Contents

1
Foreword

3
From the Chair’s Desk

4
Rick and Anne Matsen Honorary Professorship for Shoulder Research

6
New Faculty

7
Department of Orthopaedics and Sports Medicine Faculty

Zebrafish: An Emerging Model for Orthopedic Research 13 Björn Busse, PhD, Jenna L. Galloway, PhD, Ryan S. Gray, PhD, Matthew P. Harris, PhD, and Ronald Y. Kwon, PhD

Independent Investigative Inquiry 25 William D. Lack, MD

Triangles of Pain; Understanding the Symptoms that Accompany Sternoclavicular Pathology 26 Winston J. Warme, MD

2019 Japanese Traveling Fellows 28 Victoria M. Cannon, BA, Conor P. Kleweno, MD, and Reza Firoozabadi, MD, MA

University of Washington Medical Center and Northwest Hospital Orthopaedics 29 William D. Lack, MD and Albert O. Gee, MD

Seattle Children’s Hospital Orthopaedics 31 Gregory A. Schmale, MD

Harborview Medical Center Orthopaedics 33 Carlo Bellabarba, MDCM

VA Puget Sound Orthopaedics 35 Nicholas P. Iannuzzi, MD

Orthopaedic Surgery Residency Program 36 Christopher Y. Kweon, MD, Nicholas P. Iannuzzi, MD, Stephen A. Kennedy, MD, FRCSC, and Lisa A. Taitsman, MD, MPH
38
Graduating Residents

40
Incoming Residents

42
ACEs and Fellows

44
Research Grants

47
Department Publications 2019-2020

54
Alumni

57
Endowments
In this time of unprecedented global upheaval, it is my humble privilege to present to you what I hope is a brief respite from another day of worrisome news and widespread illness. Managing Editor Fred Westerberg, the three co-editors Drs. Chris Allan, Steve Kennedy and Will Lack and all of the contributors have put together another stellar annual summary of the Department, Discoveries 2020, while using their ingenuity and skill to take advantage of the modern collaborative tools that permit working closely together while physically separated.

Perhaps even an understatement, but nothing has been the same for our Department since the first case of coronavirus disease 2019 (COVID-19) was detected in the Pacific Northwest on January 20. That is the day that the first patient in the United States, in Snohomish County, was identified to have severe acute respiratory syndrome (SARS-CoV-2) due to infection with COVID-19. This case set off a national cascade of events and consequences that perhaps only a few epidemiologists and authors of fiction could have envisioned. Of course, the consequences for the rest of the planet have been no less disruptive and deadly, and in some countries quite a bit worse.

The initial patient had returned to Washington from Wuhan, China on January 15. There were predictions of rapid spread but the six-week interval before the first death was reported may have led to a false sense of security. By this time, dozens of residents at the Life Care Center in Kirkland were sick with COVID-19 and many would not survive. Elderly residents of other nursing homes around the country were eventually similarly severely afflicted. Subsequently many public schools with COVID-positive students began to voluntarily close as did some organizations, notably on March 4 the Fred Hutchinson Cancer Research Center instructed all employees performing “nonessential” work to work from home – this order has now been extended through the month of August.

By March 5 many large companies followed the actions of the “Hutch” and on March 6, UW announced that in-person classes would be cancelled for the rest of the semester. On March 13, all schools in the state were instructed to close and on March 23, following the decrees of several mayors and requests by the public, Governor Inslee issues a shelter-in-place order for the state. Initially to be in place for at least 2 weeks, the stay-at-home order was extended to May 4 and then again to May 31.

Despite these early measures and successfully “flattening the curve”, the “surge” of patients with COVID-19 stressed our infrastructure and front-line health care providers who displayed incredible fortitude and courage in caring for so many critically ill patients who were isolated from their loved ones. The emotional toll on our ED and critical care physicians, staff and advanced-practice providers cannot be underestimated. While the impact on the orthopaedic faculty, staff and trainees was not as direct, we also had to Rapidly adapt to the risks of exposure and to the needs of our patients and health care system. Most impactful from a financial perspective was the governor’s decree on March 19 that restricted “non-urgent” surgical procedures.

The lifting of restrictions on elective surgery and social gathering have been accompanied by a very gradual return to something that nobody would refer to as “normal”. Every employee must sign an attestation to their health every day they show up for work while many continue to work from home. Every surgical patient needs to be tested for COVID-19 and all employees will be gradually tested for the presence of antibodies that would indicate previous exposure to COVID.

Many more outpatient visits are being handled via telehealth modalities and many patients continue to be wary of the risks of contracting COVID while outside of their home and particularly while in a health care setting. The financial consequences of this tumult are predictions of up to a 500 million-dollar annual deficit for UW Medicine, employee furloughs, unpaid voluntary leave and voluntary salary reductions.

Aside from the inconceivable number of deaths, perhaps what is most jarring is the conversion of routine face-to-face interactions to mask-to-mask interactions. Barring development of effective treatment or vaccines which hopefully will occur within the next 1-2 years, the medical recovery from the COVID pandemic will likely be lengthy with intermittent surges and tightening of infectious precautions. Unfortunately, most experts predict that the economic devastation may not be
entirely reversed for at least five years. “Life” in UW Medicine and the Department continues, albeit with physical distancing and a large dose of “zoom” conferences. We have had faculty join the Department over the past year as well as several of our faculty announce their retirement. Dr. David Fitz has joined our team at the Northwest Campus where he will focus on adult reconstructive surgery and management of patients with arthritis of the hip and knee. For more information on Dr. Fitz please see Dr. Gee’s site update in this issue of Discoveries.

For 16 years Dr. Michael Goldberg has been a linchpin of Seattle Children’s Hospital’s skeletal dysplasia program and served as the Director of the Skeletal Health Program, a multidisciplinary clinic involving both orthopaedic surgeons and pediatric geneticists. While you are probably familiar with Dr. Goldberg’s renowned clinical and scientific expertise in the realm of skeletal dysplasia, you may not know that he also dedicated (an understatement) time every year to the children at Camp Korey, a camp for children with life altering conditions, including orthopaedic conditions such as skeletal dysplasias.

Dr. Michael Goldberg has been extremely prolific and I attribute this to his seemingly having several successful careers all tied together by his commitments to evidence-based care delivered by compassion and humanistic caregivers. His life as an orthopaedic surgeon has been bracketed by a focus on evidence-based care in the earlier phases of his career and a focus on burnout and compassionate care in the later phases. No doubt it is this focus that led the Schwartz Center for Compassionate Healthcare in Boston to recognize the wisdom of bringing Dr. Goldberg into their program. Perhaps most notably, throughout his career he has been a passionate advocate for his patients, children with the most complex syndromes, and their families. So, after 16 years at SCH, what Dr. Goldberg refers to as his second retirement is about to begin. Please join me in congratulating Michael and his wife Fran and wishing them a long healthy retirement.

Dr. Kevin Smith came to Seattle in 1995 to spend one year doing his Shoulder & Elbow Fellowship with Dr. Rick Matsen and Dr. Doug Harryman. As fate would have it, he never left! Kevin completed his residency in Orthopaedic Surgery at McLaren Regional Medical Center in Flint, MI before coming to do his fellowship at the University of Washington School of Medicine. Kevin then spent more than a decade in the Department based at UWMC where he was beloved by his colleagues, nurses and the residents. In fact, for his excellent clinical and educational skills, the residents awarded him Teacher of the Year. He also ran the residency interview and selection process for years and made the process both effective and fun.

After he left the UW as an Associate Professor, Dr Smith practiced briefly at the now defunct Group Health Cooperative before moving to Northwest Hospital where he practiced for the past decade. In the end he came full circle this past January and re-joined the Department of Orthopaedics & Sports Medicine. It was great to have him back in the Department and my good friend “Kev” said that it was a difficult and sad decision, but he decided to retire from orthopaedic surgery this past April. “Gosh, I’ve had a ball and we’ve accomplished soooo much. It’s been a WONDERFUL ride, personally as well as professionally, but it’s time for me to move on and pursue new adventures”. Amongst many great qualities, what I will always remember about Dr. Smith is his dedication to his patients and to his residents and colleagues. He was a stalwart of call coverage and took on any patient regardless of complexity or social issues. I wish Kevin and his wife Diane good health and a wonderful retirement where they get to spend more time with their two daughters.

Please stay in good health and good cheer through these challenging times. In the 2021 issue of Discoveries I hope to be reporting on the sustained financial health of the Department of Orthopaedics and Sports Medicine and more importantly, on the progress of our nation’s battle against COVID-19 and its societal and economic consequences. Do not hesitate to reach out to myself, Fred Westerberg, or any of the co-editors with questions and suggestions for future editions of Discoveries.

Howard A. Chansky, MD
Professor and Chair
Members of our department from disparate backgrounds have understandably expressed sadness and outrage at the recent deaths Ahmaud Arbery, Breonna Taylor and now George Floyd. I share their sentiments. The UW Medicine community has endured several struggles over the past year - radioactive cesium upending laboratories at the R&T building, aspergillus severely curtailing care of children at SCH, and the coronavirus pandemic leading to massive loss of life. However, the senseless deaths of these three and other African-Americans have occurred at the hands of our fellow citizens or those who enlisted to protect us, and they serve as a pointed reminder of our nation’s history of racism.

The sheer nonchalant brutality of the killing of Mr. Floyd, televised for the world to view, has captured our attention and I am sure many of us are trying to make any sort of sense of it and explain it to our children or to friends outside of the United States. These tragic and senseless deaths unfortunately are not isolated, in fact they are just the latest three that have come to light in a long legacy of similarly horrific deaths. At this point I am not even sure what “horrific” means in the context of events that occur with such disheartening regularity. We all share the same sense of outrage over these deaths and yet expressing outrage - “horrific” and “enough is enough” - is clearly not enough if we are to see real change.

I cannot profess to have the answers to this long-standing stain on our community and our nation and we will all have our own personal approaches. While we won’t see the abolition of racism and violence in our country in the span of our lives, the status quo isn’t acceptable and we are not free from the moral imperative to help, to at least reach out and express our shame and support, and to listen to our black neighbors, colleagues and members of our department. Perhaps the best next step is listening closely to their everyday fears - fears that are existential and fears that most of us live our lives without needing to pay any regard to. Fears that do not arise out of paranoia but fears that spring from words, deeds and events in our daily lives. Fears that are now greatly magnified and made manifest by recent events.

Many are hurting, disillusioned and fearful - this is a time to care for each other, our trainees, and particularly those members of our department of color. Express solidarity, ask how you can help, listen to their perspective. Support the department’s efforts at encouraging and pursuing diversity and inclusion. Take your usual excellent care of the neediest in our community to another level. Ask our leaders in government - our sheriff, mayor, governor, representatives - what they are doing to address endemic racism and violence and let them know that their words and actions are important for your continued support. Vote. Let your partners, staff and residents know that they are welcome in our department. Even small gestures and efforts, consistently applied, can make a difference as we strive for a more perfect department, community and nation.

Howard A. Chansky, MD
Professor and Chair
It is my great pleasure to announce the new Rick and Anne Matsen Honorary Professorship for Shoulder Research. Dr. Jesse Roberts, a grateful patient of Dr. Matsen’s, funded this professorship in honor of Dr. and Mrs. Matsen (pictured to the right). As we all know, Dr. Matsen is one of the world’s foremost surgeons and pioneers of modern shoulder surgery. And Rick would be the first to tell anyone that he could not have achieved this without the support of his wife Anne.

The goal of this professorship is to support a member of the Department who can best advance the field of shoulder care and surgery through innovative patient-centered research and secondarily to provide strategic support to the Department of Orthopaedics and Sports Medicine. The committee charged with selecting the first holder of this professorship has chosen Dr. Jason Hsu. The committee made their selection based on Dr. Hsu’s “growing international academic reputation, his outstanding surgical care, his thoughtful clinical and research mentorship, and his willing service, inspiring leadership and exemplary professionalism align directly with the intent of the donors.”

This wonderful gift and professorship will advance the goals of the department by helping to retain critical faculty such as Dr. Hsu and it will advance the field of shoulder surgery. Please join me in congratulating Jason Hsu and Rick and Anne Matsen.

[Signature]

Howard A. Chansky, MD
Professor and Chair
Dr. Jason Hsu is an Associate Professor in the Department of Orthopaedics and Sports Medicine. Dr. Hsu completed his medical degree at Northwestern University Feinberg School of Medicine, followed by his residency at the University of Pennsylvania followed by a fellowship at Washington University. He came to UW Medicine in 2014 and has become a highly valued educator, surgeon and leader in the Department of Orthopaedics and Sports Medicine. Dr. Hsu’s clinical interest lies in arthroscopic rotator cuff repair, arthroscopic and open procedures for shoulder instability, primary and revision shoulder replacement surgery. His research interests have focused on the prevention, diagnosis and treatment of periprosthetic shoulder infections. Dr. Hsu has distinguished himself as a national leader in shoulder and elbow surgery and there is no more fitting first holder of the Rick and Anne Matsen Honorary Professorship for Shoulder Research.
David W. Fitz, MD
Assistant Professor
Northwest Hospital
Hip and Knee
dwfitz@uw.edu

David Fitz, MD is an Assistant Professor at the University of Washington Department of Orthopaedics and Sports Medicine. He specializes in Adult Joint Reconstruction. His areas of clinical interest are hip and knee arthroplasty, partial knee replacement, post-traumatic reconstruction of the hip and knee, as well as geriatric fracture care. He is based at our Hip & Knee Center at Northwest Hospital.

Dr. Fitz attended college at Harvard and medical school at Northwestern University, where he also completed his internship and residency. After graduation, he completed at fellowship at Massachusetts General Hospital in Boston, MA.

Dr. Fitz has published original research on "Differences in Post-Operative Outcome Between Conversion and Primary Total Hip Arthroplasty", "The Impact of Metabolic Syndrome on 30-Day Complications Following Total Joint Arthroplasty", "Preoperative Opioid Use Negatively Affects Patient-reported Outcomes After Primary Total Hip Arthroplasty", "Relationship of the Posterior Condylar Line and the Transepicondylar Axis: A CT-Based Evaluation", as well as many other articles in orthopaedics.

He is also active in the orthopaedic community as a member of American Association of Hip and Knee Surgeons and American Academy of Orthopaedic Surgeons.

Christian M. Peterson, DO
Clinical Assistant Professor
Northwest Hospital
Sports Medicine
chrismp@uw.edu

Christian M. Peterson, DO is board certified by the American Osteopathic Board of Orthopedic Surgery and the National Board of Osteopathic Medical Examiners. He attended medical school at Kirksville College of Osteopathic Medicine, completed his internship and residency at Doctors Hospital in Columbus, Ohio, and completed fellowships in spine surgery at Ohio University and in sports medicine and arthroscopy at the Institute for Bone and Joint Disorders in Phoenix, Arizona.

