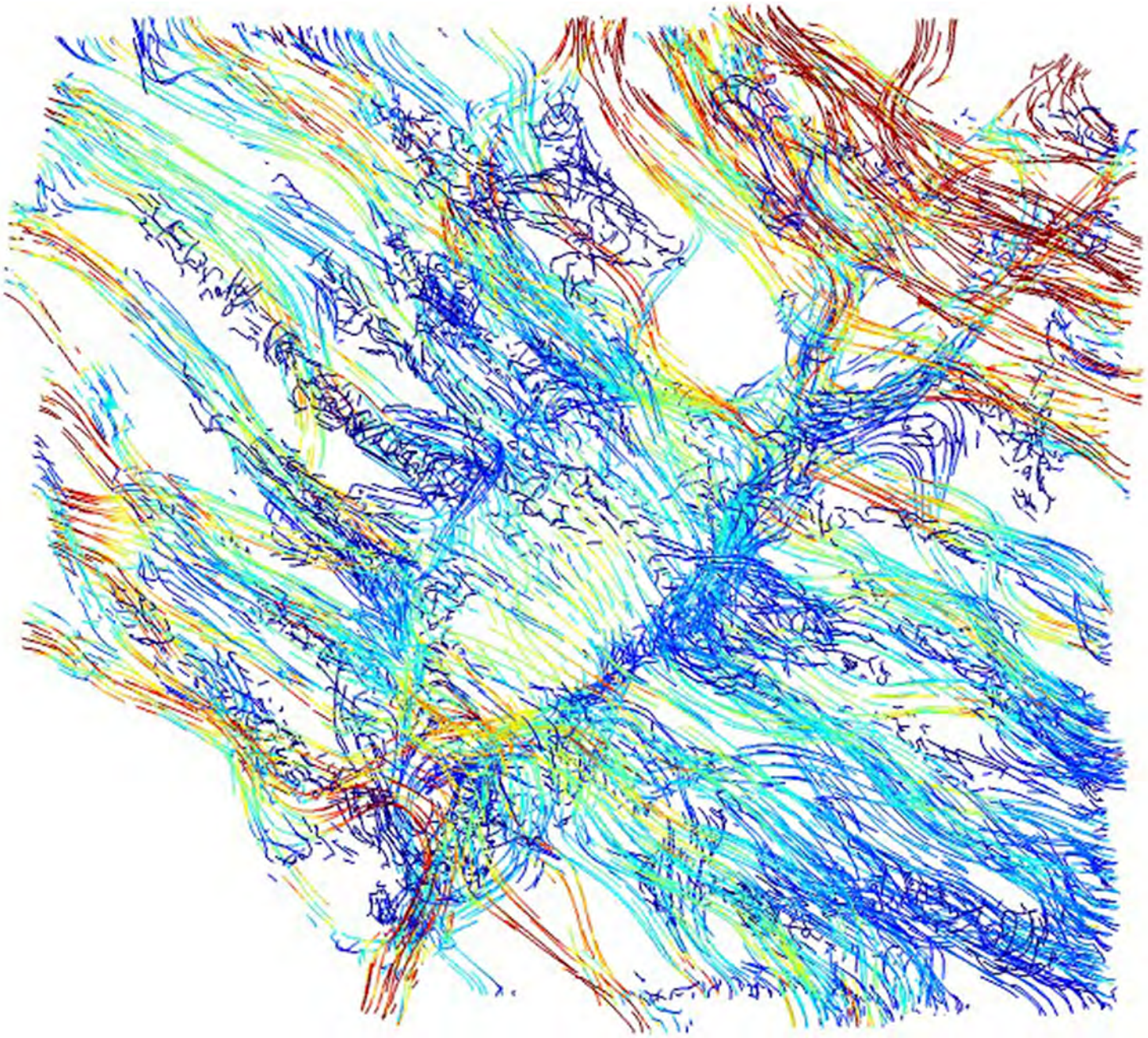
Research Report

Highlights in Musculoskeletal Research 2020



UCSF Orthopaedic Surgery

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Produced by Maryam Farshad, Kathleen Jay, and Erin Simon.

May 14, 2021

Cover image: Visualization of flow lines from dynamic finite element fluid modeling representing fluid shear within the pericellular space of a single osteocyte lacunae and its associated canalicular dendrites from mouse cortical bone. A special thanks to **Charlie Shurman** (Graduate student, Alliston Lab) **Stefaan Verbruggen,** and **Tamara Alliston, PhD**.

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UCSF Orthopaedic Surgery

Message from the Chair of the UCSF Department of Orthopaedic Surgery

Dear colleagues and friends,

The year 2020 will be remembered as a remarkable year of change, challenge, and loss as well as growth, resilience, achievements and success by our researchers.

Our day-to-day lives may have been disrupted by the pandemic, but as a Department we learned to adjust and continued to focus on our core objectives: looking to the future, answering fundamental questions, and providing the best available evidence-based data from all disciplines of musculoskeletal research. We continue to fuel curiosity by exchanging ideas and encouraging collaborations in orthopaedic research -- basic science, clinical and translational. Even if it's over a Zoom.

In 2019, we took great pride in sharing that UCSF was the top public recipient of funding from the National Institutes of Health (NIH), and as a Department we received $39,103,498 in peer-reviewed NIH research grants. Although 2020 posed challenges -- -- including safe ways to re-open labs and conduct clinical research with our patients-- nonetheless, our Department received an additional $5,127,654 in NIH Funding to continue our innovative research.

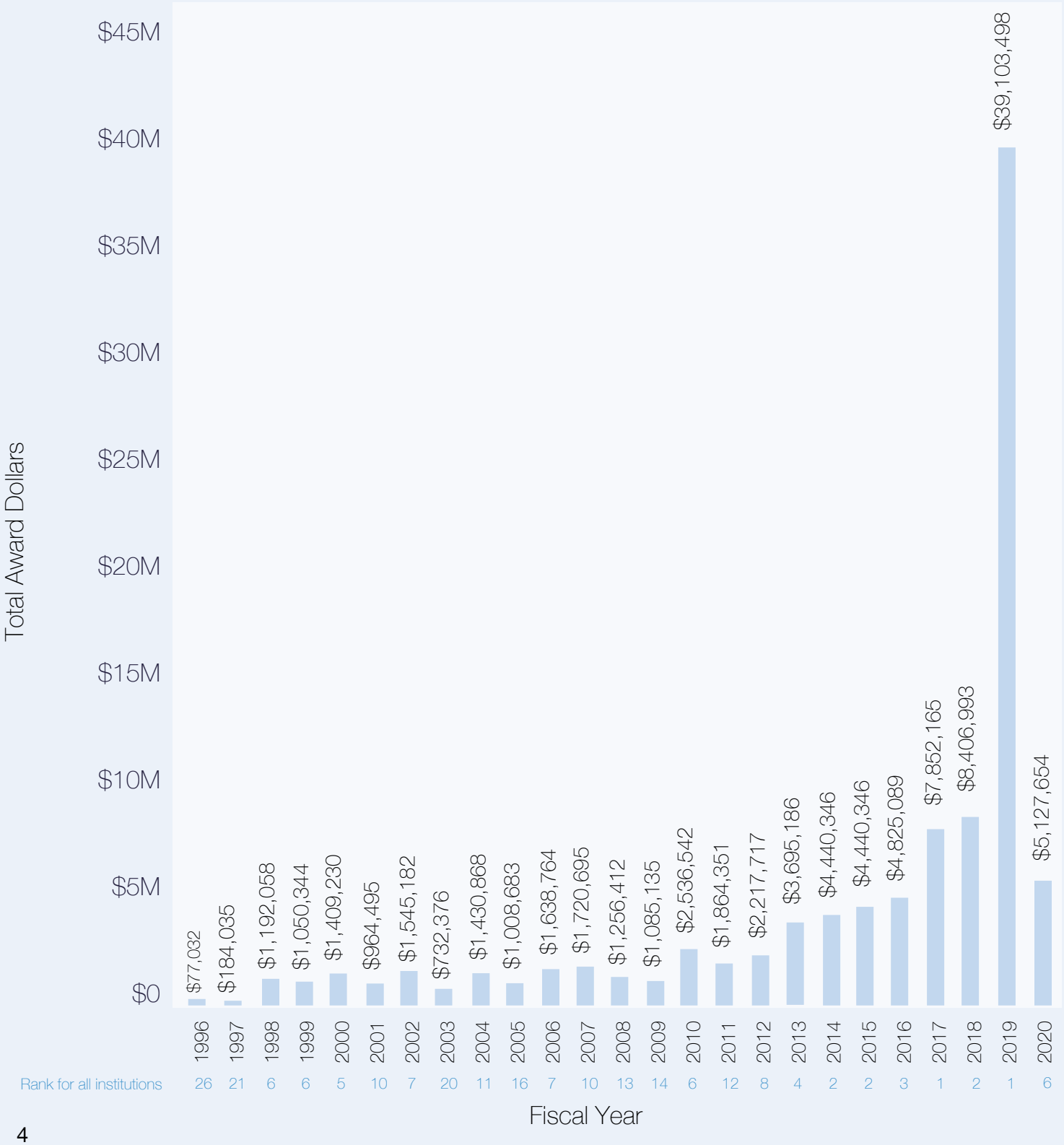
Building upon our sustainable model, we look forward to continuing success, innovative studies and evidence-based breakthroughs. Plans are underway to expand and remodel labs in 11 HSE and 95 Kirkham, and our faculty are actively engaged in the process of re-envisioning the entire research community on the Parnassus campus.

We are very proud of all of our researchers for riding out these challenges and slowly, carefully and safely returning to a new normal. I look forward to our research enterprise growth throughout 2021 and well beyond!

Thomas Parker Vail, MD
James L. Young Professor
Chair, Department of Orthopaedic Surgery

NIH Ranking

NIH Research Grants for UCSF Department of Orthopaedic Surgery



Our Vision

Pioneering musculoskeletal discovery and innovative care to transform lives.

Devante Horne, a graduate student, performs musculoskeletal reseach in the Lotz Laboratory for Orthopaedic Tissue Engineering and Regeneration on UCSF's Parnassus campus.

Research Programs and Activities

Researchers in the Department of Orthopaedic Surgery conduct innovative clinical, basic science, and translational research in musculoskeletal biology to improve the delivery and outcomes of orthopaedic care. Neha Dole, PhD,above, performs musculoskeletal research in the Alliston Laboratory for Skeletal Mechanobiology at UCSF's Parnassus Campus.

Basic, Translational and Clinical Research

The UCSF Department of Orthopaedic Surgery has a diverse and broad basic and translational research program in musculoskeletal biology. This is in addition to our clinical research program, which spans all orthopaedic subspecialties. Each of our various research programs are aimed at bringing new insights to our understanding of the musculoskeletal system. A major goal is to develop novel treatments for defects, diseases, conditions, and injuries that affect musculoskeletal function. We are driven by the desire to improve the delivery and outcomes of orthopaedic care.

Additionally, the Department has a strong tradition in clinical research across all subspecialties. Over the past decade, clinical researchers have established a large collaborative network both within UCSF as well as with national and international clinical researchers. This has improved the impact and depth of our clinical research.

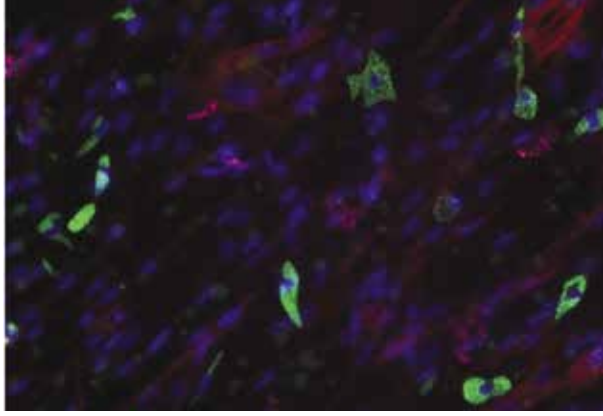
Over the past year, clinical research has been published in all major orthopaedic surgery journals including the Journal of Bone & Joint Surgery (JBJS), Journal of Shoulder and Elbow Surgery (JSES), Journal of Orthopaedic Trauma (JOT), Spine journal, Journal of Pediatric Orthopaedics (JPO), Clinical Orthopaedics and Related Research (CORR), and the American Journal of Sports Medicine (AJSM). Faculty, fellows, and residents presented at American Academy of Orthpaedic Surgeons (AAOS), Orthopaedic Research Society (ORS), the American Orthopaedic Society in Sports Medicine (AOSSM), International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS), the Hip and Knee Society, and the Orthopaedic Trauma Association (OTA), among other national and international meetings. For a full list of our departmental contributions to the 2020 AAOS and ORS conferences, please visit https://orthosurgery.ucsf.edu/education/courses/.

While the individual projects are too numerous to list in detail, there have been several highlights of collaborative research across spine surgery, osseointegration, 3D printing for improving surgical outcomes, shoulder arthroplasty and instability, imaging analysis using high resolution MRI and CT, global health through UCSF's Institute for Global Orthopaedics and Traumatology (IGOT), pediatrics and pediatric sports medicine.

Orthopaedic Translational Research

UCSF VA Health Center, Research Facility at Mission Bay

The Laboratory for Orthopaedic Translational Research is directed by **Hubert Kim, MD, PhD** and **Alfred Kuo, MD, PhD** at the UCSF VA Research Facility at Mission Bay.



Stem cells found within the rotator cuff muscle can be stimulated into fibrotic tissue (red) or fat tissue (green) depending on the stimulus (Feeley-Liu Laboratory for Stem Cell Regeneration and Translational Research)

The focus of the team's research effort is to examine the molecular and cellular mechanisms responsible for secondary injury cascades that are set in motion after trauma. There is particular interest in tissues that have an extremely limited capacity for healing and regeneration, where preservation of existing cells and tissue may be of great clinical significance. The intention is to apply lessons learned in the laboratory to design better treatments for patients.

Additionally, Brian Feeley, MD directs the Laboratory for Stem Cell Regeneration and Translational Research, located on the UCSF/VA Mission Bay campus focusing on muscle injury problems. Brian Feeley, MD collaborates with Xuhui Liu, MD and researchers at UCSF on developing models to study the molecular mechanisms and cellular mechanisms that are responsible for the development of muscle atrophy and fatty infiltration after rotator cuff tears.

The focus of the research is to understand the cellular and molecular changes that occur within the muscle after different injuries, but particularly rotator cuff tears. They have developed novel injury and repair models to study the acute and chronic effects of rotator cuff injury on the important signal transduction pathways that govern muscle cell size and stem cell fate within the muscle. They also focus on understanding how muscle injury patterns affect the stem cell populations within the muscle (satellite cells, FAP cells) in an effort to determine treatment strategies that would improve muscle function after orthopedic injuries.

Within the UCSF VA Health Center, the Orthopaedic Rapid Intelligent Fabrication Group led by Alan Dang, MD and Alexis Dang, MD focus on translating orthopaedic ideas into orthopaedic products. They maintain a 3-axis CNC mill as well as a small fleet of 3D printers with customized extruders, firmware, and other software optimizations. Active projects include the development of advanced surgical lighting technology as well as surgical instrumentation and implants.

Orthopaedic Edge Innovations Laboratory

Multi-Campus Laboratory

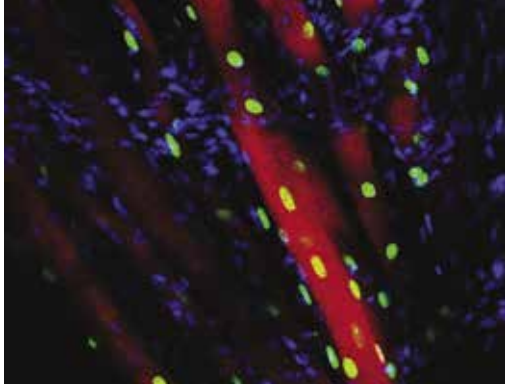
The Edge Innovations Lab is led by **Aenor Sawyer, MD, MS, Alexis Dang, MD** and **Alan Dang, MD** and is focused on Engineering, Designing, and Growth Enabling digital (EDGE) and manufacturing technologies.

This group is responsible for clinical 3D printing across the many campuses of the Department including UCSF Parnassus Heights, The Orthopaedic Institute at Mission Bay, ZSFGH, SF VAHC, UCSF Benioff Children's Hospital Mission Bay, and UCSF Benioff Children's Hospital Oakland. Currently, the focus is on 3D printing of Precision Anatomic Models for surgical pre-operative planning and conducting the research to assess the efficacy and economics of the technology.

As a result of their work in the 3D imaging arena, Alexis Dang, MD and Alan Dang, MD won the San Francisco Federal Executive Board "Federal Employee of the Year" award in Science & Technology related to 3D printing in orthopaedics. https://gsablogs.gsa.gov/febsanfrancisco/programs/public-service-recognition/. The Board represents approximately 70,000 federal, postal and military employees throughout the nine bay area counties (Alameda, Contra Costa, Marin, Napa, San Francisco, San Mateo, Santa Clara, Solano, Sonoma), as well as agencies in the Sacramento area.

Edge Innovation Laboratory is led by Aenor Sawyer MD, MD, Alexis Dang, MD, and Alan Dang, MD.

Additionally, Dr. Aenor Sawyer, Dr. Alexis Dang and Dr. Alan Dang spearheaded a multidisciplinary initiative, together with the Pediatric Heart group and Radiology, to develop 3D+ printing technologies at UCSF. The "+" includes augmented reality, virtual reality, and 4D imaging (3D-imaging with a time component). This has received $1.4 million in funding.



Human muscle stem cells and regeneration (Brack Laboratory for Skeletal Muscle Regeneration and Aging). Image by Annarita Scaramozza, PhD

Stem Cell Laboratory

Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research on Parnassus Heights

The Brack Laboratory for Skeletal Muscle Regeneration and Aging is directed by **Andrew Brack, PhD**, and focuses on the development of strategies to accelerate skeletal muscle repair.

During aging or in response to radiotherapy, the capacity for muscle repair is diminished, leading to reduced mobility and strength.

The Brack Lab uses state of the art machine learning and molecular biology to determine the causes of muscle dysfunction and identify strategies to rejuvenate the regenerative potential of skeletal muscle.

In the future, the Brack Lab hopes that current projects will lead to strategies that reverse aging and improve recovery after radiotherapy.

Andrew Brack, PhD, has developed collaborations with clinical faculty, including sports medicine and oncology. Active studies include studies on muscle aging and muscle recovery after radiotherapy.

Skeletal Mechanobiology

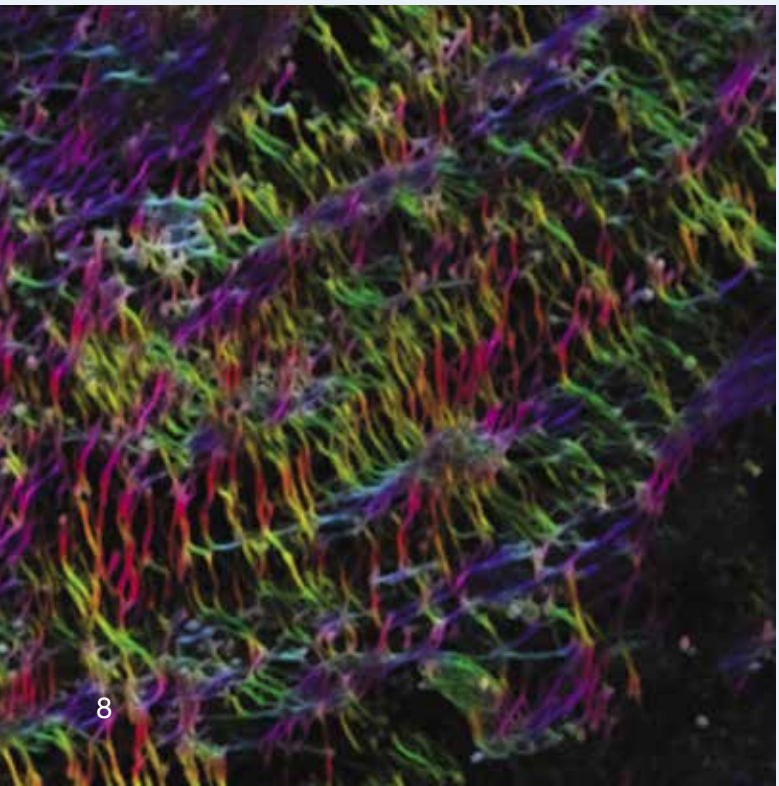
UCSF Parnassus Heights

The Laboratory for Skeletal Mechanobiology is directed by **Tamara Alliston, PhD.**

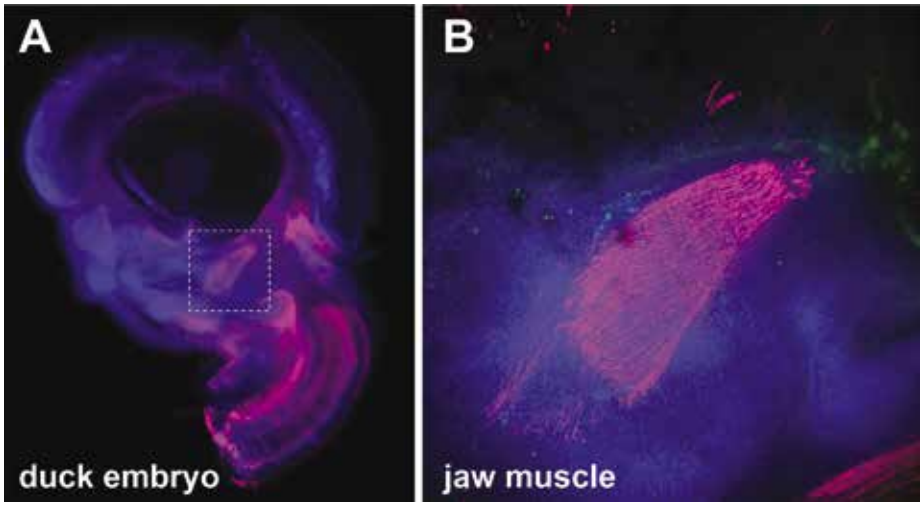
The Alliston Laboratory investigates the molecular pathways controlling skeletal cell behavior, how these pathways coordinate with physical cues to influence mechanical integrity of healthy bone and cartilage, and how they can be harnessed to repair tissue damaged in degenerative skeletal diseases like osteoporosis and osteoarthritis. To answer these questions they combine molecular, cellular, physiologic, and materials science approaches.

