The University of Pennsylvania Orthopaedic Journal

Volume 29 June 2019

ELSA® AL

ADJUSTABLE LORDOTIC INTEGRATED LLIF SPACER

ADJUSTABLE LORDOSIS

UP TO 30°

ALLOWS FOR SAGITTAL BALANCE CORRECTION

GLOBUS MEDICAL

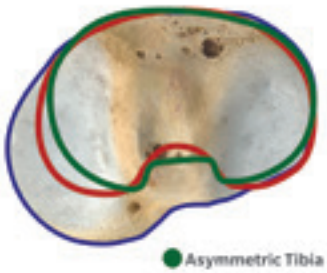
Find the right balance at
GlobusMedical.com/ELSA

Life moves us

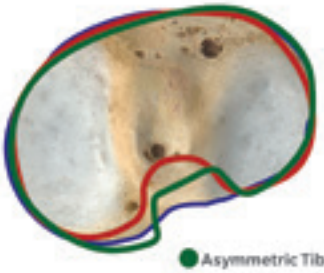
SHAPE MATTERS

Achieve Both

Proper Rotation



Maximum Coverage



Persona®
THE PERSONALIZED KNEE

The shape of other tibias impose a choice between proper rotation and bone coverage. This leads to variability in rotational alignment. This is important, because several studies have shown a correlation between mal-rotation and anterior knee pain.[1–4]

Mal-rotation of implants may lead to over **50% of painful TKA cases.[5]**

Anatomic shape of the Persona Tibia is designed to achieve proper rotation and optimal coverage, resulting in:

Statistically significant **decrease in anterior knee pain** *in vivo*[7]

92%
bone coverage[6]

Statistically significant improvement in medial plateau fit for Asian populations[8]

Lower incidence of downsizing[6]

3% anatomic **vs.** **50%** non-anatomic

To learn more visit **zimmerbiomet.com.**

1. Nicoll, D. and Rowley, DI. Internal rotational error of the tibial component is a major cause of pain after total knee replacement. Journal of Bone and Joint Surgery (British) 92-B:1238–44. 2010. 2. Barrack, Robert L., et al. Component Rotation and Anterior Knee Pain After Total Knee Arthroplasty. Clinical Orthopaedics and Related Research. Number 392, pages 46–55. 3. Matsuda, et al. Effect of femoral and tibial component position on patellar tracking following total knee arthoplasty. American Journal of Knee Surgery. 14:152-156; 2001. 4. Bedard, M. et al. Internal rotation of the tibial component is frequent in stiff total knee arthroplasty. Clinical Orthopaedics and Related Research, Vol. 469, no. 8, pages 2346–2355; 2011. 5.Martin, et al. Maximizing Tibial Coverage Is Detrimental to Proper Rotational Alignment, CORR January 2014. 6.Dai, Y., et al. Anatomical Tibial Component Design Can Increase Tibial Coverage and Rotational Alignment Accuracy: A Comparison of Six Contemporary Designs. Knee Surg Sports Traumatol Arthrosc. 22:2911-2923; KSSTA 2014. 7.Indelli, et al. Relationship between Tibial Baseplate Design and Rotational Alignment Landmarks in Primary Total Knee Arthroplasty. Hindawi Publishing Corporation Arthritis. Volume 2015, Article ID 189294, 8 pages. 8. Jin, C., et al. How Much Does the Anatomical Tibial Component Improve the Bony Coverage in Total Knee Arthroplasty? The Journal of Arthroplasty. In Press 2017. Online http://dx.doi.org/10.1016/j.arth.2016.12.041.

ZIMMER BIOMET
Your progress. Our promise.®

U·P·O·J

The University of Pennsylvania Orthopaedic Journal

Volume 29, June 2019

Editorial Board

Philadelphia Orthotics & Prosthetics, Inc.

Our Goal...

PO&P strives to increase the quality of life for all our patients by providing the finest O&P solutions, hi-tech devices, excellent treatment, and dependable follow-up care by skilled professionals.

Orthotics

FOOT
- Custom Foot Orthotics
- UCBL's

LOWER EXTREMITY
- Ankle Foot Orthoses
- Knee Ankle Foot Orthoses
- Custom and Sports Knee Orthoses
- Fracture Orthoses

HIP
- Pre and Post-Operative

SPINAL *HIGHLY SPECIALIZED*
- Soft, semi-rigid and rigid Spinal Orthoses
- LSO, TLSO, TLSO with Cervical Extension
- Scoliosis Orthoses (Boston, Charleston etc.)

CERVICAL SPINE
- HALOS
- Rigid Collars (Miami-J, Aspen)
- Philadelphia Collars
- Soft Collars

UPPER EXTREMITY
- Humeral Fracture Orthoses
- Forearm Fracture Orthoses
- Wrist Splints
- Thumb Spica's

CRANIAL
- Custom Head Helmets
- Protective Helmets

Prosthetics

BELOW KNEE
- Partial Foot Prostheses
- Ultra-light materials

ABOVE KNEE
- Ischial containment sockets
- Microprocessor knees

UPPER EXTREMITY
- Shoulder Caps (cosmetic)
- Above and Below Elbow

Bill Penney, CPO/LPO
President & Clinical Specialist

Two Convenient Locations

301 South Eighth Street, Ste B2
Philadelphia, PA 19106
(215) 829-5733

709 Somerdale Road
Voorhees, NJ 08043
(856) 428-4201

Now service Pennsylvania Hospital, Presbyterian Hospital, and Hospital of the University of Pennsylvania

Philadelphia O&P Orthotics & Prosthetics INCORPORATED

Specializing in Quality In-Patient and Out-Patient Orthotic and Prosthetic Care

Visit our web site for detailed directions.
www.philaop.com

U·P·O·J

The University of Pennsylvania Orthopaedic Journal

Volume 29 June 2019

Table of Contents

Resident and Fellow Updates

Residents

Hospital System Updates

Research Articles

Clinical Research Sections

Trauma

Basic Science Section

Bone

Cartilage

Tendon

Your partner in specialized orthopaedic care for kids.

The Division of Orthopaedics at Children's Hospital of Philadelphia is one of the largest and most active pediatric orthopaedic centers in the world. We have expertise in every area of the field, including sports injuries, hip disorders, trauma, spine deformities, upper and lower extremity disorders, brachial plexus injuries, thoracic insufficiency syndrome, cerebral palsy, foot and ankle disorders, neuromuscular conditions, and tumors. Our surgeons and specialists partner with referring physicians to help ensure today's orthopaedic treatment takes into account tomorrow's growth and long-term quality of life.

For peer-to-peer consultations with our surgeons and specialists, or to make a referral, call 800-TRY-CHOP and press 2.

