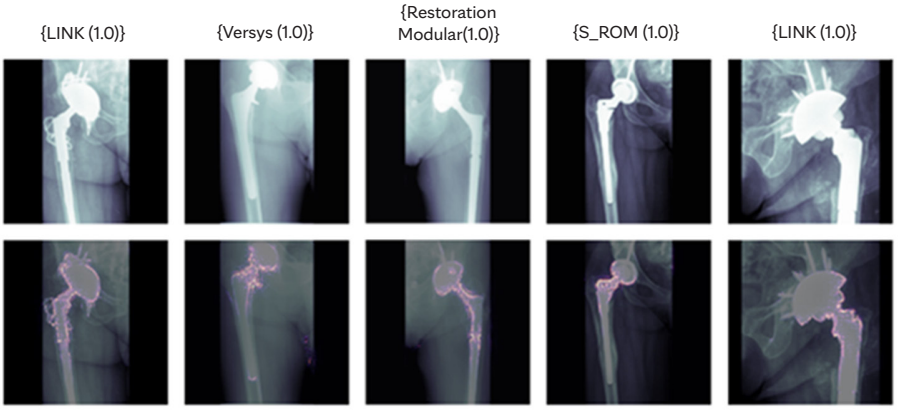
Finally, members of the Hip and Knee division, in collaboration with the ANCHOR group and first author John C. Clohisy were awarded with the 2024 Kappa Delta Lanier Award, for their work on "Development and Implementation of a Roadmap for Improving Quality of Care in Pre-Arthritic Hip Disease: A Journey Over 20 Years."

**Figure 1.**



Biomechanics Fixture prepared for testing Dual Mobility Dissociation. The study was awarded with the Stinchfield award from the Hip Society.

**Figure 2.**




THA-AID identifies THA Implants on postoperative radiographs with 99% accuracy for both femoral and acetabular components and works equally well on AP, lateral, and oblique view.

## DIVISION OF ORTHOPEDIC ONCOLOGY

**Division Chair: Peter S. Rose, M.D.**

**Division Research Director: Matthew T. Houdek, M.D.**

The Mayo Clinic Orthopedic Oncology Division continued its tradition of multidisciplinary care and research in 2023. This year provided the highest total case number of our division ever, with 762 primary cases and 128 secondary cases among the division surgeons. The secondary case volume is equally important to the primary case volume, as these represent our multidisciplinary collaboration throughout the institution to care for patients whose tumors impact musculoskeletal structures. Our most frequent collaboration is with colleagues in Colorectal Surgery for complex, curative intent resections of locally advanced colorectal malignancies.

The Oncology Division Team continued to lead internationally with collaborative research within and beyond Mayo. Members of the division published 38 articles in the medical literature, authored two book chapters, and presented 17 works at national and international conferences. A particular recent focus has been Dr. Houdek's work on scapular resections and reconstructions, forwarding a new evidence-based classification to guide treatment and predict outcomes in patients receiving these procedures.

The influence of the division is widely felt. Dr. Houdek serves as the invited North American co-chair of the international consortium to define standards in the care of chondrosarcoma and serves as the section co-editor for the journal Cancers; he additionally reviews for 15 other peer-reviewed publications. Dr. Rose continues as the editor-in-chief of the *Journal of the American Academy of Orthopaedic Surgeons* and as an elite reviewer for the Journal of Bone and Joint Surgery. Perhaps most impactfully in Rochester, Dr. Houdek was honored as Teacher of the Year by the Mayo Orthopedic Residents.

Moving forward, our division is engaged in the Bold, Forward initiative at Mayo to increase the integration of cancer care for patients in Rochester and around the world. Current efforts look to harness AI to predict wound complications around soft tissue sarcoma resections, a major source of morbidity and to continue our strong clinical tradition of sacropelvic tumor resections. Our goal is to positively impact the care of our patients and those worldwide with difficult cancer presentations. We are welcoming Ms. Leilani Garaya-Cruz as a medical student researcher to spend a year immersed in the division and look forward to her contributions as well.