In particular, they seek to define the function of TGF□ in synergistically coordinating physical and biochemical cues in bone and cartilage cells. Since TGFβ is a powerful regulator of homeostasis throughout the skeleton, understanding this signaling pathway has helped their team uncover fundamental new cellular mechanisms that participate in skeletal health and disease.

This research has provided important new insight on factors that cause common musculoskeletal problems, like joint injuries, osteoarthritis, and bone fragility in aging men and women. Now the research team is building on what they have learned in the laboratory to discover new therapeutic strategies to prevent skeletal disease and to improve skeletal repair.



Osteocyte canalicular networks visualized in silver stained bone. Image by Charlie Schurman 2018 (Alliston Laboratory for Skeletal Mechanobiology)



(A) Skeletal muscle from a duck embryo showing muscles of the head and neck (stained pink with an anti-myosin antibody). (B) At higher magnification (dashed inset box), striated fibers of the jaw closing muscles and their insertions points within skeletal precursor cells can be observed (Schneider Laboratory for Developmental and Evolutionary Skeletal Biology, confocal images by Dr. Jessye Aggleton).

Development and Evolutionary Skeletal Biology

UCSF Parnassus Heights

The Schneider Laboratory for Developmental and Evolutionary Skeletal Biology is directed by **Richard A. Schneider, PhD.**

Research is broadly aimed at understanding how the developing musculoskeletal system achieves its structural and functional integration.

To address this question, the lab has created a unique surgical transplantation system that involves embryos from two distinct types of birds (quail and duck), which differ considerably in their functional anatomy and growth rates.

Transplanting skeletal and other progenitor cells between them challenges the resulting chimeric “quck” and “duail” embryos to integrate two different species-specific developmental programs.

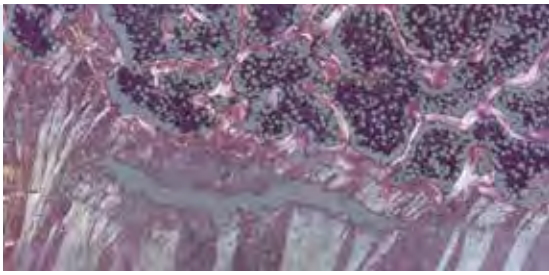
By focusing on donor- versus host-controlled changes to embryonic patterning and growth, this strategy has illuminated molecular and cellular mechanisms that regulate the musculoskeletal system and enable bones, cartilages, tendons, muscles, and other tissues to achieve their proper size, shape, orientation, and integration.

A goal is to devise novel molecular- and cell-based therapies for repairing and regenerating musculoskeletal tissues affected by birth defects, disease, and injury. Work from the Schneider Lab has also helped elucidate the role of development in evolution.

Orthopaedic Tissue Engineering and Regeneration

UCSF Parnassus Heights

The Orthopaedic Tissue Engineering and Regeneration Laboratory is directed by **Jeffrey C. Lotz, PhD.**



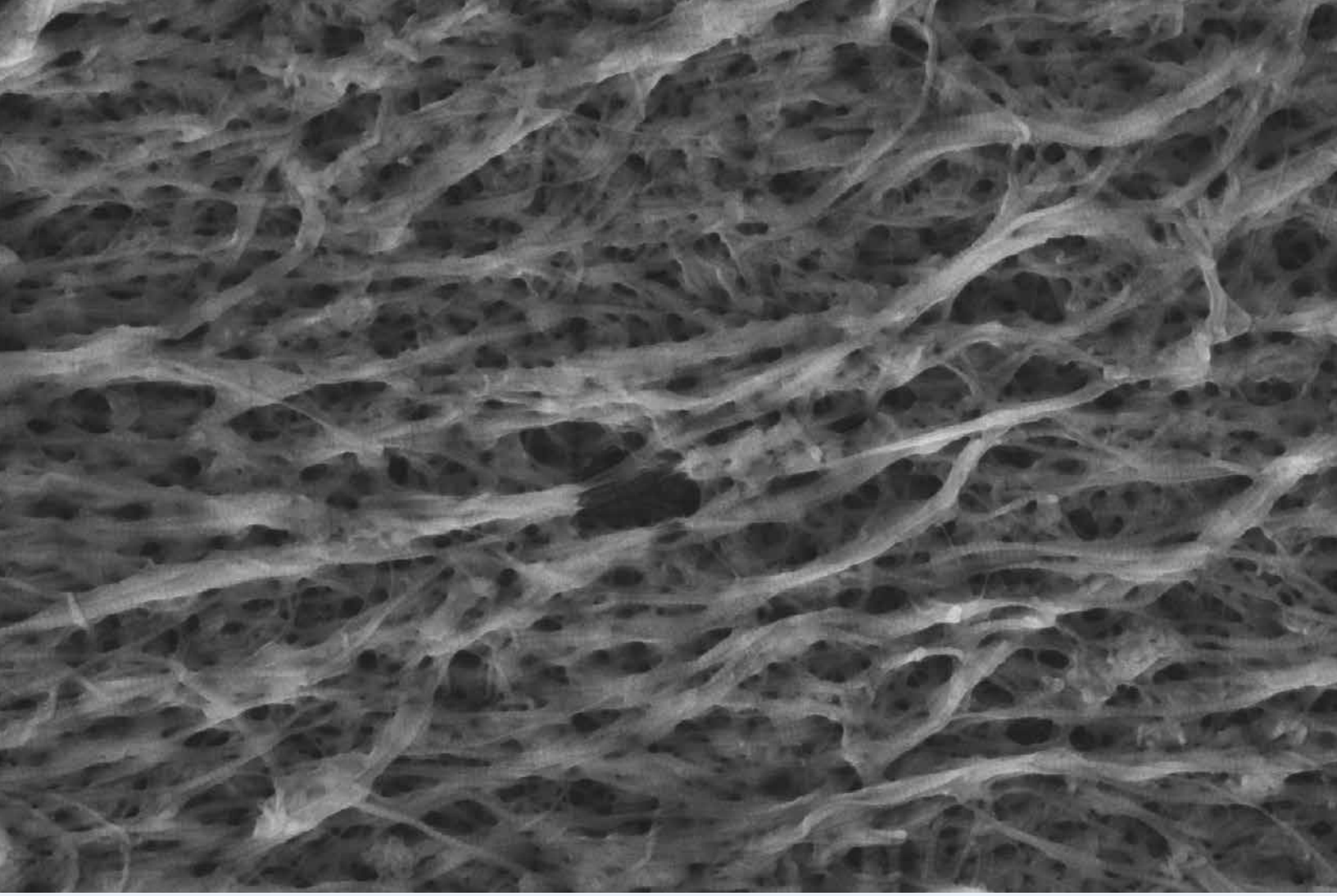
The Lotz Laboratory has pioneered biomechanical, anatomic, and imaging studies of the human disc/vertebra interface (Lotz Laboratory for Orthopaedic Tissue Engineering and Regeneration).

The Lotz Laboratory is devoted to conducting basic research in several areas of orthopaedics including biomechanics of the spine, knee, and hand. Biomechanical studies serve to investigate the physical properties of musculoskeletal (MSK) tissues, as well as functional performance of MSK patients.

The Lotz Laboratory is collaborating with UC Berkeley engineers to design and validate in-clinic tools and sensors that quantify patient movement and augment traditional physical tests and patient-reported data. Similar studies are being conducted with NASA astronauts to understand the adverse effects of microgravity, and to develop countermeasures to maintain astronaut health and safety on long-duration space flight, such as the planned Mars missions. Additionally, they have focused on understanding the etiology of different diseases (e.g., disc degeneration, osteonecrosis) and comorbidities (disc degeneration and diabetes).

In the area of regenerative medicine, the Lotz laboratory is exploring various uses of mesenchymal stem cells for new therapies for disc, cartilage, and bone regeneration.

The diverse research team includes bioengineers, biologists, biochemists, histologists, and orthopaedic surgeons.



Fields Laboratory for Orthopaedic Biomechanics and Biotransport

Orthopaedic Biomechanics and Biotransport

UCSF Parnassus Heights

The Orthopaedic Biomechanics and Biotransport Laboratory is directed by **Aaron Fields, PhD.**

The broad research interests of the Fields Lab are related to structure-function relationships in musculoskeletal tissues, with a particular focus on the mechanisms of nutrient transport in bone and cartilage, and harnessing nutrient transport for tissue repair and regeneration.

The lab combines engineering and biology approaches for: (1) understanding the effects of aging and disease on structure-transport relationships, and (2) developing translatable diagnostic and therapeutic strategies. An overall theme of this research is the use of advanced experimental and computational tools to measure how tissue constituents at the nano- and microscales impact whole-organ behavior. The research involves close collaborations with clinicians including spine surgeons, physiatrists, and radiologists.

Active projects include: (1) translational studies aimed at harnessing nutrient transport for disc repair and regeneration; (2) clinical studies testing new diagnostic MRI tools for selecting patients that would most benefit from disc regenerative therapies; and (3) basic science studies comparing healthy vs. pathologicdisc cell phenotype. These studies are funded by grants from the National Institutes of Health and the North American Spine Society.

Skeletal Regeneration/Molecular and Cellular Biology

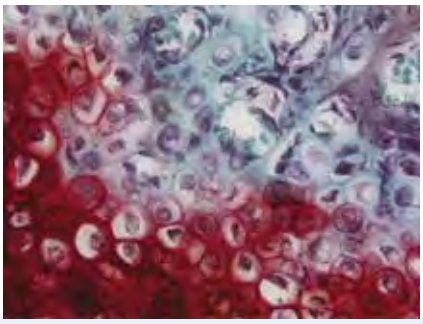
Zuckerberg San Francisco General Hospital (ZSFGH)

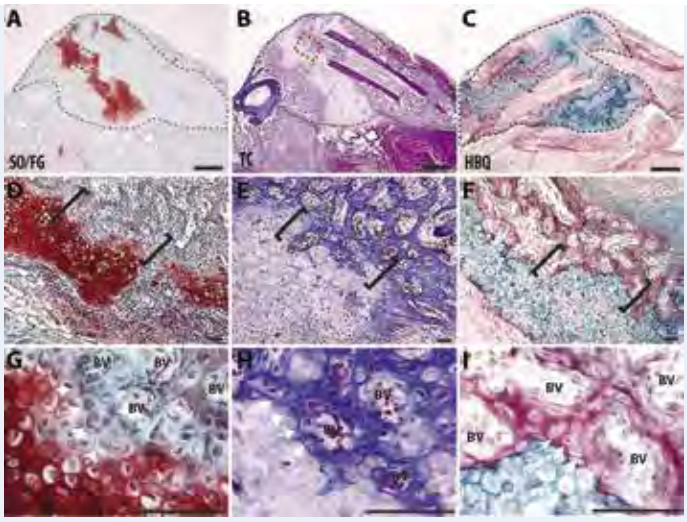
The Molecular and Cellular Biology Laboratory is directed by **Ralph Marcucio, PhD,** and **Ted Miclau, MD.**

The major focus of the work performed is to examine the processes that occur during bone regeneration after traumatic injury. Understanding the events that occur during fracture repair is essential for developing therapies to help people that exhibit difficulties in bone healing. For example, delayed or non-union afflict approximately 10% of all people undergoing fracture repair. By understanding how the body normally responds to orthopaedic trauma, they are laying the foundation for the development of new therapeutic regimens to treat a wide variety of skeletal pathologies.

The research utilizes a murine tibia fracture model that was developed by members of the laboratory and is used in other laboratories throughout the national and international orthopaedic research community. Current areas of study include, the role of muscle in bone healing, the role of inflammation in bone healing, the role of angiogenesis in bone healing, genotype-phenotype correlations during skeletal development, and the role of continuous phenotypic variation in disease production.

Image is from the Molecular and Cellular Biology Laboratory.





Visualization of the chondro-osseous transition zone in a fracture callus. (A-C) Low magnification of a murine fracture callus, outlined with black dashed line, stained with (A) Safranin-O/Fast Green (SO/FG), (B) Modified Milligan's Trichrome (TC) or (C) Hall and Brunt Quadruple Stain (HBQ). (D-F) A magnified region of cartilage and bone from the fracture callus, outlined with a red box (A-C), with the TZ indicated by black brackets. (G-I) High magnification images of the TZ show the invading vasculature and the chondro-osseous junction. (Bahney Laboratory for Musculoskeletal RegenerationMusculoskeletal Regeneration).

Musculoskeletal Regeneration

Zuckerberg San Francisco General Hospital (ZSFGH)

The Laboratory for Musculoskeletal Regeneration is directed by **Chelsea S. Bahney, PhD.**

The Bahney Laboratory utilizes a developmental engineering approach to discover novel therapeutic targets for regenerative medicine by first studying the normal mechanisms of repair, then utilizing engineered biomaterials to deliver bioactive signals to promote improved regenerative outcomes.

Currently, the focus of the Bahney Lab is primarily on the process of cartilage turning into bone, either naturally during fracture repair, or in disease processes such as osteoarthritis.

A long-term research goal is to translate new biologics that change healthcare options in fracture healing and post-traumatic osteoarthritis.

Laboratory for Evolutionary Anatomy

Zuckerberg San Francisco General Hospital (ZSFGH)

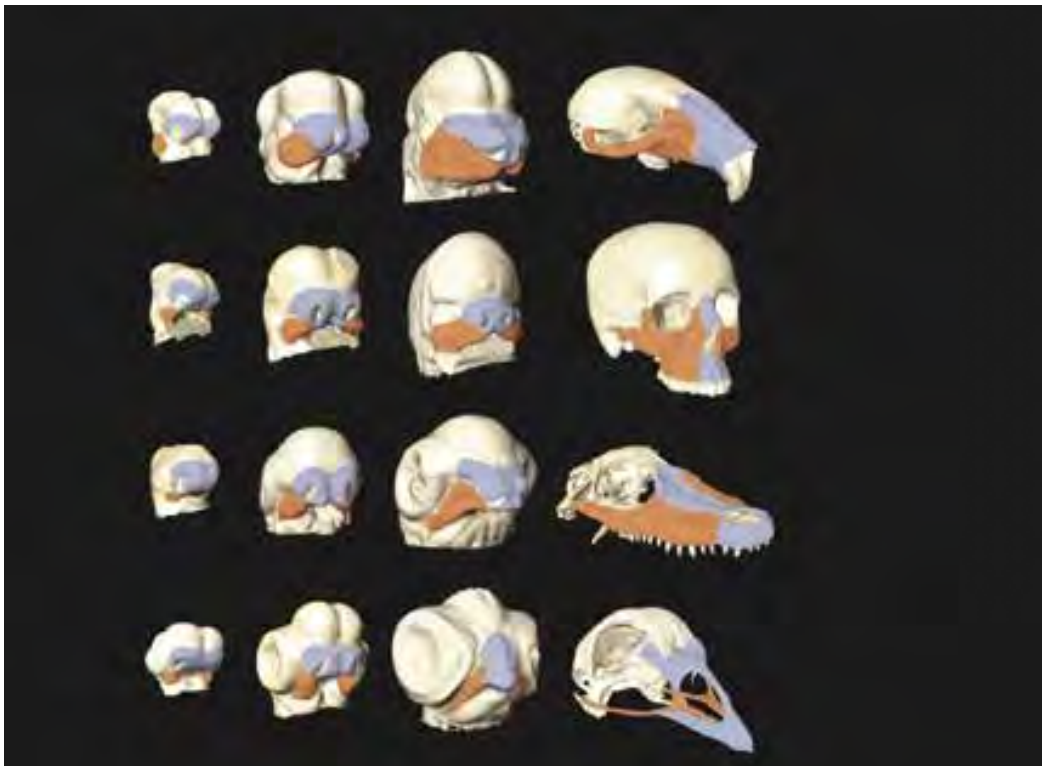
The Laboratory for Evolutionary Anatomy is directed by **Nathan Young, PhD.**

The Young Laboratory addresses biomedical basic research through the lens of evolution, utilizing functional compromise and historical constraint as fundamental explanatory principles. When combined with mechanistic insights from experimental systems, this approach yields significant insights into the generation of individual phenotypes, both normal and abnormal.

The lab research program combines classical embryology, modern experimental and genetic tools, and advanced methods for quantifying and comparing phenotypes at a range of scales.

This approach has significance for understanding not only the processes that contribute to and constrain evolutionary diversity, but also the individual phenotypic differences found within species and among individuals, including dysmorphologies associated with human disease states. Research includes the study of normal mechanisms of development as well as the etiology of congenital developmental defects, and is strongly relevant to longstanding goals of providing personalized and predictive medicine.

Comparison of facial development from embryos to adults in mouse, human, alligator, and chicken (Young Laboratory for Evolutionary Anatomy).



Testing facility, Safa Herfat PhD, Transtibial prosthetic socket being 3D printed for a patient at the OTI O&P clinic (OTI Biomedical Engineering Lab).

Orthopaedic Trauma Institute (OTI) Biomedical Engineering Lab

Zuckerberg San Francisco General Hospital (ZSFGH)

Directed by **Safa Herfat, PhD,** the OTI Biomedical Engineering Lab specializes in experimental biomechanical testing and finite element analysis of orthopaedic fracture fixation strategies and implants.

The lab also collaborates with the UCSF Orthotics & Prosthetics clinics on prosthetic innovation projects incorporating 3D scanning and printing to design and manufacture patient-specific prosthetic solutions. The lab houses its own 3D lab, with four 3D printers, a high accuracy white light 3D scanner, and a high-end design workstation. A Hearts Grant from the San Francisco General Hospital Foundation has also generously funded a large 3D printer capable of printing large lower limb sockets, as well as funding the development of a custom pressure sensor system to objectively monitor prosthesis fit in the clinic.

The lab is collaborating with other UCSF and UC Berkeley labs on an NSF grant-funded project to develop an implantable sensor to monitor fracture healing.

International Research at the Institute for Global Orthopaedics and Traumatology (IGOT)

Zuckerberg San Francisco General Hospital (ZSFGH)

IGOT Research Projects Led by Saam Morshed, MD, MPH, PhD and David Shearer, MD, MPH,:

Tanzania- Intramedullary Nailing Versus External Fixation for Open Tibia Fractures Randomized Controlled Trial Long-Term Follow-Up

Open tibia fractures are among the most common and debilitating injuries faced in low-income countries due to high rates of infection and nonunion. This study aims to address the question of whether internal or external fixation is better as definitive treatment for open tibia fractures in Tanzania. The study has enrolled and randomized 240 patients and achieved greater than 90% 1 year follow up. The study is currently conducting final data analysis, and we anticipate publication in the near future.

Tanzania- Cost-effectiveness of Prosthetics for Above Knee Amputees

Although the need for greater access to prosthetic services in low- and middle-income countries is well-established, literature on the long-term sustainability and cost-effectiveness of these prostheses in low-resource settings is lacking. This study will provide longitudinal follow-up to a previously conducted cost analysis of above knee prostheses in a low-resource setting, examining the original target study population to assess the long-term durability and impact of the prosthesis on quality of life, functional outcomes, and cost-effectiveness. The study is currently awaiting Tanzanian ethical approval, and we anticipate beginning patient enrollment and data collection in the near future.

Tanzania- Cost-effectiveness of Prosthetics for Below Knee Amputees

Limb loss has profound economic, social, and psychological effects on both the individual and the community, and these effects are especially pronounced in low- and middle-income countries. However, countries with already strained financial resources rarely prioritize rehabilitation services, and thus there is a need for economic analyses evaluating cost-effective, sustainable, and appropriate prosthetic technology in LMICs. This multisite, prospective cohort study aims to measure the impact of below knee prostheses on quality of life, functional outcomes, and cost-effectiveness in a low-resource setting. The study is currently awaiting Tanzanian ethical approval, and we anticipate beginning patient enrollment and data collection in the near future.

Tanzania - Low-cost Intramedullary K-wires for Pediatric Femur Fractures

Femoral shaft fractures in children are commonly treated with surgery using flexible nails to avoid damage to growth plates. However, titanium flexible nails that are commonly used in high-income countries are cost-prohibitive for many families in low-income countries where governments do not subsidize implant costs. Substituting titanium flexible nails with stainless steel “Kirschner wires” could reduce the cost of these implants nearly 40-fold, thereby markedly increasing access to surgery for children globally. IGOT is supporting a randomized controlled trial in Tanzania comparing these low-cost implants to the high-cost titanium nails for children with femoral shaft fractures.

Tanzania - A Pilot Masked, Randomized Controlled Trial Evaluating Locally-applied Gentamicin versus Saline in Open Tibia Fractures (pGO-Tibia)

Tibial shaft fractures are the most common long-bone fracture. Deep infection remains a common, devastating complication of open injuries leading to lifelong impairment that disproportionately affects low- and middle-income countries (LMICs). Thorough surgical debridement, followed by fracture stabilization using internal or external fixation, is the mainstay of treatment. One proposed adjunctive measure is prophylactic local antibiotic delivery, which can achieve much higher antibiotic concentrations at the surgical site than can be achieved safely with systemic administration. There is a growing body of literature evaluating local antibiotic administration in both aqueous and powder form at the time of wound closure. While demonstrating potentially promising results, these studies are heterogeneous, of poor general methodologic quality, and none originate from LMICs where this technique would have the greatest potential benefits. Local gentamicin is particularly promising given the broad spectrum of activity against common pathogens in osteomyelitis (staphylococcus, gram-negative rods), wide availability, and low cost (<1$ per 80mg vial). IGOT propose a prospective, blinded, randomized controlled trial enrolling adult open tibial shaft fractures at the Muhimbili Orthopaedic Institute (MOI) in Dar es Salaam, Tanzania. At the time of initial debridement, participants will be randomly assigned to receive aqueous gentamicin after closure or placebo saline injection. The primary outcome will be deep surgical site infection at 1 year. Secondary outcomes include health-related quality-of-life (HRQOL), modified Radiographic Union Scale for Tibial Fractures (mRUST), FIX-IT score for clinical healing, and cost of treatment using time-driven activity-based costing (TDABC) and survey methods.

Tanzania – Total Joint Replacement Registry

Our partners at Muhimbili Orthopaedic Institute in Tanzania created an excel sheet registry ten years ago with 900+ patients. This project will use this excel sheet to create and implement a formal registry prospectively using REDCap for total joint replacement procedures.