Children's Hospital of Philadelphia®
Division of Orthopaedics

Letter from the Editors

Liane Miller, MD and Matthew Counihan, MD

Liane Miller, MD

Matthew Counihan, MD

It is with great honor and pride that we welcome you to the 29th edition of the University of Pennsylvania Orthopaedic Journal (UPOJ). The journal began in 1986 under the leadership of Dr. Carl T. Brighton as the nation's first completely resident-run journal of orthopaedic surgery, and has been a source of distinction for the department since its foundation. We are privileged to continue this tradition and would like to recognize all the contributors that have made this journal possible, including residents, surgeons, scientists, and faculty.

We are thrilled to dedicate this edition to Dr. Paul A. Lotke, an inspiration in the field of orthopaedics and a foundational member of the University of Pennsylvania Orthopaedic Department. Dr. Lotke was a talented and productive surgeon-scientist during his 50 plus years of practice, and continues to be a gifted clinician educator and an advocate for driving the future of orthopaedic practice forward.

The theme of this year's journal is inspired not only by Dr. Lotke's tremendous legacy but also by the unwavering dedication and ambition of our chairman, Dr. Levin, to constantly push the department forward and adapt in the ever-changing landscape of medicine. The editorials focus on the importance of advancing our orthopaedic knowledge by fostering our leadership skills through a new dedicated curriculum and expanding our humanitarian influence with international outreach.

We have continued this year with highlighting original scientific research through an "extended abstract" format, to allow for increased representation of both clinical and basic science work. In addition, each clinical division has provided a tips and tricks article with various surgical techniques or unique case presentations to further encourage discussion and inquiry. We have had the honor of reviewing articles from nearly all clinical divisions and primary investigators of the Department of Orthopaedic Surgery at the University of Pennsylvania. Finally, this year's edition includes a comprehensive update on the many programs and divisions of the department including our multiple new faculty and facility additions and a spotlight on our increasing advanced practice provider workforce.

We would like to thank Dr. L. Scott Levin for his unparalleled support in the production of this journal year after year. Additionally, we would like to acknowledge the ten year anniversary of Dr. Levin's tenure as department chair. The department has consistently grown and improved in nearly every quantifiable measure under his guidance for the past ten years. Moreover, Dr. Levin has graduated 80 residents in his time as department chair, many of whom have gone on to major faculty and leadership positions of their own. As both a leader and a teacher, Dr. Levin has been changing the landscape of orthopaedics both within Penn Medicine and beyond. We are tremendously grateful for his tireless efforts, and look forward to what the next chapter of his tenure will bring.

We would also like to thank and our faculty advisors, Dr. Jaimo Ahn and Dr. Samir Mehta for their continued support and guidance in the production of this journal. As a fully resident-run publication, the UPOJ would not be possible without the contributions from our section editors: Joseph Koressel (Arthroplasty), James Friedman (Foot and Ankle), Andrew Tyler (Spine), Matthew Stein (Shoulder and Elbow), Kelsey Bonilla (Tumor), Brandon Haghverdian (Pediatrics), Agnes Dardas (Trauma), Matthew Webb (Sports), David Falk (Hand), Ivan Zapolsky (Orthoplastics), Viviana Serra Lopez (Bone), Adnan Cheema (Tendon and Ligament), and Michael Eby (Cartilage).

The UPOJ has been financially independent from the Department of Orthopaedic Surgery since 1997 thanks to the generous financial support from our advertisers. We wish to sincerely thank our sponsors, on behalf of our department, for supporting the educational and research missions of Penn Orthopaedics.

The journal is viewable for free online and all mobile devices at www.upoj.org. On behalf of all the contributors to the UPOJ this year, we hope that you find this edition educational, inspiring, and thoughtful.

Letter from the Chair

L. Scott Levin, MD, FACS

Paul B. Magnuson Professor of Bone and Joint Surgery, Chair of the Department of Orthopaedic Surgery, University of Pennsylvania School of Medicine

As I approach the end of my first decade at the University of Pennsylvania school of medicine, I look back on the last 3650 days with pride in all that our team has accomplished. As the oldest Orthopaedic Surgery department in the country, we now rank among the top five, according to a recent JAAOS article that analyzed the characteristics that determine success is academic Orthopaedic Departments. (Namavar et al. *J Am Acad Orthop Surg*. 2019 Feb 1;27(3):e118-e126.) This study was well designed and executed, and the conclusions are scientifically validated.

I believe that good leaders should admit when they fall short in terms of realizing their vision and facilitating group success. My BHAG if you recall (big hairy audacious goal as described by Jim Collins in his book *Good to Great*) was to become a top five Orthopaedic Department in five years. We even had T shirts made- "Top Five in Five"-Penn Orthopaedics. We failed with regards to the ambitious timeline that I set for this goal but we eventually arrived…5 years later than predicted. This lesson in humility will serve me well as I continue our quest for "number 1". That being said, our Penn Orthopaedic research program funding has doubled in the last 10 years and our research rank according to the NIH has consistently been among the **top five** programs in the country for more than 10 years. What an achievement by Lou Soslowsky and his colleagues!

Our clinical mission has expanded tremendously. Currently our Penn Orthopaedic Brand is present in 7 hospitals in our health system compared to our initial footprint at three downtown hospitals in 2009. Under the leadership of Ralph Muller, we have purchased three health systems: Chester County Hospital, Lancaster General Hospital and Princeton Health. We now have a significant presence in New Jersey based on our affiliation agreement with Princeton Orthopaedic Associates, our partners Kevin McHale and Stanley Michael at Cape Regional Hospital (part of the Penn system) and our combined Adult Reconstructive Fellowship at Virtua Health System. Our Cherry Hill outpatient center is magnificent and was modelled after our Philadelphia Musculoskeletal Center on the Presbyterian Medical Center Campus. Our new Grand View Hospital Orthopaedic partnership is providing affiliation with an outstanding Orthopaedic group that shares our values with regards to excellence in value based musculoskeletal care. Under the leadership of our COO, Neil Ravitz, we recently organized a Joint Replacement summit that included every entity in our health system. More than 120 people attended, from physicians, administrators, nurses, quality officers and service line leaders. This event was a huge success and demonstrates alignment across our health system with regards to Penn Medicine's commitment to value and quality of care delivery for patients undergoing joint replacement.

Our reach goes beyond US borders. An exchange program with Princess Grace Hospital in Monaco adds value to our Shoulder and Elbow fellowship. Our Spine Deformity outreach led by Vincent Arlet in Trinidad provides world class care to a deserving population that has limited access to complex spine reconstruction. Neil Sheth is making strides in building a hospital in Tanzania as a tribute to the legacy of Enyi Okereke, MD. We are proud of our evolving global influence.

The construction of a $1.5 billion new Hospital Pavilion across from HUP is a testimony to the leadership of UPHS CEO Ralph Muller, our EVP, and Dean Larry Jameson, as well as a testament to the financial strength of Penn Medicine. Our orthopaedic oncology program will be based at the new Pavilion and continues to expand at HUP. The addition of Robert Wilson has helped support Orthopaedic Oncology on the HUP campus.