**Figure 1.**

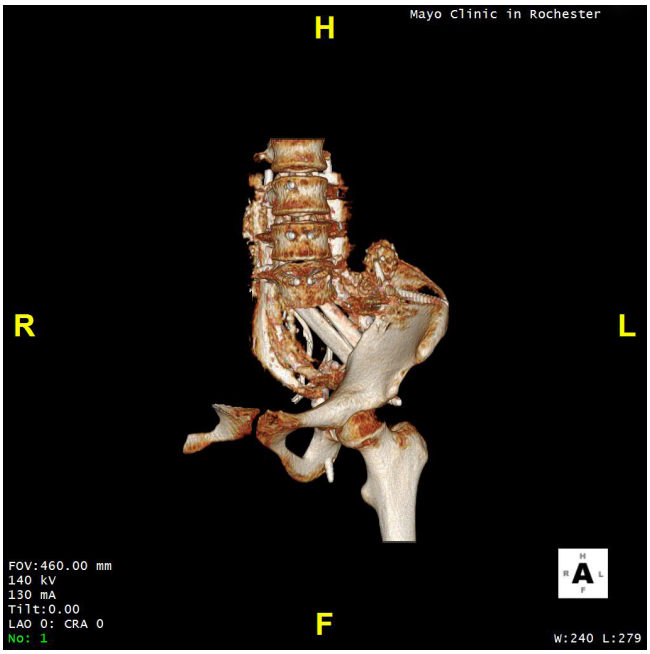
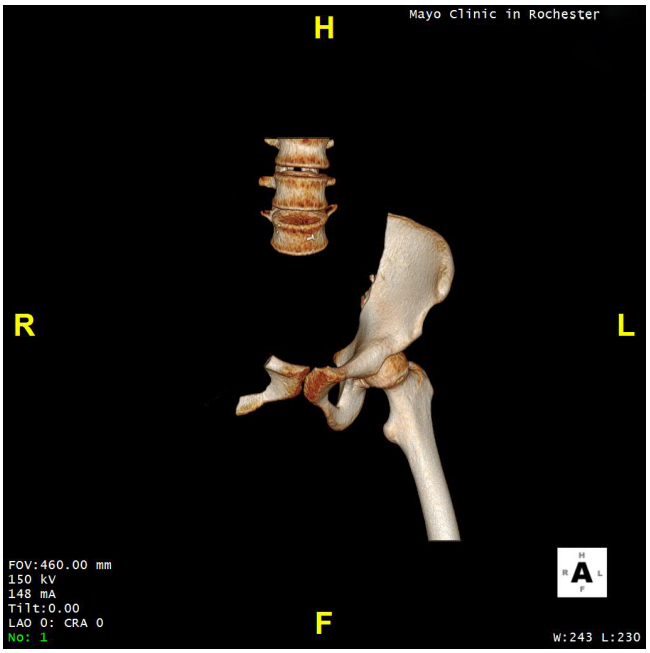



**Figure 2.**



## DIVISION OF ORTHOPEDIC TRAUMA

**Division Chair: Brandon J. Yuan, M.D.**

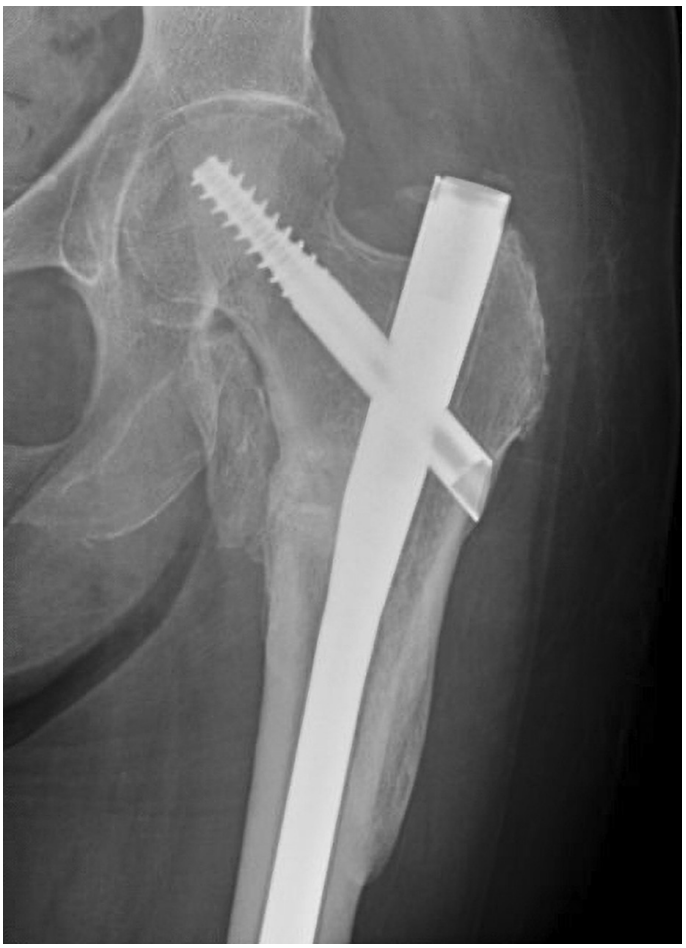
**Division Research Director: Jennifer Tangtiphaiboontana, M.D.**

The Mayo Clinic Orthopedic Trauma Service prioritizes the care of the acutely sick and injured in and around the Southeast Minnesota region. For over 20 years, the Orthopedic Trauma Service has tracked and collected data on outcomes of surgical treatment of a multitude of different fractures, and analysis of this data has led to continued improvements in patient care.