Africa– Open tibial shaft fracture treatment practices in Africa

Open tibial shaft fractures are the most common open long bone fracture and a significant source of morbidity and mortality in low- and middle-income countries (LMICs). Appropriate management of open tibia fractures includes timely antibiotic administration, surgical debridement, and definitive stabilization, which have been shown to reduce long-term morbidity and function. Due to the increase in road traffic injury, these injuries pose a rising burden in LMICs; however, the majority of research and guidelines regarding the treatment of open tibial shaft fractures comes from high-income countries (HICs). Practice patterns in HICs may differ from LMICs due to injury patterns, surgeon training, resource

availability, and treatment setting. Characterizing open tibial shaft fracture treatment patterns in Africa will allow for more appropriate resource allocation, development of treatment guidelines, and improved patient care. This study will identify current treatment practices of open tibial fractures in Africa, identify barriers to care of open tibial fractures in Africa and understand barriers to implementing evidence-based care.

International- SIGN Database Study

The significance of timely debridement in preventing fracture-related infection is still poorly understood but may have a substantial impact on minimizing patient morbidity and optimizing perioperative care. This retrospective review of the SIGN Online Surgical Database aims to determine whether time to operative debridement affects the development of fracture-related infection after treatment of open long bone fractures with intramedullary nail fixation. Over 10,000 unique fractures were included, with a wide geographic distribution of cases. The study is currently conducting preliminary data analysis, and we anticipate completing final analysis in the near future.

International- COACT: Motivations and Impact of Resident Rotations Qualitative Follow-Up

There is growing interest among orthopaedic residency programs in North America to pursue clinical rotations in resource-limited settings. However, little is known regarding the motivations of orthopaedic residents in North America for participating in such international rotations and the impact of these elective rotations on the host community. Potential concordance in motivations for participating in international clinical rotations between North American residents and their hosts has not been explored in the orthopaedic context. Furthermore, there are no best practice guidelines for establishing an effective and mutually beneficial orthopaedic training partnership between academic institutions in North America and their overseas partners in lower-middle-income countries (LMICs). This qualitative study aims to explore the themes found in the initial survey, "Motivations and impact of international rotations for orthopaedic residents: Is there concordance in perceptions amongst stakeholders at academic centers in North America and their partners in Low and Middle-income countries?".

Ghana – Predictors of Quality of Life and Economic Impact after Open Tibia Fractures

This study is led by our resident PGY4, Heather Roberts, under the mentorship from Drs. Saam Morshed and Dave Shearer.

This is a prospective study of open tibia fracture management in Kumasi, Ghana. The purpose of this study is to examine the influence of socioeconomic status on type of treatment for open tibia fractures, and in turn the influence of type of treatment on clinical and economic impact after open tibia fractures. The results of this study will impact policies that support investment in surgical care and inform evidence-based protocols in low-resourced settings where the burden of orthopedic trauma is highest.

Latin America - Quality of Life and Outcomes after Open Tibia Fractures

There is a limited understanding of the current state of treatment and resultant clinical outcomes for open tibial shaft fractures in Latin America. Therefore, the study aims to address the current state of treatment for open tibial shaft fractures across Latin America, including injury to hospital presentation, antibiotic prohphylaxis, debridement, and definitive bony stabilization. This prospective multicenter observational study is enrolling patients with open tibial shaft fractures at multiple time points over a period of a year. The study is taking place across multiple centers in Latin America.

Institute for Global Orthopaedics & Traumatology (IGOT) Global Research Initiative team with IGOT's Tanzania research partner, Dr. Billy Haonga.)

Latin America - Research Priorities in Latin America Delphi Study

The burden of musculoskeletal trauma internationally, and particularly in low- and middle-income countries, is substantial. Research capacity aimed to address these deficiencies is severely lacking compared to high-resource settings such as the United States, Canada, and Europe. LMIC providers therefore often rely on reports largely from high-income countries (HICs), extrapolating them to their own populations. This lack of population-specific research limits countries' abilities to improve care for patients with musculoskeletal injuries, advocate for necessary clinical resources, and inform research and policy priorities. This study will use a modified Delphi process to determine the clinical research priorities of orthopaedic surgeons in Latin America in order to set the agenda for future studies.

Latin America - Soft-Tissue Management and Wound Vacuum Survey

Open fractures, particularly Gustilo-Anderson Classification Type IIIB open tibial shaft fractures, characterized by massive soft-tissue defects, are the most common open long bone fractures, and are a frequent cause of morbidity and mortality in low- and middle-income countries (LMICs). Successful management of these injuries often requires acute management decisions that can have a substantial impact on a patient's short- and long-term recovery prognosis. Management of soft-tissue wound coverage varies in LMICs in Latin America based on numerous factors including: fracture type, surgeon expertise, resource limitations, and treatment setting. This study is assessing the treatment of soft-tissue coverage of open fracture wounds in Latin American countries and examining the availability of resources specific to their hospital and country. The survey will be administered to members of the organization, Asociación de Cirujanos Traumatólogos de las Americas (ACTUAR), and to Latin American orthopaedic surgeons who are members of national orthopaedic societies.

Latin American Research Consortium- Asociación de Cirujanos Traumatológos de las Americas (ACTUAR)

ACTUAR held its 3rd Annual Research Symposium on November 1-2 in Hermosillo, Mexico at the Federación Mexicana de Colegios de Ortopedia y Traumtologia conference (FEMECOT) National Congress. ACTUAR is the product of a group of Latin American orthopaedic surgeons interested in a collaborative initiative focused on building research capacity across institutions. Theodore Miclau, MD Professor and Vice Chair, Director of Orthopaedic Trauma at UCSF represented ACTUAR, IGOT, and OTI.

Research Publications

IGOT Global Research Initiative team has been active in publishing several intriguing articles, check out few of the recent publications!

1. Donnelley CA, von Kaeppler EP, Roberts HJ, Haonga B, Shearer DW, Morshed S. Monoplanar external fixation of comminuted open tibial shaft fractures predicts loss of alignment by one year compared to a statically locked intramedullary SIGN nail. Injury. 2020 Oct 17:S0020-1383(20)30898-6. doi: 10.1016/j.injury.2020.10.078.

2. Albright PD, MacKechnie MC, Roberts HJ, Shearer DW, Padilla L, Segovia J, Quintero JE, Amadei R, Baldy dos Reis F, Miclau T, and ACTUAR Open Tibia Study Group. Open Tibial Shaft Fractures: Treatment Patterns in Latin America. J Bone Joint Surg Am. Oct. 2020. doi:10.2106/JBJS.20.00292

3. Donnelley, CA, Won, N, Roberts, HJ, von Kaeppler, EP, Albright, PD, Woolley, PM, Haonga, B, Shearer, DW, Sabharwal, S. Resident Rotations in Low- and Middle-Income Countries. JBJS Open Access. 2020, 5(3). doi: 10.2106/JBJS.OA.20.00029

4. Chokotho L, Wu HH, Shearer D, Lau BC, Mkandawire N, Gjertsen JE, Hallan G, Young S. Outcome at 1 year in patients with femoral shaft fractures treated with intramedullary nailing or skeletal traction in a low-income country: a prospective observational study of 187 patients in Malawi. Acta Orthopaedica. 2020 Jul 22:1-8.

5. Cordero DM, Miclau T, Paul AV, Morshed S, Miclau T, Martin C, Shearer DW. The global burden of musculoskeletal injury in low and lower-middle income countries. OTA International. 2020 June, 3(2): e062 doi: 10.1097/OI9.0000000000000062

6. Von Kaeppler E, Donnelley C, Roberts HJ, O'Hara NN, Won N, Shearer DW, Morshed S. Impact of North American Institutions on Orthopedic Research in Low-and Middle-Income Countries. Orthop Clin N Am. 2020; 51:177–188. Doi: 10.1016.

7. Haonga BT, Liu M, Albright P, Challa ST, Ali SH, Lazar AA, Eliezer EN, Shearer DW, Morshed S. Intramedullary Nailing Versus External Fixation in the Treatment of Open Tibial Fractures in Tanzania: Results of a Randomized Clinical Trial. J Bone Joint Surg Am. 2020 Feb 5. doi: 10.2106/JBJS.19.00563. [Epub ahead of print] PubMed PMID: 32028315.

Grants and Fellowships

The 2020-2021 IGOT Morgan and Madison McClellan International Research Fellow, Mayur Urva, is involved with multiple research projects with IGOT. This year we have a research resident from UCLA through the GloCal Fellowship, Abigail Cortez. Her main research projects with IGOT include Intramedullary Nailing Versus External Fixation for Open Tibia Fractures Randomized Controlled Trial, Cost-effectiveness of Prosthetics for Below Knee Amputees, and Cost-effectiveness of Prosthetics for Above Knee Amputees.

Dr. Dave Shearer was awarded the OREF Career Development Grant of $225k for IGOT's Masked, Randomized Controlled Trial Evaluating Locally-applied Gentamicin versus Saline in Open Tibia Fractures (GO-Tibia) study.

The Orthopaedic Trauma Institute Clinical Research Center

Zuckerberg San Francisco General Hospital (ZSFGH)

The Clinical Research Center (CRC), led by **Saam Morshed, MD, MPH, PhD,** is dedicated to designing and implementing clinical studies to answer the most important questions in the care of patients with musculoskeletal injuries. In collaboration with industry and other major trauma medical centers, the CRC develops innovative clinical trials to evaluate the latest technologies and innovative treatment approaches in orthopaedic trauma. In particular, they are interested in the treatment and management of lower extremity fractures, surgical site infections, and lower limb amputations.

Dedicated to conducting safe and impactful research, our professionally trained clinical research team includes specialists in clinical research methodology, grant administration, data management, and quality control. The CRC also provides training in clinical research for post-doctoral fellows, graduate students, orthopaedic residents, medical, and undergraduate students.

For more information about our research Internship opportunities, please contact the clinical research manager Tigist Belaye, MPA, CCRP (tigist.belaye@ucsf.edu).

A list of our current projects include:

Transtibial Amputation Outcomes Study (TAOS): Comparing Transtibial Amputation with and without a Tibia-fibula Synostosis (Ertl) Procedure

Site Co-Investigators: Theodore Miclau, MD, and Saam Morshed MD, MPH, PhD.

A multi-center randomized clinical trial comparing the functional outcomes of patients undergoing tibia-fibula synostosis (Ertl procedure) versus a standard posterior flap procedure (Burgess procedure). The primary outcome is to assess the fit and alignment of the prosthesis with the level of comfort and satisfaction of each treatment. We will also examine the rate of re-hospitalizations for complications, resource utilization, and overall treatment cost.

Sponsor: Department of Defense Congressionally Directed Medical Research Program (DoD CDMRP).

Prosthetic Fit Assessment in Transtibial Amputees Secondary to Trauma (ProFit)

Principal Investigator: Saam Morshed, MD, MPH, PhD.

The PROFIT trial's objectives are to investigate prosthesis fit, alignment, and conditions of the residual limb in patients currently enrolled in the Transtibial Amputation Outcome Study (TAOS). The goal of this study is to validate and refine the prosthetic assessment tool (ProFit) that was developed by an expert panel of certified prosthetist orthotists (CPOs), orthopaedic trauma investigators, a measurement scientist and a biomedical engineer from the BADER consortium.

Sponsor: Department of the Army – U.S. Army Medical Research Acquisition Activity (USAMRAA)

A Prospective Randomized Trial to Assess PO versus IV Antibiotics for the Treatment of Post-op Wound Infection after Extremity Fractures (POvIV)

Site Co-Investigators: Theodore Miclau, MD, and Saam Morshed MD, MPH, PhD.

A multi-center clinical trial comparing the efficacy of oral antibiotics (PO) versus intravenous (IV) antibiotics in patients that develop a deep post-operative infection after fracture fixation. The differences in rates of re-hospitalization, infection, non-union, and amputation will be assessed. This will also determine the rates of compliance and medical costs associated with each treatment.

Sponsor: Department of Defense Peer Reviewed Orthopaedic Research Program (DoD PRORP)

A Pragmatic Randomized Trial Evaluating Preoperative Aqueous Antiseptic Skin Solutions in Open Fractures (A-PREP)

Site Co-Investigators: Saam Morshed MD, MPH, PhD, and Theodore Miclau, MD.

A-PREP is a multi-center clinical trial comparing the effectiveness of aqueous pre-operative antiseptic skin preparation with 10% povidone-iodine versus 4% chlorhexidine gluconate (CHG) for management of open fractures. Effectiveness will be evaluated by the occurrence of surgical site infection and unplanned fracture-related reoperations.

Funders: US Department of Defense (DoD), Physician Services Incorporated, and McMaster University Surgical Associates

PREPARE: A Pragmatic Randomized Trial Evaluating Pre-operative Alcohol Skin Solutions in FRactured Extremities

Site Co-Investigators: Meir Marmor, MD, and Saam Morshed MD, MPH, PhD.

The overarching objective of this multicenter trial is to compare the effectiveness of iodine povacrylex (0.7% free iodine) in 74% isopropyl alcohol versus 2% chlorhexidine gluconate (CHG) in 70% isopropyl alcohol for the management of extremity fractures that require surgical treatment. The primary outcome for comparison is surgical site infection (SSI), and the secondary outcome is unplanned fracture-related reoperation.

This study is funded by the Patient-Centered Outcomes Research Institute (PCORI).

The Pediatric Orthopaedic Surgery team, back row (left to right), Sanjeev Sabharwal, MD, MPH, Coleen S Sabatini, MD, MPH, Mohammad Diab, MD, and Jason E Jagodzinski, MD; front row: Nirav K Pandya, MD, Kristin S Livingston, MD, and Ravinder K Brar, MD, MPH. Not pictured: Eliana Delgado, MD, and Rhonda Watkins, MD, MPH and Ishaan Swarup, MD.

Pediatric Orthopaedic Surgery, Clinical Research

UCSF Benioff Children's Hospital, Oakland and UCSF Benioff Children's Hospital, San Francisco

The Pediatric Orthopaedic Surgery group strives to provide comprehensive care for all musculoskeletal conditions in children and young adults, to lead in medical education, and to advance the field through fundamental and enduring research.

The clinical research carried out by the Pediatric Orthopaedics team spans a diverse range of topics, some of which include research on fractures, scoliosis, sports medicine, limb deformity, health disparities, and musculoskeletal diseases at the global health level.

Project Highlights

• CORTICES – Children's Orthopaedic Trauma and Infection Consortium for Evidence-Based Studies. Dr. Sabatini and Dr. Swarup

• PSSG – Pediatric Spine Study Group, Multicenter Study, Dr. Swarup, Dr. Diab, and Dr. Metz

• Multicenter Prospective Cohort Study on Current Treatments of Legg-Calvé-Perthes

Disease, International Perthes Study Group - Dr. Swarup.

• Emotions and Pain with Surgery on Broken Bones – Dr. Gornitzky and Dr. Swarup

• Access to Healthcare for Freelance Professional Dancers during COVID-19 – Dr. de Borja

• Changes in Pediatric Orthopedic Referrals during COVID-19 Pandemic – Dr. de Borja and Dr. Diab

• Frontal Deformity in Scoliosis Patients - Surface Topography and Impact on Psychosocial Functioning – Dr. de Borja and Dr. Diab

• Accessing the Electronic Health Record Pædiatric Orthopædics: Preferences and Experiences of Teens versus Parents – Dr. Diab

• The Tether: Clinical Use of HDE/HUD – Dr. Diab

• Risk factors for post-operative urinary tract infections in children after surgery: a NSQIP study – Livingston and Brar

• Patient Satisfaction in Pediatric Orthopaedic Surgery – Dr. Livingston, Dr. Diab

• Prevalence of COVID-19 in Pediatric Patients Undergoing Orthopaedic Surgery –Dr. Pandya and Swarup

• Complications with the Use of Bio-Absorbable Fixation in The Treatment of Osteochondral Lesions of the Knee – Pandya

• Outcomes after Meniscus Surgery in Pediatric and Adolescent Patients – Pandya

• Tuberculosis osteomyelitis of long bones in children and adolescents in Uganda- Sabatini

• Does Access to an Online Educational Resource Change Practice for Orthopaedic Surgeons in LMICs? – Sabatini

• Impact of Time to Operating Room on the Management and Outcomes of Pediatric Supracondylar Humerus and Femoral Shaft Fractures - Sabatini

• Assessment of Rates and Risk Factors of Repeat Subsequent Surgery in Pediatric Patients with Septic Arthritis of the Knee – Swarup

• Efficacy of Patient Education in Pediatric Orthopaedic Trauma – Swarup

To learn more, visit the Pediatric Clinical Research website: **https://orthosurgery.ucsf.edu/research/clinical-research/Pediatric-Clinical-Research.html**

Orthopaedic Clinical Research

Sports Medicine Clinical Trials

UCSF Sports Medicine is currently performing several prospective clinical trials focusing on arthritis, rotator cuff tears, and cartilage injuries. Current studies include:

A Phase 3 Prospective, Randomized, Partially Blinded Multi-Center Study to Measure the Safety and Efficacy of NOVOCART® 3D, Compared to Microfracture in the Treatment of Articular Cartilage Defects

Principal Investigator: C. Benjamin Ma, MD

This prospective, randomized, partially-blinded multi-center study is being conducted to compare NOVOCART® 3D relative to Microfracture for the treatment of knee cartilage defects. Subjects with articular knee defects will be randomized to receive either Microfracture or NOVOCART® 3D, an autologous chondrocyte transplantation system. Subjects will be followed for five years in total and will be evaluated for safety and efficacy (by pain and function).

Sponsor: Aesculap Biologics

A Phase 2, 52 Week, Single Center, Open-Label Study Utilizing Imaging Techniques and Evaluating the Safety and Efficacy of SM04690 Injectable Suspension for the Treatment of Moderately to Severely Symptomatic Knee Osteoarthritis

Site Co-Investigators: C. Benjamin Ma, MD and Drew Lansdown, MD

This study investigates the safety and efficacy of SM04690, an injectable small-molecule inhibitor of the Wnt pathway, in driving progenitor cells resident in the joint to become chondrocytes and potentially enhance cartilage formation. Following a single injection, patients with moderate to severe knee osteoarthritis are evaluated over 52 weeks using advanced MRI techniques to measure changes in cartilage volume, thickness, and quality.

Sponsor: Samumed LLC.

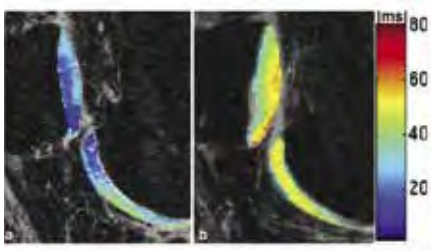
Operative vs. Non-Operative Treatment for Atraumatic Rotator Cuff Tears: A Multicenter Randomized Controlled Pragmatic Trial

Site Co-Investigators: C. Benjamin Ma, MD, Brian Feeley, MD, Christina Allen, MD, Alan Zhang, MD, Drew Lansdown, MD, Anthony Luke, MD, and Carlin Senter, MD

The Arthroscopic Rotator Cuff (ARC) Trial is a large, multicenter, randomized clinical trial comparing operative and non-operative treatment for rotator cuff tears that develop over time. This study aims to find out which treatment works better and for whom, in order to help patients in the future select the best treatment for them.

Funding: Patient-Centered Outcomes Research Institute (PCORI)

Image is from the Sports Medicine Clinical Trials in Knee and Shoulder Surgery group.



Prospective, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Safety and Efficacy of Pulsed Electromagnetic Field (PEMF) Therapy as an Adjunctive Treatment to Surgical Repair of Full Thickness Rotator Cuff Tears

Site Investigator: Brian Feeley, MD

Using a non-invasive therapeutic device, this study aims to evaluate the safety and efficacy of applying pulsed electromagnetic fields (PEMF) to rotator cuff repairs. It hopes to demonstrate that exposure to PEMF therapy following surgical repair will reduce tendon re-tear rates, improve clinical outcomes and range of motion, and decrease fatty infiltration.

Sponsor: Orthofix Medical Inc.

Evaluation of Muscle Stem Cells in Rotator Cuff and Other Muscle Injury Models

Principal Investigator: Brian Feeley, MD and Xuhui Liu, MD

Our previous data has highlighted the presence of fibro-adipocyte precursor (FAP) cells within muscle in mice, their ability to proliferate after injury, and their capability to regulate muscle quality with pharmacologic modulation. However, their presence and capabilities in human musculoskeletal conditions are not known. This study aims to evaluate the cellular plasticity, differentiation capability, and functional role of human fibro-adipocyte precursor cells (hFAPs) harvested from patients with musculoskeletal injuries.

Funding: NIH, REAC Grant

Prospective Post Market Clinical Follow-Up Study of the Zimmer® Trabecular Metal™ Reverse Shoulder System

Site Co-Investigators: C. Benjamin Ma, MD and Brian Feeley, MD

To assess the long-term performance of the Trabecular Metal Reverse Shoulder System, patients undergoing primary or revision reverse shoulder arthroplasty are evaluated annually over a span of 10 years.

Sponsor: Zimmer Biomet Inc.

Comparison of Outcomes Utilizing Blood Flow Restriction Training as a Rehabilitative Protocol in Post-operative Meniscus Repair Patients

Principal Investigators: Sachin Allahabadi, MD, Brian Feeley, MD, and Drew Lansdown, MD

Blood flow restriction (BFR) is a training tool that has been shown to be useful in the rehabilitative setting, but its utility in patients undergoing meniscus surgery is unknown. This study therefore seeks to understand whether BFR is a useful rehabilitation tool in this population. BFR is a unique and promising strategy for surgical patients, as it is low-load and can be used in early phases of rehabilitation, including non-weight bearing periods. This would be helpful for the many post-operative patients who are faced with a period of non-weightbearing status or limited activity after surgery, which constrains current rehabilitation practices and often results in poorer patient outcomes, including muscular atrophy, increased risk of injury, and delayed return to activity/sports. This study will help clarify whether BFR can reduce these complications and improve patient strength and function in patients undergoing meniscus repair surgery. If successful, this concept could be applied across other surgeries and disciplines within orthopaedics.

Orthopaedic Clinical Research

Benjamin Ma, MD, treating a patient in the Sports Medicine clinic.