Dr. Peterson belongs to the American Academy of Orthopedic Surgeons, the American Osteopathic Association, the American Osteopathic Association of Sports Medicine, the Association of Professional Team Physicians, the Washington Osteopathic Medical Association and the Washington State Orthopedic Association.

Dr. Peterson’s clinical interests include advanced arthroscopic procedures and sports medicine.

Dr. Peterson is the team physician for Bishop Blanchet High School and Bellevue Community College. He is also a consulting physician for Seattle Pacific University.

He joins our department as a Clinical Assistant Professor based at Northwest Hospital.
Discoveries 2020

Department of Orthopaedics and Sports Medicine Faculty

Howard A. Chansky, MD
Professor and Chair
VA Puget Sound Health Care System
University of Washington Medical Center
Northwest Hospital
Adult Reconstructive Surgery
chansky@uw.edu

Carlo Bellabarba, MD
Professor
Division Chief
Harborview Medical Center
Spine and Trauma
cbella@uw.edu

Christopher H. Allan, MD
Associate Professor
University of Washington Medical Center
Hand and Wrist
callan@uw.edu

Stephen K. Benirschke, MD
Professor
Harborview Medical Center
Foot and Ankle
beniskb@uw.edu

Steven D. Bain, PhD
Research Associate Professor
Harborview Medical Center
Research
sdbain@uw.edu

Sarah D. Beshliant, MD
Clinical Associate Professor
Northwest Hospital
Hand and Wrist
sarbesh@uw.edu

David P. Barei, MD
Professor
Harborview Medical Center
Trauma
barei@uw.edu

Todd J. Blumberg, MD
Assistant Professor
Seattle Children’s Hospital
Pediatric Orthopaedics
todd.blumberg@seattlechildrens.org

Jennifer M. Bauer, MD, MS
Assistant Professor
Seattle Children’s Hospital
Pediatric Orthopaedics
jennifer.bauer@seattlechildrens.org

Michael E. Brage, MD
Associate Professor
Harborview Medical Center
Foot and Ankle
bragem@uw.edu

Daphne M. Beingessner, MD
Professor
Harborview Medical Center
Trauma
daphneb@uw.edu

Richard J. Bransford, MD
Professor
Harborview Medical Center
Spine
rbransfo@uw.edu
Department of Orthopaedics and Sports Medicine Faculty

Kenneth Chin, MD
Clinical Assistant Professor
Northwest Hospital
University of Washington Medical Center
Foot and Ankle
kenchin@uw.edu

Reza Firoozabadi, MD, MA
Associate Professor
Harborview Medical Center
Trauma
rezaf2@uw.edu

Robert S. Clawson, MD
Clinical Associate Professor
Northwest Hospital
Fractures & Trauma
robert.clawson@nwhsea.org

David W. Fitz, MD
Assistant Professor
Northwest Hospital
Hip and Knee
dwfitz@uw.edu

Mark C. Dales, MD
Clinical Associate Professor
Seattle Children’s Hospital
Spine
mark.dales@seattlechildrens.org

Edith M. Gardiner, PhD
Research Associate Professor
Harborview Medical Center
Research
edigar@uw.edu

Robert P. Dunbar, MD
Associate Professor
Harborview Medical Center
Trauma
dunbar@uw.edu

Albert O. Gee, MD
Associate Professor
Division Chief
University of Washington Medical Center
Sports Medicine
ag112@uw.edu

Russell J. Fernandes, MSc, PhD
Research Associate Professor
University of Washington Medical Center
Research
rjf@uw.edu

Michael Githens, MD, MS
Assistant Professor
Harborview Medical Center
Trauma
mfg28@uw.edu

Navin D. Fernando, MD
Assistant Professor
Northwest Hospital
Hip and Knee
navinf@uw.edu

Ted S. Gross, PhD
Professor
Vice Chair, Research
Harborview Medical Center
Research
tgross@uw.edu
Department of Orthopaedics and Sports Medicine Faculty

Mia S. Hagen, MD
Assistant Professor
University of Washington Medical Center
Sports Medicine
smia@uw.edu

David M. Hudson, PhD
Research Assistant Professor
University of Washington Medical Center
Research
dmhudson@uw.edu

Douglas P. Hanel, MD
Professor
Harborview Medical Center
Hand and Wrist
dhanel@uw.edu

Nicholas P. Iannuzzi, MD
Assistant Professor
Division Chief
VA Puget Sound Health Care System
General Orthopaedics
iannuzzi@uw.edu

Jared L. Harwood, MD, MBA
Assistant Professor
University of Washington Medical Center
Tumor
harwoodj@uw.edu

Stephen A. Kennedy, MD, FRCSC
Associate Professor
Northwest Hospital
Harborview Medical Center
Hand and Wrist
sajk@uw.edu

Jonah Hebert-Davies, MD
Assistant Professor
Harborview Medical Center
Trauma
jdavies2@uw.edu

Conor P. Kleweno, MD
Associate Professor
Harborview Medical Center
Trauma
ckleweno@uw.edu

Jason E. Hsu, MD
Associate Professor
University of Washington Medical Center
Shoulder and Elbow
jehsu@uw.edu

Walter F. Krengel III, MD
Clinical Professor
Seattle Children’s Hospital
Spine
wally.krengel@seattlechildrens.org

Jerry I. Huang, MD
Associate Professor
University of Washington Medical Center
Hand and Wrist
jihuang@uw.edu

Christopher Y. Kweon, MD
Assistant Professor
University of Washington Medical Center
Sports Medicine
ckweon@uw.edu
Department of Orthopaedics and Sports Medicine Faculty

Ronald Y. Kwon, PhD  
Associate Professor  
Harborview Medical Center  
Research  
ronkwon@uw.edu

Vincent S. Mosca, MD  
Professor  
Seattle Children’s Hospital  
Pediatric Orthopaedics  
vincent.mosca@seattlechildrens.org

William D. Lack, MD  
Assistant Professor  
Northwest Hospital  
General Orthopaedics  
wdlack@uw.edu

Sean E. Nork, MD  
Professor  
Harborview Medical Center  
Trauma  
nork@uw.edu

Seth S. Leopold, MD  
Professor  
University of Washington Medical Center  
Northwest Hospital  
Adult Reconstructive Surgery  
leopold@uw.edu

Viral R. Patel, MD  
Acting Instructor  
University of Washington Medical Center  
Spine  
pviralr@uw.edu

Antoinette W. Lindberg, MD  
Clinical Assistant Professor  
Seattle Children’s Hospital  
Orthopaedic Oncology  
antoinette.lindberg@seattlechildrens.org

Christian M. Peterson, DO  
Clinical Assistant Professor  
Northwest Hospital  
Sports Medicine  
chrismp@uw.edu

Paul A. Manner, MD  
Professor  
University of Washington Medical Center  
Northwest Hospital  
Adult Reconstructive Surgery  
pmanner@uw.edu

Bruce J. Sangeorzan, MD  
Professor  
Harborview Medical Center  
Foot and Ankle  
bsangeor@uw.edu

Frederick A. Matsen III, MD  
Professor  
University of Washington Medical Center  
Shoulder and Elbow  
matsen@uw.edu

Michael G. Saper, DO  
Assistant Professor  
Seattle Children’s Hospital  
Pediatric Orthopaedics  
michael.saper@seattlechildrens.org
Department of Orthopaedics and Sports Medicine Faculty

**Gregory A. Schmale, MD**  
Associate Professor  
Acting Division Chief  
Seattle Children's Hospital  
Pediatric Orthopaedics  
gregory.schmale@seattlechildrens.org

**Winston J. Warme, MD**  
Professor  
University of Washington Medical Center  
Shoulder and Elbow  
warmewj@uw.edu

**Suzanne E. Steinman, MD**  
Clinical Associate Professor  
Seattle Children's Hospital  
Pediatric Orthopaedics  
suzanne.steinman@seattlechildrens.org

**Klane K. White, MD, MSc**  
Professor  
Seattle Children's Hospital  
Pediatric Orthopaedics  
klane.white@seattlechildrens.org

**Lisa A. Taitsman, MD, MPH**  
Professor  
Harborview Medical Center  
Trauma  
taitsman@uw.edu

**Suzanne M. Yandow, MD**  
Professor  
Seattle Children's Hospital  
Pediatric Orthopaedics  
suzanne.yandow@seattlechildrens.org

**Scott Telfer, EngD**  
Research Assistant Professor  
University of Washington Medical Center  
Research  
telfers@uw.edu

**Suzanne Unno, MD**  
Acting Assistant Professor  
Northwest Hospital  
Trauma  
unno@uw.edu

**Matthew Thompson, MD**  
Assistant Professor  
University of Washington Medical Center  
Orthopaedic Oncology  
mthomp2@uw.edu

**Haitao Zhou, MD**  
Assistant Professor  
Harborview Medical Center  
Spine  
hzhou71@uw.edu
## Department of Orthopaedics and Sports Medicine Faculty

### Emeritus Faculty
- Stanley J. Bigos, MD  
  Professor Emeritus
- Peter R. Cavanagh, PhD  
  Professor Emeritus
- David R. Eyre, PhD  
  Professor Emeritus
- Sigvard T. Hansen, Jr., MD  
  Professor Emeritus
- M. Bradford Henley, MD  
  Professor Emeritus
- Roger V. Larson, MD  
  Associate Professor Emeritus
- Douglas G. Smith, MD  
  Professor Emeritus
- Lynn T. Staheli, MD  
  Professor Emeritus
- Carol C. Teitz, MD  
  Professor Emeritus
- Theodore A. Wagner, MD  
  Clinical Professor Emeritus

### Joint Faculty
- Monique S. Burton, MD
- Randall M. Chesnut, MD
- Armagan Dagal, MD
- Jeffrey B. Friedrich, MD
- Kimberly Harmon, MD
- Mark A. Harrast, MD
- Stanley A. Herring, MD
- Thomas Jinguiji, MD
- Brian Krabak, MD
- John Lockhart, MD
- John W. O'Kane, Jr., MD
- John E. Olerud, MD
- Celeste Quitiquit, MD
- Nicholas B. Vedder, MD
- Fangyi Zhang, MD

### Adjunct Faculty
- Roger E. Bumgarner, PhD
- Cora C. Breuner, MD
- Charles H. Chesnut III, MD
- Randal P. Ching, PhD
- Joseph Cuschieri, MD
- Gregory C. Gardner, MD
- Dennis Kao, MD
- Erin Miller, MD
- Grant E. O'Keefe, MD
- Susan M. Ott, MD
- Michael L. Richardson, MD
- Miqin Zhang, PhD

### Affiliate Faculty
- William R. Ledoux II, PhD
- Jeremy S. Somerson, MD
- Sundar Srinivasan, PhD

### Senior Fellow
- Charlotte Gistelink, PhD

### Clinical Instructor
- David Gendelberg, MD

### Acting Instructor
- Claire Watson, PhD

### Teaching Associate
- Hannah Bae, ARNP
- Alexander L. Bertelsen, PA
- EChing V. Bertelsen, PA
- Edward G. Blahous, DPM
- Lauren A. Colpo, PA
- Emily H. Clayton, PA
- Mahra Davidson, PA
- Jason S. Erickson, PA
- Aaron J. Eusterbrock, PA
- Joseph L. Fiorito, PA
- Peter C.A. Hall, PA
- Jennifer S. Hamilton, PA
- Douglas J. Ichikawa, DPM
- Sophia Jeannot, ARNP
- Cherie H. Johnson, DPM
- Tony D.H. Kim, PA
- Julianne V. Krause, PA
- Kaitlen E. Laine, PA
- Erik C. Lilja, DPM
- Connie U. Ly, PA
- Sara Mahmood, DPM
- Jason E. Maris, PA
- Katie L. Moore, ARNP
- Rockwell G. Moulton, DPM
- Janice M. Olivo, PA
- Amanda L. Pedersen, PA
- Dena R. Pruitt, PA
- Priya Shah, PA
- Jennifer L. Stambaugh, PA
- Michael D. Taylor, PA
- Emily M. Thach, PA
- Kirsten M. Thompson, PA
- Stasia Turner, ARNP
- Wyatt Visca, PA
Zebrafish: An Emerging Model for Orthopedic Research

Björn Busse, PhD¹, Jenna L. Galloway, PhD², Ryan S. Gray, PhD³,
Matthew P. Harris, PhD⁴, and Ronald Y. Kwon, PhD⁵

Abstract

Advances in next-generation sequencing have transformed our ability to identify genetic variants associated with clinical disorders of the musculoskeletal system. However, the means to functionally validate and analyze the physiological repercussions of genetic variation have lagged behind the rate of genetic discovery. The zebrafish provides an efficient model to leverage genetic analysis in an in vivo context. Its utility for orthopedic research is becoming evident in regard to both candidate gene validation as well as therapeutic discovery in tissues such as bone, tendon, muscle, and cartilage. With the development of new genetic and analytical tools to better assay aspects of skeletal tissue morphology, mineralization, composition, and biomechanics, researchers are emboldened to systematically approach how the skeleton develops and to identify the root causes, and potential treatments, of skeletal disease. © 2019 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J. Orthop. Res

Keywords
zebrafish; bone; tendon; muscle; cartilage

Introduction

Small animal models amenable to rapid-throughput biology are needed to accelerate the discovery of new treatments for clinical disorders of the musculoskeletal system. Complex, multi-cellular interactions are difficult to recapitulate in a dish. While such processes can be studied in animal models, ready-made mutant lines often do not exist (e.g., see section “Disease loci”). The zebrafish (Danio rerio) is a small, tropical freshwater fish that, by virtue of its unique experimental attributes (e.g., small size, low cost, genetic tractability, and optical transparency), has opened powerful avenues for biomedical research (including studies of development,¹,² neuroscience,³ regeneration,⁴ and disease⁵) that are difficult in other vertebrate models. Such avenues include in vivo imaging of cell dynamics, and genetic and chemical screens. Moreover, zebrafish can be used as a pre-screening tool to prioritize more labor and cost-intensive studies that require de novo mutant mouse generation. The potential benefits of incorporating zebrafish into a research program must be weighed with limitations, including infrastructure costs (which vary depending on institution), differences in zebrafish and human genetics and physiology, and the fact that many experimental approaches are still in their infancy, and thus remain to be rigorously validated. Indeed, the use of zebrafish to understand clinical disorders of the musculoskeletal system has only begun to be established. Here, we introduce the experimental advantages of the zebrafish, discuss its genetic and physiological similarities and differences to humans, and survey recent applications to musculoskeletal development and disease. This review elaborates on a workshop of the same name at the 2019 Orthopaedic Research Society Meeting, conducted by the authors, the purpose of which was to introduce emerging orthopedic research in zebrafish to facilitate cross-talk, establish foundations, and develop new models of clinical disorders.