History was made this past March, when Kristy Weber, MD was inducted as of AAOS President. As many of you know, Dr. Weber serves as vice chair of Orthopaedic Surgery and Director of the Penn Medicine Sarcoma program. Her presidential remarks emphasized diversity and inclusion. I am proud to share that this year's intern class includes three remarkable women who will begin our residency in June 2019. We have more than 30 percent women in our program. We walk the walk and talk the talk. We are proud of the leadership of Dr. Weber.

Other Society leaders include John Kelly who is serving as President of the Eastern Orthopaedic Association. I am currently serving as the President of the American society of Surgery of the Hand. The emphasis on leadership skills and training for our residents and faculty will continue thanks to the efforts of John Kelly and Derek Donegan. Our partnership with the Wharton School of Business provides unprecedented opportunities for our residents to learn about leading and leadership.

This summer we will appoint a new chief at the VA hospital. Dr. Marlene DeMaio is stepping down, and will remain a valued member of our faculty. Dr. Richard Grant will be appointed as VA Chief, and brings to Penn a wealth of clinical educational and leadership experience. As past Chair at Howard Orthopaedics and President of the ABOS he is poised to provide educational impact and coaching for our residents and fellows.

Our Musculoskeletal service line is continuing to innovate and is recognized as a leading service line in the Penn Medicine. Led by Neil Ravitz, our COO, Sean Looby (outreach director) and supported by our Quality Officer Hannah Lacko we have

an administrative "dream team" that drives our clinical success. Opioid reduction programs, PROMIS capture and value based purchasing are programs that benefit our patients and our health system. Reduction in costs and standardization of care are among the many achievements that have brought well deserved recognition to our department. Penn Orthopaedics has led the health system in digital patient scheduling and same day access. My moto has been "If you call us today with a musculoskeletal problem, we will see you today". The strong work ethic of our faculty and the phenomenal group of PA's and NP's allow us to keep this promise.

Our residency and fellowship programs continue to attract the brightest students and residents from around the country. We have extended our fellowships to physicians from outside the USA in order to be considered an educational system that is global rather than local. Fellows from India, Canada and Israel benefitted from their time with us and have returned to their countries to practice and represent the Penn Orthopaedic training experience. Craig Israelite, Jaimo Ahn, and Andrew Milby have provided outstanding oversight for our residents and students. I am grateful for their tireless dedication to the educational mission.

Ten years passes quickly. While we are in a good place, we are not complacent with our successes. There is still much work to be done and higher mountains to climb. Penn Orthopaedics is department comprised of an outstanding group of talented individuals that functions exceptionally well as a team. We will continue to improve our efforts across all missions. There will be many changes ahead in the practice of medicine, our team is positioned well for the future challenges of health care delivery. Our values and culture are sound and are accepted by all. As Coach Vince Lobardi once said "if we seek perfection, we will find excellence." As the coach of this great team, our quest will continue for perfection. We will settle for nothing less than excellence. With appreciation and profound gratitude for the opportunity to lead and be part of such a magnificent team.

Letter from the Program Director

Craig Israelite, MD

With each year, I look forward to the publication of The University of Pennsylvania Orthopaedic Journal. The reason is that it gives me pause for reflection on the past and present academic year. It is truly a privilege and honor to continue to serve as program director of this prestigious orthopaedic program. Since being appointed program director almost 10 years ago, I have witnessed significant positive changes to one of the oldest orthopaedic programs in the country.

Under Dr. Levin's continuing leadership, the faculty has grown substantially in numbers and diversity. This has offered our residents the opportunity to learn advanced techniques by leaders in their respected fields. While this can put a strain on any program, we have been fortunate enough to increase the numbers of our tremendous physician extenders in order to allow residents to spend more time pursuing academic and clinical interests. As such, our faculty and residents continue to lead. A recent JAAOS review article just ranked The University of Pennsylvania Orthopaedic Department as #4 in the nation with respect to academic impact and productivity. Our residents are extraordinarily productive with numerous peer reviewed articles and national presentations. Our reputation as a training leader places our residents in a position to garner the most prestigious fellowship programs in the nation. It also allows us to attract the most competitive residents to our own numerous fellowship programs.

The combination of dedicated and stellar faculty, along with superlative residents, continues to allow Penn to attract the best and brightest medical students available. Recruitment of gifted students has not been, nor will it be, a problem in the future.

I would ask the readers of UPOJ to go on-line and search the numerous offerings our department continues to provide. Our grand rounds, daily conferences and visiting professorship series are the envy of many other peer institutions.

Finally, our culture, which has been established by our chairman Dr. Levin, is one of Team. Penn Orthopaedics is truly a championship team. Our Penn team consists of coaches [faculty], players [residents] as well as administrative support staff. Shannon Savelloni has taken over the duties of program coordinator from Shanna Kurek, who has moved with her husband to continue his residency. Shannon has already shown herself to ably steward the program. She has begun instituting her organizational expertise which will benefit all of our activities.

Finally, the backbone of any program is our residents. Truly the strength of our residency. Each resident contributes to our successes. My heartfelt thanks and gratitude goes out to our graduating academic chief residents. Luke Lopas, Nicki Zelenski and Kristen Buterbaugh have done a remarkable job this past year. All of our graduating residents will be missed and we wish them well as they embark on their fellowships.

If you have not been back to Penn for a while, please join us and I have no doubt that you will amazed at our growth as well as our trajectory.

2018-2019 Dedication: Paul A. Lotke, MD

Matthew Counihan, MD

Paul A. Lotke, MD

It is with great honor that we dedicate the 29th edition of the University of Pennsylvania Orthopaedic Journal to Dr. Paul A. Lotke, a tremendous surgeon and leader within the orthopaedic community for greater than 50 years. He is recognized as a foundational member of the University of Pennsylvania Orthopaedic Department and an essential figure that has guided the growth and development of the department into the present day.

Dr. Lotke is native to the greater Philadelphia area. Born and raised locally, he attended Cheltenham high school before moving on to Dickenson College, graduating in 1959 with a Bachelor of Science in physical chemistry. He thereafter attended medical school at the University of Pennsylvania, graduating in 1963. He recalled that orthopaedics was a field in which he had an innate interest, and furthermore, at that time the research components of the field seemed to be only primitively developed. As such, he saw this as an area in which he could have a great impact during his career.

His post-graduate medical training first started with a year of internal medicine at the University Hospital in Madison, Wisconsin. This was followed by a 2-year appointment at the Naval Medical Research Institute in Bethesda, MD, where his lab used canine models to define the parameters of rejection and limits of preservation in kidney transplants. After completion of this research appointment, Dr. Lotke moved on to a year of general surgery at Cedars-Sinai Medical Center in Los Angeles. His time in LA was interrupted by a 2-month stint in Russia on a cultural exchange program, where he would continue research in a lab dedicated to transplant work. After his time in Russia, he returned to Cedars-Sinai to complete his general surgery year, though during that trip abroad he had developed a deep appreciation for the value of international travel and service that would reappear later in his career.