Sports Medicine Patient-Centered Clinical Outcomes Research

To better provide patient-centered treatments, active collection of patient-reported outcomes measurements is paramount. To fulfill this mission, the UCSF Orthopaedic Sports Medicine Group currently participates in multiple prospective clinical outcome registries.

UCSF is an active member of the Multicenter ACL Revision Study (MARS) group. This group is responsible for collecting outcomes of revision ACL reconstruction with over 30 other institutions across the United States. This is the largest cohort of revision ACL reconstruction patients (over 1,200) reported. Numerous research grants as well as awards have been given to this study. Christina Allen, MD serves as a member of the scientific advisory board for the MARS group, providing input into current and future directions for evaluating research proposals and manuscripts. The MARS study began its 10 year follow-up program phase, and UCSF will be one of the sites for performing in-person follow-up with patients.

UCSF is also an active member of the Multicenter Orthopaedic Outcomes Network (MOON) shoulder group. Along with 12 other institutions across the United States, they actively follow patients undergoing surgery for shoulder instability and rotator cuff repairs. They have collected information on over 1400 patients with shoulder instability, which is the largest cohort reported.

Locally, C. Benjamin Ma, MD, has enrolled over 1,400 patients in a prospective shoulder arthroplasty database that has successfully published over 20 abstracts and scientific papers. With this database, the team has been able to establish important factors that contribute to the outcomes of shoulder replacement, including a novel technique to decrease the rate of re-infections after shoulder replacements, and techniques to decrease pain. Other studies include the evaluation of socioeconomic status, return to sport, and other factors that influence outcomes in shoulder replacement surgery.

Additionally, Alan Zhang, MD, is actively collecting outcomes measurements on patients undergoing hip arthroscopy surgery. Over 700 patients have been enrolled in this on-going study, yielding multiple research publications.

Digital Health

UCSF Digital Orthopaedics

Digital Health is led by **Stefano Bini, MD.** Digital Health research focuses on using commercial grade sensors to predict patient outcomes following surgery.

Value based care is a powerful concept that is fundamentally changing the way health care is being delivered in the United States and elsewhere. Arthroplasty as a specialty is front and center in this movement. The advent of vast quantities of patient generated health data (PGHD) created by commercial grade wearable sensors has raised the question as to whether these devices may provide objective data through which to quantify and compare clinical outcomes in surgical patients. However, many questions remain to be answered relative to these sensor generated data sets such as what data points are predictive of what outcomes, how many data points are needed for accuracy, and over what time frame data needs to be collected. They use PROMs as ground truth for outcomes as these measures are currently considered the gold standard surrogate for clinical quality.

With funding through CDHI Stefano Bini, MD coupled the power of AI with the data collection capabilities of wearable sensors to test the hypothesis that machine learning can be used to predict clinical outcomes following TKA based on PGHD in the early post-operative period. 22 patients undergoing total knee replacement were prospectively enrolled and tracked for 6 weeks after surgery and generated over three million data points. With the aid of AI, he and a team of residents including Jeff Barry MD, now faculty, Ilya Bendich MD, Kevin Hwang MD, Joseph Patterson MD, and Jeffrey Mulvihill MD, showed that, amongst other things, 42 day PROMs can be predicted with reasonable accuracy using data collected as early as 11 days following surgery. The first paper, “Changes in Prospectively Collected Longitudinal Patient-generated Health Data are Associated with Short-term Patient-reported Outcomes after Total Joint Arthroplasty: a Pilot Study,” accepted for publication (Arthroplasty Today, 2019 Mar; 5(1):61-63. PMID: 31020024) from this research was authored by Ilya Bendich, MD and several other papers followed (PMID: 31439405, PMID: 31445866 and PMID: 32235178).

Having concluded this longitudinal study, Stefano Bini, MD was awarded a second grant from CDHI to use similar technology to test post-operative patients at fixed time points to identify a data set that can accurately measure a patient’s recovery at a specific moment in time rather than using longitudinally collected data. Novel to this project was the use of commercially available running shoes with embedded sensors. The research is being conducted at the UCSF Human Performance center and shows the potential for interaction between different labs within the department.

This study in turn lead to a research project in partnership with Google. This project, funded through a gift from Google intended to support Dr. Bini’s research, intends to train machine learning algorithms to process continues data collected through smart sensors to directly output values optimized to reproduce as closely as possible values output by traditional gait lab tests. This novel approach bypasses the need to correlate surrogate endpoints created by sensors (such as step counts) to the gait lab data. Furthermore, as part of the agreement with Google, Dr. Bini and his team at UCSF HPC lead by Anthony Luke, MD, will make all data collected through this and future projects public. The roadmap with Google will include an extended multicenter data collection project to create the first crowd sourced public access sensor data base to be used for the study of knee mechanics through ML algorithms. Such promising collaborations show the potential for collaboration with industry and the resources available in our department.

Orthopaedic Clinical Research

Multicenter Trials on Hip and Knee Surgery

Led by surgeons Dr. Thomas Vail, MD; Erik Hansen, MD; and Stefano Bini, MD, UCSF's Arthroplasty Group participates in, and designs research studies, that are on the cutting edge of digital health and technology. Projects include longitudinal studies utilizing the post-surgical follow-up to gauge the effectiveness of advancing techniques and knowledge of arthroplasty surgeries, such as the prevention and treatment of periprosthetic joint infections (PJIs)

Project Highlights

Perioperative Antibiotic Prophylaxis in Patients Undergoing Elective Total Knee Arthroplasty: A prospective, randomized, open-label controlled multi-center trial.

Site Co-Investigators: Erik Hansen, MD; Stefano Bini, MD; Jeff Barry, MD; Derek Ward, MD.

Sponsored by Duke University

Despite advances in surgical care and implant technology, PJRIs and surgical site infections (SSIs) after total knee arthroplasty (TKA) present long-term catastrophic complications. Administration of prophylactic antibiotics before surgery is a well-established strategy to prevent PJIs and SSIs; yet, discussions linger regarding the choice of antibiotic, duration of prophylaxis, optimal dosage and timing, and route of administration. Level I data on antibiotic use for elective TKAs are limited, thus determining an effective protocol can deter PJIs and SSIs. And, so, this open-label trial is designed to identify the comparative effectiveness of various perioperative strategies for antibiotic delivery as prophylaxis against PJI and SSIs in elective TKAs.

One Stage versus Tow Stage or Periprosthetic Hip and Knee Infection

Site Co-Investigators: Thomas Vail, MD; Erik Hansen, MD; Stefano Bini, MD; Jeff Barry, MD; Derek Ward, MD.

Sponsored by OrthoCarolina Research Institute

This clinical trial intends to investigate the outcomes of one-stage and two-stage exchange arthroplasty for the management of patients with chronic PJIs. We hypothesize that one-stage exchange arthroplasty, if performed on the appropriate patient population, carries similar success rate for the treatment of chronic PJI as two-stage exchange arthroplasty and avoids many of the problems associated with two-stage exchange arthroplasty. Participants are randomized into either surgical approach and monitored thru the duration of their recovery.

How to Improve the Results of Irrigation and Debridement for PJI through the use of Intraosseous Antiboitics

Site Co-Investigators: Erik Hansen, MD; Jeff Barry, MD; Derek Ward, MD.

Sponsored by OrthoCarolina Research Institute

The investigators are looking to improve upon irrigation and debridement (I&D) procedures for PJIs, and limit the number of times one undergoes the procedure. One method involves utilizing intraosseous regional administration of antibiotics at the time of I&D as a deterrent for future PJI. Participants are closely followed-up to monitor the effectiveness of the approach.

Biodistribution of 11C D-methionine Positron Emission Tomography In Normal Subjects and Those with Suspected Infection

Site Co-Investigators: Erik Hansen, MD; Stefano Bini, MD; Jeff Barry, MD; Derek Ward, MD.

In collaboration with the UCSF Department of Radiology and Biomedical Imaging

Diagnosis of PJI utilizing radiographic imaging techniques comes with unique challenges, particularly with the focus on identifying nonspecific structural abnormalities that often occur late in the disease process and/or can be explained by other physiological processes. The goal of this project is to assess the ability of a positron-emitting agent in directly detecting bacterial infection in human subjects, which localize to bacteria but not mammalian cells. Such technique can further the identification process of PJI that can assist in proper control of invading organisms.

Orthopaedic Clinical Research

Youth Sports Injury Assessment and Prevention Center

The UCSF Sports Medicine Center for Young Athletes is a comprehensive, integrated clinical and research program which brings together orthopedic surgeons, physical therapists, athletic trainers, primary care physicians, and kinesiologists to provide cutting edge care for athletes under the age of 18.

Led by Nirav Pandya, MD, and Anthony Luke, MD, MPH, the center has successfully published and presented nearly 30 abstracts and scientific papers. They are also one of the few centers in the country participating in a prospective multicenter adolescent clavicle fracture registry as well as an adolescent shoulder instability registry.

Anthony Luke, MD, MPH treats a patient in the Sports Medicine clinic.

Motion Analysis Technology

The group is also using motion analysis technology to study normal and abnormal motion patterns with a mobile depth camera. This innovative work is designed to assess for lower extremity injury risk, return to play after knee injuries, and prevention of ACL tears. The study is a collaborative effort that is funded by the National Institute of Health (NIH).

Additionally, there has been a tremendous rise in athletic injuries in the skeletally immature population. This can be tied to the rise of sport specialization in this age group. The risks of sport specialization have only recently become known. Furthermore, with this rise in sports specialization, an increasing number of adult-type injuries are seen in younger patients. Yet, there are factors which differentiate the treatment of these injuries from their adult counterparts. Nirav Pandya, MD and Brian Feeley, MD have worked together, combining the expertise of the adult and pediatric sports medicine services, to publish multiple studies in this topic area.

Research topics covered include: 1) studies on patella instability; 2) shoulder dislocations; anterior cruciate ligament reconstructive techniques; and 3) revision surgery in the immature population.

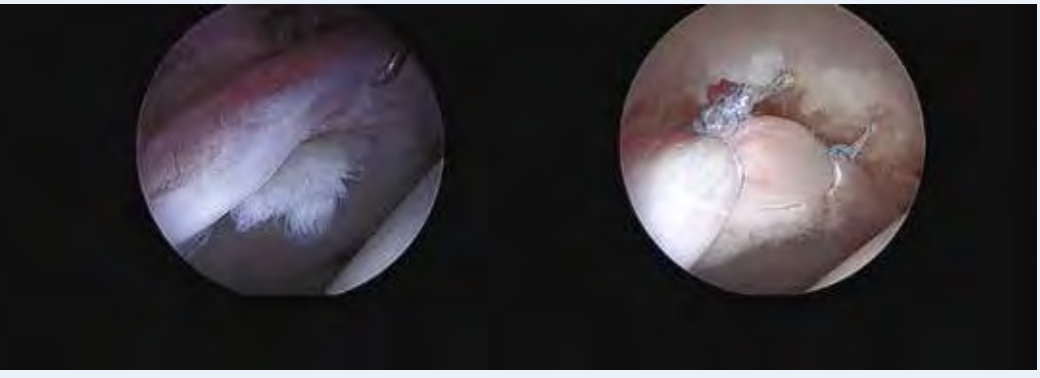
Orthopaedic Clinical Research

UCSF Hip Preservation Center

As Director of the UCSF Hip Preservation center, **Alan Zhang, MD** leads clinical and translation research on hip injuries in active individuals.

Dr. Alan Zhang has prospectively collected clinical outcomes measurements on over 600 patients who have undergone hip arthroscopy at UCSF and has published numerous articles to improve patient-centered care in this arena.

In collaboration with Sharmila Majumdar, PhD, Richard Souza, PhD, PT, and Thomas Link, MD, PhD, the hip preservation center is also conducting ongoing research on whether early hip arthroscopy treatment for labral tears and femoroacetabular impingement can decrease the risk of future arthritis in the hip.



A large tear of the hip Labrum (left) is repaired with Darthroscopic surgery (right), Hip Preservation Center.

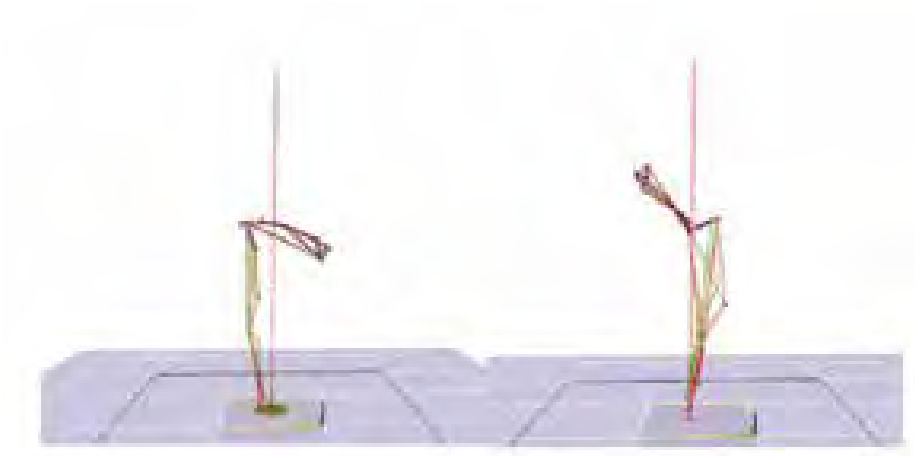
Orthopaedic Clinical Research

Clinical assessment of three-dimensional spine motion, Motion Analysis

The Motion Analysis Research Clinic is directed by S**hane Burch, MD**.

Motion Analysis studies the three-dimensional motion of the spine in adults with spinal deformity prior and after surgery. The main goal of this project is to quantify angular change on segments of the spine including C7-T12, T12-S1, C7-S1, and C7 Pelvis along with other kinematic and kinetic parameters. Data obtained through our motion analysis system Cortex is post-processed and analyzed in three different ways: individually (per subject), within groups (same level fusion), and between groups (groups with different LF and cohort group). Ultimately, this study aims to understand how changes in spinopelvic parameters correlate to patient Health-Related Quality of Life Scores (HRQL).

Full body length flexion and extension trial including reaction Force. Image by Luana Leal, 2020



Orthopaedic Clinical Research

Translational Quantitative Imaging Center

Advanced Translational Imaging Research Core

The Sports Medicine group at UCSF utilizes advanced biomedical imaging techniques to study different conditions of the knee, shoulder and hip. Magnetic resonance imaging (MRI) scans produce high-resolution three-dimensional images. Specialized MRI sequences can also provide detailed information about the biochemical composition of tissue, tissue architecture, or the function of joints. The Sports Medicine group closely collaborates with the UCSF Department of Radiology and the MQIR (Musculoskeletal Quantitative Imaging Research) group to leverage these advanced technologies to better evaluate patients and the effects of non-surgical and surgical treatment.

Knee Imaging

Knee ligament injuries and cartilage injuries are common conditions, especially in active people. Following anterior cruciate ligament (ACL) tears, patients are at an increased risk of developing knee arthritis. We can track the composition of cartilage using two advanced MRI sequences: T1rho and T2 mapping. The T1rho mapping sequence can measure the content of proteoglycans, which are an important component of healthy cartilage. The T2 mapping sequence gives information on the structure of collagen in cartilage. Both sequences can detect the breakdown of cartilage early in the degenerative process. These sequences have been used to monitor improvement after cartilage repair surgery and evaluate for early cartilage breakdown in patients with ACL tears.

Additionally, this group has also used kinematic MRI to evaluate the alignment and motion of the knee after injury to the ACL and following ACL reconstruction surgery. They obtain MRI scans, with a weight applied to the foot, to simulate standing in the scanner. They use images with the knee straight and then also bent. From this, they can then reconstruct three-dimensional models of the knee and better understand the complex function of the knee through motion. As a result, by combining these imaging technologies, they have linked abnormal knee motion to early cartilage breakdown.

Shoulder Imaging

This research has applied advanced imaging techniques to study patients with rotator cuff injuries. The muscles of the rotator cuff undergo degenerative changes following rotator cuff tears, with the muscle both shrinking in size (atrophy) and being replaced by fat (fatty infiltration). Both degenerative changes are associated with worse outcomes after surgical treatment. Advanced MRI sequence, IDEAL imaging, are used to measure the fat content in the shoulder muscles. The images show that increasing fat content can be observed in larger rotator cuff tears. Additionally, researchers have also studied how the fat content changes after surgical repair of a rotator cuff tear and they have demonstrated that lower fat content prior to surgical repair is associated with a higher chance of successful tendon repair.

Hip Imaging

In Hip Imaging, researchers have applied the T1rho and T2 mapping sequences to track the cartilage health of the hip. In femoroacetabular impingement (FAI), bony mismatch between the femoral head (ball) and the acetabulum (socket) are associated with labral tears and cartilage breakdown. Ultimately, this has shown that T1rho and T2 mapping can identify hip cartilage injuries better than traditional MRI.

Orthopaedic Oncology/Osseointegration

UCSF Mission Bay

UCSF Orthopaedic Oncology is dedicated to exemplary patient care, education, and research in the area of pediatric and adult bone and soft tissue tumors and tumor-like conditions.

Headed by **Rosanna L. Wustrack, MD** as Section Chief, our musculoskeletal oncologists are involved in a wide array of basic, translational, and clinical projects at UCSF, as well as regionally, nationally, and internationally. Dr. Wustrack's research, supported through the generosity of Dr. and Mrs. James O. Johnston, focuses on immunotherapy for sarcomas, functional outcomes in cancer patients, osseointegration, and optimizing treatment for metastatic disease. She is also interested in global health and osteoporosis in cancer survivors.

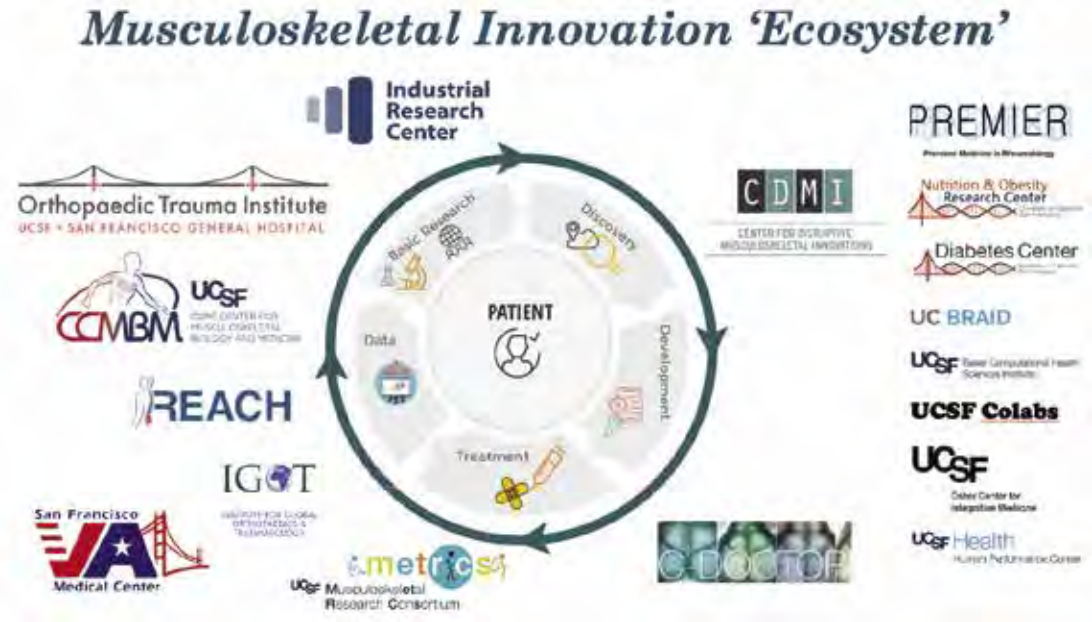
Richard J. O'Donnell, MD works in research administration and program development as Director of the iCORES (UCSF international Center for Osseointegration Research, Education and Surgery) and METRiCS (UCSF Musculoskeletal Research Consortium) efforts.

Melissa N. Zimel, MD has joined the group's studies directed towards normalizing function in patients with limb preservation and limb loss. The trio has spearheaded the development of the Sarcoma Program at UCSF, and of an Orthopaedic Oncology Research Collaborative in the Western States, involving colleagues at UCLA, UC Davis, Stanford, Kaiser Permanente, the University of Oregon, and the University of Utah. Drs. Wustrack and Zimel serve on the National Comprehensive Cancer Network's (NCCN) Bone Cancer and Soft Tissue Sarcoma Panels, respectively. International efforts include participation in the randomized prospective Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial, as well as the COVIDSurg Collaborative. Dr. Zimel is the Diversity, Equity and Inclusion Champion for the Department.

Melissa Zimel, MD, at left, Richard O'Donnell, MD and Rosanna Wustrack, MD lead the iCORES research.

MSK Innovation Centers

UCSF Musculoskeletal Innovation Ecosytem



The Core Center for Patient-centric Mechanistic Phenotyping Center Level Activities

Core Center for Musculoskeletal Biology & Medicine (CCMBM)

The NIH-supported P30 Core Center for Musculoskeletal Biology & Medicine (CCMBM) is one of five such centers nationally. The goal of CCMBM is to stimulate and support UCSF transdisciplinary collaborations to accelerate translational research in the musculoskeletal field through grants, core services, mentorship, and networking.

The CCMBM began its seventh year of funding under the new direction of Dr. Tamara Alliston, and has cultivated a diverse membership of over 150 faculty and trainees that span across three Schools and 23 Departments at UCSF. The Center provides research services through its three cores: imaging; biology and biomechanics; and epidemiology, biostatics and study design. Over the last seven years, the CCMBM has funded 14 pilot/feasibility grants, 13 tools and technology grants, and 24 awards supporting junior and early stage investigators. The CCMBM provided over $511K in funding and has leveraged an additional $1.1M in grant support for CCMBM members.

The UCSF community can participate in the Center through its various events including retreats, scientific symposia, seminars, technical workshops, and networking events that are offered throughout the year.

To learn more, visit ccmbm.ucsf.edu.

CCMBM
CORE CENTER FOR MUSCULOSKELETAL BIOLOGY AND MEDICINE UCSF

Center Level Activities

Core-Center for Disruptive Musculoskeletal Innovations (CDMI)

The Center for Disruptive Musculoskeletal Innovations (CDMI) is a National Science Foundation (NSF) Phase II Industry/University Cooperative Research Center (IUCRC). Representatives from a broad array of companies (medical devices, biomaterials, injury prevention, product manufacturing) form the CDMI Industry Advisory Board, and contribute to supporting 'industry-inspired' fundamental research and student training. Projects span a range of areas that include healthcare economics, biomedical science, biomechanics, biomaterials, injury prevention, and clinical outcomes, all while leveraging the increasing need for digital health resources.