Genetics

Genetic similarity to humans
A key criterion in the selection of an appropriate disease model is its genetic similarity to humans. Approximately, 71% of human protein-coding genes possess at least one zebrafish ortholog.⁶ This is comparable to mouse, as ~80-90% of human protein-coding genes possess at least one ortholog in mouse (http://www.informatics.jax.org/homology.shtml). As zebrafish arose from a common ancestor that underwent an additional round of whole-genome duplication relative to mice and humans, zebrafish can have multiple co-orthologs for human genes (e.g., human RUNX2 has two zebrafish co-orthologs, runx2a and runx2b). While this can complicate testing of gene function due to issues such as functional redundancy, such difficulties can be alleviated through simultaneous knockdown or knockout of co-orthologs.¹,⁷ In other cases, maintenance of two copies of a gene in the zebrafish often is balanced by the partitioning function of a gene, or subfunctionalization. As such, the retention of co-orthologs in the zebrafish often permits nuanced analysis of gene function in genes that might be lethal in mice. In mouse, analysis of many genes often requires combinatorial genetic techniques to provide conditional spatial or temporal regulation of gene function, whereas in the zebrafish simple genetic alterations can be studied (e.g. Fgfr1⁸). The often partitioned function of paralogues in the zebrafish also permits loss-of-function analysis to the model the effect of more nuanced alleles such as regulatory shifts in gene function underlying many common skeletal pathologies. Such pathologies cannot easily be modeled with knockout strategies in the mouse and due to the complex anatomical nature of many skeletal disorders, often cannot be modeled in vitro even when allele-specific cell lines are constructed. A large number of skeletal disease models have been identified in zebrafish,⁹-¹¹ and this number is steadily increasing.

Techniques
The ease of forwarding genetics in zebrafish gives this model an advantage for unbiased discovery of mutant phenotypes. N-ethyl-N-nitosourea (ENU) mutagenesis screens in zebrafish have uncovered a large number of variants relevant to fundamental aspects of skeletogenesis,¹²-¹⁴ morphological evolution,¹⁵ and human skeletal diseases.¹⁶-²⁰ Early examples involved the identification of a large collection of mutants with defects in formation of
the jaw and branchial arches. The same screen also identified mutations, specifically affecting the adult form. The mutants identified in these early large-scale screens served as foundation for experimental analysis and were proof that not only could specific mechanisms of skeletal development be identified, but that mutation could be in genes homologous to human genes associated with skeletal diseases. Such screens often yield specifically defined point mutations which provide nuanced changes in gene function that simple loss-of-function mutations or frameshifts cannot. Screens for dominant mutations affecting skeletogenesis, in which mutations often lead to dominant-negative properties as well as alleles with increased functions (hyper- or neomorphic alleles), are proving to be informative and useful in disease modeling. For example, recent screens have identified dominant mutants closely mirroring collagenopathies and osteogenesis imperfecta (OI) (col1a1a/b, col1a2), Adams-Oliver Syndrome (dll4), and hyperhidrotic ectodermal dysplasia (edan). Finally, the Zebrafish Mutation Project, which has phenotyped a large number of zebrafish mutant alleles and made them available to the community, demonstrates the feasibility of systematic genome-wide analysis.

In addition to forward genetics, zebrafish are also readily amenable to reverse genetics, that is, testing for phenotypic consequences following the targeted interference of gene function. The advent of TALEN and CRISPR-based gene editing has substantially expanded the means by which the scientific community can approach reverse genetics in zebrafish. For gene editing using CRISPR, administration of Cas9:gRNA ribonucleoproteins (RNPs) generates double-stranded breaks at defined loci. Errors in the non-homologous end joining (NHEJ) repair mechanism lead to insertions and deletions (indels) at the cut site, often leading to loss of function (e.g., due to non-sense-mediated decay triggered by a premature stop codon). Alternatively, multiple RNPs can be used to induce site-spanning deletions that delete promoter regions or entire gene loci, which may help reduce activation of compensatory pathways triggered by messenger RNA degradation. Moreover, Cas9:gRNAs can be co-injected with a donor template which, following homology-directed repair (HDR), can result in precise gene edits. Because zebrafish develop externally, hundreds of embryos can be injected by a single user in one morning. This allows for efficient creation of induced mutations or replacements at specific genetic loci. Screening phenotypes in injected G0 founder “crispant” animals can further enable rapid and cost-effective assessment of gene function.

In addition to alleviating the time and resources needed to breed alleles to homozygosity, G0 screens are also amenable to multiplexing strategies, in which multiple genes are targeted in the same animal. The ability to detect adult skeletal phenotypes in G0 zebrafish for genes associated with recessive forms of OI (bmp1a and plod2) was recently demonstrated. Zebrafish also provide a versatile system to test gene function through the use of transgenesis. This allows for stable or inducible (e.g., heat shock-induced) protein expression, or conditional gene targeting (e.g., Cre-mediated recombination). The Tol2 transposon system is commonly used for introducing transgenes. There exists a large, growing panel of zebrafish fluorescent reporter lines for cell types within the musculoskeletal system (Table 1). As zebrafish are also relatively transparent and develop externally, development can be easily observed.

Table 1: Transgenic Lines for Visualizing Cells Relevant to the Musculoskeletal System

<table>
<thead>
<tr>
<th>Tissue/Cell Type</th>
<th>Transgene</th>
<th>References</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early neural crest and CNC- derived cartilages</td>
<td>Tg(sox10:GFP)</td>
<td>26</td>
<td>Tamoxifen-inducible Cre</td>
</tr>
<tr>
<td>Early neural crest and CNC- derived cartilages</td>
<td>Tg(sox10-CreER2)</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Cartilage/chondrocytes</td>
<td>Tg(col2a1a:EGFP)</td>
<td>28</td>
<td>Membrane-tagged EGFP</td>
</tr>
<tr>
<td>Cartilage/chondrocytes</td>
<td>Tg(Col2a1a:Cherry)</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Cartilage/chondrocytes</td>
<td>Tg(1.7col2a1a:EGFP)</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Tendon cells</td>
<td>Tg(-0.5unc45b:mCherry)</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Muscle cells</td>
<td>Tg(unc45b:Cherry)</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Bone/pre-osteoblasts</td>
<td>Tg(mk7:EGFP)</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoblasts</td>
<td>Tg(bac:Cre)</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoblasts</td>
<td>Tg(bac:CreER2)</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoblasts</td>
<td>Tg(Ola.Sp7:NLS-GFP)</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoblasts</td>
<td>Tg(þnic5α:Cre)</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Bone/mature osteoblasts</td>
<td>Tg(tg:GFP)</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoclasts</td>
<td>Tg(ctsk:YFP)</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Bone/osteoclasts</td>
<td>Tg(ctsk:DaRed)</td>
<td></td>
<td>Nuclear localization signal-tagged GFp</td>
</tr>
</tbody>
</table>

EGFP, enhanced green fluorescent protein.
in real-time. With these two attributes, use of transgenic reporters for particular cell types and proteins have provided an unmatched ability to visualize the dynamics of skeletal patterning and regeneration. These advantages also permit the visualization of cell behaviors in specific genetic contexts to gain mechanistic understanding of disease etiology.

Because of their small size and low cost, zebrafish are also amenable to drug discovery via chemical screens. In such screens, large libraries of small molecules are tested to identify specific compounds that affect gene function or developmental processes. In a typical screen, zebrafish embryos/larvae are dispensed into 48- or 96-well plates, drugs are administered by adding them to the water, and phenotypes are assessed (e.g., via morphological, fluorescent, or behavioral readouts). This strategy can be adapted to adults. The identification of dorsomorphin as a selective inhibitor of bone morphogenetic protein (BMP) type I receptors were discovered in a large zebrafish chemical screen and led to the development of analogs for the treatment of heterotopic ossification. In another screen, phosphodiesterase (PDE) inhibitors were found to alter phenotypes in a zebrafish model of Duchenne muscular dystrophy. See Wiley et al. for a recent review of chemical screens in zebrafish.

Formation and Integration of the Zebrafish Musculoskeletal System

Development and patterning

Fully developed, the zebrafish skeleton comprises several functional groups including the cranial skeleton, axial skeleton, caudal skeleton, unpaired fins (dorsal, anal, the caudal fins), paired fins (pectoral and pelvic fins), and elasmoid scales (Fig. 1A-D). As in all vertebrates, the zebrafish cranial skeleton and its associated connective tissues, tendons and ligaments, arise from the cranial neural crest; the fin skeleton elements arise from the lateral plate mesoderm, and the myosepta and axial skeleton from somitic paraxial mesoderm. The cranial musculoskeletal system forms rapidly and can function by 5 days post fertilization (dpf). The pectoral fin cartilage and muscles are also developing at this time. Although the axial skeleton does not form cartilage and bone until later stages, it has the same somitic compartments, sclerotome, syndetome, and myotome, fated to become skeletal, tendon, and muscle tissues as in higher vertebrates. Prior to 5 dpf, the axial musculoskeletal structures primarily are composed of muscle and myosepta, a scleraxis- expressing myotendinous tissue that links the myomers. The bony elements form through direct/intramembranous ossification, or via a cartilage or cartilage-like template (e.g., via perichondral or endochondral ossification). The modes of ossification can differ in zebrafish and mammals in similar bones. For example, in mouse, the vertebrae form by endochondral ossification, in zebrafish, vertebrae form by direct mineralization of the notochord sheath (perichondral ossification), without passing through a cartilaginous stage. In some bones, osteoblasts and osteoclasts act in concert to model bone shape into adulthood. Although uncommon, osteon-like structures in zebrafish have been reported for lateral ethmoid bone. Notably, these structures contained solely one lamella and no osteocytes. Indeed, most skeletal elements in adult zebrafish skeletons are osteocytic and do not show osteons or hemiosteons indicative of human-like secondary remodeling. In vertebrae of adult zebrafish, osteocyte lacunar orientation shows a preferred orientation (Fig. 1E). While the mecanosensing and remodeling characteristics of osteocytic bone in zebrafish remain to be fully understood, lacunae in zebrafish indicate smaller volumes with less numerous canaliculi compared with mice and humans.

Tendons are the tissue interface between the muscle and bone. Concurrent to skeletal development, transcripts of scleraxis (scx) are found in the forming tendon cells adjacent to the developing cartilage and muscle by two dpf. These cells aggregate and differentiate, turning on expression of tendon matrix genes, tenomodulin (tmnd), thrombospondin-4 (tsp4b), and type I collagen (col1a1a1b, col1a2). As in mammals, initiation of the axial tendon program depends on signals from the muscle. Cranial and fin tendons form in the absence of muscle, but require muscle for tendon maintenance. FGF and transforming growth factor-β (TGF-β) are also important for proper tendon formation, and cyp26b1 loss of function studies suggest that retinoic acid is required for tendon cell condensation. Recent studies have shown that mechanical force, through release of TGF-β, regulates the formation of tendon cell projections, which are thought to be involved in extracellular matrix (ECM) production. In the adult, the cranial tendons have similar ultrastructure to mammalian tendons with highly ordered type I collagen fibrils observed by transmission electron microscopy. In addition, they can be readily visualized using second harmonic generation (SHG) imaging (Fig. 1F).

Analogous to higher vertebrates, striated muscle of zebrafish contain three main components: contractile proteins, lipids, and connective tissue. Vertebrae are connected by intervertebral ligaments. Zebrafish possess both slow- and fast-twitch muscle fibers, which are topographically separated. Together with cellular mineralized bone tissue, muscles, tendon, and other soft tissues, the zebrafish skeleton facilitates locomotion, provides mechanical support, and protects internal organs. In Figure 2, we compare the inter-vertebral space in the zebrafish and mouse as a case study of how skeletal structures in each species typically exhibit both morphophysiological similarities and differences.

Conservation of Developmental programs

The molecules that govern zebrafish skeletal development are highly conserved with mammals. Sox9, a transcription factor necessary for chondrogenesis and skeletal development, has two co-orthologs in the zebrafish, sox9a, and sox9b. They are expressed in overlapping and complementary patterns during development with sox9a in the pharyngeal arches and later restricted to the pre-chondrogenic mesenchyme that will form the jaw cartilage and fin scapulocoracoid, and with sox9b in the premysteric neural crest and fin endochondral disc. The sox9a expressing chondrocytes also express col2a1 and are Alcian Blue positive before three dpf. These skeletal elements will undergo perichondral or endochondral ossification and later become Alizarin red-positive cranial
bones. In perichondral ossification, perichondral cells become *runx2a/b*, *osterix* (*sp7/osx*), and *collagen 10* positive osteoblasts and initiate ossification. Similar to other vertebrates, *indian hedgehog* co-orthologs (*ihha/b*) are expressed by chondrocytes and are thought to signal to patched, Hh receptors (*ptc1/2*) in the perichondrium and mediate bone formation. Other cranial elements, such as the maxilla undergo direct intramembranous ossification via *osx*-expressing osteoblasts. For many of these genes and cell types, reporter and lineage-tracing transgenic zebrafish lines have been generated, which, along with the optical access provided by zebrafish, allow unprecedented ability to visualize skeletogenesis (Fig. 3).

**Physiology During Development and in Homeostasis**

The skeleton serves as a key organ which mediates systemic signaling affecting the physiology. Although many of these non-structural functions of the skeleton are just being identified, it is clear that many have conservation between humans and zebrafish. One key function of the skeleton is to facilitate mineral homeostasis. The skeleton participates in part by regulating phosphate homeostasis in the kidney through bone-kidney crosstalk. There is evidence that Fgf23, which in humans and mice, is synthesized in osteocytes and regulates kidney phosphate reabsorption, also regulates phosphate homeostasis in zebrafish.