Several projects to highlight include high-quality prospective research studies, including a randomized study on the use of tranexamic acid at the time of initial evaluation for patients with intertrochanteric hip fracture. The results of the study were presented at the 2023 Orthopaedic Trauma Association meeting and won the "Resident Paper Memorial Award," which is given to the best resident lead study and podium presentation. Dr. Krystin Hidden was also awarded the $200,000 Benefactor Career Development award to support her project on gait analysis after surgical treatment of distal femur fractures and the $65,000 Foderaro-Quattrone Grant for AI Innovation in Orthopaedic Surgery for her study on chest X-ray findings to help predict hospital disposition and morbidity in hip fracture patients. The Orthopedic Trauma Service is also involved in a multicenter randomized trial looking at single versus dual implant fixation of distal femur fracture and outcomes of time to surgery for hip fractures.

Additionally, the Orthopedic Trauma Service has collaborated with the Hip and Knee Division and the Shoulder/Elbow Division on several projects. Together, they have worked together to answer questions about periprosthetic fractures, infections, and acute fractures. Their collaboration has led to new ideas and perspectives and a better understanding of how to describe and manage these complex injuries.

**Figure 1.**



The Orthopedic Trauma Service is working with the Department of Orthopedic Surgery at Mayo Clinic to modernize and expand the collection of data on surgical and patient-centered outcomes for our patients. Using computer algorithms and machine learning, we hope to create a more complete picture of the effect of trauma on our patients going forward, yielding additional insights that will help improve surgical treatments for all patients in the future.

## DIVISION OF PEDIATRIC ORTHOPEDICS

**Division Chair: Todd A. Milbrandt, M.D.**

**Division Research Director: A. Noelle Larson, M.D.**

The Pediatric Orthopedic division at Mayo Clinic Rochester performs class-of-one research to advance care for children with musculoskeletal disease, with a focus on spine, trauma, and hip conditions. In 2023, our group completed our first vertebral body tethering procedure using a new, thicker cord designed to prevent loss of correction over time. Our group was among the first in the U.S. to have access to this device, and our FDA post-approval registry to study this device is now open. We are one of the few centers offering all three novel motion-sparing scoliosis surgeries through the U.S. FDA Humanitarian Device Exemption. We hosted many visiting surgeons in 2023 who were interested in this novel technology, including five Scoliosis Research Society (SRS) traveling fellows and SRS Emerging Technologies Fellow Alice Baroncini, M.D., who selected Vancouver, BC, and Mayo Clinic as the two sites to visit for her learning program and spent two weeks learning about motion-sparing scoliosis surgery.

Another goal of our group is to hasten the development of automated registries and develop scalable tools that can be used to process and study large imaging registries. Dr. Larson presented Deep Learning Classification of Spinal Radiographs for Use in Large Scale Imaging Registries at the awards session at the Annual Meeting of Pediatric Orthopaedic Society of North America, which was funded by the Angela S.M. Kuo Memorial Award. With the Mayo Orthopedic AI Lab, we developed an automated measurement tool to calculate the angle subtended by the vertebral body tethering screws. This provides us with a fast and reliable way to process large radiographic databases to measure curve correction over time. With our scientific collaborations, we aim to leverage artificial intelligence and deterministic biomechanical principles to aid in preoperative spine modeling and risk prediction to improve the outcomes of scoliosis surgery.