Faculty from UCSF, University of Toledo, The Ohio State University, and Northeastern University, along with industry partners collaborate to target novel technologies that will decrease healthcare costs and improve the lives of patients with musculoskeletal conditions. Partnerships with the FDA have initiated several programs in regulatory science related to medical implants and digital sensor technologies.

Over its first five years, CDMI received about $1.8 million in industry membership support to fund 60 projects across its university sites. These projects have generated pilot data that led to $4.5M of additional extramural funding plus $1.1M in related 'enhancement' projects with the industry partners.

In December 2019, under the direction of Dr. Jeffrey Lotz, the CDMI team successfully became a Phase II center and secured another five years of funding. During Phase II, the CDMI will significantly expand its impact via integration of data and expertise spanning the manufacturing, insurance, healthcare, and office work environments. The CDMI is now recruiting additional industry partners and growing its faculty research network across the four partner universities.

To learn more, visit nsfcdmi.org.

Center Level Activities

Center for Dental, Oral, & Craniofacial Tissue & Organ Regeneration (C-DOCTOR)

The Center for Dental, Oral, & Craniofacial Tissue & Organ Regeneration (C-DOCTOR) is one of two national NIDCR-funded Tissue Regeneration Resource Centers. C-DOCTOR is a partnership among several California institutions to recruit, nature, and translate promising tissue regeneration technologies to human clinical trials. Participating universities include: UC San Francisco, UC Berkeley, UC Davis, UC Los Angeles, USC, and Stanford University.

C-DOCTOR has built an infrastructure to integrate a comprehensive and dynamic team of clinicians, research scientists, biostatisticians, regulatory scientists, and pre-clinical/clinical trial experts to enable the clinical adoption of innovative approaches for dental, oral, and craniofacial (DOC) tissue and organ regeneration. C-DOCTOR has awarded $4.5M to 17 interdisciplinary translational project (ITP) teams from across the US. C-DOCTOR is currently working with its industry advisor network to advance the most commercially viable products, and preparing those select ITPs for a pre-IND meetings with the FDA.

In 2020, the C-DOCTOR successfully received $3.9M in Stage 3 NIDCR funding. Over the next five years, this funding will be used to build on the Stage 2 successes and become a sustainable, comprehensive national resource center that enables the clinical translation of innovative regenerative technologies to replace DOC tissues or organs lost to congenital disorders, traumatic injuries, diseases, and medical procedures.

To learn more, visit c-doctor.org.

The vision forC-DOCTORis to be a national resource for the clinical translation of innovative regenerative technologies to replace dental and craniofacial tissues and organs lost to congenital disorders, trauma, and disease.

Center Level Activities

Industry Research Center (IRC)

Industrial Research Center

The Industry Research Center (IRC) goal is to facilitate efficient industry/university alliances and provide biomechanics, biochemistry, imaging, and animal testing and project management support to industry and faculty and residents in the Department of Orthopaedic Surgery.

For more information, please contact the IRC Director of Operations, Dezba Coughlin, PhD (mailto:dezba.coughlin@ucsf.edu).

Center Level Activities

UCSF MSK Center: UCSF Musculoskeletal Center

This newly formed campus-wide center integrates musculoskeletal (MSK) research at UCSF across schools, departments, and disciplines. Fueled by an outstanding community of musculoskeletal research leaders and a uniquely collaborative culture, the UCSF MSK Center will stimulate breakthrough discovery.

Our aspirations are bold. Prevent and cure conditions that adversely affect the musculoskeletal system such as osteoporosis, osteoarthritis, and diabetes. Pioneering musculoskeletal research has the potential to end health disparities and accelerate transformative advances that impact overall human health. The UCSF MSK Center will foster collaboration among basic, translational, computational, and clinical investigators, within and beyond musculoskeletal research, in 4 research areas to tackle big challenges in musculoskeletal research:

- Bio/Engineering: The unmet promise of MSK development and regeneration
- Data Science: The need for data science solutions in MSK biology, mechanics, and medicine
- Systems Biology: The unknown but emerging role of MSK tissues in systemic health, aging, and disease
- Health Disparities: The disproportionate impact of MSK disease on women and communities of color

In partnership with research leaders throughout UCSF, the MSK Center will achieve these goals by strengthening the MSK research community with new programmatic efforts, expansion of research space, and recruitment of new faculty. Tamara Alliston, PhD is the Director of the UCSF Musculoskeletal Center.

For more information, please contact Tamara Alliston, PhD (mailto:tamara.alliston@ucsf.edu)

Center Level Activities

Core Center for Patient-centric, Mechanistic Phenotyping in Chronic Low Back Pain (REACH)

The Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (REACH) is a $30M NIH-funded Mechanistic Research Center that is part of the NIAMS Back Pain Consortium Research Program (BACPAC) under the HEAL Initiative to stem the national opioid health crisis. BACPAC was funded to support studies in chronic low back pain (cLBP) since it is the most common, non-cancer reason for opioid prescription in the US. In its second year, REACH is an interdisciplinary consortium of basic and clinical scientists dedicated to developing precision medicine approaches for managing cLBP that factor in the interconnection between biology, biomechanics, psychology, and socio-environmental factors.

Under the direction of the Department of Orthopaedic Surgery (Drs. Jeffrey Lotz and Conor O'Neill), the goal of REACH is to define cLBP phenotypes and pain mechanisms that can lead to effective, personalized treatments for cLBP patients, as well as developing a clinical utility roadmap for clinicians. REACH is one of three BACPAC Mechanistic Research Center that consists of six cores: 1) Administrative Core; 2) Clinical Core; 3) Analytics Core; 4) Bio-behavioral Core; 5) Pathophysiology Core; and 6) Physical Function and Biomechanics Core. These cores provide support to a single research project that is focused on developing validated and adoptable tools that enable comprehensive yet routine clinical assessment and treatment of cLBP patients.

REACH also fosters scientific exchange through an Enrichment Program that enables REACH investigators, faculty, students, and the general public to interact with one another. The program includes seminars featuring local and visiting scientists, an annual retreat, and half-day symposia with a rotating topic relevant to the biopsychosocial model of cLBP. Another vital REACH component is its Ancillary Studies Program that provides seed money to leverage REACH clinical data and cores. Overall, the object of REACH is to catalyze discovery and translation of novel diagnostics and therapeutics that improve outcomes of cLBP patients.

To learn more, visit www.bacpac-reach.org or Tweet @ BacpacReach.

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To learn more, visit www.bacpac-reach.org or Tweet @ BacpacReach.

Center Level Activities

Human Performance Center

The Human Performance Center (HPC) is the key center for exercise related science serving the Department of Orthopaedic Surgery and the UCSF community. The HPC optimizes people's function and performance, emphasizing multidisciplinary solutions to advance discovery. With use of cutting-edge biomechanics and exercise physiology approaches, the HPC provides accurate and precise quantitative assessments of human movement and fitness. The state-of-the-art equipment and expert staff enable the center to handle a diverse range of research projects, from knee osteoarthritis to prostate cancer and more.

"We emphasize a team approach on solving problems. Our studies and programs involve experts across the UCSF community, crossing lines and sharing knowledge to join forces. We explore how exercise can improve people's daily function and prevent disease," explains Anthony Luke MD, MPH who is the Director of the HPC and Benioff Distinguished Professor in Sports Medicine.

The Human Performance Center is managed by Brooke Schultz, MS, who also serves as the full time Biomechanist for the Vicon Motion Capture system and AMTI force plates. Brooke has graduate level training in both physics and kinesiology as well as a decade's worth of experience as an American Council on Exercise (ACE) certified Personal Trainer. She utilizes her diverse background to blend expertise in movement science technology with patient care.

Neil Panchal, MS, ACSM-CPT, serves as the exercise physiologist of the lab. With multiple years of designing and modifying exercise prescriptions and administering graded exercise testing amongst a variety of populations, Neil conducts metabolic and physiological testing including VO2max, lactate threshold, RMR, and administering CPETs.

"Our aim is to use quantitative analysis that is accurate and precise when analyzing physical function. Our goal is to utilize novel technology and approaches to advance science; revealing new information about pathology and human function. We can consult, administer assessments and data collections, or provide comprehensive support for anyone investigating human performance." Richard Souza, PT, PhD, HPC, Director of Research.

2020 Projects

Hip Osteoarthritis

Dr. Souza leads a team of biomechanists, post-docs, and PhD students on an R01 funded project investigating the progression of hip osteoarthritis; tracking participants over a period of three years. In conjunction with radiology's evaluation of joint tissue health, the study uses the Vicon system, AMTI force plates, and BTE Primus dynamometer to analyze the participants while moving through standard activities of daily living such as walking, stair ascent and decent, as well as squatting.

Orthotics and Prosthetics

A proud partnership exists between the Orthotics and Prosthetics division of Orthopaedics and the HPC. Four studies are in an active data collection phase. Our orthopaedic team is building an expansive database for normal, able-bodied gait under both barefoot and shoe conditions. The control data set will be used in all forseeable research projects for O&P including the current biomechanical evaluation of transtibial amputee gait. The PROPEL program launched by Matthew Garibaldi, MS CPO in 2020 is a multidisciplinary approach to a 12-week wellness intervention for patients with lower limb loss. Evaluation of patient function, gait, strength, quality of life, and pain are assessed pre and post training program. The HPC continues to assisted Dr. Richard O'Donnell's Osseointegration program by evaluating metabolic cost and gait kinematics & kinetics of prosthetic patients pre- and post-implant surgery.

Diabetic Neuropathy

Victor Cheuy, PhD, Assistant Professor in the Department of Physical Therapy and Rehabilitation Sciences uses the HPC to investigate lower extremity biomechanics of people with diabetic neuropathy and to promote clinical research of skeletal muscle through novel technology. Dr. Cheuy's current RAP award assesses intersegmental foot kinematics and dynamic plantar pressure kinetics to explore their relationships with intrinsic foot muscle quality (MRI) and metatarsal microarchitecture (HR-pQCT). In addition, Dr. Cheuy was funded a RAP shared technology award (co-PI: Dr. Souza) which brings a new electromechanical dynamometer to the HPC. This device broadens the scope of our research potential by providing a more complete picture of skeletal muscle function, enabling strength measures, muscle power and activity, all integrated and available in one device.

Parkinson's Syndrome

The Michael J. Fox Foundation funded Neurology's Dr. Doris Wang, MD PhD's investigation into decoding the neural control of normal and abnormal gait patterns in Parkinson's disease using adaptive neurostimulation to understand and improve circuit mechanisms of human gait control. Patients have either the Medtronic Activa PC+S or Medtronic Summit RC+S device implanted in their brain. Subjects perform a treadmill-based gait retraining task in the HPC, during which signals from the implanted device are synced with the Vicon motion capture system, Xsens motion capture system, and wireless Delsys EMG to evaluate gait kinematics.

The HPC continues to partner with Neurology by way of the SPARX3 program led by Nijee Luthra, MD PhD. Staff members from the HPC team implement a treadmill-based exercise training program utilizing Heart Rate Zones on early stage Parkinson's patients. A VO2max fitness assessment with our Parvomedics Metabolic Cart will be measured at Baseline, six, twelve and eighteen month timepoints in addition to disease biomarkers and other functional movement tests.

Prostate Cancer

The HPC continues to work with the Department of Urology to conduct the exercise interventions of their large studies, including VO2max fitness testing and monitoring in patients with prostate cancer. June Chan, ScD Professor of Epidemiology & Urology, is working to determine the effect of aerobic training on prostate genomic signatures that predict risk of prostate cancer progression or aggressive disease in men on active surveillance for low-risk prostate cancer. We are now 4 years into a randomized controlled trial looking at how introducing regular vigorous exercise associated may reduce prostate cancer progression and cancer-specific mortality, as has been shown with other cancers. This project includes metabolomics so that we can have more in depth understanding of the effects of a 16-week exercise program in prostate patients and controls without cancer.

Similarly, Stacey Kenfield ScD, Associate Professor in Urology completed the data collection phase for the CHAMP study and has now received funding through the Movember Foundation to begin a new longitudinal study, GAP4. This will be a multicenter investigation to determine if supervised high intensity aerobic and resistance training can increase overall survival and reduce disease progression, skeletal-related events and pain among men with advanced metasatic prostate cancer. Fitness levels, including muscular strength (1RM), aerobic (VO2max) and functioncal capacity will be evaluated in the HPC, in addition to regularly providing exercise coaching for the patients and monitoring the safety and feasibility of the exercise programs. Finally, the HPC assists Dr. Kenfield with exercise interventions and one-on-one coaching performed solely via remote web-based communication for the Department of Urology's Prostate 8 research program. We are now 2 years into the study investigating the long term wellness program using exercise and/or diet lifestyle interventions and their potential impact to prevent the reoccurrence of cancer. The goals are to improve biological, clinical, and quality of life outcomes in men who choose surgery as the primary treatment for prostate cancer.

Center Level Activities

METRiCS: UCSF Musculoskeletal Research Consortium

UCSF Parnassus Heights

Envisioned in 2018 as a means to foster collaborative interaction between like-minded clinicians and scientists, the UCSF Musculoskeletal Research Consortium, or METRiCS Program, has been demonstrably successful in supporting translational projects that leverage inter-Departmental, cross-campus, and multi-School interactions. By definition, METRiCS focuses on outcomes, in terms of securing extramural grant and philanthropic funding, highlighting patient-centric health-related quality of life measures, and advancing knowledge through educational efforts and peer-reviewed publications.

METRiCS has brought together researchers from across the UCSF School of Medicine, including from the Departments of Orthopaedic Surgery, Physical Therapy, Radiology, Anesthesia, and Otolaryngology, as well as from UC Berkeley. Jeannie Bailey, PhD's work entitled, Assessing biomechanical function and hip stabilizing muscle quality associated with transfemoral osseointegration received $350,000 in funding from the Congressionally Directed Medical Research Program (CDMRP), Orthotics and Prosthetics Outcomes Research Program (OPORP). Current METRiCS proposals include: Quantifying and predicting risk of fracture and implant failure in individuals with transfemoral osseointegrated prostheses (Rob Matthews, PhD, PI); The influence of biomechanical contributions and patient-specific risk factors on the development of chronic low back pain symptoms in lower extremity amputees (Jeannie Bailey, PhD, PI) and Phantom limb pain multimodal neuroimaging (Steven Cheung, MD, PI). These studies will supplement ongoing efforts in the UCSF international Center for Osseointegration Research Education and Surgery (iCORES) Program, already the recipient of more than $6 million in federal contracts and grants, including a gift from Dr. and Mrs. Richard Stern.

Directed by Richard J. O'Donnell, MD, the METRiCS Lab has a bricks-and-mortar home at 95 Kirkham Street, where major support from the Department of Orthopaedic Surgery is transforming this southwestern corner of a re-imagined Parnassus Heights campus into a state-of-the-art gait analysis facility. Undergraduates, post-doctoral fellows, and Faculty members with basic, translational, and clinical expertise are developing lab-based, in-clinic, and at-home motion capture tools for assessing amputee rehabilitation that can be used to better understand kinematics in patients with a wide range of orthopaedic pathology, including hip and knee arthritis and degenerative conditions of the spine. A portion of the studies associated with the Department's $29.4 million National Institutes of Health (NIH) Helping to End Addiction Long-Term (HEAL) Initiative award will be conducted in the METRiCS Lab.

The METRiCS group hopes to use these biomechanical assessments to inform assistive device design and control. Based on pioneering biomechatronic work with electronic percutaneous osseointegrated implants that enable bi-directional volitional motor control of, and sensory/proprioceptive feedback from, external prostheses, METRiCS aims to formulate brain-machine interface platform technology that can be applied to a broad range of motion disorders, including paralysis. Meanwhile, for patients with phantom limb pain, METRiCS plans to identify brain functional connectivity mechanisms of chronic pain emergence and pain severity, as well as neuroimaging-based biomarkers and neuropsychological risk factors to stratify patients susceptible to chronic pain for earlier treatment, to personalize interventions to achieve greater benefit, and to develop novel neuromodulation therapies.

Orthotics and Prosthetics Research

Mission Statement

The mission of the UCSF Orthotic and Prosthetic research (OPR) team is to improve patient care through developing evidence- based programs and protocols. The OPR group utilizes an interdisciplinary approach gathering patient reported and functional outcome measures to determine the impact of orthotic and prosthetic devices on patients' quality of life and goals.

Project Collaborations

The overarching aim of the OPR team is to use research to inform clinical decision making and enhance outcomes for orthotic and prosthetic patients around the globe. The OPR group has multiple collaborations within UCSF Orthopaedic Surgery, most notably with the HPC, iCORES and METRICs on osseointegration and IGOT, on cost benefit analyses of prosthetic use in Tanzania.

Select Projects Include:

Optimization of Cranial Remolding Orthoses

Site Investigator: Chrysta Irolla, MS, MSPO, CPO

For babies diagnosed with plagiocephaly or brachycephaly the standard treatment is a cranial remolding orthosis (CRO). This retrospective chart review is investigating the impact of treatment parameters like age and cranial deformity on CRO efficacy.

Empirical Measurement of Dosing Efficacy in Pectus Carinatum Bracing: A Prospective Cohort Study

Site Investigator: Chrysta Irolla, MS, MSPO, CPO

Pectus carinatum is a chest wall deformity most commonly seen in teenage boys. Prior to skeletal maturity, correction of this prominence can be achieved with the use of a pectus carinatum orthosis (PCO). This study is collecting wear time data, in-brace pressure data and patient reported outcome measures to optimize the orthotic treatment.

Sponsor: American Orthotic and Prosthetic Association

Physical Rehabilitation Optimization and Patient Education for Life (PROPEL) Site Investigator: Matthew Garibaldi, MS, CPO

This study is assessing the impact of a new comprehensive wellness program for persons with lower limb loss using a multidisciplinary team approach. The personalized 12-week wellness program incorporates strength training, nutrition education, and pain management. The changes in physical function are measured through assessing muscle strength, balance, and endurance pre and post program. The improvements in quality of life and pain are being measured through patient-reported outcomes administered before, throughout, and at the end of the 12-week program.

Proximal Junctional Kyphosis Rates after the Introduction of the UCSF Soft TLSO

Site Investigator: Vedat Deviren, MD

This is a retrospective study (chart review) looking at the incidence of proximal junctional kyphosis (PJK) in UCSF patients who have received a soft TLSO (backpack brace) post-operatively. The UCSF soft TLSO was designed to restrict trunk motion with the intention of decreasing the likelihood of PJK, and we are interested in how effective it is. Sponsor: UCSF NOVA Grant

Starting in 2021:

The Impact of Knee Orthoses on Community Involvement for Osteoarthritis Patients

Site Investigator: Erik Hansen, MD

This study will measure the effects of unloader knee orthoses on activity and pain levels of participants with unilateral knee osteoarthritis. An Actigraph activity monitor in addition to various outcome measures will be used to investigate the out of-clinic benefits of the unloader knee orthoses.

Sponsor: American Orthotic and Prosthetic Association

New Faculty

The UCSF Dept. of Orthopaedic Surgery is pleased to welcome four new faculty members, all of whom have unique research interests.

Rhonda Watkins, MD, MPH

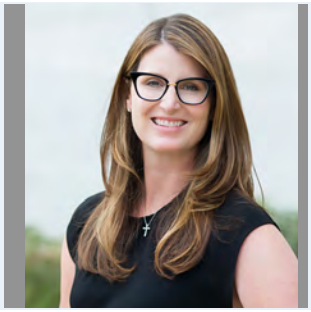
Pediatric Orthopaedics

Lyndly Tamura, MD

Non-Op Spine

Joelle Gabet, MD

No- Op Spine



Sara Edwards, MD

Sports Medicine

Stephanie Wong, MD

Sports Medicine

Lan Chen, MD

Foot and Ankle

Lauren Shapiro, MD

Hand and Upper Extremity

Lauren Santiesteban, MD

Hand and Upper Extremity

New Faculty

Courtney Sagar, MD

Pediatric PM&R

Kathryn Sigford, MD

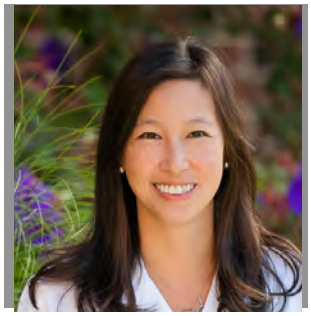
Pediatric PM&R

David Gendelberg, MD

Trauma/Spine

Ashraf El-Naga, MD

Trauma/Spine



Jennifer Tangtiphaiboontana, MD

Trauma/Sports Medicine

Residency Highlights

The year 2020 marks another successful year for the UCSF Dept. of Orthopaedic Surgery Residency Program in terms of outstanding research that directly improves patient care.

Residents performed international, clinical, and basic science research that was published in leading orthopaedic journals across several subspecialties, and presented at national and international meetings. The UCSF Dept. of Orthopaedic Surgery residents were awarded several awards for research, as well as for clinical care and leadership, as highlighted below.

In the upcoming year, we continue to expand the goals of our research. We will continue to have second year residents apply for the Orthopaedic Research and Education Foundation (OREF) research grant, and will also expand that opportunity to the interns, with the goal of establishing a research track for longitudinal studies earlier in their research career.

We will continue to expand our Web site and provide information and support on grant writing, manuscript preparation, and how to perform specific studies, such as meta-analyses and systematic reviews, as well as cost effective analyses.

The beginning of 2021 is already a landmark year, with many of the residents presenting at the American Academy of Orthopaedic Surgeons (AAOS) and Orthopaedic Research Society (ORS) annual meeting, and we look forward to the rest of the year and the innovative research that our residents continue to perform.