In mammals, the skeleton also serves as a calcium and phosphorus reservoir. Because calcium regulation can occur through the gills in fish, compared with humans, the physiological role of the skeleton in calcium homeostasis in fish may differ. Another function of the mammalian skeleton is acting as a site of hematopoiesis, as well as fat storage, in the marrow cavities. Zebrafish possess bone marrow spaces, which is evident in endochondral bones, which are filled with fatty tissue. However, unlike in humans, this is never colonized by hematopoietic stem cells (HSC). Thus, zebrafish bone marrow spaces lack hematopoietic tissue. A number of zebrafish bones possess adipocytes within their marrow spaces, however, it is unknown whether this adiposity responds to the metabolic demands, as it does in mice. Finally, the skeleton can regulate the metabolic processes independent of mineral metabolism. For instance, the bone-derived hormone osteocalcin has been implicated in glucose homeostasis, cognition, and male fertility. Whether the zebrafish skeleton functions as an endocrine organ through osteocalcin secretion requires further investigation.
Aging

Compared with early development, processes such as homeostasis and aging have not been studied in depth in the zebrafish. As certain debilitating conditions arise in the skeleton as a function of age, such as osteopenia and osteoporosis, the ability of the zebrafish to model components of these processes could be important. Zebrafish typically have a lifespan of approximately 2-3 years (though 5 years or more is possible),74 and exhibit growth throughout life. There is evidence that zebrafish skeletal function declines with age. For instance, tendon mechanical properties diminish with age.75 Moreover, alterations of vertebral bone and disc are observed in aged zebrafish.76 The bone dependence on estrogen has been modeled in another small teleost, medaka, and thus the basic properties of the etiology are likely present in zebrafish.77 With more analysis of late developmental stages, it is likely more insight will emerge from the zebrafish into how the skeletal system ages and its consequences.

Regeneration and Repair

Zebrafish have not been used as a common model for understanding human fracture repair. This is in part due to lack of accessible long bones, as well as its high regenerative capacity, which may utilize different repair mechanisms than in mammals. Previous studies have examined the repair properties of damaged membranous bones of the skull roof78 as well as mandible.79 Although these are not directly comparable with analysis of long bone fractures studied in mouse and most commonly seen in patients, there were some similarities in terms of the genes and cell types involved. For example, runx2+ cells in the periostium were likely involved in new bone formation and proper formation of the cartilage callus relied upon Indian hedgehog a (ihh).79 In addition to examination of intrinsic regenerative mechanisms, the transparency of the zebrafish permits the analysis of extrinsic cell populations in the healing process. Studies have shown that the immune system plays an important role in mediating tissue regeneration.80,81 Visualization of immune infiltration after injury can be accomplished through the use of transgenic reporter lines that either label all leukocytes (cd45:DsRed)82 or are specific for neutrophils (mpx:GFP177479)83 or macrophages (mpeg:GFP).84 There are also several methods to functionally deplete immune cell populations (reviewed in Keightley et al.85), which can permit temporal control over cell type-specific cell ablation to assess the role of immune cell populations at different stages of the regenerative process, as has been performed for tail fin regeneration.86

Zebrafish have a significant capacity for epimorphic regeneration.5,14 One example is the caudal fin, which regenerates following amputation.86 Similar to salamander limb regeneration, fin regeneration involves a heterogeneous pool of progenitors called the blastema, which is comprised, at least in part, of mature cells at the amputation stump that dedifferentiated, including osteoblasts.86 A variety of pathways known to be important for skeletogenesis in mammals are recapitulated during fin redevelopment, as reviewed in Watson et al.86 An intact musculoskeletal system is required for normal regeneration as zebrafish subjected to injection of botulinum toxin, which inhibits synaptic release at cholinergic nerves, exhibit impaired regeneration.87 This model has also revealed the existence of mesenchymal progenitor populations within specific regions that robustly respond to injury and generate new osx+ osteoblasts.88,89 Dedifferentiation of mature osteoblasts also occurs during repair of zebrafish fin fractures and skull injuries.79 While osteoblast dedifferentiation is more limited in mammals, fin repair after fracture exhibits some similarities to mammalian long bone fracture, including formation of a remodeling callus,90 and recruitment of osteoclasts.81 Recently, it was shown that neutrophils dynamically colonize the fracture site. When infected with Staphylococcus aureus, neutrophils were retained in the fracture site and repair was reduced.91 Further studies examining the utility of the fin fracture model to study the aspects of fracture biology are warranted.

Musculoskeletal Loading

While the zebrafish skeleton has a reduced role in resisting gravitational loads relative to humans, there is evidence that the zebrafish skeleton can respond to exercise, as well as disuse. Swim training routines have been established to force exercise and stimulate natural modes of skeletal loading in zebrafish. In this way, the complex interplay of cellular, structural, and compositional bone characteristics can be assessed using multiscale approaches in zebrafish to study the effects of genetic and environmental interactions on the skeletal system in vivo. During early development in zebrafish, swim training alters timing of skeletogenesis.85 In adult zebrafish, swim training increases vertebral bone formation and alters quality.86 Moreover, this type of forced exercise also induces muscle adaptations in adult zebrafish.83 This paradigm opens up avenues for genetic and small molecule screens to identify signaling pathways critical for musculoskeletal adaptation to loading and exercise.

Phenotyping

MicroCT

The three dimensional (3D)-high-resolution micro-computed tomography has become established as a powerful method to assess bone morphology and microstructure in zebrafish.18,58,94,95 Using a 5 μm voxel size, bone structure indices as vertebral bone volume, thickness, and eccentricity can be characterized.18,58 Neural arch area, which reflects modeling arising from osteoblast and osteoclast activity, can also be captured.94 Because of their small size, whole body, high-resolution scans are readily acquired.95 Software for semi-automated segmentation enables in-depth phenotyping at a large number of skeletal sites. By quantifying hundreds of measures this was shown to increase the sensitivity in discriminating mutant populations.95 Moreover, the osteocyte lacunar network in the vertebral tissue can be imaged at high resolution with lab-based nano-CTs and 3D X-ray Microscopy (3DXRM). The orientation of the osteocyte lacunae in relation to the long and short axis of the vertebral bodies, sphericity, mean lacunar volume and lacunar density can be quantified.18,58 Finally, synchrotron-based X-ray microCT, when combined with tissue-contrast stains, can yield whole-organism images suitable for cell-level quantitative histological phenotyping in zebrafish.96

Histomorphometry

In zebrafish, histologic sections stained using von Kossa/van
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Gieson, Goldner’s modified Masson-trichrome, and toluidine blue enable static bone histomorphometry, and is performed in accordance with standardized nomenclature set forth by the ASBMR nomenclature committee for practitioners of bone histomorphometry. Calcein labeling or double labeling with calcien and Alizarin Red S can be performed and double labels can be evaluated for dynamic bone histomorphometry. Such an approach was used to quantify increases in mineral apposition rate (MAR), mineralizing surface per bone surface (MS/BS), and bone formation rate (BFR) at the vertebral endplates in zebrafish subjected to swimming exercise.

Assessment of Bone Composition, Mineral Density Distribution, and Mechanical Properties

Recently, quantitative backscattered electron imaging (qBEI) has been established as an effective means to measure the bone mineral density distribution in zebrafish. Gray value histograms were used to assess the mean calcium content in the mineralized bone tissue, as well as the homogeneity of mineralization. Vibrational spectroscopy methods (e.g., Fourier transform infrared spectroscopy (FTIR) and Raman spectroscopy) have also been adapted to zebrafish bone. Parameters such as the mineral-to-matrix-ratio, carbonate-to-phosphate ratio, cross-link-ratio (collagen maturity), and crystallinity (purity, size of mineral crystals) of the bone were shown to provide information about the molecular and compositional bone characteristics. Finally, nanoindentation of vertebrae at the vertebral endplates in zebrafish subjected to swimming exercise.

Disease Applications

Collagenopathies

OI is a disease of the collagen matrix, which results in brittle bones and skeletal deformities. In humans, collagen type I is a heterotrimer composed by two alpha chains, α1(I) and α2(I), which trimerize in a 2:1 ratio, respectively, to form a fibril with a triple-helix structure. In zebrafish, the collagen type I triple helix is composed of three α chains, α1(I), α2(I), and α3(I), which are encoded for by the genes col1a1a, col1a2, and col1a1b, respectively. Most human patients with OI are attributed to mutations in type I collagens, with the majority of mutations disrupting the conserved Gly-X-Y motifs responsible for fibrillar assembly of the collagen heterotrimers. In zebrafish, several dominant mutants have been identified carrying heterozygous glycine substitution in the α1 chain of collagen type I, and which exhibit severe, pathological features of classical OI. This was demonstrated in the chihuahua mutant, which exhibited changes in vertebral tissue composition. A large panel of zebrafish mutants of col1a1 genes with qualitative and quantitative defects in collagen type I have been identified.
Spinal Curvature

Adolescent idiopathic scoliosis (AIS) is defined as scoliosis without underlying vertebral malformations. While the pathogenesis of this disease is still controversial, the zebrafish has made significant advances in our understanding of this disorder. AIS-like scoliosis was demonstrated in cc2d2a mutant zebrafish, which has a role in vesicle trafficking and fusion at the transition zone of photoreceptor connecting cilium in the eye. Recently, mutant zebrafish displaying larval or late-onset scoliosis without vertebral malformations, analogous to AIS, have been described for c21orf59, cdc40, cdc151, dyx1c1, kif6, and ptk7. A common mechanism has emerged from these studies, where loss of ependymal cell cilia function lining the ventricles of the brain, leading to reduced cerebrospinal fluid flow can generate AIS in zebrafish. Interestingly, maternal-zygotic ptk7 mutant zebrafish display scoliosis with vertebral malformations, while strictly zygotic ptk7 mutant fish display late-onset AIS without vertebral malformations. This suggests that the severity of scoliosis can be on a spectrum based on temporal requirements for gene function, which may explain the strong association of AIS in families of children with CS.

The cellular mechanism of AIS in ptk7 was demonstrated by a foxj1,ptk7 transgenic zebrafish, which can completely rescue the onset of scoliosis phenotypes observed in ptk7 mutant zebrafish. Foxj1 is a master transcriptional regulator of motile cilia, which labels motile cilia of the ventricles of the brain and in the pronephros but also labels a subset of central canal lining ciliated (CSF)-fluid contacting neurons. Indeed, disruption of a major signaling receptor, pdk21, of CSF-contacting neurons led to mild alterations in spine curvature in zebrafish. While it is still unclear how these disruptions of CSF physiology cause scoliosis, recent studies demonstrated that CSF flow helps to stimulate the proper formation of the extracellular Reissner’s fiber, which can directly contribute to body straightness during embryonic development, via an unknown mechanism; and (ii) that CSF flow transports adrenergic signals, which stimulate the expression of urotensin neuropeptides from CSF-contacting neurons along the spinal cord and mutant zebrafish of the urotensin receptor uts2ra display AIS. How these studies will translate to mammalian physiology is still unclear. However, at least one candidate gene for AIS uncovered in zebrafish kif6 does not recapitulate AIS phenotypes when mutated in mouse or human.

Although having early differences in vertebral specification compared with mammals, the zebrafish may also serve as a model for aspects of congenital scoliosis (CS). Disruption of the extracellular sheath through chemical disruption of lysyl oxidases or specific genetic disruptions of the sheath extracellular matrix components of the notochord sheath such as: colba1a, col27a1a/b, or calymp][-15,16 can generate CS-like scoliosis with vertebral malformations in zebrafish suggesting potential underlying components of zebrafish development that can be used to assess gene function in CS etiology.

Disease loci

Human genome-wide association studies (GWAS) are a powerful means to understand the genetic risk factors for chronic diseases such as osteoarthritis and osteoporosis. These loci may harbor novel drug targets for orthopedic diseases, as evidenced by the fact that OPG/RANK/RANKL and LRP5/SOST, all genes at BMD loci, are members of pathways targeted by osteoporosis drugs (Denosumab and Romosozumab, respectively). A recent analysis of UK-Biobank data identified 515 loci associated with eBMD. The causal genes responsible for most associations have yet to be assigned, and thus gene discovery in animal models is needed to complement GWAS in human populations. One limitation with knockout mice is the lack of coverage of genes at BMD loci. For instance, of the >23,000 protein-coding genes in the mouse genome, <5% have been rigorously analyzed for bone phenotypes in knockout mice within ancillary bone phenotyping projects of the International Mouse Phenotyping Consortium. A recent study demonstrated the potential to rapidly generate mutations in CRISPR-edited G0 zebrafish to attribute functional contributions of candidate genes at bone disease loci. Skeletal abnormalities have been observed in fish with altered function in other genes at BMD loci, including LRP5, OSX, SP7, and RANKL. This provides further evidence that the identification of genes that contribute to human osteoporosis-related traits in zebrafish is feasible. The utility of zebrafish for human skeletal genomics is reviewed in Kwon el al.

Osteoarthritis

Recent data has shown that zebrafish can be used to study the development of synovial joints and osteoarthritis. Mutations in col11a2 in zebrafish leads to joint pathologies reminiscent of early-onset osteoarthritis in humans. Further, as in humans and mice, zebrafish lubricin or proteoglycan-4b (prg4b) expression was found within some joint regions, such as articular chondrocytes in the jaw. These joint regions also expressed col10a1, acana, and matrilin1, which together with prg4b, show similarities to genes expressed in mammalian synovial joints. Loss of both prg4 orthologs resulted in synovial hyperplasia and deterioration of the joint surface by 6-12 months of age. This phenotype recapitulates that found in mouse where loss of Prg4 results in joint disease by 2 months. Although it is unknown why there is a significant delay in timing of osteoarthritis onset in the zebrafish compared with mouse genetic models, possible explanations are the zebrafish’s robust regenerative abilities combined with different mechanical environments. Even with these differences, this work establishes the conservation in synovial joint gene expression and function in the zebrafish.

Summary / Future Directions

The genetic causes of skeletal disorders are rapidly becoming identified, and it is now clear that many common musculoskeletal disorders are fundamentally complex in their causes. The field is faced with the need to more fully interrogate the functional consequences of genetic
and environmental stresses in how the skeleton and its connecting tissues are formed, how it integrates with broader physiology, and how it repairs the damage. There is now a strong rationale to validate newly discovered disease candidate genes in the zebrafish prior to extensive mouse analyses. The refinement of clonal analyses of gene function will expedite the combinatorial analysis of gene function and permit a systematic testing platform for genetic association studies and analysis of genetic modifiers. With the ability to visualize cellular dynamics during the formation of the skeleton as well as during repair, in different genetic contexts, the zebrafish provides a powerful system to bring functional characterization in line with the rate of genetic discoveries.

As the use of zebrafish for orthopedic research is still in its relative infancy, there are a number of open questions regarding the developmental stages, bones, and phenotypic traits in zebrafish that best serve as a model for human skeletal biology. Morphophysiologival differences can make one-to-one modeling of human skeletal phenotypes in zebrafish challenging. Origins of mammalian bones and their connections to fish bones (e.g., the mammalian middle ear bones, which derive from bones that form the jaw in fish) can sometimes be revealed through evolutionary analyses, however, such relationships cannot always be made. In this context, a community effort to phenotype zebrafish mutants for orthologs of genes examined in mutant mouse phenotyping consortia may aid in identifying zebrafish phenotypes that are most consistently associated with phenotypic changes in the orthologous mutant mouse.