**Figure 1.**

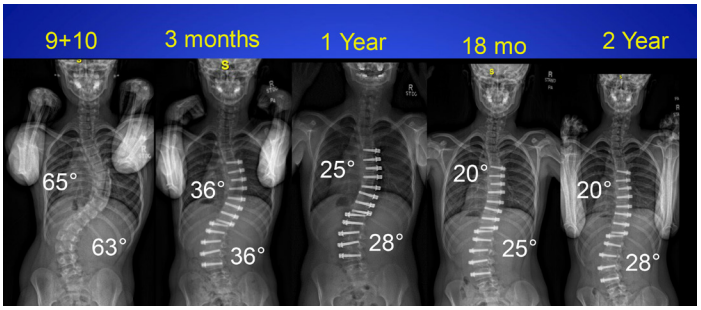
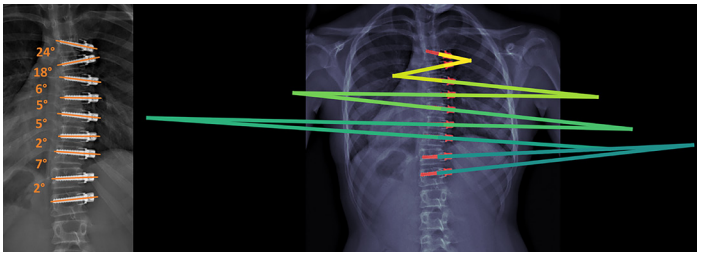



**Figure 2.**




Our group participates in the Pediatric Spine Registry, Harms Study Group Registry, Setting Scoliosis Straight Surgeon Performance Program, and the International Perthes Registry. Dr. Milbrandt is Vice-President of the Pediatric Orthopedic Society of North America. Dr. Larson served as program chair at the International Congress on Early Onset Scoliosis, attended by surgeons from 21 different countries. By serving as international leaders in research and education we can drive the science forward to find new cures for our patients at Mayo and beyond.

### Research Highlights

**38** peer-reviewed publications

**48** national/international research presentations

**3** national society board memberships

Mulford KL, Regan C, Nolte CP Jr, Pinter ZW, Milbrandt TA, Larson AN. Automated measurements of interscrew angles in vertebral body tethering patients with deep learning. Spine J. 2024 Feb;24(2):333-339. doi: 10.1016/j.spinee.2023.09.011. Epub 2023 Sep 27. PMID: 37774982.

## DIVISION OF SHOULDER AND ELBOW SURGERY

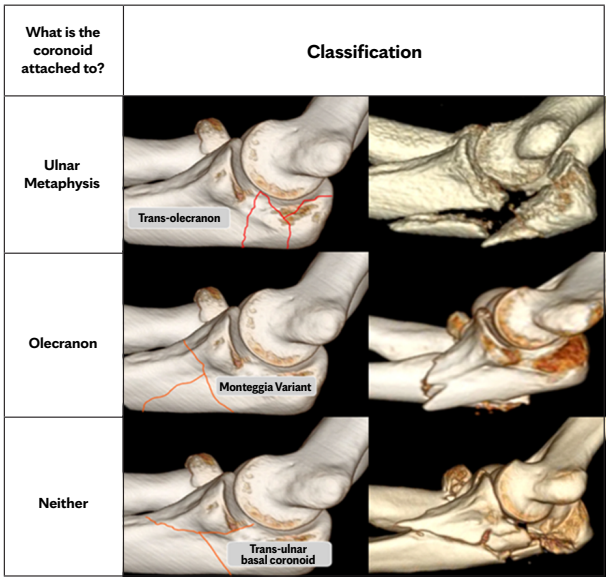
**Division Chair and Division Research Director:**
**Joaquin Sanchez-Sotelo, M.D., Ph.D.**

For the Division of Shoulder and Elbow Surgery at Mayo Clinic Orthopedics in Rochester, 2023 was a very productive research year. All members of our division (Drs. Sanchez-Sotelo, O'Driscoll, Sperling, Morrey, Camp, and Barlow) published numerous research projects in peer-reviewed journals and presented at national and international meetings.

**Shoulder arthroplasty.** Our Division led a multicenter study that for the first time proved the accuracy of mixed reality navigation for shoulder arthroplasty **(Figure 1)**. Research from our Division provided original information on various other topics, including the comparative long-term outcome of hemiarthroplasty for acute fracture and fracture sequelae, the comparative outcome of hemiarthroplasty and total shoulder arthroplasty in B2 glenoids, the higher risk of infection when vancomycin is administered incompletely, the outcome of arthroplasty on sickle cell disease, the influence of preoperative anemia on complications of shoulder arthroplasty, and the outcome of shoulder arthroplasty in patients with prior stroke, prior radiation, and prior bariatric surgery.

**Rotator cuff and shoulder instability.** Our focus this year was to understand the relative value and indications of superior capsule reconstruction and transfer of the lower trapezius **(Figure 2)**. We also published on the outcome of rotator cuff repair in inflammatory shoulders, a systematic review on both lower trapezius and latissimus dorsi transfer for the irreparable cuff tear, an update on the role of the subacromial balloon, surgery for shoulder instability in a large cohort of patients with underlying seizure disorders, as well as surgery for patients older than 50 with shoulder instability.