After completing his general surgery internship, Dr. Lotke started his orthopaedic residency at the Hospital for Special Surgery in 1967. Among the most important lessons instilled in him during his residency was the concept of being a lifelong learner, a value that would continue throughout his career and no doubt drive his many advancements in the field of orthopaedics. Another significant component of his residency was the camaraderie among his fellow co-residents. In fact, on his arrival to HSS he met one of his senior residents, Dr. Malcom Ecker, who would himself become a pillar of the Penn Orthopaedic community. They developed a life-long friendship during their residency that continues to this day. Dr. Lotke completed his orthopaedic residency in 1970, followed an additional year-long research fellowship at HSS completed in 1971.

After his residency and fellowship, Dr. Lotke returned to Philadelphia, taking a position at the University of Pennsylvania Orthopaedic Department. The department, under the guidance of Dr. Edgar Ralston at the time, was quite different in 1971, having less then 10 full-time physicians and operating out of a small office in the bottom of the Maloney building. Dr. Lotke, as with all of his colleagues at that time, started in general orthopaedics, but it wasn't long before his practice headed toward specializing in the knee. He noted that at the start of his career, the surgical options for knee arthritis were scarce and, when utilized, not well received. It was an area in which he saw great potential for development and improvement. He recalls, "I said to the chair at the time 'I'm going to know more about the knee than anyone in the city of Philadelphia' and I dedicated myself to that aim." Soon, he would push to develop the first specialty knee clinic at Penn. Dr. Lotke recalled that the idea was not easily sold to the department at first, as there was some resistance to specialty clinics at the time. After a bit of a "fight to get it started", Dr. Lotke became the director of the Knee Clinic, which was only the second specialty clinic in department history (the hand clinic was the first). As will become apparent, this specialty clinic was one of several prescient ideas Dr. Lotke pursued that would later become hallmarks of present day orthopaedics.

Figure 1: Dr. Lotke at his desk, buried in paperwork.

Dr. Lotke soon became a leader in knee replacements, having a significant impact on the development and progression of knee arthroplasty techniques throughout his career. He recalled that when the first total knee designs came to the market,

guides for their placement did not exist. Surgeons had only an angular rod to help judge the plane of the femoral cut, and a simple osteotome to judge the plane of the tibial cut. He was among the first vocal advocates for the idea that well-positioned components were vital for a good outcome. This concept is evidenced by many of his early publications, including the landmark paper "Influence of Position of Prosthesis in Total Knee Arthroplasty", which was published in JBJS in 1977 and to this day remains among the most cited pieces of literature concerning knee arthroplasty. As he recalled, "implants that were put in well had better results, and those that were put in poorly failed quickly. Now this seems like a pretty obvious conclusion, but back in the 70's that wasn't known…this finding started the need to get good [guide] instruments in total knees so we could get reproducible results." His work in this area was integral to the growth of the arthroplasty service at Penn, as well as to improving the technique of total knee arthroplasties around the world.

Dr. Lotke was also a strong advocate early in his career for the use of aspirin for DVT prophylaxis in orthopaedics as opposed to other, more aggressive pharmacologic regimens. He remembers this as a "decade-long battle with the powers that be", and "one of two or three topics" that took over his career. At the start of his practice, post-operative protocols were much more sedentary as compared to the present day, and as such the risk of DVT and PE was higher. As a result, pharmaceutical companies "overdeveloped" their pharmacologic regimens, but Dr. Lotke always felt that the side effects of these regimens were too great and under reported. He recalls using an aspirin regimen during that same time with good results and limited complications. With his data, he embarked on an aggressive campaign advocating for the use of aspirin, offering support for the medication regimen on a lecture circuit that spanned many universities and institutions. Ultimately, his efforts were realized when the American College of Chest Physicians first officially recommended aspirin for DVT prophylaxis, and in the present day his viewpoint continues to be supported by the American Academy of Orthopaedic Surgeons.

Dr. Lotke has devoted a great deal of his time abroad during his career working with Orthopaedics Overseas, visiting many different countries including Pakistan, Vietnam, and Bhutan, among others. He holds these experiences in high regard, recalling that these trips changed the lives of both him and his children, who would often accompany him on the trips. He continues to strongly endorse these experiences to orthopaedic residents and physicians as opportunities to not only give back to the community and help underserved populations, but also for personal growth and enrichment.

During his esteemed career, Dr. Lotke has held numerous leadership, editorial, and administrative roles, has been the recipient of many honors and fellowships, and held positions in several surgical societies. Highlights include roles as the chief of the Implant Service at Penn from 1977 to 2001, President of the Knee Society from 1992-1993, a member on the Board of Directors for Orthopaedics Overseas from 2001-2007, and a senior associate editor of Clinical Orthopaedics and Related Research from 2008 until 2014. He has authored

Figure 2: Example of one of Dr. Lotke's handcrafted boats

over 150 original publications, over 50 editorials, reviews, and book chapters, and has been the author/editor of 13 different textbooks. He has been invited to visiting professorships around the world, most recently as the Honorary President of the Japanese Orthopaedic Society in Tokyo, Japan in 2007.

Dr. Lotke moved toward retirement in 2008, though he still enjoys regularly attending grand rounds and visiting professorships. In his retirement, he has become an avid woodworker, with extensive shops in both Pennsylvania and Maine. Among his more impressive achievements, he has crafted two boats, a 16 ½ foot Herreshoff sailboat and 17 foot Westport skiff (Figure 2), as well as many pieces of furniture. Another long-standing hobby of his is keeping several different types of animals at his Pennsylvania barn. At various times in the past he has bred llamas and sheep, as well as kept horses, dogs, cats, and chickens. To this day he still always has several chickens around, though he got out of the "llama game" long ago. He continues to enjoy spending time his wife, Dorothy Sue, and their three children and grandchildren.

Recalling his tenure at Penn, Dr. Lotke remembers this time with fondness and amazement at the extraordinary changes that have taken place since he first started, further stating that many of the most significant changes have occurred in the last several years. He was present during the leadership of 7 different department chairs, and notes that, while each of these individuals had a positive impact, "I don't think I saw a chair that made as much of an impact as the current chair, Scott Levin. He has taken the department to a level that was not previously attainable." When asked what advice he has for current residents, Dr. Lotke remarked "nothing I did when I was a resident, would I still do today. Everything changes… you have to be prepared for that, be willing to accept that, and be willing to make those changes throughout your career." He further said that, while his career ventures onto editorial boards and leadership positions were rewarding, he also simply stated, "there was nothing more fun than operating".

Dr. Lotke is an extraordinary figure in the field of orthopaedic surgery. He is a surgeon known for his exceptional technical skills, an inquisitive scientist who has published research with great impact across the orthopaedic community, a great humanitarian giving back to underserved communities internationally, and an advocate for driving the future of orthopaedic practice toward the best patient care possible. It is our great honor to dedicate this edition of the University of Pennsylvania Orthopaedic Journal to Dr. Paul A. Lotke.