With the extension of zebrafish work into phenotypes of the skeleton beyond early development, the broad utility of this model has emerged. While there are differences stemming from the use of a non-mammalian vertebrate for modeling human disorders, the zebrafish model provides both genetic and anatomical foundations, in which informed analyses can be made concerning the etiology of disorders and also serves as a tool to refine potential therapeutic strategies.

Authors' Contribution

B.B., J.L.G., R.S.G., M.P.H., and R.Y.K. drafted and revised the manuscript. All authors have read and approved the final submitted manuscript.
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Authors

1 Department of Osteology and Biomechanics, University Medical Center Hamburg-Eppendorf, 22529, Hamburg, Germany

2 Center for Regenerative Medicine, Harvard Stem Cell Institute, Department of Orthopaedic Surgery, Massachusetts General Hospital, Harvard Medical School, 185 Cambridge Street Boston, MA 02114, United States of America

3 Department of Pediatrics, Dell Pediatric Research Institute, The University of Texas at Austin, Dell Medical School, Austin, Texas, United States of America

4 Department of Genetics, Harvard Medical School; Department of Orthopedic Research, Boston Children’s Hospital, 300 Longwood Avenue, Boston, MA, 02115, United States of America

5 Department of Orthopaedics and Sports Medicine; Department of Mechanical Engineering; Institute for Stem Cell and Regenerative Medicine, University of Washington, Seattle, Washington, United States of America

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AII University of Washington medical students complete Independent Investigative Inquiry (III) during the summer after their first year. The program maintains relationships throughout WWAMI (UW School of Medicine’s one-of-a-kind, multi-state medical education program serving Washington, Wyoming, Alaska, Montana and Idaho). Through III, students are connected with opportunities here and at other institutions. Organizations or faculty who would like to become mentors for summer or long-term projects can list opportunities through our office. Students select a project of interest and execute their scholarly work under the guidance of a Faculty Mentor over the Summer term between years one and two of medical school. Students will work on their research projects full-time (~30 hours per week) for nine weeks during the Summer term between the first and second years of medical school.

The University of Washington Department of Orthopaedics and Sports Medicine is deeply connected with this program, mentoring a number of students annually. This is primarily through the Scholarship for Discovery and Scholarship for Integration pathways.

Quotes from Past Students:

This experience “…showed me how to treat patients with compassion and dignity, and taught me qualities I can emulate as a person, future physician and researcher”

– Anonymous student

“I couldn’t have asked for a better summer research experience. In addition to taking part in a really interesting project, I was able to meet some great people and make long lasting friendships.”

– Anonymous student

Laboratory Highlight:

In conjunction with clinical faculty collaborators over the last 3 years, the CoRE laboratory has supported 8 medical students in the Independent Investigative Inquiry (III) and Medical Student Research Training (MSRTP) programs. These students have worked on diverse projects, from using 3D surface scanning to monitor knee swelling after ACLR reconstruction surgery to studying how bone density in the sacrum changes with age. During their weeks in the laboratory, all students proved to be highly motivated, intellectually curious, and provided positive feedback about their experience. Several have continued to work on their research projects in their spare time after the end of the program. Their work has led to a growing number of conference abstracts and journal articles, benefiting both the students’ future career and the department’s research dissemination efforts.

Scholarship of Discovery is empirical research in which new discoveries are made through original investigation. The project can be initiated by the student or by a faculty mentor, as long as the student has an independent role and makes an intellectual contribution to the project. Students selecting this program can expect to learn the steps and rationale in trying to resolve an empirical question through data collection and analysis. A hypothesis is made regarding the relationship between variables and a study attempts to validate the hypothesis through observation. The study may take the form of a basic laboratory study, a survey, a secondary analysis of an existing data set, a chart review, a qualitative study, or a prospective clinical trial. This empirical research may be directed toward a question in any field related to medicine and may include laboratory or clinical research and quality improvement studies. The project will culminate in a poster presentation at the annual Medical Student III Poster Session held every Fall quarter at their Foundations Site.

Scholarship of Integration involves a complete systematic literature review to answer an unresolved scientific question relevant to medicine. Alternatively, students can complete a systematic literature review to analyze an issue in medicine or to perform a historical investigation. In the process, they work with our Health Sciences Librarian to learn to effectively search medical databases and are guided by a Faculty Mentor as they interpret studies and synthesize this information to draw a conclusion.

This III program culminates in a final paper due in September after the Summer term. Students in this program are welcome to present a poster of their work at the Fall 2019 Medical Student III Poster Session held at their Foundations Site, but this is not a requirement.

For more information:

Primary contact:
Education Specialist:
Rachel Liao, somiii@uw.edu
Faculty Director:
Dr. Shobha Stack
Website:
https://sites.uw.edu/somcurr2/iii-scholarship-requirement/start-here/
The sternoclavicular joint (SCJ) can develop all of the same conditions seen in the body’s other diarthrodial joints, including arthritis, instability and intra-articular disk tears. Pathological changes in the joint can produce effusions, abnormal motion, or pain. And like other joints, patients may perceive pain arising from the SCJ as pain in that location, or it may be perceived elsewhere, a phenomenon called referred pain. When the SCJ refers pain elsewhere, the result is often an orthopaedic misdiagnosis or, even worse, a patient being told that there is nothing wrong when (s)he may have a treatable joint problem.

A knowledge of how referred pain occurs—first described by 19th-century anatomist John Hilton in his classic monograph “On Rest and Pain”—can keep orthopaedic surgeons from being fooled, and their patients from being mistreated or written off as having psychosomatic illness.

Hilton, who was sometimes called “Anatomical John” by his colleagues, famously stated that in patients with referred pain “one of the earliest symptoms is remote from the actual seat of mischief” (1). When we apply this to the SCJ, we find that symptoms there can masquerade as neck, shoulder and infraclavicular pain.

SCJ symptoms can be understood if one considers the innervation of the sternoclavicular joint, the related anatomical structures and Hilton’s Law. First articulated in 1863, (2) and revisited recently, (3) Hilton’s Law holds that “The same trunks of nerves whose branches supply the groups of muscles moving a joint furnish also a distribution of nerves to the skin over the insertions of the same muscles; and…the interior of the joint receives its nerves from the same source.”

For example, patients with adhesive capsulitis (“frozen shoulder”) may present with pain in the axillary sensory distribution (that is, in the C5 dermatome); they—and sometimes their surgeons—may be confused as to why the outside of the arm upper arm hurts when the problem arises from the shoulder. Understanding Hilton’s Law is the key to the answer.

Applying this to the SCJ, we find that the relevant neuroanatomy of the SCJ explains why patients will often describe “triangles of pain” that they feel, which can radiate up their SCM, down the trapezius and even below the clavicle and out to the acromioclavicular joint. Some patients will mainly experience pain in one of these areas, such as under the clavicle, or along the SCM and do not describe a whole triangle as painful. (See the diagram below to review the muscular anatomy and the described triangles.)

The SCJ capsule is innervated by branches from the medial supraclavicular nerve (C3,4) as well...
as branches from the nerve to the subclavius (C5,6). Many muscles that attach to this joint capsule have similar innervation, including the subclavius muscle. This can account for pain that SCJ patients feel along the undersurface of the clavicle that follows the subclavius muscle out towards the ACJ. Similarly, the sternothyroid and sternohyoid muscles, which attach near the posterior SCJ capsule, are innervated by the ansa cervicalis (C1-3). The common root C3 contributes to the medial supraclavicular nerve. Therefore, it is not surprising that patients with SCJ pathology will have some altered sensation in the neck and describe swallowing issues and even a sensation of neck fullness. Moreover, apart from the neurologic connection, when one recognizes that the sternothyroid and sternohyoid muscles connect from the SCJ capsule to the thyroid cartilage and hyoid bone respectively, the simple act of swallowing can pull on the inflamed sensitive capsular tissue.

It is not clear that the spinal accessory nerve, which also innervates the trapezius and sternocleidomastoid muscles, has any direct articular branches to the SCJ. However, the trapezius receives ventral rami from C3 and C4 and the SCM receives ventral rami from C2 and C3. Hence there may be neural connections from the C3 and C4 roots that explain how SCJ capsular distension or stretching from instability issues will radiate along the SCM and even along the trapezius toward the lateral clavicle, just as hip joint injury can refer pain to the medial aspect of the knee, along the termination of the obturator nerve. It is also plausible that patients with SCJ pain will subconsciously “splint” the joint by maintaining increased tone in the trapezius, SCM, subclavius and even pectoralis major and thus experience additional pain in these muscles from overuse.

Of course, the proximity of other structures such as the trachea, brachiocephalic veins, and other anterior mediastinal structures, as well as the sequelae of severe trauma to that area (sometimes causing posterior SCJ dislocations) all must be considered and when present addressed appropriately.

But even patients with more-subtle sternoclavicular swelling or instability may report a sensation of fullness in the throat, or even discomfort with swallowing—all without any obvious anatomical disruptions in those parts of their bodies. Other patients will share that the pain travels up the neck to behind the ear, from that area down to the ipsilateral shoulder, and even pain under the clavicle that runs towards the acromioclavicular joint.

These patterns may cause an inexperienced physician to conclude erroneously that more than one problem is present, and perhaps even obtain otolaryngology or spine consultations. As most orthopaedic surgeons are more familiar with managing problems of the acromioclavicular joint, they may try acromioclavicular joint injections or even perform needless distal clavicle resections to ameliorate symptoms stemming from the more medial “epicenter”—tactics that, of course, will do nothing for pain arising from the SCJ.

A keen diagnostician is one who has learned to listen to his or her patients—they're trying their best to tell us what is wrong—but where complicated anatomy is concerned, as is the case around the SCJ, good diagnosticians will follow in the path of “Anatomical John”. Paying attention to patterns of referred pain around that joint, which are readily decoded using Hilton’s Law, can help patients understand their symptoms, allay their fears, save them unnecessary consults and interventions, and hasten their journey to healing.

Bibliography

The University of Washington Department of Orthopaedics and Sports Medicine hosted the Japanese Orthopaedic Association (JOA) Traveling Fellowship July 16-19, 2019. In conjunction with the American Orthopaedic Association (AOA), the fellowship promotes travel for the exchange of medical ideas. On even years US Fellows are chosen and travel to Japan, while on odd years Japanese Fellows are chosen and hosted by American institutions. To date, the department has four alumni of the JOA Traveling Fellowship, Conor Kleweno, MD in 2018, Reza Firoozabadi, MD in 2016, Sean Nork, MD in 2004, and Bruce Sangeorzan, MD in 1994. This year, we were happy to host Taku Hatta, MD from Sendai, Gen Inoue, MD from Sagamihara, Takashi Kaito, MD from Suita, Tomoyuki Matsumoto, MD from Kobe, Shinji Miwa, MD from Kanazawa, and Hiroaki Nakashima, MD from Nagoya.

Upon arrival, they had a meet and greet with Dr. Reza Firoozabadi before Grand Rounds at Harborview Medical Center early the following morning. At Grand Rounds, they each gave six-minute presentations on a topic of their choosing. Dr. Hatta talked about “Shoulder Biomechanics of Treatment for Rotator Cuff Tear.” Dr. Inoue presented on “Application of the Allograft Bone for Spinal Surgery: Differences Between the US and Japan.” Dr. Kaito spoke on the “Intervertebral Disc Regeneration with Small Compounds and Cell-Based Therapy.” Dr. Miwa spoke on the “Risk Factors for Postoperative Deep Infection in Bone Tumors.” Lastly, Dr. Nakashima talked about “Lateral Access Surgery.” Each presentation provided great opportunities for group discussion and learning for all attendees.

Following Grand Rounds on Wednesday, the fellows were escorted for photos with Drs. Howard Chansky, Reza Firoozabadi, and Conor Kleweno, then on to the OR to observe a couple cases in spine surgery and one foot and ankle case with Dr. Bruce Sangeorzan. They enjoyed their afternoon with lunch at Aerlume followed by a walk through Pike Place Market. Afterwards, they had a private tour of T-Mobile Park with Dr. Kleweno including a chance to walk onto the field. All of the fellows were excited to pay homage to their hero Ichiro Suzuki. The day ended with a traditional barbeque dinner at the home of Drs. Reza Firoozabadi and his wife, Dr. Suzette Miranda, where the fellows were able to socialize with Drs. Bruce Sangeorzan, Conor Kleweno, David Gendelberg, and a few other guests.

The fellows spent Thursday with Dr. Albert Gee, where they were given a tour of the Sports Medicine Clinic and Husky Stadium, and also had the opportunity to observe Dr. Chansky in the OR at the University of Washington Medical Center. The fellows and Dr. Gee had a relaxing afternoon with fish n’ chips for lunch at Ivar’s followed by an afternoon of boating with Jason Maris, PA-C. They ended their trip with a lovely dinner at the Chanskys’ home, where many faculty and family were invited to socialize and further their discussions from earlier in the week.

Drs. Firoozabadi, Kleweno, Gee, and Chansky were happy to host the six traveling fellows from Japan and hope it was a productive experience to everyone involved.
The overarching story this year is the COVID-19 crisis which has touched almost every facet of our lives including the operations of the University of Washington, UW Medicine and our Department.

However, we want to first share the good news and positive changes we had prior to the onset of the pandemic. We successfully completed the merger of what were formerly UW Medical Center (UWMC) and Northwest Hospital into a single medical center on 2 campuses (UW Medical Center is now formally known as UWMC - Montlake and Northwest Hospital has been renamed UWMC - Northwest). The union of these two hospitals leverages the efficiencies, agility and accessibility of a community hospital with the cutting-edge care, research and teaching of UW Medical Center (UWMC). The merger was successfully completed on January 1st, 2020 and we are excited for this next chapter and the exciting possibilities that came with it. We welcomed a host of new clinical faculty to our Department who had been a part of NW Hospital and this included:

Edward Blahous, DPM
Douglas Ichikawa, DPM
Cherie Johnson, DPM
Anthony Kim, DPM
Erik Lilja, DPM
Sara Mahmood, DPM
Christian Peterson, DO

(See below for a full list of our combined clinical faculty and advanced practice providers for UWMC)

Other faculty additions included Dr. David Fitz who is the latest member of our Arthroplasty Service at UWMC - Northwest and joined us just this past Fall after completing his fellowship at Massachusetts General Hospital. As we look to the future, we are very excited to report the successful recruitment of Dr. Jesse Roberts who will join Drs. Thompson and Harwood on the Tumor Service beginning this October. He is completing his Sarcoma Fellowship at the University of California-Davis and prior to that completed his residency at the University of Colorado. He will divide his time between UWMC – Montlake and Seattle Children’s Hospital. He comes highly recommended by all who have worked with him throughout his training and we are confident he will make a great addition to the faculty at both sites.