Figure 1.

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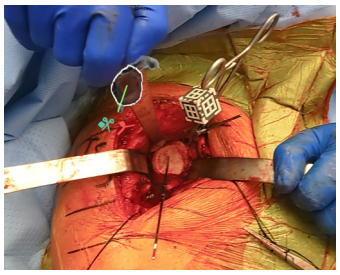
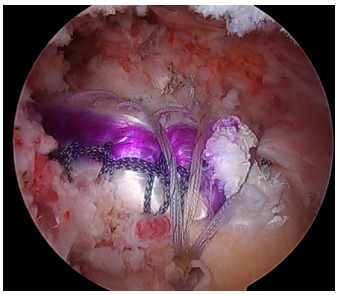
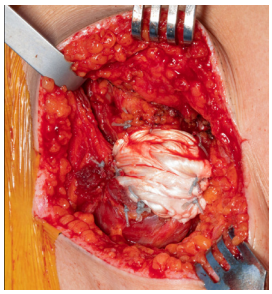


Figure 3.





**Elbow surgery.** A major focus area of our division was centered around understanding transulnar fracture dislocations **(Figure 3)**: in close collaboration with the Division of Orthopedic Trauma, a new Mayo classification was developed and validated, and we also completed a systematic review on reported outcomes of surgical management by category. We also reported on a very complex group of patients presenting with almost no remaining humeral bone stock after failed elbow arthroplasty requiring reconstruction with large humeral allograft from an anterior approach. Other studies analyzed the higher risk of infection after elbow arthroplasty when cefazolin is not used prophylactically, the safety of intraoperative modification of elbow arthroplasty implants, the long-term fate of partial thickness distal biceps tendon tears, the long-term outcome of arthroscopic debridement for elbow OCD, the comparative outcome of surgery versus nonoperative treatment for elbow OCD, baseball performance, and new data on the biomechanics of elbow instability.

**AI.** One of our most relevant studies used machine learning to help identify subscapularis tears. Another foundational AI study led to a pipeline to automatically classify reverse shoulder X-rays. To help the busy shoulder and elbow surgeon understand the new field of AI, our division also summarized in a comprehensive review article current AI clinical applications, as well as the rising number of publications in the field. One of our AI projects also identified risk factors for early reoperation due to reverse dislocation.

## DIVISION OF SPINE SURGERY

**Division Chair: Brett A. Freedman, M.D.**

**Division Research Director: Arjun S. Sebastian, M.D.**

The Division of Spine Surgery at Mayo Clinic had a very productive research year in 2023. All members of our division participated in numerous projects, resulting in 35 peer-reviewed publications. Division members also presented work at several prestigious national and international society meetings, including the Cervical Spine Research Society, Lumbar Spine Research Society, Scoliosis Research Society, North American Spine Society, AO Spine North America, American Academy of Orthopaedic Surgeons, and the International Society for the Study of the Lumbar Spine. Research from the spine division has been recognized for best paper awards at Cervical Spine Research Society as well as the North American Spine Society.

**Prospective clinical trials.** Currently the division is leading the way nationally to investigate new motion-sparing technologies for the spine. This includes the recently completed Total Posterior Spine System trial, led by Dr. Ahmad Nassr, as well as the ongoing 3Spine trial. In addition, the group is collaborating in two prospective trials to evaluate bone biologics for spinal fusion, including the Ankasa trial led by Dr. Freedman and the ongoing Medtronic Investigational Device Exemption trial. In addition, Dr. Sebastian is actively enrolling patients in the SPY wound angiography trials to identify ideal closure techniques to optimize care for our patients with complex spinal disorders.

**Institutional and extramural funding.** The Division of Spine Surgery has been awarded several grants for its ongoing research. Dr. Huddleston and his team recently received institutional funding to improve the use of AI in assessing spinal radiographs and implants. Dr. Sebastian and his team received extramural funding to lead an educational trial to improve surgical skills for residents and fellows, in addition to extramural funding to create a database of spinal fusion cages to assess results and improve clinical outcomes. Dr. Sebastian and his colleagues also recently received institutional funding to study the impact of sacroiliac disease on long-segment spinal fusions. The group was again selected as a top-tier AO Spine-funded fellowship program, and our fellows each presented their research at the Banff Fellows Forum.

**Bone health.** The Division of Spine Surgery and our collaborators in the Department of Neurosurgery are fast becoming nationally and internationally recognized as experts in bone health optimization for spinal fusion surgery. We have developed and clinically validated approaches for best defining bone health in patients undergoing spine surgery, and just as importantly, demonstrating the efficacy of anabolic osteoporosis medications in reducing osteoporosis-related complications.