In Memoriam: Dr. Robert Campbell (1951-2018)

John M. Flynn, MD

Penn Orthopaedics and CHOP lost a dear friend and giant in the field when Robert "Bob" Campbell, Jr. passed away peacefully on July 29th, 2018. Bob's innovative thought-leadership and inventions changed the world's approach to children with complex, life-threatening spine and chest wall deformities. The essence of Bob's contribution to pediatric orthopaedics was a paradigm shift: the focus of treating children with complex spine and chest wall deformities should be on pulmonary function, not on Cobb angle measurement of their scoliosis. His tenacious drive to evangelize the critical importance of preserving or improving pulmonary function, and his success inventing devices to support spine and chest wall growth, explain why colleagues refer to Bob Campbell as "the Charnley of early onset scoliosis".

Born on May 7, 1951, Bob was raised in Nashville, TN, graduating from Father Ryan High School in 1969. He matriculated to Vanderbilt University where he played football ("I was the smallest linebacker in the SEC"), then transferred to Johns Hopkins, graduating with a BS in Natural Sciences in 1973. After completing Georgetown Medical School in 1977, he did his surgical internship at Tripler Army Medical Center in Honolulu, Hawaii, then his orthopaedic residency at Fitzsimmons Army Medical Center in Aurora, CO. After four years of military service at Kimbrough Army Hospital in Fort Meade, Maryland, Bob completed the pediatric orthopedic fellowship at A.I. DuPont Hospital under the tutelage of G. Dean McEwen.

In 1986, Bob began his career at Christus Santa Rosa Children's Hospital/UT San Antonio, rising to Tenured Professor and holder of the President's Council/Dielmann Chair in Pediatric Orthopaedic Surgery. In 2008, Bob was recruited to the Children's Hospital of Philadelphia to take a leadership role in CHOP's rapidly growing multi-disciplinary Thoracic Insufficiency program. In 2009, Bob launched CHOP's Center for Thoracic Insufficiency (CTIS), attracting infants and children from around the world, many of whom were told "nothing can be done". He grew the team approach to care, collaborating closely with pulmonologists, thoracic surgeons, intensivists and radiologists to optimize treatment of children with severe spine and chest wall deformities.

Bob invented the VEPTR (Vertical Expandable Prosthetic Titanium Rib) device, taking a customized solution for a single child in San Antonio in desperate need of chest wall support through conceptualization, fabrication, testing and the arduous regulatory pathways of the FDA. His invention became the standard of care throughout the world for children with severe deformities of the spine and chest, saving or extending the lives of children with previously untreatable conditions. From 1991-2004, Bob led the FDA Feasibility Study: Thoracodorsal Reconstruction in Children with Vertical Expandable Prosthetic Titanium Ribs, travelling worldwide to train surgeons on the indications and surgical techniques to treat thoracic insufficiency using the VEPTR device. One of the least heralded contributions Dr. Campbell made to the field of pediatric surgical care was facilitating new device development through his involvement with the FDA. Dr. Campbell leveraged the relationships he built at the FDA to foster countless other devices through the regulatory process. He was named by the agency one of the 30 "Heroes of the FDA". Bob made frequent trips to FDA headquarters to advise and educate, and created an annual course for surgeons, scientists, device manufacturers and FDA device personnel to promote mutual understanding. In recent years, the regulatory approval processes have eased considerably, paving the way for a new wave of implants to help children; this is in no small part due to Bob's work, expert collaboration and influence.

Bob received numerous awards and honors, including Congressional recognition (Bill no. 1499, 111th Congress, 2nd session "Honoring the achievements of Dr. Robert M. Campbell, Jr.), The Pediatric Orthopaedic Society of North America Heune Award, The Scoliosis Research Society Walter Blount Humanitarian Award, and the Johns Hopkins University Distinguished Alumnus Award. Bob held 6 US Patents.

Far beyond awards and patents, Bob patient-families knew him for his unwavering devotion to their child's care; the large and growing yearly reunion of CTIS families at CHOP is a testament to impact he has had on so many. Bob will be dearly missed by his family, patients and colleagues at CHOP and around the world, but he has left a lasting legacy through his ideas, inventions, and the many surgeons and physicians he trained. "Don't be afraid to take a chance" Bob said. "It takes someone who can start a marathon without a finish line. If it's for a child, it's worth it. Don't be afraid. You can succeed." As Bob's colleagues and trainees, we are determined to do just as he advised, and build his legacy into something even greater. With generous support from his Faculty partners, patients, the

Children's Surgical Associates and CHOP, The Robert Campbell Chair in Orthopaedics has been endowed. The yearly proceeds with drive forward the care of children whose lives are threatened by spine and chest wall deformities, and help CHOP orthopaedics maintain its world leadership in their care.

Photo collage of Dr. Campbell with one of the many patients and families whose lives have been changed by the VEPTR device.

The Penn Orthopedic Leadership Program: Training Surgeons as the Leaders of Tomorrow

John Kelly IV, MD

Leadership is simply the art of motivating others to realize a goal. Orthopedic surgeons are necessarily called to lead a health care team toward the singular goal of exemplary musculoskeletal care. We are the de facto 'captain of the ship' in surgery and in clinic and others look to us to exercise proper decision making. In addition, the achievement of any great organizational goal, be it philanthropic, research, surgical innovation or advocacy, requires effective leadership. Great leaders accomplish great things and can be agents of cataclysmic positive change. However, the ability to effectively lead is indeed a ***skill*** which can be learned.

Penn has enjoyed a rich tradition of training leaders in Orthopedic Surgery; many graduates have lead departments and served as program directors while others have helped develop new paradigms in research and clinical care. The Penn leadership legacy can be greatly enriched with targeted leadership training.

The Penn Orthopedic Leadership Program was conceived in order to equip our residents with the skills needed to realize their dreams and become positive agents of change for our esteemed vocation. While many great leaders have received 'on the job training', the *study* of leadership has evolved greatly and much is to be learned from formal educational training.

The Penn Leadership Program goal is to arm our graduates with skills necessary to effectively lead and realize their *professional and life* goals. The leadership curriculum is comprised of periodic leadership journal clubs, guest lecturers, and an annual leadership forum where local leaders share wisdom on topics such as team building, personal responsibility and execution of priorities.[1] The cornerstone of the curriculum is the Wharton spring retreat where residents receive highly relevant didactic sessions orchestrated by Dr. Mike Useem, the highly esteemed Director of the Center for Leadership and Change Management at Wharton.

Figure 1. Dr. Mike Useem, Director of the Center for Leadership and Change Management at Wharton, leading a discussion with the residents during the annual leadership forum.

By partnering with the Wharton School, we have developed a highly efficient curriculum for residents to: increase their emotional intelligence, appreciate the importance of integrity, develop a leadership identity, assist in building effective teams, and implement skills into their careers as the next generation of surgeon leaders. We truly believe the skills learned in our program can assist our young graduates to effectively lead the next generation of Orthopedic Surgeons at a time when leadership is needed most.