The merger affected clinical care, teaching and research activities. Challenges regarding attending and resident coverage of call across hospitals was managed through discussion between stakeholders (orthopaedic resident and attendings as well as representatives of other departments). Under the leadership of Dr. Kweon, the resident call schedule and team allocation was adjusted, leading to excellent care and a superb educational experience for residents across the two UWMC campuses. The merger has also improved the ease with which research may be carried out at UWMC - NW, and multiple orthopaedic studies have been initiated already this year.

Like the rest of the world, the COVID-19 pandemic has had a dramatic effect on all of our lives. Our city and state were ordered to lockdown in an effort to slow the spread of the disease and “flatten the curve”. Elective surgeries were postponed in order to conserve resources and prepare for the surge of COVID positive patients. UWMC - NW took the brunt of UW Medicine’s overall COVID patient census and as a result all of the ORs there were closed to divert personnel, supplies and equipment to support the efforts in caring for infected patients.

We continued emergent and urgent orthopaedic surgeries at UWMC – Montlake throughout the lockdown period and it truly was a collaborative effort as the faculty came together to cover surgical cases and share OR time. The educational mission of the residency was maintained via videoconferencing technology. We rapidly accelerated the planned incorporation of telemedicine throughout the health system virtually overnight. This was a critical tool in continuing to care for our patients and most everyone found that the delivery of care in this manner was better than...
many had expected (so much so that many of us are plan to continue its use beyond the current crisis).

COVID-19 crisis notwithstanding, we are happy to report that the faculty, trainees, APPs and staff at both UWMC campuses remain stable, productive and steadily growing as we look to explore the changes, benefits and challenges of our new paradigm of one medical center comprised of 2 campuses.

Full List of Faculty and APPs at UWMC

**Arthroplasty**
Howard Chansky, MD, Paul Manner, MD, Seth Leopold, MD, Navin Fernando, MD, David Fitz, MD, Peter Hall, PA-C, Michael Taylor, PA-C, Jason Erickson, PA-C

**Hand**
Jerry Huang, MD, Sarah Beshlian, MD, Stephen Kennedy, MD, Nicholas Iannuzzi, MD, Erin Miller, MD, Dennis Kao, MD, Amanda Pedersen, PA-C, Kaitlen Laine, PA-C, Jennifer Stambaugh, PA-C

**Podiatry**
Edward Blahous, DPM, Douglas Ichikawa, DPM, Cherie Johnson, DPM, Anthony Kim, DPM, Erik Lilja, DPM, Sara Mahmood, DPM

**Shoulder and Elbow**
Frederick Matsen, MD, Winston Warme, MD, Jason Hsu, MD, Alex Bertelsen, PA-C, Kirsten Harvey, PA-C, Emily Thach, PA-C

**Spine**
Viral Patel, MD, Carlo Bellabarba, MD, Julianne Krause, PA-C, Connie Ly, PA-C, EChing Bertelsen, PA-C

**Sports**
Albert Gee, MD, Christopher Kweon, MD, Mia Hagen, MD, Ken Chin, MD, Christian Peterson, DO, Jason Maris, PA-C, Lauren Colpo, PA-C, Priya Shah, PA-C, Mahra Davidson, PA-C

**Trauma**
William Lack, MD, Florence Unno MD, Wyatt Visca, PA-C

**Tumor**
Matthew Thompson, MD, Jared Harwood, MD, Jesse Roberts, MD, Jennifer Hamilton, PA-C, Stasia Turner, ARNP

Orthopaedic Inpatient Service (Montlake)
Janice Olivo, PA-C and Hannah Bae, ARNP

Orthopaedic Inpatient Service (Northwest)
Katie Moore, PA-C and Sophie Jeannot, ARNP
Pediatric orthopedic surgery remains one of the largest and most active divisions of care at Seattle Children’s. For the second year in a row, we exceeded 42,000 outpatient clinic visits and performed over 2100 surgeries despite numerous challenges with operating room access. Our programs in general pediatric orthopaedics, pediatric trauma led by Dr. Mark Dales, hand and upper extremity led by Dr. Suzanne Steinman, foot and ankle led by Dr. Vince Mosca, tumor led by Dr. Antoinette Lindberg, as well as the specialty programs noted below continue to thrive.

After five years of exceptional leadership, with growth of our division in both number of care providers and presence on the national meeting scene, Dr. Suzanne Yandow has moved on to focus her efforts as Associate Surgeon in Chief at Seattle Children’s, helping coordinate incident command response to past operating room challenges and now the COVID-19 pandemic. We have so appreciated her leadership.

Pediatric Spine

This year we want to especially thank Dr. Walter Krengel III for his exemplary leadership of the spine division since 2008 as he steps back into a supportive role for the division and department, staffing outreach clinics and being available for major OR-case assistance, as well as a leading the design of the new SCH operating rooms. He is known nationally for his clinical care, particularly for pediatric cervical spine as well as complex thoracolumbar deformity, and in being so elevated the level of our clinical program. Wally has been a unifying presence throughout the last decade in the department and ushered in a number of quality and safety initiatives for the division, including standardizing perioperative spine management, QSVI dashboards, the Spine at Risk pre-anesthetic program, and a drawn-out battle for patient reported outcome collection. The spine division leadership has now been transferred to Dr. Jennifer Bauer who looks to build on what Dr. Krengel created.

The next year will bring continued involvement and enrollment in international research groups, including the Pediatric Cervical Spine Study Group (PCSSG) and the Pediatric Spine Study Group (PSSG), which focuses on early-onset scoliosis, both of which feature SCH faculty in leadership positions and have yielded a number of research projects the past year. Dr. Klane White, most active in PSSG along with SCH pulmonologist Dr. Gregory Redding, continues to focus on lung function and quality of life in early onset scoliosis, with several presentations at national meetings this year. Dr. Todd Blumberg has added depth to his hip practice with a 3-month Boston Children's Hip Preservation Fellowship this past winter, and will grow this program as he continues to care for spine patients.

Skeletal Health and Dysplasia

The Skeletal Health and Dysplasia program at Seattle Children’s is a global leader in the healthcare of children with rare bone disorders and has recently been designated as one of five “Centers of Excellence” in the United States by the NIH funded consortium – Lysosomal Disease Network (LDN). Patients receive both specialized clinical care and access to international medical trials through our program, which is currently offering both phase II and III trials for patients with achondroplasia. Our faculty and medical staff represent Seattle Children’s and University of Washington by maintaining a strong presence within Little People of America (both nationally and locally), the Osteogenesis Imperfecta Foundation and the National MPS Society, among others. Dr. White serves on the LPA and Camp Korey Medical Advisory Boards and the Scientific Advisory Board of the National MPS Society.

This year marks a heartfelt milestone for the Skeletal Dysplasia team. After 15 remarkable years and momentous contributions, Dr. Goldberg will be retiring from clinical practice and returning to Boston full-time. His legacy will indeed live on in the DNA of this program (pun intended!). Patients, families, and staff alike are wholly indebted to his contributions to the Skeletal Health and Dysplasia program at Seattle Children’s Hospital, and we are deeply grateful for the many gifts.
Sports Medicine

The Seattle Children's Sports Medicine Program is a multi-disciplinary collaborative program that includes sports orthopedic surgeons (Drs. Michael Saper and Greg Schmale), sports medicine trained pediatricians (Drs. Monique Burton, Tom Jingui, John Lockhart, Kyle Nagle and Celeste Quitiquit) and a physiatrist (Dr. Brian Krabak), an adolescent medicine physician (Dr. Cora Breuner), physician assistants (Jeanette Kotch, Leslie Rodriguez, Kari Robertson), 6 in clinic certified athletic trainers, 54 certified regional high school athletic trainers, and over 20 sports physical therapists.

We deliver care at multiple sites metropolitan Seattle sites as well as regional clinics including Yakima, Wenatchee and Olympia. Our sports providers see over 6000 visits annually. We provide care for sports and physical activity related injuries and medical concerns. Our visits include comprehensive evaluations that address not only their current concerns, but also any predisposing factors and ways to prevent injury in the future. Our sports concussion program provides detailed evaluations and management plans for over 500 concussion patients annually.

Our two full-time sports surgeons, Drs. Michael Saper and Gregory Schmale, remain busy treating patients with ACL tears, patellar instability, and shoulder instability, as well as osteochondritis dissecans of the elbow, knee, and ankle, having performed nearly 350 sports-related surgeries in the past year. Each of our surgeons are members of the Pediatric Research in Sports Medicine society Research Interest Groups and are currently participating in multicenter studies of meniscal tears and discoid menisci, tibial spine fractures, rehabilitation after ACL injury, and the treatment of medial epicondyle fractures.

Our sports pediatricians and physiatrist provide sports medicine coverage at local high schools as well as international events including USA Track and Field, USA Swimming, USA Ski and Snowboarding including World Championships, World Cups an Olympic Games.

Now in its twelfth year, the Athletic Training Program has emerged as the regional leader in providing on-site healthcare for young student-athletes and is one of the largest of its kind in the country. Our high school athletic trainers are located at 41 greater Puget Sound area high schools, providing excellent care for our student-athletes as well as involved in over 100 outreach organizations including the Reign Academy, Girls on the Run, Special Olympics, Disc NW, Derby Brats and UW sports camps. This group provided over 65,000 assessments including over 600 concussions and over 100,000 treatments to young athletes.

Areas of Future growth and development are related to aspects of being a young physically active person, including continued incorporation of musculoskeletal ultrasound within our sports medicine practice, integration of sports medical conditions and subspecialties, growth of our care for athletes with disabilities, and the addition of sport psychology and sports nutrition.

Seattle Children's cares for all young people in the diverse aspects of their life. A child's "job" is to learn and play. Our sports program's goal is to provide multi-disciplinary collaborative care to patients of all abilities to help restore, and ideally, enhance their level of function whatever that may be. We will continue to expand upon our current sports program foundation to provide care for the whole child whether that may be adaptations after recovering from a serious medical condition, general wellness and fitness goals, elite athlete performance aspirations, or sports related injury or illness, and get them back to what they enjoy most, which is to play.

Neuromuscular Program

Our program in the care of patients with neuromuscular disorders led by Dr. Suzanne Yandow continues to grow, with over 11,000 clinic visits at Seattle Children's in the last year for patients with cerebral palsy, treated in collaboration with Pediatric Rehabilitative Medicine, Neurodevelopmental Medicine, Neurology, Neurosurgery, Physical Therapy and Orthotics.

Multidisciplinary Orthopedic/Rehabilitation and Surgical Tone Management clinics help to develop integrated care plans. Dedicated specialized physical therapists with expertise in neuromuscular disorders work with practitioners and orthotists to optimize the care of our children with cerebral palsy.

Many patients are enrolled in the Cerebral Palsy Research Network with opportunities to participate in ongoing research studies. A Motion Analysis Lab and expansion of outcomes research are planned for 2020/2021.

Research

With more than 100 open studies, including industry sponsored clinical trials, investigator initiated research grants, as well as multi-center national studies, our faculty at Seattle Children's are actively involved in research for a wide variety of pediatric conditions. This year, Dr. Bauer was the recipient of Seattle Children's Academic Enrichment Fund for her study on pediatric spinal fusions. Drs. Schmale and Blumberg are the site PIs for national studies funded by the Pediatric Orthopedic Society of North America (POSNA).

Our faculty continue participating in national and international research groups such as The Children's Spine Foundation, CORTICES, CoULD registry, SDMC and PRiSM with presentations at numerous academic societies, including AAOS, POSNA, SRS and PRiSM. It is our goal to strengthen our involvement in outcomes research and continue to increase the national recognition of our clinical and research programs.
2019-20 saw the well-deserved promotions of Lisa Taitsman, MD to Professor, and Stephen Kennedy, MD to Associate Professor in the Department of Orthopaedics and Sports Medicine. Dr. Taitsman has also been elected as new Director for the American Board of Orthopaedic Surgery. Dr. Kennedy has been appointed as Associate Residency Program Director, joining the other Associate Directors, Dr. Taitsman and Dr. Nick Iannuzzi.

Daphne Beingessner, MD, has been appointed Vice-Chair of Quality Improvement for the Department of Orthopaedics & Sports Medicine, which she has added to her existing role as Harborview’s Surgical Director for Quality Improvement. Rick Bransford, MD has been elected as Chair of the AO Spine North America Education Committee. Brad Henley, MD is currently Chair of the AAOS Governance Committee and Chair of the AAOS Coding, Coverage and Reimbursement Committee. Dr. Henley is also the Physician Operations Lead for the University of Washington Physicians. Conor Kleweno, MD is completing his term as member of the AO North America Fellowship Committee and the Orthopaedic Trauma Association Podcast Committee. Dr. Kleweno is also the newly elected Chair of the Orthopaedic Trauma Association Membership Committee and has been appointed to the Washington State Department of Health, Technology Review Committee.

Medical Center
Harborview was operating in a ‘business as usual’ fashion until late winter, grappling with the challenges associated with high patient demand for both trauma and elective care that exceeded hospital capacity, until the institution’s focus shifted sharply in mid-March to provide for the region’s needs during the current Coronavirus Pandemic. The institution is currently returning to a modified version of usual operations as the need to care for Covid-19 patients decreases.

Clinical Care
The 2019-20 year has seen continued stability in terms of orthopaedic faculty and had seen an equally stable volume and complexity of orthopaedic conditions being treated. In mid-March, we joined other departments and the institution as a whole in adapting our practices to allow for a shift in resources to pandemic-readiness. As with most individuals, businesses and industries, we continue to adapt to our new circumstances, which have resulted in a significant change in the way we function and a considerable economic impact on the Department and the Medical Center. Although non-urgent surgical procedures were canceled for two months, from mid-March through mid-May, our role as the region’s level one trauma center kept the various orthopaedic services functioning at over 50% of our normal capacity during this designated two-month hiatus, with our clinical workload having since returned to near-normal levels.