**Biomechanics.** We fostered national and international multicenter collaborations, including exciting, advanced imaging- based biomechanical assessment methods with investigators at the Imperial College London. We are also working with our Biomechanics team at Mayo Clinic to use finite element analysis to better understand the impact of our surgical intervention on spinal kinematics.

**Regenerative medicine.** Working collaboratively with our regenerative medicine research group in the Department of Orthopedics, the Division of Spine Surgery has been recently looking into the functionalization of spinal implants and bone grafts to improve the value of spine care. The division is also currently working to establish potentially better therapeutics for the management of degenerative disc disease.

**Figure 1. Schematic demonstrating the total posterior spine system device affixed to pedicle screws.**

## DIVISION OF SPORTS MEDICINE

**Division Co-Chairs: Daniel B.F. Saris, M.D., Ph.D., and Jacob L. Sellon, M.D.D.**

**Division Research Director: Daniel B.F. Saris, M.D., Ph.D.**

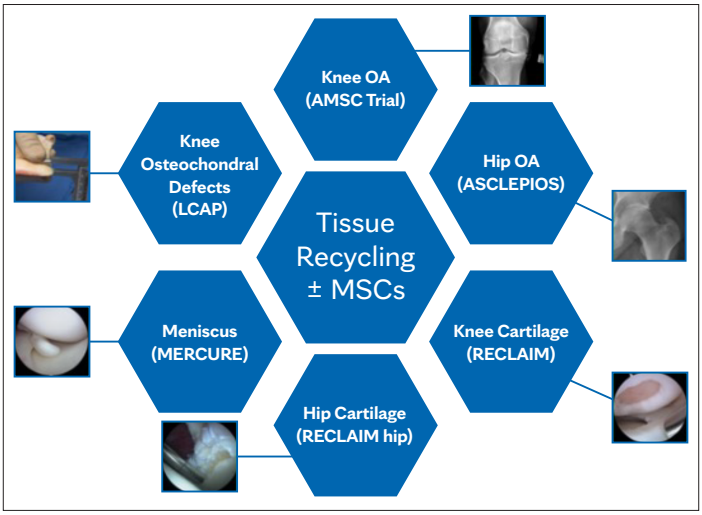
The goals of the Division of Sports Medicine are to provide world-class evidence-based clinical care, to conduct innovative translational research, and to deliver high-value education to our patients and trainees. Our passion and focus are to ensure that patients' needs come first and that our team works with our patients to help them achieve their goals of returning to their desired sports activities and lifestyle.


Our specialty clinics and research focus are closely connected, which enables effective translational innovation. Our collaborative, multidisciplinary teams of surgeons, physicians, researchers, nurses, physical therapists, and athletic trainers work together to address the unmet needs of our patients.

The year 2023 was highly productive for our team. We published over 140 peer-reviewed publications in high-impact journals and book chapters. We made important contributions to national and international research and educational events as educators and leaders in our respective fields. Our team has actively contributed to the mission of being a world leader in orthopedic care, innovation, research, and education.

In the field of injectable orthobiologics, we have a multitude of innovative ongoing clinical trials. We are studying the safety and effectiveness of autologous, culture-expanded MSCs for symptoms of knee and hip arthritis in early onset degenerative

**Figure 1.**




disease. We are investigating novel injectable solutions, such as alpha-2-macroglobulin-rich plasma and refining the use of established biological products like platelet-rich plasma, bone marrow aspirate concentrate, and microfragmented adipose tissue. This enables us to provide the best evidence-based advice to help patients on individually manage their care.

One of our innovative laboratory-to-clinical practice successes is the RECLAIM trial for cartilage repair in the knee. RECLAIM examines the safety and effectiveness of recycling cartilage from a patient's knee defect, combining them with allogeneic MSCs in a fibrin glue, and implanting this combination of cells back into the defect in a one-stage surgical procedure. The first clinical trial is supported by the Regenerative Medicine Minnesota program and the Mayo Clinic Transform the Practice Award. Our enrollment was completed, and we are continuing to follow up with our patients two years post-surgery. This RECLAIM approach has been expanded for application to the hip and is now being studied by our translational research team for meniscus and tendon repair.

In addition to our cell-based and regenerative medicine approaches, we are researching methods to improve meniscus preservation or replacement in various patient populations. The ongoing studies include examining the role of surgical meniscus root repair compared to conservative treatments and determining whether the novel concept of reducing the extruded meniscus by centralization technique with fixation is feasible, in addition to repairing the torn root or posterior horn tear.