2019 JOJ Research Recipients

Leah Demetri, MD

- JOJ grant
- Resident Stryker/JRGOS grant ($2,500)

Favian Su, MD

Publications

- Su, F; Allahabadi, S; Bongbong, D; Feeley, B; Lansdown, DA. Minimal Clinically Important Difference, Substantial Clinical Benefit, and Patient Acceptable Symptom State of Outcome Measures Relating to Shoulder Pathology and Surgery: A Systematic Review. Current Reviews in Musculoskeletal Medicine. Accepted 12/8/20.
- Friedman, J; Su, F; Zhang, AL; Feeley, B; Allen, C; Souza, R; Ma, CB; Li, X; Lansdown, DA. Patient Reported Activity Levels Correlate with Early Cartilage Degeneration after Anterior Cruciate Ligament Reconstruction. American Journal of Sports Medicine. Accepted 9/9/20.
- Allahabadi, S; Su, F; Lansdown, DA. A systematic review of orthopaedic and sports medicine injuries and treatment outcomes in Women's National Basketball Association and National Basketball Association players. Orthopaedic Journal of Sports Medicine. Accepted 8/31/20.

Presentations

- Su, F; Cogan, C; Bendich, I; Zhang, N; Wooley, M; Kuo, AC. The Effect of Hepatitis C in Total Shoulder Arthroplasty among US Veterans. California Resident Research Symposium. 9/25/20.

Heather Roberts, MD

Grants

• AO Trauma North America Resident Research Grant: $10,000, 10/2019-6/2022

• AO Alliance: $10,000, 10/2019-10/2020

• JOJ: $5000, 7/2019-6/2020

• CTSI: $4000, 6/2019-6/2020

Presentations

• Roberts, HJ; Albright, P; Shearer, DW; Won, N; MacKechnie, M; Coughlin, RR; Miclau, T; Morshed, S; Sabharwal, S. "Motivations and impact of international rotations in low- and middle-income countries for orthopedic surgery residents: Are we on the same page?" Accepted for podium presentation at the Association for Surgical Education Annual Meeting, April 28-30, 2020 (conference canceled due to COVID).

• Roberts, HJ; Rogers, S; Ward, D; Kandemir, U. "Protocol-Based Multidisciplinary Comanagement for Hip Fracture Care: Three Years of Experience at an Academic Medical Center." Podium presentation at the 2020 Orthopedic Trauma Association Annual Meeting, October 21-24, 2020.

• Solarczyk, J; Roberts, HJ; Kandemir, U; Ward, D. "Will Medicare's Bundled Payments Program Threaten Patient Access? Early Experience With Bundled Payments for Care Improvement Advanced for Internal Fixation of the Hip and Femur." Poster at the 2020 Orthopedic Trauma Association Annual Meeting, October 21-24, 2020.

Publications:

• von Kaeppler, EP; Kramer, EJ; Donnelley, CA; Wu, HH; Marseille, E; Eliezer, E; Roberts, HJ; Shearer, DW; Morshed, S. "The initial economic burden of femur fractures on informal caregivers in Dar es Salaam, Tanzania." Malawi Med J (in press).

• Roberts, HJ; Albright, P; Shearer, DW; Won, N; MacKechnie, MA; Coughlin, RR; Miclau, T; Morshed, S; Sabharwal, S; and the COACT Resident Rotation Study Group. "Motivations and impact of international rotations in low- and middle-income countries for orthopaedic surgery residents: Are we on the same page?" Am J Surg (in press).

• Coburn, A; Shearer, DW; Albright, P; Ali, S; Roberts, HJ; Haonga, B; Eliezer, E; Chu, K; Morshed, S. "Evaluating reliability and validity of modified radiographic union scale for tibia (mRUST) among North American and Tanzanian surgeons." OTAI (in press).

• Albright, P; MacKechnie, M; Roberts, HJ; Shearer, DW; Padilla, LG; Segovia, J; Quintero, JE; Amadei, R; Baldy dos Rios, F; Miclau, T. "Open tibial shaft fractures: Treatment patterns in Latin America." J Bone Joint Surg Am 102(22), e126, 2020.

• Donnelley, C; Won, N; Roberts, HJ; Von Kaeppler, E; Albright, P; Woolley, PM; Haonga, B; Shearer, DW; Sabharwal, S. "Resident Rotations in Low- and Middle-Income Countries: Motivations, Impact, and Host Perspective." J Bone Joint Surg OA 5(3), 2020.

• Donohoe, E; Roberts, HJ; Miclau, T; Kreder, H. "Management of Lower Extremity Fractures in the Elderly: A Focus on Post-Operative Rehabilitation." Injury 51(Suppl 2), S118-S122, 2020.

• Von Kaeppler, E; Donnelley, C; Roberts, HJ; O'Hara, NN; Won, N; Shearer, DW; Morshed, S. "Impact of North American Institutions on Orthopedic Research in Low- and Middle-Income Countries." Orthop Clin N Am 51, 177-188, 2020.

Alejandro Cazzulino, MD

Publications

• Swarup I, Cazzulino A, Williams BA, Spiegel D, Shah AS. Outcomes after Surgical Fixation of Posterior Sternoclavicular Fracture-Dislocations in Children. Journal of Pediatric Orthopedics, October 2020.

• Swarup I, Hughes M, Cazzulino A, Spiegel D, Shah A. Open Reduction and Fixation of Acute Sternoclavicular Fracture-Dislocations in Children. Journal of Bone and Joint Surgery 2020.

• Meza BC, Swarup I, Woodard T, Cazzulino A, Talwar D, Shah AS. Pediatric Orthopedic Surgery in Opioid-Naïve Patients: Incidence and Risk Factors for Obtaining Opioid Prescription Refills. Journal of Pediatric Orthopedics. 2020.

• Cazzulino A, Gandhi R, Woodard T, Ackshota N, Janjua B, Arlet V, Saifi C. Utilization of hooks at the upper instrumented level in adult spinal deformity surgery. The Journal of Spine Surgery. 2020.

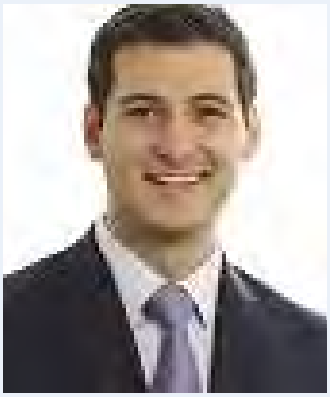
• Cazzulino A, Wu W, Allahabadi S, Swarup I. Management of Unstable SCFE: A Critical Review Analysis. The Journal of Bone and Joint Surgery.

Presentations:

• Cazzulino A, Swarup I, Williams BA, Spiegel D, Shah AS. Patient Reported Outcomes after Surgical Fixation of Acute Posterior Sternoclavicular Physeal Fractures and Dislocation in Children. Orthopedic Research and Education Foundation California Region Resident Research Symposium. Virtual. September 25, 2020.

• Cazzulino A, Gandhi R, Woodard T, Ackshota N, Janjua MB, Arlet V, Saifi C. Soft Landing: Can it prevent Proximal Junctional Kyphosis and Proximal Junctional Failure in Adult Spinal Deformity?. Scoliosis Research Society (SRS) 55th Annual Meeting. Phoenix, Arizona. September 9-12, 2020.

• Meza B, Swarup E, Woodard T, Cazzulino A, Shah A. Opioid-Seeking Behavior After Pediatric Orthopaedic Surgery: An Analysis of Incidence and Risk Factors. American Academy of Orthopedic Surgery (AAOS) Annual Meeting. Orland Fl. March 24-28 2020.



Alex Gornitzky, MD

Presentations

• Nguyen T, Khanna K, Gornitzky AL, Diab M. Idiopathic stroke after syndromic and neuromuscular scoliosis surgery: a case report and literature review. AME Case Reports. eCollection 2019.

• Gornitzky AL, Kim AE, O'Donnell JM, Swarup I. Diagnosis and Management of Osteomyelitis in Children: A Critical Analysis Review. JBJS Reviews. 2020; 8(6):e1900202

Sachin Allahabadi, MD

Awards

• Oct 2019 - 2nd place award in the clinical science category, Orthopaedic Research and Education Foundation 2019 California Resident Research Symposium

• Aug 2019 - Omer A. Ilahi Donor Award for paper in the clinical sciences, Western Orthopaedic Association 2019 meeting (awarded to co-author, Jonathan Cheah)

Presentations

• Allahabadi S*, Hagen M, Zhang AL, Feeley BT, Grace T, Ma CB. A randomized single-blinded trial of early rehabilitation versus immobilization after reverse total shoulder arthroplasty. Orthopaedic Research and Education Foundation California Resident Research Symposia, 2019. 2nd place award, clinical sciences. Podium presentation.

• Cheah J, Allahabadi S*, Cortes X, Sequeira N, Kim H, Vail T. Supporting orthopaedic resident education and advancement in leadership skills. Omer A. Ilahi Donor Award for paper in the clinical sciences. Western Orthopaedic Association Annual Meeting, 2019. Podium presentation.

William Rubenstein, MD

Awards

• 3rd place, OREF Research Symposium

Obiajulu Agha, MD

Awards

• OREF Research Symposium 2020, basic: 2nd Place

Trainee Highlights

The UCSF Dept. of Orthopaedic Surgery Laboratories have had another successful year in terms of musculoskeletal research. For example, our Parnassus Heights Labs continue to grow in size and extramural funding. In 2020, the Parnassus Heights Labs welcomed more than 16 new employees to its research enterprise. The Labs currently have more than 35 trainees including postdocs, fellows, visiting scholars, graduate students, technicians, interns, and staff researchers. Their efforts continue to advance the field of musculoskeletal biology through outstanding contributions in the study of bone, cartilage, tendon, and muscle.

Trainees from various Dept. of Orthopaedic Surgery Laboratories were awarded competitive and highly prestigious NIH awards including F30, F31, and F32 grants. Additionally, they have presented at a broad range of national and international meetings, including the Orthopaedic Research Society (ORS) and Gordon Research Conferences. Our basic research scientists continue to publish in leading journals and each day, are accelerating the discovery of novel strategies for healing the musculoskeletal system.

Because of these sustained contributions and our ongoing success, the Department has maintained its high ranking in NIH funding. We look forward to the rest of the year and the innovative research that the lab personnel continue to achieve.

Alliston Laboratory Highlights

Neha Dole, PhD,
Assistant Researcher,
Alliston Laboratory

- Awarded the prestigious ASBMR 2020- John Haddad Young Investigator Award.
- Received the Outstanding Abstract Award from the Endocrine Society.
- Publication: Dole, NS ; Yee, CS; Mazur, CM; Acevedo, C; Alliston, T. TGF beta Regulation of Perilacunar/Canalicular Remodeling Is Sexually Dimorphic. Journal of Bone and Mineral Research. August 2020. DOI: 10.1002/jbmr.4023.

Karsyn Bailey, MD/PhD Candidate,
Alliston Laboratory

- Presented a moderated poster at the Orthopaedic Research Society Annual Meeting Osteocytic TGFβ Contributes to Post-traumatic Osteoarthritis through Control of Subchondral Bone Plate Thickness, February 2020
- Presented an e-poster at the American Society for Bone and Mineral Research Annual Meeting. Mechanosensitive Control of Articular Cartilage and Subchondral Bone Homeostasis Requires Osteocytic TGFβ Signaling, September 2020
- Invited speaker to Stanford Joint and Osteoarthritis Imaging with Novel Technology (JOINT) group meeting. Bone/cartilage crosstalk in joint disease: a role for osteocytes, September 2020
- Publications: Bailey KN, Nguyen J, Yee CS, Dole NS, Dang A, Alliston T. Mechanosensitive Control of Articular Cartilage and Subchondral Bone Homeostasis Requires Osteocytic TGFβ Signaling. Arthritis Rheumatol. 2020 Oct 6. doi: 10.1002/art.41548. Epub ahead of print. PMID: 33022131.
- Graduated with her PhD from the UC Berkeley/UCSF Graduate Program in Bioengineering and returned to UCSF School of Medicine to complete her MD

Charles Schurman, Graduate Student, Alliston Laboratory

• Awarded Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship (F31) through September 2021: Age-related Control of Bone Quality by Osteocyte TGF-beta Signaling

• Oral Presentation at the 2020 American Society for Bone and Mineral Research Annual Meeting: Disrupted Lacunocanalicular Networks, Mass Transport, and Osteocyte Mechanosensation in Bone with Aging and Disrupted TGF Signaling

• Publications: Schurman, C.A., Verbrugen S.W., Alliston, T., Disrupted Osteocyte Connectivity and Pericellular Fluid Flow in Bone with Aging and Defective TGFβ Signaling. PNAS (In Review)

Jihee Yoon, DDS/PhD Candidate, Alliston Laboratory

• Awarded UCSF Program in Craniofacial Biology's Caroline H. Damsky Award, April 2020

• Advanced to PhD candidacy, May 2020

• Successfully passed qualifying examination in the UCSF Graduate Program in Oral and Craniofacial Sciences to advance to candidacy for a PhD

• Awarded an NIH F30 research grant to support her training as a Dentist-Scientist

• Awarded the UCSF Caroline Damsky grant to pursue a project on the role of osteocytes in orthodontic tooth movement

Jean Luke Campos, Graduate Student, Alliston Laboratory

• Successfully passed qualifying examination in the UCSF Graduate Program in Developmental and Stem Cell Biology to advance to candidacy for a PhD

Serra Kaya, PhD-Postdoc, Alliston Laboratory

• Awarded a UCSF COral Presentation at the Orthopaedic Research Society Annual Meeting,

Enrichment for genetic predictors of bone quality using unbiased analysis of mouse transcriptome and human genome-wide association study, February 2020

• Poster Presentation at American Society for Bone and Mineral Research Annual Meeting,Transcriptomic analysis of aged mouse bone identifies novel genes enriched for genetic associations with bone fracture and bone mineral density in human, September 2020

• Poster Presentation at the CCMBM Retreat and Awarded Best Postdoc Scholar Poster, Transcriptomic analysis of aged mouse bone identifies novel genes enriched for genetic associations with bone fracture and bone mineral density in human, September 2020

• Reviewer, Calcified Tissue International 2020

• Publication: Monteiro, D. A., Dole, N. S., Campos, J. L., Kaya, S., Schurman, C. A., Belair, C. D., Alliston, Tamara. Fluid shear stress generates a unique signaling response by activating multiple TGFβ family type I receptors in osteocytes. The FASEB Journal. (Accepted, in publication) 2020

• Established mouse2human.org - a public online resource that facilitates computational analysis of laboratory-based datasets using UK Biobank data from 500,000 humans to identify new genetic determinants of skeletal health

David Monteiro, PhD, Graduate Student, Alliston Laboratory

• Graduated with his PhD from the UC Berkeley/ UCSF Graduate Program in Bioengineering and is pursuing a career as a data scientist in Boston, MA

• Publication: Monteiro DA, Dole NS, Campos JL, Kaya S, Schurman CA, Belair CD, and Alliston T. Fluid shear stress generates a unique signaling response by activating multiple TGFβ family type I receptors in osteocytes. The FASEB J. (2020, in press)

• Presentation: Doctoral exit seminar (defense). Title: Physical cues regulate the localization and activation of TGFβ receptors to control the quantity and quality of signaling pathway activity. December 7, 2020.

• Presentation: American Society for Bone and Mineral Research Annual Meeting. Poster: Fluid Shear Stress Rapidly Activates TGFβ Family Signaling in Osteocytes. September 11-15, 2020.

Collaborative lab publications:

• Dole, N. S., Yee, C. S., Schurman, C. A., Dallas, S. L. & Alliston, T. Assessment of Osteocytes: Techniques for Studying Morphological and Molecular Changes Associated with Perilacunar/Canalicular Remodeling of the Bone Matrix in Skeletal Development and Repair 2230, 303–323 (Humana, New York, NY, 2021)

Schneider Laboratory Highlights

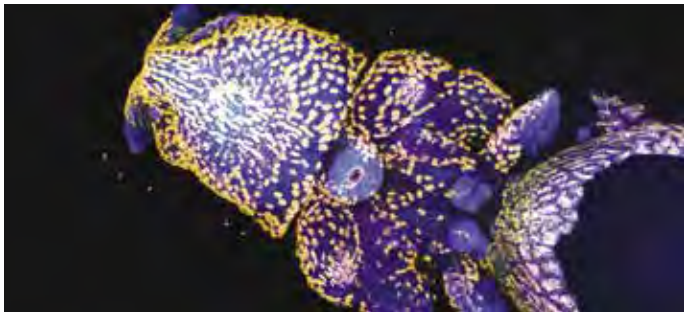
An Nguyen, PhD Candidate

• Awarded an NIH F30 research grant through August of 2021

Zuzana Vavrušová, PhD Candidate

• Awarded an NIH F30 reConference chair: Craniofacial Morphogenesis and Tissue Regeneration (GRS); title: Interconnecting Concepts of Craniofacial Development and Disease to Incite New Therapies, February 2020.

• Presented at: Zuzana Vavrušová, Daniel Chu, Jennifer L. Fish, and Richard A. Schneider. The role of Shh signaling in regulating species-specific jaw size. 43rd Annual SCGDB Meeting, online, October 2020, talk.



• Presented at: Zuzana Vavrušová, Daniel Chu, Jennifer L. Fish, and Richard A. Schneider. The Role of SHH Signaling in Regulating Species-Specific Jaw Size. SDB 79th Annual Meeting, Online, July 2020, poster.

• Presented at: Zuzana Vavrušová, Daniel Chu, Jennifer L. Fish, and Richard A. Schneider. Species-Specific Regulation of SHH Signaling and Jaw Size. Gordon Research Conferences: Craniofacial Morphogenesis and Tissue Regeneration, Lucca (Barga, Italy), February 2020, poster.

• Publication: Daniel Chu, An Nguyen, Spenser S. Smith, Zuzana Vavrušová, and Richard A. Schneider. Stable Integration of an Optimized Inducible Promoter System En- ables Spatiotemporal Control of Gene Expression Throughout Avian Development. Biology Open, 2020.

Spenser Smith, PhD, Postdoc

• Awarded an NIH F32 research grant, runs through 2021

Collaborative lab publications:

• Smith SS, Chu D, Qu T, Schneider RA. 2020. Differential sensitivity to TGFβ signaling and regulatory changes in the Mmp13 promoter underlie the development and evolution of the avian jaw skeleton. BioRxiv https://doi.org/10.1101/2020.12.23.424223.

• Stable integration of an optimized inducible promoter system enables spatiotemporal control of gene expression throughout avian development. Biol Open. 2020 Oct 06; 9(10). Chu D, Nguyen A, Smith SS, Vavrušová Z, Schneider RA. PMID: 32917762.

Poster Presentations:

• Developing an in vivo system for PGC migration using xenotransplantation. Afonso, L., Chacon, B., Vavrušová, Z., Nguyen, D., Tao, Y., Schneider, R. A., Clark, A., and D. Laird. Society for Developmental Biology (SDB) 79th Annual Meeting, Online, July 9th-15th.

• Smith,S., Chu, D., Lucena, A., Qu, T., and R. A. Schneider. Runx2 Gene Evolution and Isoform Expression: Effects on transcriptional activity and the regulation of Mmp13 during jaw development. Society for Developmental Biology (SDB) 79th Annual Meeting, Online, July 9th-15th.

• The Role of SHH Signaling in Regulating Species-Specific Jaw Size. Vavrušová, Z., Chu, D., Fish, J., and R. A. Schneider. Society for Developmental Biology (SDB) 79th Annual Meeting, Online, July 9th-15th.

• Smith SS, Chu D, Qu T, Krish G and Schneider R. Sept 2020. Differential sensitivity to TGF signaling and regulatory changes to the Mmp13 promoter under species-specific variation in bone resorption and jaw length. ASBMR 2020 Meeting, P-374.

• Qu T, Smith SS, and Schneider R. March 2020. The Role of TGF Signaling in Neural Crest-Mediated Jaw Bone Remodeling. AADR General Session, #2417, Washington D.C.

• Smith SS, Chu D, Qu T, and Schneider R. February 2020. Multiple levels of gene regulation in the development and evolution of the jaw. Craniofacial Morphogenesis and Tissue Regeneration conference. Barga, Italy.

Podium Presentation:

• The Role of SHH Signaling in Regulating Species-Specific Jaw Size. Vavrušová, Z., Chu, D., Fish, J., and R. A. Schneider. Society for Craniofacial Genetics and Developmental Biology (SCGDB) 43rd Annual Meeting, Online, October 19th-20th.

Linshanshan Wang, Undergraduate Research Intern

• Presented at Orthopaedic Research Society Annual Meeting

• Talk: T2* mapping of human cartilage endplate: spatial differences and association with adjacent disc degeneration.

• Publications: Wang L, Han M, Wong J, Zheng P, Lazar AA, Krug R, Fields AJ. Evaluation of human cartilage endplate composition using MRI: spatial variation, association with adjacent disc degeneration, and in vivo repeatability. J Orthop Res. 2020 Jun 27. PMID: 32592504

Justin Scheer, MD, PGY-5

• Awarded an NIH NIAMS F32 research grant (declined)

• Awarded an NIH NINDS R25 research grant, runs through 2021

Jerry Jung, PhD, Postdoc

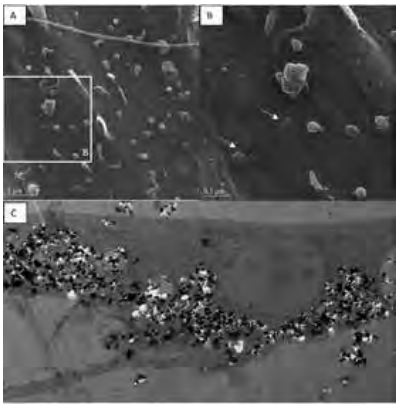
• Awarded a Molecular Foundry research proposal, “Multiscale structural characterization of the human cartilage endplate”

Mohamed Habib, PhD

• A successful collaboration with Orthofix co. to study a novel strategy for enhanced bone healing procedure. This research work has been published recently in Tissue Engineering: Part A (TEA-2020-0102) and has been submitted as an invention disclosure form to the Innovation Ventures office at UCSF (case number SF2020-120).

• Novel approaches for stimulating new bone growth are necessary to overcome the challenge of delayed bone healing. In this study, we cultured human bone marrow-derived mesenchymal stem cells with an iron-ion doped tri-calcium phosphate bone substitute (Fe-TCP) and exposed them to a pulsed electromagnetic field (PEMF) signal to investigate their effects on osteogenesis. We revealed the synergistic effects of Fe-TCP and PEMF and demonstrated that the combination of these technologies could provide a promising method for accelerating bone healing in a clinical setting.