Figure 2. Residents participating in a team building and leadership exercise at last year's annual leadership forum

Self-mastery is an imperative before one can effectively lead others. Thus, the leadership curriculum is replete with sessions on stress management, mindfulness, relationship building and proactivity. The attainment of *meaning* in work is emphasized so that joy and fulfillment can be cultivated.[2] In addition, efforts are underway to formulate 'support groups' and a more complete mentoring scheme where residents can confide in select attending surgeons when under excessive stress.

Indeed, it is an exciting time in our beloved program as we endeavor to equip our graduates with the tools necessary to live fulfilling lives and become agents of quantum change.

References:

1. Willink, Jocko, and Leif Babin. *Extreme ownership: How US Navy SEALs lead and win.* St. Martin's Press, 2017.

2. Collins, Jim. *Good to Great: Why Some Companies Make the Leap and Others Don't.* Instaread, 2016.

Quality Improvement: Achieving Quality Outcomes in Surgical Episodes and Disease Teams

Eric Hume, MD, Hannah Lacko, and Luke Lopas, MD

Introduction

While surgical teams understand quality improvement generally, we needed to incorporate formal language and structure to build quality and safety into patient care. We have morphed from focus on hip and knee arthroplasty episodes of care at Penn Presbyterian Medic Center (PPMC), to Musculoskeletal Rheumatology (MSKR) disease teams working across the University of Pennsylvania Health System (UPHS.)

Training the next generation is a key component of quality work. When our residents enter practice, they will be expected to be competent in methods to improve quality and cost. To this end, we developed a patient safety committee and curriculum with our residents.

Early Experience: Achieving Quality Outcomes in Surgical Episodes

The first formal efforts based on quality started with our Risk Stratification Tool (RST). UHC data, now Vizient, demonstrated the importance of a focus on hospital mortality for hip and knee arthroplasty patients. The proxy of unplanned ICU admissions was used for Plan-Do-Check-Act (PDCA) process-improvement (PI) cycles. Preoperative screening identified patients who would benefit from planned ICU admission, then later led to developing PAMP (Post Arthroplasty Monitoring Protocol). Our RST, optimized over four PDCA cycles, recommends postoperative care location and has reduced hospital mortality and both planned and unplanned ICU admissions.

We developed preoperative disease mitigation aimed at reducing readmissions. Readmission reduction, a prime metric of quality, prepared us to start BCPI (CMS Bundle Payment Care Initiative) and Independence Blue Cross (IBC) bundle work. The variability in IBC bundle cost (Figure 1) informed opportunities to develop postoperative care processes such as Home Safely and Hot Joint. Data showed that patients who are discharge directly to home have a lower readmission rate, and identified medical risk factors to manage before admission (e.g., diabetes, anemia, malnutrition). We are addressing smoking cessation and opioid usage before admission. "Penn Addressing the Opioid Crisis" in this UPOJ outlines these efforts more completely.

Our physician champion and a quality-trained administrator initially focused efforts on the PPMC hip and knee arthroplasty bundle initially, then extended to Pennsylvania Hospital (PAH,) and have now transitioned to MSKR service line Disease Teams across UPHS.

Achieving Quality Outcomes Through the Work of Disease Teams

Much of the quality improvement work is through the work of disease teams within the MSKR Service Line. Our disease teams are made up of focused work groups that address efficiency and value for specific care pathways within a given disease or injury. The current MSKR disease team structure is shown in Figure 2. Each fiscal year, five of the pathway teams are given the opportunity to set a goal that, if achieved, earns an incentive payment that can be reinvested into the disease teams to fund pilot projects, purchase material resources, and contribute to programmatic development and growth. Incentivized disease teams for FY19's are highlighted in blue in Figure 2.

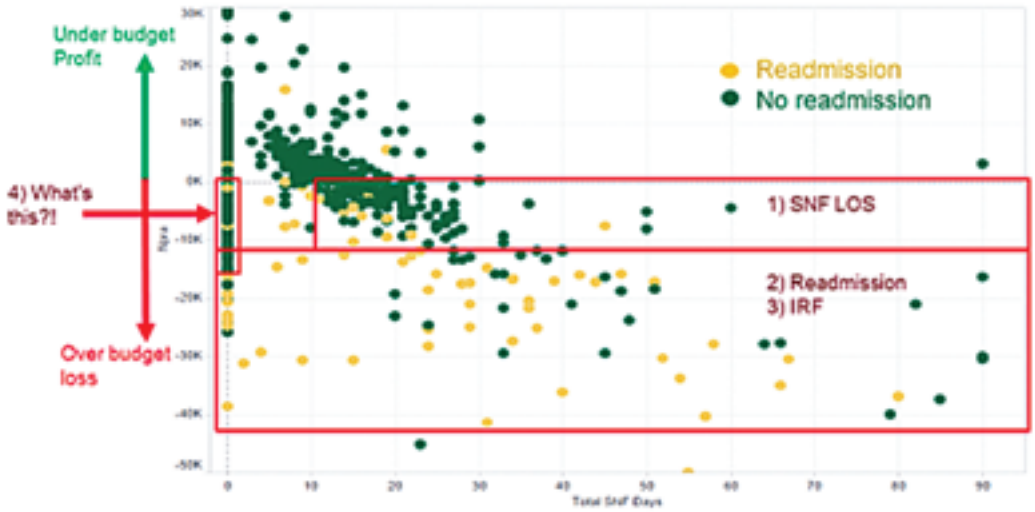


Figure 1. IBC Bundle Over- or Under-Budget Data. Cost variability demonstrates impact of readmissions, IRF, SNF, LOS.

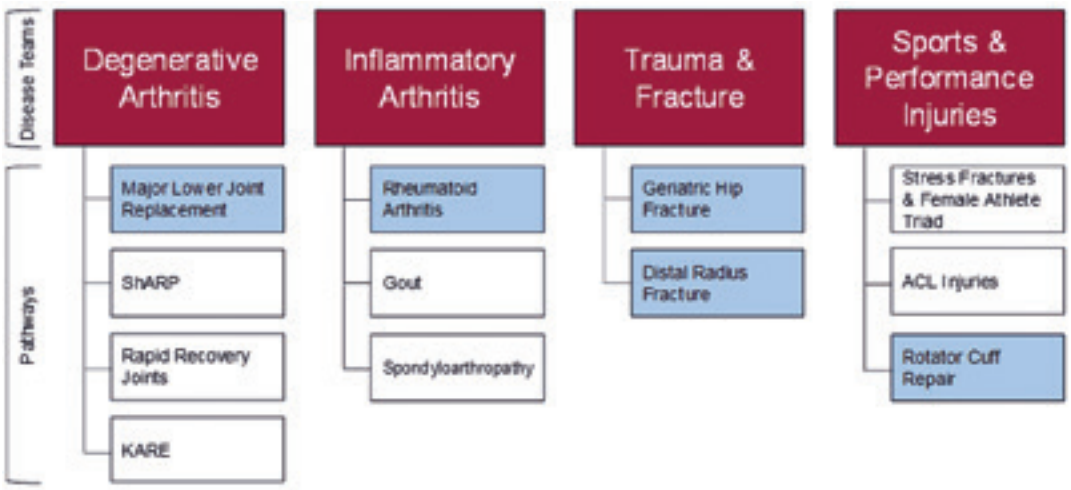


Figure 2. MSKR Disease Team Structure

Disease Team: Degenerative Arthritis
Pathway: Major Lower Joint Replacement
Goal: Increase percentage of patients discharged to home by 5%

Given the increased enterprise focus on performance in bundled payments and episodes of care, the major lower joint replacement (MLJR) care pathway team chose to focus their effort on increasing the percentage of patients who are discharged to home. Patient expectations prior to surgery are a key driver of postoperative discharge location. As such, several projects were implemented to ensure that expectations for discharge to home were being communicated clearly throughout the episode.