## New Consultant Spotlight

**Mimi Sammarco, Ph.D.**

Dr. Sammarco joined the faculty in the Department of Orthopedic Surgery at Mayo Clinic in 2023. Her laboratory research focuses on the mechanisms underlying bone and soft tissue regeneration after amputation. Dr. Sammarco's research program is funded by the NIH and focuses on several different regenerative mechanisms and how they promote bone and soft tissue replacement with the objective of harnessing these mechanisms to develop regenerative therapies. Her lab seeks to understand how cell metabolism modulates bone and soft tissue regeneration in the limb (grant) R01HD107034). Drugs can be used to modulate cell metabolism and promote bone formation. Additionally, this bone formation needs to be in the correct place. These studies have expanded to understanding how cell metabolism not only replaces bone, but also plays a role in the shape, patterning, and location of the bone (grant R01HD112474). Her lab also investigates the role of sensory nerves in promoting limb regeneration. While motor neurons are known to have a huge impact on tissue regeneration, these studies seek to understand how sensory nerves, nerves not thought to be involved in regeneration, interact with neighboring cells to promote regenerative outcomes (grant R21HD106162). Dr. Sammarco is also working in collaboration to generate a finite element model to predict where bone regeneration will occur. Identifying where bone grows, and what gene expression is affiliated with this bone growth helps us develop therapies that will dictate where bone should form and generate stronger structures using gene-based mechanisms. These signals can then be harnessed to promote regenerative therapies (grant R03HD112824). Future directions aim to expand Dr. Sammarco's basic science research to translational approaches using the synergy of the Department of Orthopedics.

Dr. Sammarco received her bachelor's degree in cell and molecular biology and biochemistry from Colby College, and her Ph.D. in pathology from Louisiana State University Health Sciences Center. She completed her postdoctoral work at Tulane University before joining the Department of Surgery as an assistant professor at Tulane School of Medicine.

# T32 Musculoskeletal Research Training Program

**Director: Jennifer Westendorf, Ph.D.**

The goals of the T32 Musculoskeletal Research Training Program are to provide transdisciplinary research and training opportunities in musculoskeletal science and medicine to postdoctoral fellows, graduate students, and medical students and to train future leaders in musculoskeletal research.

Trainees participate in faculty-directed programs and acquire new skill sets that will differentiate them for long-term careers in musculoskeletal research. Cross-departmental opportunities are coordinated within collaborative faculty projects.

Multispecialty training experiences are deployed at various learner levels and rely on high-functioning teams to complement the ultimate learning experience.

**Areas of focus include** *biomechanics, bone biology, data sciences, joint tissue biology, orthopedic surgery, sports medicine, regenerative sciences, and skeletal muscle biology.*

# 2023 T32 Trainee Highlights

**Haydee Torres, Ph.D.**

I was born in the cultural melting pot of Miami, FL, as the youngest daughter of Cuban exiles. Until recently, I was a young trainee from a less familiar institute and studied rare bone disease, but I was inspired to pursue a position in Dr. Jennifer Westendorf's laboratory after getting to know her as a collaborator and because of her outstanding scientific contributions in skeletal development and regeneration. Mayo Clinic also happened to be an excellent place to pursue my training goals, as it is the top regional research and medical facility and a world-renowned leader in cutting-edge research. The NIH T32 at Mayo Clinic has allowed me to flourish as a scientist and opened many doors that will lead to exciting new opportunities in the future. In the year and a half that I have been a T32 fellow, I have been fortunate to receive honors including the American Society for Bone and Mineral Research (ASBMR) Young Investigator Award, the ASBMR THRIVE program, and LRP-REACH, an NIH Loan Repayment Program award. My project involves understanding how inhibiting PH domain leucine-rich repeat protein phosphatases reduces post-traumatic OA pain. This avenue of research will expand our understanding of why patients have varying experiences with OA pain and one day help guide clinician decision making. Overall, I am grateful to the T32 program, for I am surrounded by a strong team of researchers in supportive environment, as well as sophisticated laboratory equipment and resources, and an outstanding training environment with outstanding seminar series and career development opportunities.

**Erica Bell, Ph.D.**

I hold a B.S. in exercise physiology and completed my Ph.D. in bioenergetics and exercise science, both from East Carolina University.