Research and Education
Under the direction of research coordinator Julie Agel, MA, and the Director of Clinical Research, Reza Firoozabadi, MD, the Harborview orthopaedic faculty continue to conduct a variety of prospective and multicenter research studies, as well as retrospective clinical studies and basic science projects, and have maintained a leadership role worldwide in helping determine how orthopaedic conditions are best evaluated and treated. Harborview also continues to be a key contributor to the multicenter Major Extremity Trauma Research Consortium (METRC), with the goal of enhancing the quality of trauma care globally. The pandemic has had a paradoxical effect on our research operations, as large-scale clinical studies have had to cease enrollment for the time being, whereas the short period of decreased clinical workload imposed by the pandemic has had the indirect benefit of providing increased time for faculty to focus on research endeavors.

Harborview remains a key component of the University of Washington Department of Orthopaedics’ teaching program, which provides ample learning opportunities for residents and fellows. The department also continues to offer a robust fellowship program in Orthopaedic Trauma, Orthopaedic Hand, and Orthopaedic Sports Medicine.

(Left to right) Lisa A. Taitsman, MD, MPH, Orthopaedic Trauma Faculty, and Stephen A. Kennedy, MD, FRCSC, Orthopaedic Hand Surgery Faculty
opportunities for a large number of our fellows, residents, medical students and advanced practice providers as well as for visiting surgeons who travel from throughout the globe year-round to immerse themselves in the Harborview orthopaedic experience first-hand. These teaching programs have also had to adapt to current circumstances. Resident rotations were temporarily altered to accommodate a shift in our needs while allowing greater distancing in order to decrease the potential for the spread of illness within the department that could compromise our ability to provide much-needed care to the community. Teaching conferences have largely been done through teleconferencing sites, for similar reasons. Our visiting surgeon programs have been suspended for the time being. We look forward to the return to pre-Covid-19 activities.
The Puget Sound Veteran’s Administration (VA) Medical Center is a tertiary referral center within the VA Northwest Health Network, helping to serve patients from Washington, Alaska, Montana, Idaho, Wyoming, and parts of Oregon. We continue to provide the highest level of care for our veterans while training future surgeons and advancing the field of orthopaedics through research.

Over the past few months, the VA has adapted to the changing healthcare landscape in response to the COVID-19 pandemic. Like other facilities within the University of Washington system, the VA has been quick to adopt telephone and video visits. Elective surgeries have been postponed, and patients are being evaluated and treated remotely when possible. The VA has adjusted staffing to prepare for a potential surge in COVID patients, and providers at the VA have volunteered their time to perform screening activities in addition to their normal clinical duties. Dr. Harwood has also given his time to respond to the COVID healthcare crisis. In April, Dr. Harwood joined his reserve unit in New York City in order to provide medical care to those affected by COVID-19. Dr. Harwood has since returned from his deployment, healthy, and we are truly appreciative of his service.

Researchers here at the VA have also been instrumental to the COVID-19 response. Members of the musculoskeletal research team have been working along with others to develop 3-D printed masks that can protect healthcare workers from the continued spread of COVID-19. As a part of this effort, Dr. Lack and myself worked with members of the team and Boeing in order to develop and fit test prototype masks. The efforts by the researchers at the VA are appreciated. We are fortunate to have such ingenious and capable colleagues. In addition to the lab director, Bruce Sangeorzan, MD, the musculoskeletal investigators group includes Bil Ledoux, PhD, Dan Norvell, PhD, Patrick Aubin, PhD, Joseph Iaquinto, PhD, Brittney Muir, PhD, Christopher Richburg, PhD, and Jiang Cheng, PhD. The work done in the Center is supported by grants from the Department of Veterans Affairs, the NIH, The DoD and other agencies.

As of July, the VA has continued a gradual reopening, and discussions remain ongoing as to how we will transition back towards more normal operations. As these normal duties resume, Drs. Lack, Harwood, Chansky, Sangeorzan, Gee, and myself will be present to cover nearly all orthopaedic subspecialties including Hip and Knee arthroplasty, Foot and Ankle surgery, Shoulder and Sports Medicine, and Hand and Upper Extremity surgery. As attendings, we have the great privilege to work with a number of residents and medical students, including a Chief Resident, two PGY-4’s, a PGY-3, and a PGY-2. We are extremely fortunate for the residents’ assistance as they work to cover a busy and diverse service.

Our physician extender team is one of the highlights of the VA. Dustin Higbee, PA-C, Steve Casowitz, PA-C, Amy Katzenmeyer, NP, Renato Rafi, PA-C, and Martin Hendricks, PA-C assist in both the operating room and clinic and provide excellent care for our veterans.

Not to be overlooked are two of the most important members of our team. Monette Foltan, RN and Katherine German, RN are our nurse coordinators, serving in this role for 16 and 8 years, respectively. Nurse Coordinator is hardly an adequate description of the role that they serve, as they manage the logistics behind complex clinic and OR schedules while serving as a primary point of contact between the veteran and the orthopaedics service. Cindy Lostonis remains our administrative assistant, but Diane Diggins has retired as our service line manager. Rosemary Melomey, our new service line manager has been an excellent new addition, and she continues to handle our day-to-day administrative duties while keeping us all in line.

The Puget Sound VA Orthopaedic Surgery Service has faced a number of challenges as a result of the ongoing COVID-19 healthcare crisis. Despite these challenges, the Orthopaedics Service has continued to provide exceptional clinical care in the service of America’s Veterans, and we look forward to continuing this service for years to come.
The University of Washington Department of Orthopaedics & Sports Medicine continues to be a top training destination for orthopaedic education. The unique challenges to our healthcare system as well as to all of our personal and professional lives during the unprecedented COVID-19 crisis has provided an opportunity for the residents, staff, and faculty to truly demonstrate the qualities that define our residency training program. Our orthopaedic surgery residents are consistently lauded as some of the hardest-working, brightest, skilled, and selfless trainees at the University of Washington. During times of stress and true crisis, they have continually lived up to our mantra of keeping patients and our community as a top priority and focus. The residents have adjusted to the challenges during the past year and have consistently taken great care of patients in unwavering fashion. Our residents are truly remarkable. The residents and faculty have demonstrated every single day what it means to be an orthopaedic surgeon at the University of Washington.

A strong and lasting bond between the department, faculty, and every graduating resident is the ultimate goal of every orthopaedic surgery residency program. Some highlights in the past year include the full integration of Northwest Hospital’s orthopaedic services into the department. This integration will provide additional opportunities for our residents to develop and enhance their skills by caring for patients with more common, community-level orthopaedic conditions. With the growing number of cases and volume, our residency has taken the opportunity to enhanced its long-standing relationship with the Madigan Army Medical Center Orthopaedic Surgery Residency Program. Additional residents from their renowned military program will rotate through the University of Washington program and will benefit from these increased educational opportunities. The program again has recruited and
matched a diverse group of talented medical students into our PGY-1 class set to start in June 2020. Our excitement as we anticipate these future physician-surgeons’ professional, personal, and academic over the next five years is matched only by their individual enthusiasm for starting the next stage of their lives in Seattle. As we look towards the future of the program, we are also thankful for those who are completing their training. The seven graduating chief residents have given so much to the program and the patients in our community over the past five years. We look forward to seeing all the ways in which they will use the skills they have developed to give to their future communities as physician surgeons.

Despite the challenges that COVID-19 has brought to the healthcare community and the uncertainty it will bring moving forward, there are several things of which we can all be certain for years to come. The University of Washington Orthopaedic Surgery Residency Program will continue to graduate skilled and compassionate physician-surgeons who make a difference in their communities and in the field of orthopaedic surgery. As we turn the chapter on a truly historic and difficult time for our country, it is this certainty that allows many of us to take comfort in what we do for the program and what we will continue to do for each other and all of our patients.
Graduating Residents

Prashoban Bremjit, MD
After graduation, Prash will be moving to Chicago to begin a fellowship in Arthroplasty and Joint Replacements at Rush University Medical Center. After his fellowship, he plans on returning home to the Pacific Northwest to start his practice alongside his fiancée and soon-to-be wife Jamie, a general surgery resident.

Matthew Folchert, MD
Matt and his wife Jacki with their golden doodle Remi will be moving to Philadelphia to complete a fellowship in Hand Surgery at the Philadelphia Hand to Shoulder Center. Afterwards, they will decide whether to stay in the greater Philadelphia area or to explore another part of the country.

Thomas Byrnes, MD
After graduation, Thomas, his wife, Mariam, and their nine-month-old daughter, Layla, will be moving to Philadelphia where he will complete a fellowship in Sports Medicine at the University of Pennsylvania. After fellowship, they will return to Seattle where Mariam will start dermatology residency at UW and Thomas will start practice.

Boris Kovalenko, MD
Boris will return to Atlanta, GA to begin a fellowship in Adult Reconstruction at Emory University. His fiancée, Maansi Dave, will stay in the Seattle area as she advances her career at Zillow. Afterwards, he hopes to return west to begin practice.
Graduating Residents

Christopher Tipton, MD
Cody, his wife, and beautiful two children, Cohen and Sloane, will be moving to Taos, New Mexico to begin fellowship in Sports Medicine. There he will assist as team physician to the United States Ski and Snowboard Team. After completion of fellowship, the Tiptons hope to return to the Pacific Northwest.

Brett Schiffman, MD
After graduation, Brett and his wife Margaret will be moving to Baltimore where he will complete a fellowship in Hand Surgery at the Curtis National Hand Center. Afterwards, they hope to settle somewhere warm and sunny.

Anthony Yi, MD
Anthony will move to Boston, Massachusetts to complete a fellowship in Orthopaedic Foot & Ankle Surgery at Harvard Brigham and Women’s Hospital. Joanna, his fiancée, will join him after she completes her Nurse Practitioner Fellowship in Hospitalist Medicine at Virginia Mason. They plan ultimately to return to Washington, where they both grew up and where their families live.
Incoming Residents

Nate Benner, MD
Nate grew up in southern Vermont. He attended the University of Vermont where he obtained a B.S. in Neuroscience and subsequently his medical degree. Outside of medicine, Nate enjoys skateboarding, snowboarding, playing guitar, and coffee.

Gabrielle Bui, MD
Gabrielle grew up in Iowa City, Iowa before attending the University of Iowa for college and medical school. Her specialties of interest include trauma, joints, and hand. In her spare time, she enjoys running, hiking, skiing, and supporting the performing arts.

Eli Bunzel, MD
Eli Bunzel grew up in New York City and attended Hamilton College, where he earned a BA in Biology and Art History. He attended medical school at the University of Utah. Outside of the hospital, Eli enjoys hiking, backpacking, trail running, skiing (both backcountry and inbounds), soccer, cooking and seeing live music.

Arthur McDowell, MD
Arthur was born and raised in Atlanta, GA and attended Morehouse College for his undergraduate studies. He earned his medical degree from Howard University in Washington, DC. His areas of interest include trauma, arthroplasty, and sports medicine. In his spare time, he enjoys watching and playing football, baseball, and basketball.
Incoming Residents

Zachary Mills, MD
Zachary was raised in Austin, Texas. He attended Rice University in Houston for his undergraduate studies. He obtained his medical degree as part of the inaugural class of UT Austin’s Dell Medical School. In his free time, Zachary bakes bread, brews coffee, and stays active working out, rock climbing, hiking, or playing tennis.

Joseph Sliepka, MD
Joey grew up in Houston, Texas. He attended Harvard University for his undergraduate studies and earned his medical degree at Baylor College of Medicine. His areas of interest include sports medicine, arthroplasty, and pediatrics. Outside of work, Joey enjoys playing baseball and piano.

Brian Vasquez, MD
Brian grew up in San Juan Capistrano, CA and attended the University of Southern California for his undergraduate studies. He completed his medical degree at the University of California, Davis. Outside of work he enjoys cooking, exercising, and spending time with his wife and family.

Jonathan Yamaguchi, MD
Jon grew up in Phoenix, AZ and graduated from the University of Arizona. He completed his medical education at Northwestern University Feinberg School of Medicine including an MS in Clinical Investigation. His current interests include trauma, spine, and oncology. Outside of work, he enjoys photography, bouldering, and cooking.
ACEs and Fellows

Adam Alibaba, MD
Foot & Ankle

J. Imani Dupree, MD
Foot & Ankle

Jonathan Kark, MD
Spine

Chelsea Boe, MD
Hand

Iain Elliott, MD
Trauma

Erik Magnusson, MD
Trauma

Sean Campbell, MD
Trauma

Derrick Foge, MD
Spine

Chelsea Mathews, MD
Foot & Ankle

Kim Driftmier, MD
Spine

Syed Gilani, MD
Oncology

Ugochi Okoroafor, MD
Hand
ACEs and Fellows

Joseph Patterson, MD  
Trauma

Jonathan Vaux, DO  
Oncology

Brian Pridgen, MD  
Hand

Stephen Wallace, MD  
Trauma

Rufus Van Dyke, MD  
Shoulder & Elbow

John Wu, MD  
Shoulder & Elbow

Samuel Van de Velde, MD  
Pediatrics

Kent Yamaguchi, MD  
Hand
Research Grants

National Institutes Of Health

A Randomized Controlled Pilot Study Evaluating the Efficacy of Early Glenohumeral Cortisone Injection in Patients with Shoulder Stiffness Following Proximal Humerus Fractures
Jonah Hebert-Davies, MD

Blood Flow Restriction for Anterior Cruciate Ligament Reconstruction
Scott Telfer, EngD

Collagen Assembly in Intervertebral disc
Russell J. Fernandes, MSc, PhD
David M. Hudson, PhD

Collagen Cross-Linking in Skeletal Aging and Diseases
David R. Eyre, PhD
David M. Hudson, PhD
Russell J. Fernandes, MSc, PhD
Jiann-Jiu Wu, PhD

Conventus CAGE™ PH for use in Proximal Humerus Fracture Fixation
Jonah Hebert-Davies, MD

Identifying osteoporosis genes by whole genome sequencing and functional validation in zebrafish
Ronald Y. Kwon, PhD

Instrumented Footwear to Measure Plantar Tissue Properties
Scott Telfer, EngD
William R. Ledoux II, PhD

Modeling, Design, and Testing of a Joint Replacement for MTPJ1
Peter R. Cavanagh, PhD, DSc
William R. Ledoux II, PhD
Bruce J. Sangeorzan, MD
Scott Telfer, EngD

AO North America

AO North America Orthopaedic Trauma Fellowship
David P. Barei, MD

AO Trauma North America
Reza Firoozabadi, MD, MA

AO Spine North America Fellowship
Richard J. Bransford, MD

American Shoulder and Elbow Surgeons

ASES 2019 Fellowship Program Grant
Winston J. Warme, MD

Acumed

Acumed Non-Clinical Biomechanical Study Using FDA Approved Device
Jerry I. Huang, MD
Kent Yamaguchi, MD
Scott Telfer, EngD