Pre-acute care: Focus was placed on patient education with improvements in our joint education class and development of educational videos distributed by email, OCR cards, and a smart phone app created in partnership with Comcast Connected Health, now Quil Health. A Shared Decision Making (SDM) module was introduced to inform patients deciding between surgical or non-surgical treatment.

Acute care: We launched a PennChart MLJR Pathway at PAH and PPMC to decrease care variability to improve patient outcomes, to provide clinical decision support for providers, and to improve value for the health system.

Post-acute care: Home safely continues to be our focus. We enabled PennChart communication of preoperative Risk Assessment and Prediction Tool (RAPT) scores to the inpatient team and continue to work with home health care and Skilled Nursing Facilities (SNF.) Our nurse navigator has lowered readmission rates. We just completed "Home Connect+" with the Penn Center for Healthcare Innovation utilizing nudge language to provide guidance and monitor pain and activity with wearables and smartphones. Finally, we are initiating the My Mobility Project using iOS wearable and smartphone devices to track outcomes.

Disease Team: Inflammatory Arthritis
Pathway: Rheumatoid Arthritis
Goal: Increase Patient reported Outcome (PRO) capture rate by 20%

The American College of Rheumatology has made recommendations regarding the collection of a patient-reported functional assessment for some inflammatory arthritic conditions. Rheumatology at Penn Medicine University City (PMUC) introduced tablets in FY18 to collect PRO data while patients were in the waiting room. In addition to these tablets, PMUC sent the PRO survey to patients prior to appointments, and allowed patients to complete the survey directly in PennChart while waiting for the provider in the exam room. The combination of these three collection methods led PMUC to a 92% capture rate, however, the other three main clinic sites (Penn Center for Advance Medicine, Cherry Hill, and Radnor) finished the year at 13%. The service line invested in tablets to capture PROs at PCAM, Cherry Hill, and Radnor, and engaged the providers to collect PROs to inform patient care, both individually and in aggregate.

Disease Team: Trauma and Fracture
Pathway: Geriatric Hip Fracture
Goal: Decrease Average Length of Stay (ALOS) by 17%

In FY18, the geriatric hip fracture care pathway teams from PPMC, PAH, and Chester County Hospital (CCH) began tracking data in alignment with the International Geriatric Fracture Society (IGFS). IGFS provides metrics, benchmarks, operational definitions, and inclusion criteria to support best-practices geriatric hip fracture care. A premier-level certification is already held at Lancaster General Hospital (LGH.) PPMC, PAH, and CCH are moving toward achieving this certification by 2021. PPMC, PAH, and CCH are already performing well for IGFS benchmarks: readmissions, time to surgery, in-hospital mortality, length of stay (LOS), medical co-management, and osteoporosis education. Co-management improves clinical outcomes for this vulnerable population.

Disease Team: Sports and Performance Injuries
Pathway: Outpatient shoulder surgery
Goal: Unchanged pain PRO score 6-weeks post-op

The department of Orthopaedic Surgery has been focused on increasing the rate of PRO capture since July 2016 to inform an evaluation of a multimodal pain protocol. This multimodal

pain protocol was previously developed in the division of Shoulder and Elbow Surgery. Through the work of the care pathway team, all patients who undergo outpatient shoulder surgery, whether under Shoulder and Elbow or Sports Surgery, are receiving the same, proven effective pain protocol, which notably contains a minimal number of opioid pills per script. The effectiveness of this protocol from the patient's point of view will be tracked using their six week postoperative pain score. The goal is to avoid worsening of patient's reported pain score while lowering opioid use.

Disease Team: Trauma and Fracture
Pathway: Distal Radius Fracture
Goal: 70% utilization of updated hand pain protocol

The introduction of the Integrated Hand Service in FY18 allowed for the creation of a new care pathway under our Trauma and Fracture disease team: Distal Radius Fracture care. This care pathway, which was developed by surgeons from both Orthopaedic Surgery and Plastic Surgery, seeks to standardize care delivery regardless of service.

As their first project, the team standardized the discharge to include existing multimodal pain management alternatives and to lower number of opioid pills per script. This protocol prompted modifications to the existing hand pain panel, making the overall panel safer and more effective for pain control.

Achieving Quality Education for Residents

Resident education and involvement surrounding safety and quality improvement processes is a growing focus for the department. Knowledge and skills in these domains are required to actively engage in 21st-century health care.

Our interns have specific educational sessions dedicated to quality improvement methodology. This early exposure introduces fluency in the language of quality and safety and facilitates involvement in the department, hospital, and health system.

Interns put the methods into practice by developing a quality improvement project. With the guidance of senior residents and faculty mentors, the interns work through the QI methodology to improve patient care. Past examples have included improving the communication among nursing, physical therapy, case management, and the physician team for discharge planning, and improving the physical inpatient work environment.

At our quarterly Quality Improvement Grand Rounds, speakers with experience in QI offer lessons learned from QI projects in different venues. Many speakers come from within UPHS, and this year, Javad Parvizi gave a superb presentation about infection prevention. We also discuss departmental data and initiatives, gather feedback, and plan next steps. Finally, our residents present their QI projects to the department to update their progress and to receive feedback to assist in optimizing their efforts.

UPHS also participates in a national program, "Pursuing Excellence in Clinical Learning Environments," with eight other university hospitals. The goal is translation of the clinical learning environment into a culture of patient safety. The institutional focus is on early learners, especially first- and second-year residents, new fellows and new advanced providers at Penn. Within this effort, we are developing a formal interdisciplinary patient safety huddle process with members of the Department of Anesthesia to discuss collaborative patient care and safety issues.

Conclusion

We have widely broadened our quality and safety improvement efforts using formal quality structure of MSKR disease team model. We have transitioned from episodes of care at individual hospitals, to MSKR disease teams working across UPHS. Understanding and managing variability with data has been a core component.