Training at Mayo Clinic instills a patient-first culture, where patient-centered care is at the core of what we do in all three shields: clinic, research, and education. As a postdoctoral research fellow, my T32 appointment has allowed me to combine the "patient-first" and patient-specific focuses in my current project which utilizes novel 4DCT dynamic imaging and image processing techniques in the wrist to identify noninvasive methods to help design interventions and reduce secondary complications of OA. With the support of the NIH T32 Musculoskeletal Research Training program, I have been able to gain the necessary research and professional experience to help me develop a career researching topics that have the potential to produce direct functional outcomes in clinical practice and performance enhancement.

Beyond traditional research training, I am passionate about being a leader in advocating for DEI in STEM academic and research spaces. I am a cofounder of the Black Biomechanists Association, a certified nonprofit service-based organization with a mission to uplift and enrich Black biomechanists in their academic and professional careers. It is extremely important to not only advocate for my own career, but also to help pave a pathway to make academic and research spaces more accessible for Black students and scientists. I am thankful for the training and funding provided by the Musculoskeletal Research Training Program that has equipped me with a strong technical and professional skill set and the ability to thrive in environments working with diverse multidisciplinary teams.

# Orthopedic Surgery Research Gap-Year Program

**Medical Director: Christopher L. Camp, M.D**

In 2023, the Division of Orthopedic Surgery Research unveiled the Gap Year Research Program — a dynamic 12-month clinical research training initiative meticulously designed for second and third-year medical students with the first cycle beginning in 2024. This program introduces an exciting opportunity for exceptionally driven individuals to fortify their candidacy for the Orthopedic Surgery Match.

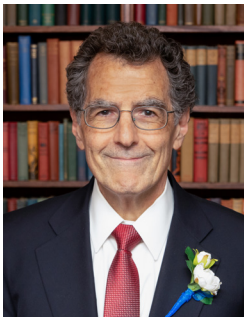
Participating students will embark on a journey of professional growth, guided by consultant mentors in Sports Medicine, Hip and Knee, Trauma, Shoulder/Elbow, Oncology, and Pediatrics. Within this immersive experience, a spectrum of research avenues are available, including project design, scientific literature exploration, data collection, and manuscript preparation.

Beyond the confines of traditional research, Gap Year Program students will have the opportunity to participate in a one-month clinical rotation, complemented by weekly didactic sessions spanning various disciplines within orthopedic surgery. This holistic approach aims to foster a robust foundation of knowledge, ensuring a comprehensive understanding of the field.

At the core of the Gap Year Program is a formalized curriculum led by distinguished Orthopedic Surgery faculty and featuring the three pillars of: Basics of Research, Leadership, and Orthopedic Career Mentorship. Within this program, passion meets purpose through a structured framework crafted to mold the Orthopedic Surgeons of tomorrow.

# Orthopedic Surgery Named Professors

**Matthew P. Abdel, M.D.**
Andrew A. and Mary S. Sugg Professor of Orthopedic Research



**Peter C. Amadio, M.D.**
Lloyd A. and Barbara A. Amundson Professor of Orthopedics

**Daniel J. Berry, M.D.**
L. Z. Gund Professor of Orthopedics

**Kenton R. Kaufman, Ph.D.**
W. Hall Wendel, Jr. Musculoskeletal Research Professor

**Jennifer J. Westendorf, Ph.D.**
Margaret Amini Professor of Orthopedic Regenerative Medicine Research

**Aaron Krych, M.D.**
John and Posy Krehbiel Professor of Orthopedics Honoring Bernard F. Morrey, M.D.

# Philanthropy

**Fueling the Future**

Musculoskeletal injuries and diseases are the leading contributor to disability in the world. The generosity of our benefactors delivers hope and healing for millions of people by making it possible for investigators to discover advancements that cure and prevent more of these conditions.

Mayo Clinic is not simply practicing at the forefront of musculoskeletal care. We are pushing the frontier forward. Fueled by benefactor generosity and confidence in our vision, Mayo Clinic's investigators are emboldened to transform healthcare for people around the world by:

**Advancing diagnostics and therapeautics**

**Leveraging advanced digital capabilities and data**

**Expanding clinical trials**

Generous benefactor funding helps support numerous research efforts throughout the Department of Orthopedic Surgery. Through this funding, the Department of Orthopedic surgery proudly funded 14 competitive research awards in 2023. These awards have become a pillar of support amongst our investigators, facilitating rapid access to funding to address strategically important research topics for orthopedic surgery. Opportunities such as these enable our team to drive transformation and rapidly translate research discoveries to patient care.

On behalf of our patients and people everywhere, thank you for your generosity and support.

For information on supporting Mayo Clinic, please contact the Department at **800-297-1185 or** mayoclinic.org/development

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MC2048-16rev042924