• Publications: Mohamed Habib, Devante A. Horne, Khaled Hussein, Dezba Coughlin, Erik I. Waldorff, Nianli Zhang, James T. Ryaby, and Jeffrey C. Lotz (2020). Magnetic Nanoparticles Synergize with Pulsed Magnetic Fields to Stimulate Osteogenesis In Vitro. Tissue Engineering: Part A (TEA-2020-0102)



Representative images demonstrate the interaction between MSCs and MNBS. SEM images at low magnification (A) and high magnification (B), light MNBS cell-surface attachment and internalization just below the cell surface (arrows) as single nanoparticles. TEM image (C) confirm MNBS internalization by MSC, mesenchymal stem cell.

Bailey Laboratory Highlights

Collaborative lab publications:

• Saul Pacheo Elorza (2019 Undergraduate Research Volunteer) presented his work on “In-clinic motion assessments as objective outcomes for tracking shoulder function during post-operative recovery” at the 2020 Annual Meeting of the Orthopaedic Research Society in Phoenix, AZ.

• Priya Nyayapati (2020 Medical Student Volunteer) presented her work on “Predicting lumbar multifidus fat fraction from T2 MRI” at the 2020 Annual Meeting of the Orthopaedic Research Society in Phoenix, AZ.

Karim Khattab, Bioengineering Graduate Student

• Awarded NIH HEAL training fellowship to investigate “How pain-related measures and psychological factors influence compensatory movement biomechanics and biophysical outcomes in chronic low back pain”, running through 2022 and in collaboration with the UCSF REACH Project. Karim is being co-mentored by Jeannie Bailey and Jeff Lotz.

Marcucio Laboratory Highlights

Heather Atwood

• Awarded an NIH NIDCR F32, research grant through 2021

News and Media

Congratulations to Tamara Alliston, Ph.D.
2020 Adele L. Boskey Award Recipient

Tamara Alliston, Ph.D., is a Professor in the UCSF Department of Orthopaedic Surgery and the Director of the UCSF Musculoskeletal Center. With a focus on TGFβ signaling and mechanobiology, her laboratory investigates the interaction between physical and biochemical signals in the control of skeletal cell differentiation and the role of these pathways in bone fragility and osteoarthritis. Supported by the NIH, NSF, and DOD, her group employs approaches from molecular and cell biology, materials science, and engineering to identify mechanisms of skeletal disease in order to advance the development of new therapeutic strategies.

"As the pioneer of bone quality research, Adele Boskey cleared a path that I have followed ever since. Early in my career, Adele encouraged *our work on the biological control of bone quality before others saw its relevance, even as her own team's brilliant research provided the framework to understand bone quality and its clinical significance. For these reasons, I am especially proud to receive an award that honors this groundbreaking scientist and leader.*

Thank you to my mentors, James Shinkle, JoAnne Richards and Rik Derynck, and colleagues, Jennifer Westendorf, Robert Nissenson, and Farshid Guilak for their nomination. I am especially grateful to the colleagues, trainees, and staff who have fearlessly joined me in exploring the vast and exciting territory between bone cell biology and materials science. Your scientific creativity, intellectual courage, and playful curiosity inspire me and give rise to the best science and scientists."

~ Tamara Alliston, Ph.D.

UCSF Department of Orthopaedic Surgery appoints Carlin Senter, MD, as Director of Primary Care Sports Medicine

The UCSF Department of Orthopaedic Surgery is pleased to announce that Carlin Senter, MD has been appointed as the Director of Primary Care Sports Medicine Service within the Division of Sports Medicine and Shoulder Surgery.

“Our team is comprised of a group of physicians specifically trained in primary care as well as sports medicine,” Dr. Senter said. “Our goal is to help patients recover from injuries or illnesses that prevent them from being as active as they want to be. We determine whether a patient’s condition requires surgery or if the problem can be managed by other types of treatment. We are also very dedicated to teaching current and future physicians how to practice musculoskeletal medicine, as well as actively involved in research to help solve common and yet complex sports medicine conditions that affect all of us.”

The UCSF Department of Orthopaedic Surgery is pleased to announce the appointment of Stephanie Wong, MD, Assistant Professor of Clinical Orthopaedic Surgery

Dr. Stephanie Wong is a board-eligible orthopaedic surgeon specializing in sports medicine and minimally-invasive arthroscopic surgery of the hip, knee and shoulder. In the hip, she frequently treats labral tears, FAI (femoroacetabular impingement), hamstring injuries, gluteus tears, and various athletic hip injuries. Dr. Wong is a specialist in advanced hip arthroscopy for hip preservation, performing labral repair and reconstruction. In the knee, she specializes in ACL tears, meniscus tears, and cartilage injuries- regularly performing ACL reconstruction and meniscus repairs. In the shoulder, she treats rotator cuff tears, shoulder dislocation/instability, and biceps injuries.

UCSF Sports Medicine launches new podcast: 6-8 Weeks: Perspectives on Sports Medicine

The UCSF Department of Orthopaedic Surgery is proud to announce the launch of a new podcast by the Division of Sports Medicine: **6-8 Weeks: Perspectives on Sports Medicine.**

Hosted by Nirav Pandya, MD, Brian Feeley, MD and Drew Lansdown, MD, the podcast presents the people and stories behind sports medicine at UCSF and our community of learners.

The podcast is available from the links below, as well as on iTunes and Spotify.

The UCSF Department of Orthopaedic Surgery is pleased to announce the appointment of Lan Chen, MD, Associate Clinical Professor, Foot and Ankle Surgery

Dr. Lan Chen, MD, is a board certified orthopaedic surgeon who specializes in foot and ankle surgery. She treats all conditions of the foot and ankle, including arthritis, bunions, flat feet, tendon disorders and fractures, and performs surgeries ranging from minimally invasive procedures to complex reconstructions. Her goal is to offer treatment options that enable patients to regain a high level of function and improve their quality of life.

Podcast: Ishaan Swarup, MD featured in "Best of POSNA 2020"

Dr. Ishaan Swarup, MD, a pediatric orthopaedic surgeon in the UCSF Department of Orthopaedic Surgery, was recently featured in a podcast from the Journal of Pediatric Orthopaedics. This podcast includes executive summaries of recent studies and interviews with authors and guest commentators.

This episode is titled "Best of POSNA 2020 – QSVI" and features the best articles from the Pediatric Orthopaedic Society of North America (POSNA) Annual Meeting.

Dr. Richard Gosselin has been appointed as the Inaugural Chief Orthopaedic Surgeon for the International Committee of the Red Cross

Dr. Richard Gosselin has been appointed as the Inaugural Chief Orthopaedic Surgeon for the International Committee of the Red Cross.

Dr. Gosselin is a long-time clinical UCSF faculty member and co-founder of the Department's initiative, the Institute for Global Orthopaedics and Traumatology (IGOT). He has dedicated the bulk of his career to international medicine and orthopaedic care.

The UCSF Department of Orthopaedic Surgery is pleased to announce the appointment of Joelle Gabet, MD, Clinical Instructor, Non-Operative Spine

Dr. Joelle Gabet, MD, is a physical medicine and rehabilitation specialist who cares for patients with neck and back pain. She specializes in improving function and decreasing pain in patients with spinal disorders. Her clinical interests also include neuromuscular medicine, neurorehab, spasticity, and amputee medicine. She will also be a member of the Department's osseointegration program. She will be seeing patients at the Orthopedic Institute and at the San Mateo Primary and Specialty Care Clinic.

Thomas A. Peterson, PhD, to lead Informatics for the UCSF REACH Center for Chronic Low Pack Pain

The UCSF Department of Orthopaedic Surgery is pleased the appointment of Thomas A. Peterson, PhD, an Assistant Professor, who will serve as Director of the Informatics Core for the UCSF REACH Center for Chronic Low Back Pain.

Patricia Zheng, MD, to lead UCSF's Integrated Spine Service

The UCSF Department of Orthopaedic Surgery is pleased to announce that Patricia Zheng, MD, a non-operative spine specialist, will take on the leadership role as Director of the Integrated Spine Service (ISS) at UCSF.

Erik McDonald, MD, Recipient of Teaching Excellence Award for Cherished Housestaff

Erik McDonald, MD, a resident in the UCSF Dept. of Orthopaedic Surgery, is the recipient of the Teaching Excellence Award for Cherished Housestaff (T.E.A.C.H.) from the UCSF School of Medicine, reflecting his outstanding didactic skills and abiding commitment to the education of medical students and residents.

The UCSF Department of Orthopaedic Surgery is pleased to announce the appointment of Sara L. Edwards, MD Associate Clinical Professor of Orthopaedic Surgery

Dr. Sara Edwards is a board-certified orthopaedic surgeon, who specializes in treating shoulder, elbow and knee injuries, non-operative management of shoulder arthritis, and sports-related injuries in all age groups and all levels – from recreational to elite athletes.

News and Media

International Women's Week at UCSF Honors our Orthopaedic Leaders, Commitment to Diversity

The UCSF Department of Orthopaedic Surgery is pleased to announce a special celebration to honor the women of our Department during UCSF's annual International Women's Day, which will be recognized worldwide on Sunday, March 8. This year's theme is #EachforEqual -- promoting the concept that an equal world is an enabled world.

Dr. Nirav Pandya featured on KQED Forum's piece on 'Newsom Proposal Could End School Fitness Exams'

SAN FRANCISCO (Feb. 11, 2020) -- Dr. Nirav K. Pandya, MD, a pediatric orthopedic surgeon and sports medicine specialist within the UCSF Dept. of Orthopaedic Surgery, was interviewed this week on KQED News Forum on the topic: Newsom Proposal Could End School Fitness Exams.

Amir Matityahu, MD, selected as Chair of Surgery at Regional Medical Center of San Jose

The UCSF Dept. of Orthopaedic Surgery is pleased to announce that Amir Matityahu, MD, an orthopaedic surgeon specializing in trauma and problem fractures and a Clinical Professor within the Department, has recently been selected as the new Chair of Surgery at Regional Medical Center of San Jose, a Level II Trauma Center that contracts surgical services from the UCSF Orthopaedic Trauma Institute.

UCSF appoints Jason Jagodzinski, MD, Informatics Lead for Pediatric Surgical Services

The UCSF Dept. of Orthopaedic Surgery is pleased to announce that Jason Jagodzinski, MD, pediatric orthopaedic surgeon, has accepted the position of Informatics Lead for Pediatric Surgical Services for UCSF Benioff Children's Hospital Oakland.

UCSF Dept. of Orthopaedic Surgery appoints Derek Ward, MD, as MarinHealth Physician Service Lead

As the MarinHealth Physician Service Lead, Derek Ward, MD will be responsible for planning, organizing, and directing daily clinical operations for the Orthopaedics Department at MarinHealth Medical Center in Kentfield, Calif. (Photo: UCSF Dept. of Orthopaedic Surgery)

Grants and Fellowships

Sachin Allahabadi, MD

• UCSF JOJ Ortho Resident Grant

Comparison of outcomes utilizing blood flow restriction training as a rehabilitation protocol in post-operative meniscus repair patients

7/1/2020-6/31/2021

$5,000

Jessye Aggleton, PhD

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

06/02/2020

$250

Tamara Alliston, PhD

• NIH NIDCR R01 A135199

The Mechanistic Control of Bone Quality and Joint Crosstalk by Osteocytes

6/3/2020-5/31/2025

$2,983,593

• NIH Natl Inst Arthr, Musculoskel & Skin P30 A133258

Core Center for Musculoskeletal Biology and Medicine

7/1/2019-6/30/2024

$3,866,912

• Sutter West Bay Medical Foundation A135898

Longevity Consortium

8/1/2020-5/31/2023

$94,902

• DOD US Army Med. Res. Acq. Activity W81 A132062

Identification of Novel Osteocyte-Regulatory Therapies to Prevent and Treat PTOA in Warfighters

9/30/2018-9/29/2021

$999,946

• NSF A128025

Mechanoregulation of Growth Factor Receptor Assembly and Signaling

9/1/2016-8/31/2020

$400,000

• NIH NIAMS R21 A129741

miRNA Coordination of TGF-beta / Wnt Signaling in Osteocyte Mechanotransduction

8/1/2017-7/31/2020

$383,570

• NIH NIDCR R01 A123992

The Mechanistic Control of Bone Extracellular Matrix Material Properties by TGFb

8/1/2014-5/31/2020

$2,261,281

• New Equipment, Department of Orthopaedic Surgery, UCSF

Developing a State-of-the-art Zebrafish Facility at Parnassus Heights

7/01/2020-6/30/2021

$50,000

• UCSF Institutional Matching Instrumentation Award

MicroComputed Tomography in the UCSF Skeletal Biology & Biomechanics Core

1/22/20-1/21/21

$122,000

• NIH NIAMS P30AR075055 (CCMBM Tools and Technology Grant)

Development of M2Hbone - a web-based tool for identification of mouse genes relevant to human bone fragility

12/17/2019 - 06/15/2020

$5,000

Heather Atwood, PhD

• NIH NIDCR F32 A132192

Mechanisms of Shape Variation in a Mouse Model of Craniofacial Birth Defects

9/1/2018-8/31/2021

$190,110

Jeannie Bailey, PhD

• DOD US Army Med. Res. Acq. Activity W81 A135195

Assessing biomechanical function and hip stabilizing muscle quality associated with transfemoral osseointegration

7/1/20-6/30/2022

$349,634

• NSF CDMI (Center for Disruptive Musculoskeletal Innovations) funded project

The effect of paraspinal muscle quality on post-operative dynamic sagittal balance outcomes for adult spinal deformity patients

11/01/2020 – 10/31/2021

$40,000

• NIH NIAMS P30AR075055 (CCMBM Pilot Feasibility Grant)

The mechanistic pathophysiology associated with paraspinal muscular degeneration and chronic low back pain

05/21/2020-12/31/2021

$39,000

Karsyn Bailey, PhD

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

06/02/2020

$108.00

Jeff Barry, MD

• OrthoCarolina Research Institute, Inc A134492

How to Improve the Results of Irrigation and Debridement for PJI Through the Use of Intraosseous Antibiotics

6/25/2019-6/24/2021

$2,500

Gaby Baylon, PhD

• NIH Diversity Supplement Award

Pairing of osteocyte tension and perilacunar material properties via perilacunar/ canalicular remodeling

7/1/18-7/31/20

$104,941

Sigurd Berven, MD

• Empirical Spine, Inc. A130354

LSS17001

A Concurrently Controlled Study of the LimiFlex" Paraspinous Tension Band in the Treatment of Lumbar Degenerative Spondylolisthesis with Spinal Stenosis, Clinical Trial

9/26/2017-9/19/2022

$51,854

• AOSpine International A134447

SDIM: Spinal Deformity Intraoperative Monitoring

5/1/2019-2/1/2022

$4,063

• AO Foundation A123247

Prospective Evaluation of Elderly Deformity Surgery: A Prospective Observational, Multicenter Study, Clinical Trial

7/1/2014-12/31/2021

$27,645

Stefano Bini, MD

• NIH Natl Institute on Aging A133586

The Oaks- A Mobile and Education Program for People with Osteoarthritis of the Knee

3/1/2019-2/29/2020

$70,000

Andrew Brack, PhD

• NIH NIAMS R01 A133478

Niche Regulation of Muscle Stem Cells

8/01/2019-5/31/2024

$2,562,213

• NIH NIA R21 A131831

Single cell activation dynamics *as a predictor and regulator of aged MuSC dysfunction.*

3/15/2019-1/31/2021

$425,252

• Department of Orthopaedic Surgery, UCSF

Develop a method to study radiotolerance inhuman muscle stem cells

7/01/2019-6/30/2020

$25,000

Shane Burch, MD

• Integra LifeSciences Corporation 106548/COV-DRSS-0002 A125223

DuraSeal Exact Spine Sealant System Post Approval Study, Clinical Trial

2/27/2015-2/27/2020

$48,580

Cindy Chang, MD

• Ossur Americas - Fellowship A135414

PCSM Fellowship program

10/1/2020-9/30/2021

$20,000

Michael Davies, MD

• Orthopaedic Research and Education Fdn. A135210

Characterizing human fibroadipogenic progenitors to decrease fatty infiltration in rotator cuff tears

12/1/2019-11/30/2020

$5,000

• AOSSM Young Investigator Grant – Basic Science YIG-2020-B

The role of age in fibroadipogenic progenitor-mediated muscle degeneration following rotator cuff tears

8/1/2020 – 7/31/2022

$40,000

Leah Demetri, MD

• UCSF JOJ Ortho Resident Grant

Health Disparities and Constriction Band Syndrome

7/1/2020-6/31/2021

$5,000

• J. Robert Gladden Orthopaedic Society/Stryker Resident Research Grant

Health Disparities and Construction Band Syndrome

8/4/2020-8/3/2021

$2,500

Sibel Demir-Deviren, MD

• Pfizer B3451002 A125917

A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficiency of Staphylococcus Aureus 4-Antigen Vaccine (SA4Ag) in Adults Undergoing Elective Posterior Instrumented Lumbar Spinal, Subcontract, Clinical Trial

9/3/2015-9/3/2022

$1,996,966

• Nocimed, LLC A128057

Clinical Development and Evaluation of the Nociscan" Virtual Discogram" Using Magnetic Resonance Spectroscopy for Identifying Painful and Non-Painful Intervertebral Discs of the Lumbar Spine, Clinical Trial

8/24/2016-12/15/2022

$1,125,112

Vedat Deviren, MD

• NOVA Department of Orthopaedic Surgery, UCSF

Determine the impact of two thoracolumnar sacral orthoses on PJK post-spinal fusion.

7/01/2020-6/30/2021

$5,000

Neha Dole, PhD

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

06/02/2020

$239

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Research Grant)

Understanding the Role of Sirt1 in Obesity-induced Metabolic Dysfunction of Osteocytes

12/22/2020-06/15/2021

$3,500

Brian Feeley, MD

• Orthofix Inc. A133456

Prospective, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Safety and Efficacy of Pulsed

7/8/19-12/31/2021

$491,556

• NIH RO1

Utilizing beige fat to improve muscle function after rotator cuff repair

07/01/2018-06/30/2022

$1,250,000 (TOTAL FUNDING)

• NIH R56

Phenotypes of pathologic vertebral endplate degeneration

09/26/2019-09/01/2021

$100,000

• NIH P30

Human Fibroadipoprogenitor (FAP) stem cells in rotator cuff disease: functional assessment of regenerative potential

01/01/2019-12/31/2021

$40,000

Aaron Fields, PhD

• NIH NIAMS R01 A129156

Role of the Cartilage Endplate in Spinal Disc Degeneration

4/1/2017-1/31/2022

$1,743,500

• NIH NIAMS UH2 A134016

Novel imaging of endplate biomarkers in chronic low back pain

9/26/2019-8/31/2021

$1,119,116

• North American Spine Society A131980

Does Enhancing Cartilage Endplate Permeability Improve Nucleus Pulposus Cell Function?

1/1/2019- 12/31/2020

$50,000

Alex Gornitzky, MD

• UCSF JOJ Ortho Resident Grant

Coping Skills after Pediatric Spine Fusion

7/1/2019-6/31/2020

$5,000

Nicholas Hanne, PhD

• NIH Natl Inst Dental & Craniofacial Res. – Fellowship A136138

Determining the Role of Extracellular Matrix Compliance and Composition on Facial Morphogenesis

12/1/2020- 11/30/2023

$204,462

Erik Hansen, MD

• Orthopaedic Research and Education Fdn. (OREF) A130350

Surgical Treatment of Chronic Periprosthetic Joint Infection: One-Stage vs. Two-Stage (STUDY), Subcontract, Clinical Trial

11/1/2017- 12/31/2020

$26,000

• American Orthotic & Prosthetic Assoc, New, P0546268 [CA-0166974]

The Effects of osteoarthritis bracing on community involvement, a pilot study

7/9/2020-7/2021

$15,000

Safa Herfat, PhD

• National Science Foundation 170 A130062

Development of a Diagnostic Device for Monitoring Fracture Healing NSF FULL SUBMISSION 11Oct2016

8/15/2017- 1/31/2021

$200,000

Chrysta Irolla, MS, MSPO, CPO

• American Orthotic & Prosthetic Assoc A130112

The Effects of a Custom Pectus Carintum Orthosis on Dosing Response and Quality of Life

7/18/2017-6/30/2021

$15,000

Igor Immerman, MD

• Super NOVA Department of Orthopaedic Surgery, UCSF

Patient Outcomes and Costs after Isolated Flexor Tendon Repairs of the Hand

6/1/19-5/31/2020

$10,000

JaeYoung Jung, PhD

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

06/02/2020

$219

Karim Khattab, PhD

• NIH HEAL Initiative Awardee Administrative Supplements to Promote Training in Clinical Research on Pain

How pain-related measures and psychological factors influence compensatory movement biomechanics and biophysical outcomes in chronic low back pain

09/23/2020 - 05/31/2024

$104,939

Alfred Kuo, MD, PhD

• Department of Orthopaedic Surgery, UCSF

Understanding racial disparities in outcomes after total knee replacement in Veterans

7/01/2020-6/30/2021

$25,000

Drew Lansdown, MD

• American Orthopaedic Soc for Sports Med A134539

The Relationship Between ACL Graft Quantitative Imaging Characteristics and Subjective and Functional Outcomes after ACL Reconstruction

8/1/2019- 7/31/2021

$49,860

• Arthroscopy Association of North America A132892

Advanced Quantitative Imaging of ACL Grafts: Comparing Autograft and Allograft Reconstructions

6/1/2019- 5/31/2021

$24,860

Tiffany Liu, MD

• Resident/Fellow Fast Track Grant

Correlation between visual appearance and histology of peripheral nerve sections (Award 3634)

1/1/21 to 12/31/21

$5000

Jeffrey Lotz, PhD

• National Science Foundation A134526

Phase II IUCRC UC San Francisco: Center for Disruptive Musculoskeletal Innovations (CDMI)

12/15/2019-11/30/2024

$499,997

• NIH NIAMS P30 A133258

Core Center for Musculoskeletal Biology and Medicine

7/1/2019-6/30/2024

$3,866,912

• NIH NIAMS U19 A134160

UCSF Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (UCSF REACH)