Antegrade Intramedullary Compression Screw Fixation of Metacarpal Fractures: a CT and Cadaver Study
Jerry I. Huang, MD
Don Hoang, MD
Research Grants

**Arthrex, Inc.**
- Arthrex Education Grant
  - Jerry I. Huang, MD
- Arthrex Fellowship Educational Grant
  - Winston J. Warme, MD

**Baylor College Of Medicine**
- Pathogenesis of Novel Forms of Osteogenesis Imperfecta
  - David R. Eyre, PhD
  - David M. Hudson, PhD
  - Russell J. Fernandes, MSc, PhD

**Brotman Baty Institute**
- Single Cell Atlas for Regeneration
  - Ronald Y. Kwon, PhD

**DePuy, Inc.**
- DePuy Synthes AO Basic Course R2s
  - Douglas P. Hanel, MD

**Foundation for Physical Therapy Research**
- The Effectiveness of Blood Flow Restriction to Increase Function Following Anterior Cruciate Ligament Reconstruction: A Pilot Randomized Controlled Trial
  - Cristine Agresta, PhD
  - Scott Telfer, EngD
  - Albert O. Gee, MD

**In Situ Therapeutic Solutions, Inc.**
- Focal Inhibition of Heterotopic Ossification
  - Steven D. Bain, PhD
  - Reza Firoozabadi, MD, MA
  - Ted S. Gross, PhD

**Integra LifeSciences Corporation**
- A Post-Market, Prospective, Non-Randomized, Multi-Center, Open-Label Clinical Evaluation of the Integra® Cadence™ Total Ankle System in Primary Ankle Joint Replacement
  - Michael E. Brage, MD

**Institute for Stem Cell and Regenerative Medicine**
- A Novel Wnt Interaction Underlying Appendage Regeneration
  - Ronald Y. Kwon, PhD

**Johns Hopkins University**
- A Prospective Randomized Trial to Assess PO Versus IV Antibiotics for the Treatment of Early Post-Op Wound Infection after Extremity Fractures
  - Reza Firoozabadi, MD, MA
  - Bruce J. Sangeorzan, MD
  - Conor P. Kleweno, MD
  - Daphne M. Beingessner, MD
  - David P. Barei, MD
  - Lisa A. Taitsman, MD, MPH
  - M. Bradford Henley, MD
  - Michael E. Brage, MD
  - Robert P. Dunbar, MD
  - Sean E. Nork, MD
  - Stephen K. Benirschke, MD

**Medical University Of South Carolina**
- Pulmonary Embolism Prevention after Hip and Knee Replacement (PEPPER)
  - Navin D. Fernando, MD

**Omega Medical Grants Association, LLC**
- Omega Shoulder and Elbow Fellowship Program Grant
  - Winston J. Warme, MD

- Omega Trauma Fellowship
  - David P. Barei, MD
Research Grants

Orthopaedic Trauma Association

An Imaging Framework for Clinically Testing New Treatments to Prevent Post-Traumatic OA
Conor P. Kleweno, MD
COTA Trauma Fellowship
David P. Barei, MD

Synthes USA

Synthes Request For Basic AO Course R2s
Douglas P. Hanel, MD

The Journal of Bone & Joint Surgery

 Resident Journal Club Program
Seth S. Leopold, MD

University of Pittsburgh

Surgical Timing and Rehabilitation (STaR) for Multiple Ligament Knee Injuries (MLKs): A Multicenter Integrated Clinical Trial
Albert O. Gee, MD
Amy Cizik, PhD, MPH
Christopher Y. Kweon, MD

US Department of Defense

Clinical Evaluation of ReHeal Negative-Pressure Wound Therapy Glove
Christopher H. Allan, MD

UW Royalty Research Fund

A Novel Wnt Interaction Underlying Genetic Risk for Osteoporosis
Ronald Y. Kwon, PhD
A list of publications authored by our faculty from January 2019 to July 2020. Our faculty members names are in bold type.


Alumni

In appreciation of the generous support over the years from the University of Washington Orthopaedic Alumni to fund Orthopaedic Resident Research and Education

1952
Park W. Gloyd, MD ★

1954
Trygve Forland, MD ★

1955
Robert W. Florence, MD

1956
J. Michael Egglin, MD ★
John E. Goeckler, MD
Robert L. Romano, MD ★

1957
John H. Aberle, MD ★
John R. Beebe, MD

1958
Samuel L. Clifford, MD
James R. Friend, MD ★
Harry H. Kretzler, Jr., MD ★
Kenneth L. Martin, MD ★★

1959
James W. Tupper, MD

1960
William V. Smith, MD ★
Irving Tobin, MD ★

1961
Robert C. Colburn, MD ★

1962
Marr P. Mullen, MD ★★★
Arthur Ratcliffe, MD

1963
Alfred I. Blue, MD
Robert A. Kraft, MD

1964
Harold J. Forney, MD ★
Theodore K. Greenlee II, MD ★★★★★
David E. Karges, MD ★
Thomas E. Soderberg, MD

1966
F. Richard Convery, MD ★
Joseph S. Mezistrano, MD ★
William A. Reilly, Jr., MD

1967
Ivar W. Birkeland, MD ★★
J. Conrad Clifford, MD ★
Robert F. Smith, MD

1968
Stewart M. Scham, MD ★★
Lynn T. Staheli, MD ★
William T. Thieme, MD ★

1969
Edward E. Almquist, MD ★★
Sigvard T. Hansen, Jr., MD ★★★★★
Edward L. Lester, MD ★
Hugh E. Toomey, MD ★★

1970
John C. Brown, MD ★
John M. Coletti, Jr., MD ★
Malcolm B. Madenwald, MD ★
Michael T. Phillips, MD ★
Robert D. Schrock, Jr., MD ★

1971
Franklin G. Alvine, MD ★★★
Bruce E. Bradley, Jr., MD ★
Nils Fauchald, Jr., MD ★
Louis A. Roser, MD ★
Jerome H. Zechmann, MD ★

1972
Thomas L. Gritzka, MD ★
Donald D. Hubbard, MD ★
David J. LaGasse, MD ★
David R. Nank, MD ★★
John A. Neufeld, MD ★

1973
Frederick J. Davis, MD ★
Larry D. Hull, MD ★
Theodore A. Wagner, MD ★★★★★
Robert P. Watkins, Jr., MD ★

1974
Samuel R. Baker, MD ★★
Richard A. Dimond, MD ★★
Ronald B.H. Sandler, MD ★★
Robert A. Winquist, MD ★★★★★★★

1975
William M. Backlund, MD, PS ★
Thomas M. Green, MD ★★★★★
Gunter Knittel, MD
Frederick A. Matsen III, MD ★★★★★★★
Larry R. Pedegana, MD ★
Donald L. Plowman, MD ★★★

1976
John F. Burns, MD ★
Douglas T. Davidson III, MD ★
Douglas K. Kehl, MD
Peter Melcher, MD
Richard A. Zorn, MD ★

1977
Carl A. Andrews, MD ★
Steven T. Bramwell, MD
Larry D. Iversen, MD ★
Mark C. Olson, MD ★
Geoffrey W. Sheridan, MD ★★

1978
John W. Brantigan, MD
Gary J. Clancy, MD ★★★★★
William Oppenheim, MD ★★
Arnold G. Peterson, MD ★★★
Robert J. Strukel, MD
Richard S. Westbrook, MD ★

1979
Allan W. Bach, MD ★★★★★
Gregory M. Engel, MD ★
Jonathan L. Knight, MD ★★
Richard L. Semon, MD ★★★

1980
John M. Hendrickson, MD ★★
Stuart R. Hutchinson, MD ★
Douglas G. Norquist, MD ★
Michael A. Sousa, MD ★★★★★★
Carol C. Teitz, MD ★★
2006
Stacey Donion, MD ★
Eric Klineberg, MD ★
Bill Montgomery, MD ★
Heidi Shors, MD ★★
Mel Wahl, MD ★
Burt Yaszay, MD ★

2007
Jamie Antoine, MD ★
Jeremiah Clinton, MD ★
Mary Cunningham, MD ★
Evan Ellis, MD ★
Joseph Lynch, MD ★
Allison MacLennan, MD ★

2008
Drew Fehsenfeld, MD ★★★
Mark Freeborn, MD ★★★
Christopher Howe, MD ★
John Howlett, MD ★
Michael Lee, MD ★
Gregg Nicandri, MD ★

2009
Rajshri Maheshwari Bolson, MD ★
Jason King, MD ★
Annie Links, MD ★
Soren Olson, MD ★
Karen Perser, MD ★
Scott Ruhlman, MD ★
Addison Stone, MD ★
Jason Wilcox, MD ★

2010
Sean Amann, MD ★
Jeremy Bauer, MD ★
Aric Christal, MD ★
Wendy Emerson, MD ★
Michael Hwang, MD ★
Lee Pace, MD ★
Christopher Wolf, MD ★
Vinko Zlomislic, MD ★

2011
Aaron Chamberlain, MD ★
Brian Daines, MD ★
Cory Lamblin, MD ★
Edward Moon, MD ★
Derek Rains, MD ★
Peter Scheffel, MD ★
Christian Sybrowsky, MD ★
Brett Wiater, MD ★

2012
Benjamin Amis, MD ★
Adam Bakker, MD ★
Gregory Blaisdell, MD ★
Joshua Lindsay, MD ★
Grant Lohse, MD ★
Matthew Lyons, MD ★
Andrew Merritt, MD ★
Nels Sampatatos, MD ★

2013
Kyle Chun, MD ★
Elizabeth Dailey, MD ★
Andrew Ghatan, MD ★
Brian Gilmer, MD ★
Jennifer Hagen, MD ★
Mark Miller, MD ★
David Patterson, MD ★
Emily Squer, MD ★

2014
Sid Baucom, MD
Nathan Coleman, MD ★
Jacques Hacqueboard, MD
Nicholas Iannuzzi, MD ★
Paul Kim, MD
Ted Sousa, MD ★
Nicholas Wegner, MD
David Zeltser, MD ★

2015
Timothy Alton, MD ★
Kenneth Gundle, MD ★
Daniel Holtzman, MD ★
Amanda Roof Larson, MD ★
Paige Mallette, MD
Courtney O'Donnell, MD
Daniel Patton, MD ★
Laura Stoll, MD ★

2016
Todd Blumberg, MD ★
Akash Gupta, MD
Sean Haloman, MD ★
Emily Harnden, MD ★
Clifford Hou, MD
Dayne Mickelson, MD ★
Jessica Telleria, MD ★

2017
Ahmad Bayomy, MD ★★★
Christopher Domes, MD
Kevin Hug, MD ★
Alexander Lauder, MD ★
Calvin Schlepp, MD ★
Shawn Schoch, MD
Neil Tarabadkar, MD ★
Sara Shippee Wallace, MD ★

2018
Kariline Bringe, MD
Romie Giby, MD
David Ibrahim, MD ★
Colin Kennedy, MD ★
Lauren MacTaggart, MD
Stuart Michnick, MD
Adam Sangeorzan, MD
Alan Swenson, MD ★

2019
Zahab Ahsan, MD
Matthew Baron, MD
Kate Bellevue, MD
Jonathan Kark, MD
Erik Magnusson, MD
Adam O'Brien, MD
Mary Kate Thayer, MD
Claudia Thomas, MD

2020
Prashoban Bremjlt, MD
Thomas Byrnes, MD
Matthew Folchert, MD
Boris Kovalenko, MD
Brett Schiffman, MD
Cody Tipton, MD
Anthony Yi, MD

Stars indicate total donations in support of the residency

★★★★★★★ = $30,000 and above
★★★★★★ = $25,000 - $29,999
★★★★★ = $20,000 - $24,999
★★★★ = $15,000 - $19,999
★★★ = $10,000 - $14,999
★★ = $5,000 - $9,999
★ = $1 - $4,999
Endowments

We express our appreciation to all who have contributed to the endowments of the Department of Orthopaedics and Sports Medicine. This assistance makes possible special research activities, educational programs, and other projects that we could not offer without this extra support from our alumni, faculty, and friends in the community. In this day and age of funding cutbacks and decreased returns on investment, an endowment in the University of Washington continues to provide above market returns and is a crucial way to support advancement of musculoskeletal medicine. If you have any questions, please contact our Chair, Howard A. Chansky, MD (chansky@uw.edu), or our Director, Ken Karbowski (kkarb@uw.edu). Thank You!

Ernest M. Burgess Endowed Chair for Orthopaedics Investigation - David R. Eyre, PhD

Sigvard T. Hansen Jr. Endowed Chair in Orthopaedic Traumatology - Ted S. Gross, PhD

Jerome H. Debs II Endowed Chair in Orthopaedic Traumatology -
Stephen K. Benirschke, MD

Bob and Sally Behnke Endowed Chair for the Health of the Student Athlete -
John W. O’Kane, MD

Endowed Chair for Women’s Sports Medicine and Lifetime Fitness -
Peter R. Cavanagh, PhD, DSc

Hansjörg Wyss Endowed Chair

Surgical Dynamics Endowed Chair for Spine Research

Douglas T. Harryman II/DePuy Endowed Chair for Shoulder Research -
Frederick A. Matsen III, MD

Synthes Spinal Surgery Outcomes Research Endowed Fund

Fracture Fixation Biology Endowed Professorship

Ostex Bone and Joint Research Endowment

Orthopaedic Traumatology Endowed Lectureship

John F. LeCocq Lectureship in Orthopaedic Surgery

Don and Carol James Research Fund in Sports Medicine and Fitness

Victor H. Frankel Endowed Award
Endowments

Esther Whiting Award

Edwin L. Laurnen, MD Award

Spine Research Endowment

James G. Garrick Endowed Lectureship in Sports Medicine

Allan Treuer - Ted Wagner, MD Endowed Chair in Regenerative Spine Surgery

Richard and Betsy Kirby Orthopaedic Resident Endowed Fund

Huang-Biu Orthopaedic Resident Endowed Support Fund

Orthopaedic Resident Endowed Support Fund

Josh and Max Myers Endowed Orthopaedic Fellowship Fund

Sarcoma Oncology Endowed Fund

Clawson Family Orthopaedic Library Endowed Fund

Kathryn E. Cramer Endowed Orthopaedics Research Fund

Evelyn E. Carman Endowed Research Fund in Women’s Sports Medicine and Lifetime Fitness

Alan J. Fraser Endowed Research Fund

Douglas P. Hanel, MD, Endowment for Orthopaedic Training and Research for Resident Education

Chansky Family Endowed Fund for Orthopaedic Resident Recruitment

Frederick A. Matsen III, MD and Anne L. Matsen Endowed Professorship in Orthopaedic Education