9/25/2019-5/31/2024

$29,513,784

• NIH NIAMS R56 A134021

Phenotypes of pathologic vertebral endplate degeneration

9/26/2019-8/31/2021

$669,247

• NIH Natl Inst Dental & Craniofacial Res. A135216

Center for Dental, Oral, and Craniofacial Tissue and Organ Regeneration (C-DOCTOR)

5/7/2020-4/30/2021

$184,139

• NIH NIDCR U24 A129002

Center for Dental, Oral, and Craniofacial Tissue and Organ Regeneration (C-DOCTOR)

3/1/2017-2/28/2021

$11,961,481

• NIH NIAMS P30 A123857

Core Center for Musculoskeletal Biology and Medicine

7/1/2014-3/31/2020

$ 2,993,910

• National Science Foundation A123593

IIP-1361975

UCRC for Technology Innovation for Novel Cost-Reducing and Quality-Enhancing Musculoskeletal Therapies

4/15/2014-3/31/2020

$520,500

• NSF CDMI (Center for Disruptive Musculoskeletal Innovations) funded project

Jeffrey Lotz, PhD and Robert Matthew, PhD

Reachable workspace

01/01/2020 – 12/31/2020

$40,000

C. Benjamin Ma, MD

• Aesculap Biologics LLC A133047

PRE CTA: A Phase 3, Prospective, Randomized, Partially Blinded Multi-Center Study to Measure the Safety and Efficacy of NOVOCART 3D Compared to Microfracture in the Treatment of Articular Cartilage Defects" Protocol # AAG-G-H-1220

1/26/2019- 1/25/2029

$8,000

• Aesculap Biologics LLC A134736

A Phase 3 Prospective, Randomized, Partially Blinded Multi-Center Study to Measure the Safety and Efficacy of NOVOCART 3D, Compared to Microfracture in the Treatment of Articular Cartilage Defects

3/30/2020- 3/29/2025

$1,722,564

• Zimmer, Inc. CMU2010-28E A117977

Prospective Post Market Clinical Follow-Up Study of the Zimmer Trabecular Metal- Reverse Shoulder System

6/15/2011-6/15/2024

$489,280

• Samumed, LLC SM04690-OA-08 A131723

A Phase 2, 52 Week, Single Center, Open-Label Study Utilizing Imaging Techniques and Evaluating the Safety and Efficacy of SM04690 Injectable Suspension for the Treatment of Moderately to Severely Symptomatic Knee Osteoarthritis

6/12/2018- 6/12/2023

$597,996

• Arthroscopy Association of North America A125441

Synovial Fluid Profile and T1p in Predicting Cartilage Degeneration after Anterior Cruciate Ligament Injuries

4/25/2015-4/25/2020

$25,000

• Vanderbilt University Medical Center VUMC63087 A130300

Operative versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears: A Multicenter Randomized Controlled Pragmatic Trial, Subcontract, Clinical Trial
7/1/2017-3/31/2020

$332,201

• Regentis Biomaterials, Ltd A132290

A Prospective, Open-Label, Multicenter Pivotal Study to Evaluate the Safety and Efficacy of GelrinC for the Treatment of Symptomatic Articular Cartilage Defects of the Femoral Condyle: A Comparison to Historical Control Microfracture

10/1/2018- 2/29/2020

$8,000

Ralph Marcucio, PhD

• Canadian Institutes of Health Research- University of Calgary A133192

The Development and Genetics of the Face (Sub-In Calgary, CIHR Prime)

7/1/2018-6/30/2025

$510,805

• NIH Natl Inst Dental & Craniofacial Res. A134688

Transcriptional regulatory landscapes underlying FEZ Formation

3/11/2020-2/28/2025

$2,434,720

• NIH NIDCR R01 DE019638 A127014

The Role of Continuous Phenotypic Variation in Structural Defects of the Face

1/1/2016-12/31/2021

$ 2,819,022

• NIH Natl Inst Dental & Craniofacial Res. R21 A131975

Understanding the Forces that Shape the Face

9/15/2018-8/31/2021

$443,098

• NIH Natl Inst Arthr, Musculoskel & Skin A127285

Regulators of Ischemic Fracture Healing

9/15/2015-7/31/2020

$750,748

• Regents of the University of Michigan A131243

Regulators of Ischemic Fracture Healing (new sub-in from UMich after transfer of Prime R01 A127285/ P0505057)

8/1/2017-4/30/2020

$441,853

Meir Marmor, MD

• Population Health Research Institute A130882

HIP fracture Accelerated Surgical Care and Treatment Track

1/1/2018- 1/31/2025

$ 60,600

• Patient-Centered Outcomes Research Inst-University of Maryland, Baltimore A134150

PREPARE: Pragmatic Randomized trial Evaluating Pre-operative Alcohol skin solutions in FRactured Extremities

2/1/2019-1/31/2021

$324,576

• NOVA Department of Orthopaedic Surgery, UCSF

Optimization of Opioid Use for Post-Operative Pain

7/01/2020-6/30/2021

$5,000

• AO Trauma North America

Wearable Devices Used to Measure Postoperative Pain Response in the Orthopaedic Trauma Patient

10/1/2020-8/31/2021

$ 9,604

• AO Trauma North America

Use of Smartphone Wearables to Evaluate Activity and Rehabilitation in Orthopaedic Trauma Patients (Smart WEAR)

10/1/2020-8/31/2021

$ 9,981

Amir Matityahu, MD

• CurvaFix, Inc A135868

A Safety and Technical Feasibility Evaluation of the Curvafix? Intramedullary RodscrEw System for FixaTion of Pelvic and AcetabulaR FracturEs - RESTORE Study

10/1/2020-9/30/2022

$73,414

Theodore Miclau, MD

• Samuel Merritt University A135247

Agreement for Training for Academic Purposes

6/1/2019-5/31/2023

$98,320

• NIH Natl Inst Arthr, Musculoskel & Skin R01 A131606

Mechanisms of Skeletal Stem Cell Dysfunctions in Traumatic Bone Injuries

7/12/2018- 4/30/2023

$ 1,514,183

• NIH Natl Inst Arthr, Musculoskel & Skin R01 A136073

Understanding the Global Burden of Disease of Skeletal Fractures: the International Orthopaedic Multi-Center Study (INORMUS) (new submission of P0521469)

9/21/2020-8/31/2022

$579,548

• Johns Hopkins University - DOD US Army Med. Res. Acq. W81XWH-10-2-0133 A123658A

Task Order: A Prospective Randomized Trial to Assess PO versus IV Antibiotics for the Early Post-op Wound Infection after Extremity Fractures (POvIV)

9/29/2012-8/31/2021

$18,700

• Johns Hopkins University - DOD US Army Med. Res. Acq. W81XWH-12-1-0588 A123658B

Task Order: Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High Energy Fracture Surgery (Oxygen)

3/1/2013- 9/30/21

$13,600

Johns Hopkins University A122597

METRC 2 - The Major Extremity Trauma Research Consortium

9/29/2012-8/31/2021

$179,800

Saam Morshed, MD, PhD, MPH

• McMaster University A124908

Fixation using Alternative Implants for the Treatment of Hip Fractures (FAITH-2), Clinical Trial

3/1/2015-3/31/2023

$1,172

• DOD US Army Med. Res. Acq. Activity A135270

Effect of Early Weight Bearing on Rehabilitation

10/1/2019-9/29/2022

$78,228

• Microbion Corporation A127989

MBN-101-201: A Phase 2a Randomized, Single-Blind, Placebo-Controlled, 24-week Escalating Dose Study to Assess the Safety, Tolerability and Clinical Activity of 3 Concentrations of Locally Applied MBN-101 to Infected Osteosynthesis

Site, Clinical Trial

8/8/2016-8/8/2021

$245,891

• DOD US Army Med. Res. Acq. Activity W81XWH-14-1-0563 A124169

Prosthetic Fit Assessment in Transtibial Amputees Secondary to Trauma (ProFit)

9/30/2014-9/29/2020

$628,030

• DOD US Army Med. Res. Acq. Activity A134521

Early Advanced Weight Bearing for Peri-articular Knee and Pilon Injuries: An RCT using the Anti-Gravity Treadmill (AlterG) (METRC Master Services Agmt)

8/1/2019-9/29/2020

$10,394

• DOD Defense Threat Reduction Agency-University of Maryland, Baltimore A132560

Aqueous-PREP: A Pragmatic Randomized trial Evaluating Pre-operative aqueous antiseptic skin solutions in open fractures

9/30/2018-9/29/2020

$121,600

• Department of Orthopaedic Surgery, UCSF

Longitudinal comparison of outcomes and cost-effectiveness of intramedullary nailing versus external fixation for the treatment of open tibial fractures in Tanzania

06/01/2019-05/31/2020

$25,000

An Nguyen, PhD

• NIH NIDCR F30 A129994

Mesenchyme-Dependent Epithelial Signals that Promote Osteogenesis in the Jaw

9/1/2017-8/31/2021

$177,211

Richard O'Donnell, MD

• DoD USAMRMC W81XWH-17-2-0060 A130749

Transfemoral Amputee Osseointegration Study (TFAOS)

10/1/2017-9/30/2022

$4,087,368

• DoD USAMRMC W81XWH-17R-BAA1 A133886

An Osseo-Neural Transtibial Prosthesis with Efferent-Afferent Neural Control

4/15/19-4/14/2022

$308,482

• DARPA W911NF-17-2-0043 A129870

An Osseointegrated Transfemoral Prosthesis Offering Long-Term Bi-Directional Efferent-Afferent Neural Transmission (MIT SubK DARPA)

3/15/2017-3/31/2021

$842,189

Conor O'Neill, MD

• NIH Center for Scientific Review - UC San Diego A134678

California Clinical and Translational Pain Research Consortium

09/30/2019-3/31/2024

$37,618

Nirav Pandya, MD

• Pediatric Orthopaedic Soc of No America A131532

The Impact of Patient Education in the Pre-Operative Holding on Post-Operative Opioid in Elective Pediatric Orthopedic Surgery Cases

6/1/2018- 5/31/2020

$1,000

Heather Roberts, MD

• Orthopaedic Research and Education Fdn. (OREF) A129158

Intramedullary Kirschner wire versus flexible nail fixation for pediatric femur fractures

7/1/2017-6/30/2020

$30,000

• Orthopaedic Research and Education Fdn. (OREF) A132990

Epidemiology, outcomes, and cost of revision total hip and knee arthroplasty

4/1/2019-3/31/2020

$5,000

Erika Roddy, MD

• UCSF JOJ Ortho Resident Grant

Does Virtual Reality Training Improve Resident Performance in Slipped Capital Femoral Epiphysis In Situ Screw Fixation?

7/1/2020-6/31/2021

$5,000

Coleen Sabatini, MD, MPH

• Pediatric Orthopaedic Society of Northern America A127489

Post-Injection Injury in Ugandan Children: Prevalence, Risk Factors, Surgical Outcomes

6/1/2016-5/31/20

$30,000

Sanjeev Sabharwal, MD, MPH

• Pediatric Orthopaedic Soc of No America A134710

Observership Opportunities in Pediatric Orthopaedics for Surgeons from Low-and-Middle Income Countries: Perceived Barriers and Impact

6/1/2019-5/31/21

$1,000

Aenor Sawyer, MD, MS

• NASA Headquarters A132254

UCSF/TRISH Space Health Innovation Program

10/1/2018- 9/30/2021

$1,950,979

Richard Schneider, PhD

• NIH NIDCR R01 DE025668 A127740

Mechanisms of Secondary Cartilage Induction and Maintenance in the Jaw

7/5/2016-6/30/2021

$1,981,250

• NIH NIDCR R01 A125490

Mesenchymal Regulation of Osteogenesis

7/1/2015-5/31/2021

$2,072,560

Charles Schurman, PhD Candidate

• NIH NIA F31 A133909

Age-related Control of Bone Quality by Osteocyte TGF-beta Signaling

9/11/2019-9/10/2022

$112,504

David Shearer, MD

• Orthopaedic Trauma Association A135783

A Pilot Randomized Controlled Trial to Evaluate Local Antibiotics after Open Tibia Fracture in Tanzania

1/1/2020 – 12/31/2021

$30,000

• Super NOVA Department of Orthopaedic Surgery, UCSF

Cost-effectiveness of transtibial prosthetic devices in Tanzania

06/01/2019 – 05/31/2020

$10,000

• Hellman Grant

A Pilot Randomized Controlled Trial to Evaluate Local Antibiotics for Open Tibia Fracture in Tanzania

06/01/2019 – 05/31/2020

$50,000

• OREF Career Development Grant

Pilot RCT to Evaluate Local Gentamicin for Tibia Fractures in Tanzania

11/1/2020-10/30/2023

$223,340

Spenser Smith, PhD

• NIH NIDCR F32 DE027283 A132095

The Role of TGF-Beta Signaling and Mmps in Neural Crest Mediated Jaw Bone Remodeling

9/15/2018- 9/14/2021

$198,774

Bobby Tay, MD

• NuVasive, Inc. A135518

2020-2021 Orthopaedic Spine Fellowship

8/1/2020-7/31/2021

$30,000

• OMeGA Medical Grants Association A134971

2020-2021 UCSF Dept of Orthopaedic Surgery Spine Fellowship

5/12/2020-5/11/2021

$50,000

• NuVasive, Inc. A133100

NuVasive Spine Fellowship 2019-2020

8/1/2019-11/30/2020

$60,000

• OMeGA Medical Grants Association A133117

UCSF Dept of Orthopaedic Surgery Spine Fellowship 2019-2020

8/1/2019-7/31/2020

$15,000

Alexander Theologis, MD

• Innovasis, Inc. A132498

A Multi-center, Patient Outcome Registry for a Hydroxyapatite infused PEEK Interbody Fusion Device

9/1/2018-9/19/2021

$20,000

• NSF CDMI (Center for Disruptive Musculoskeletal Innovations) funded project

Satellite rod configuration (in-line v. lateral) and screw type (monoaxial v. polyaxial) spanning a lumbar pedicle subtraction osteotomy (PSO): a biomechanical evaluation

11/01/2020 – 10/31/2021

$40,000

Paul Toogood,MD

• NOVA Department of Orthopaedic Surgery, UCSF

Assessment of pedagogical preferences of orthopedic faculty and residents.

7/01/2020-6/30/2021

$5,000

Zuzana Vavrušová, PhD Candidate

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

11/20/2020

$235

Hao-Hua Wu, MD

• UCSF JOJ Ortho Resident Grant

To understand the quality-of-life and economic impact of deep infection after open tibia fracturein Tanzania

7/1/2020-6/31/2021

$5,000

Rosanna Wustrack, MD

• Musculoskeletal Tumor Society A134493

Identifying and Enhancing Host Immune Response in Adult Soft Tissue Sarcoma

7/1/2019-6/30/2021

$25,000

• Canadian Institutes of Health Research SITE 36 A127607

Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY), Subcontract, Clinical Trial

6/13/2016-3/31/2021

$7,805

• James O. Johnston Immunotherapy Grant

Studying the Role of Immunotherapy in Treating Sarcomas

1/1/2014-1/1/2022

$220,000

Jihee Yoon, DDS/PhD Candidate

• NIH NIAMS P30AR075055 (CCMBM Junior Investigator Software Assistance Award)

11/19/2020

$108

Nathan Young, PhD

• NIH Natl Inst Dental & Craniofacial Res. R56DE029124 A135927

A Predictive Developmental Morphospace Model of Cleft Lip (Resubmission of P0535239 Dec 2018)

9/3/2020-8/31/2021

$382,339

Alan Zhang, MD

• Arthroscopy Association of North America – Fellowship A135177

Arthroscopy/Sports Fellowship 2020-2021

8/1/2020- 7/31/2021

$10,400

• Arthroscopy Association of North America – Fellowship A133858

Arthroscopy/Sports Fellowship

8/1/2019- 7/31/2020

$7,350

• Department of Orthopaedic Surgery, UCSF

Platelet-rich plasma for treatment of early osteoarthritis of the knee

7/01/2020-6/30/2021

$25,000

Patricia Zheng, MD

• The Spine Intervention Society A132385

ATLAS - Application to Track Longitudinal outcomes After Spine interventions

8/1/2018- 6/30/2021

$24,978

• Allergan Foundation A132233

Long-term outcomes of an Integrated Spine Service as compared to standard care for patients with chronic back pain

11/1/2018- 10/31/2020

$10,000

Research Publications 2020

Adams M, **Lotz JC,** Diederich C. In silico feasibility assessment of extracorporeal delivery of low-intensity pulsed ultrasound to intervertebral discs within the lumbar spine. Phys Med Biol. 2020 Jul 03.

Adogwa O, Buchowski JM, Sielatycki JA, Shlykov MA, **Theologis AA**, Lin J, CreveCoeur T, Peters C, Riew KD. Improvements in Neck Pain and Disability Following C1-C2 Posterior Cervical Instrumentation and Fusion for Atlanto-Axial Osteoarthritis. World Neurosurg. 2020 07; 139:e496-e500.

Agarwalla A, **Liu JN**, Wu HH, Kalbian IL, Garcia GH, Shubin Stein BE. Return to Work Following Tibial Tubercle Osteotomy for Patellofemoral Osteoarthritis and Pain. Cartilage. 2020 Apr 22; 1947603520916544.

Agha O, Diaz A, **Davies M**, Kim HT, **Liu X, Feeley BT**. Rotator cuff tear degeneration and the role of fibro-adipogenic progenitors. Ann N Y Acad Sci. 2020 Jul 29.

Agha O, Mueller-Immergluck A, Liu M, Zhang H, **Theologis AA**, Clark A, **Kim HT, Liu X, Feeley BT**, **Bailey JF**. Intervertebral disc herniation effects on multifidus muscle composition and resident stem cell populations. JOR Spine. 2020 Jun; 3(2):e1091.

Agha O, **Rugg CM, Lansdown DA**, Ortiz S, Hettrich CM, Wolf BR, **Feeley BT.** Surgical Stabilization of Shoulder Instability in Patients With or Without a History of Seizure: A Comparative Analysis. Arthroscopy. 2020 Oct; 36(10):2664-2673.e3.

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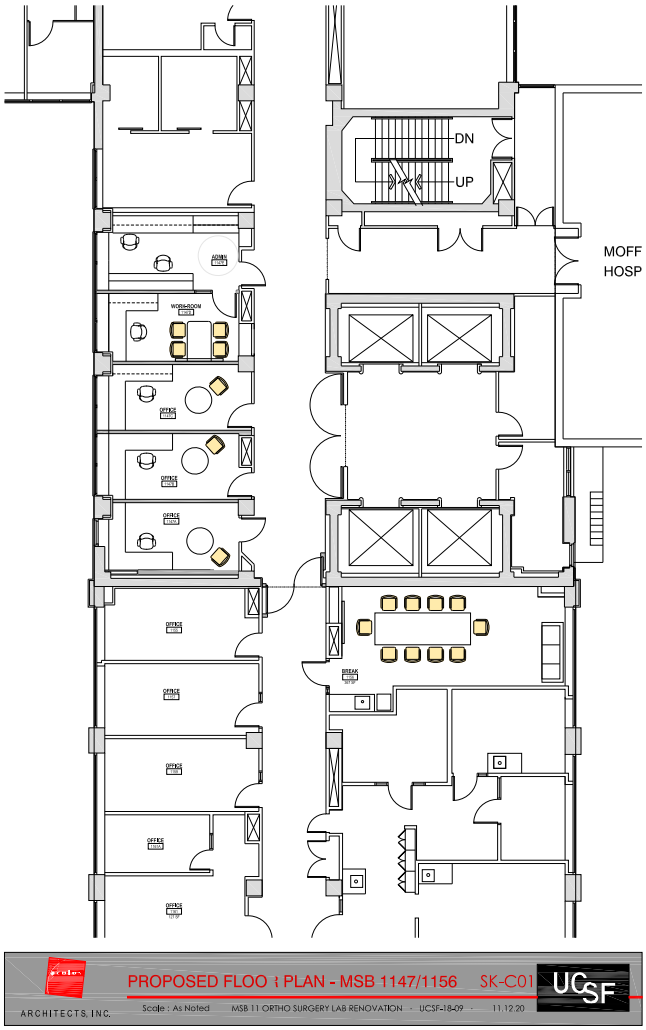
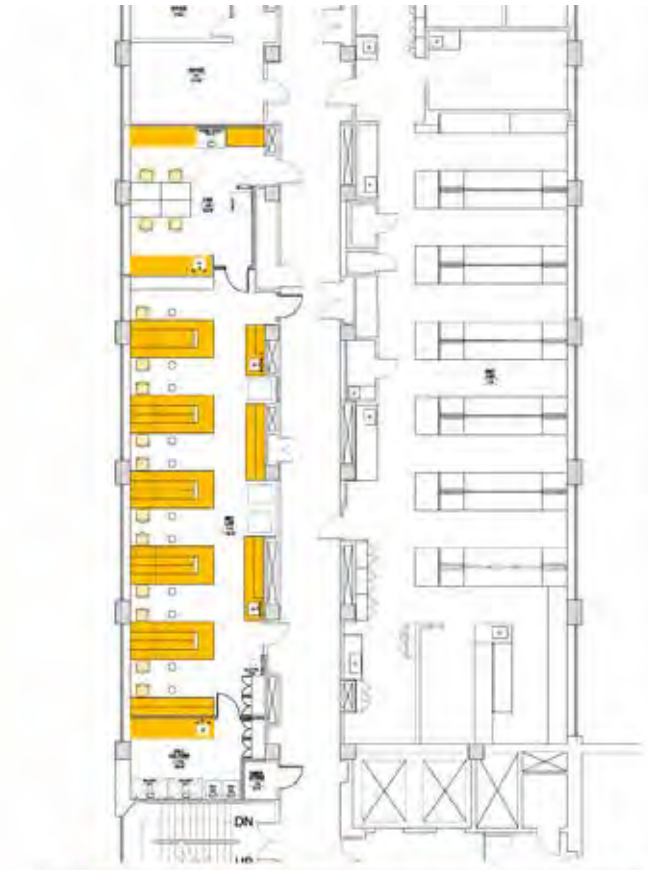
Facilities Update

Update on Parnassus renovations at Health Sciences East, 11th floor and at 95 Kirkham

- Curent square footage: 5,169.32
- New plan will be 5,169.32 (current occupied space) +1,550 (pulmonary space) +752.01 (S1147 elevator space) = 7,471.3.

- In total, we are getting about 2,302.01 of San Francisco's Parnassus campus in the new plan.





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