Training the next generation is another key component of our work. We developed a resident safety committee and a curriculum starting with half-day seminar during Intern Boot Camp. Resident participation in quality and safety work is key for their education toward future expectations of them in their careers, for patient safety, and for MSKR quality work.

Delivering Orthopaedic Care in Sub-Saharan Africa: An Update on Tanzania

W. Mack Hardaker, MS and Neil P. Sheth, MD

In Tanzania, Dr. Neil Sheth has continued to lead an expansive team, from the University of Pennsylvania and beyond, to develop a novel and sustainable solution for the delivery of orthopaedic care in East Africa. The team has formally proposed to build an Orthopaedic Center of Excellence at Kilimanjaro Christian Medical Center (KCMC) in Moshi, Tanzania. This effort is in conjunction with KCMC and the Tanzanian Ministry of Health. Surgical teams from Penn and twenty-five other partnering institutions will coordinate a rotating schedule of two week blocks to ensure year-round surgical staffing. The center will act as a collaborative training center for local health care providers including surgeons, residents, nurses, and therapists education is to be the fundamental platform at every level of this endeavor.

Over the past 18 months, the Wharton School has created a team of seven MBA students (two of whom were MD/MBA students) that formulated a formal business plan, financial model and pitch deck. The team went to Tanzania in January 2018 to acquire additional data on the ground and interface with our local partners at KCMC. The final deliverables were presented to the collective team at Penn in August 2018. The following four months were spent having independent field experts review the documents and provide feedback on how to make the overall pitch stronger. One of the independent reviewers was a team from GE Capital based in Paris, France.

In the interim, Dr. Honest Massawe, an Orthopedic Surgeon at KCMC, and a former guest at Penn in 2017, was made an adjunct professor of orthopaedic surgery at the University of Pennsylvania in April 2018. Due to Dr. Levin's leadership and continued support of this project, we have further solidified the relationship between KCMC and Penn Orthopaedics. The executive committee of KCMC has already given their approval of this project, and we are now in the process of getting additional KCMC faculty appointments at Penn.

As of February 2019, the team is working with GE Capital to create a formal investors package. There are several GE Healthcare clients that are interested in hearing more about the project and becoming potential benefactors. The final capital structure will be based on the amount philanthropic donation that is committed to the project. Recently, an orthopaedic industry partner has approached the team to become the sole provider of implants for the endeavor

this would result in significant cost savings and enhances our ability to provide democratized health care to all patients, regardless of their ability to pay. The goal is to secure funding in 2019. In July 2019, we will be able to offer opportunities for senior level (PGY4 and PGY5) residents to go to Moshi, Tanzania and spend a two-week rotation with our colleagues in Sub-Saharan Africa.

Figure 1. Proposed Orthopaedic Center in Moshi, Tanzania.

Protecting our Patients Against the Opioid Endemic: Doing Our Part at Penn Orthopaedics

Matthew Counihan, MD, Krista Tarducci, MSN, RN, and Jaimo Ahn, MD, PhD, FACS

In the past two decades, opioid misuse in the United States has become endemic and, alarmingly, opioid overdose events have reached epidemic levels. Prescriptions for opioids and subsequent use and misuse substantially grew in the 1990's and the true toll of these medications on the American population became widely apparent in following decades. Between 1999 and 2017, nearly 218,000 deaths in the US were attributed to overdoses due to prescription opioids (1). The incidence of these events increased at an unwavering pace during that time period, with nearly five times the number of deaths in 2017 as compared to 1999 (1). Unfortunately, during that same time, there was no apparent decrease in pain for patients across the US. Prescribing habits modestly improved across the medical community in the early 2010's, with CDC data showing the overall opioid prescribing rate peaking in 2012 followed by a steady decline to the present day. However, the morphine milligram equivalents (MME) prescribed per person continues to be three times the MME in 1999 (1). In the face of the continued upward trend of opioid overdose events, it was necessary for our orthopaedic community to take an active role in responding to this devastating national crisis.

Providers in orthopaedic departments across the country not only play a critical role in managing patients' pain but also bear the role of being responsible stewards of opioid prescriptions. More than 7% of all opioid prescriptions originate from an orthopaedic surgeon (2), each prescription carrying a risk of worsening misuse or provoking dependence. Managing these medications is a tremendous responsibility. In the past year, Penn Orthopaedics has embraced this responsibility as an opportunity a chance to improve the wellbeing and safety of our patient population without sacrificing adequate pain management.

Penn Orthopaedics recently undertook a quality improvement initiative to assess the opioid use among our patients and use that data to enact measures to decrease the burden of opioids within our community. For example, it was determined that in 2017, our arthroplasty patients took a mean of 32 opioid pills postoperatively but generally were prescribed 50-60 tables postoperatively. Additionally, fewer than 10% of patients continued to use opioids past four weeks despite receiving prescription regimens intended to last four to six weeks. This data presented a clear opportunity to decrease unnecessary and unused opioid prescriptions and this endeavor was implemented in each subspecialty within the orthopaedic department. As a result, we have shown a significant improvement in opioid prescribing patterns comparing fiscal year 2018 to fiscal year 2019. As of January 2019, the entire department reduced the number of pills per prescription by 28%, with certain divisions achieving far beyond that mark, including reductions of 35%, 39%, and 53% in the Foot and Ankle, Arthroplasty, and Trauma divisions, respectively (Figure 1). Furthermore, we enacted new protocols limiting the number of tablets prescribed at discharge and at follow up visits.

Addressing this crisis in a safe and effective manner requires more than simply decreasing the total number of opioid pills prescribed. Penn Orthopaedics' continued commitment to managing our patients' pain is reflected in an ongoing emphasis on multimodal pain management. This has taken the form of a renewed emphasis on long-used, dependable pain medications such as acetaminophen and NSAIDs, agents targeting nerve pain and other alternative pain pathways, and regional anesthesia. The latter of these modalities is performed by the highly skilled Anesthesia Pain Management team at Penn. In this regard, our focus has become both multimodal and multi-disciplinary. Our partnering providers not only deliver reliable regional anesthesia, but also help manage two critical categories of patients: those with chronic opioid use pre-operatively and those having difficulty weaning from opioid medications beyond 30 days post-operatively. A close collaboration with the Pain Management service has been integral to our ongoing work in this area.

Finally, one of the most important factors impacting our efforts to address opioid use is patient awareness and increased patient knowledge. Increased news coverage of the opioid crisis and state-level initiatives to reduce opioid-related overdoses have increased patient awareness of the dangers of chronic opioid use and made patients more accepting of the use of non-narcotic medications to manage postoperative pain. Providers with Penn Orthopaedics have seized this opportunity to have a more thorough and considerate physician-patient interaction in the pre-operative setting. The increased communication results in improved patient expectations and an improved sense of confidence from patients that their post-operative pain regimen will be effective, safe, and minimize the risk of side effects from opioids.

The magnitude of the country's opioid crisis means that our efforts in this area are far from over. While Penn Orthopaedics is proud of its improvements thus far, there is no doubt that

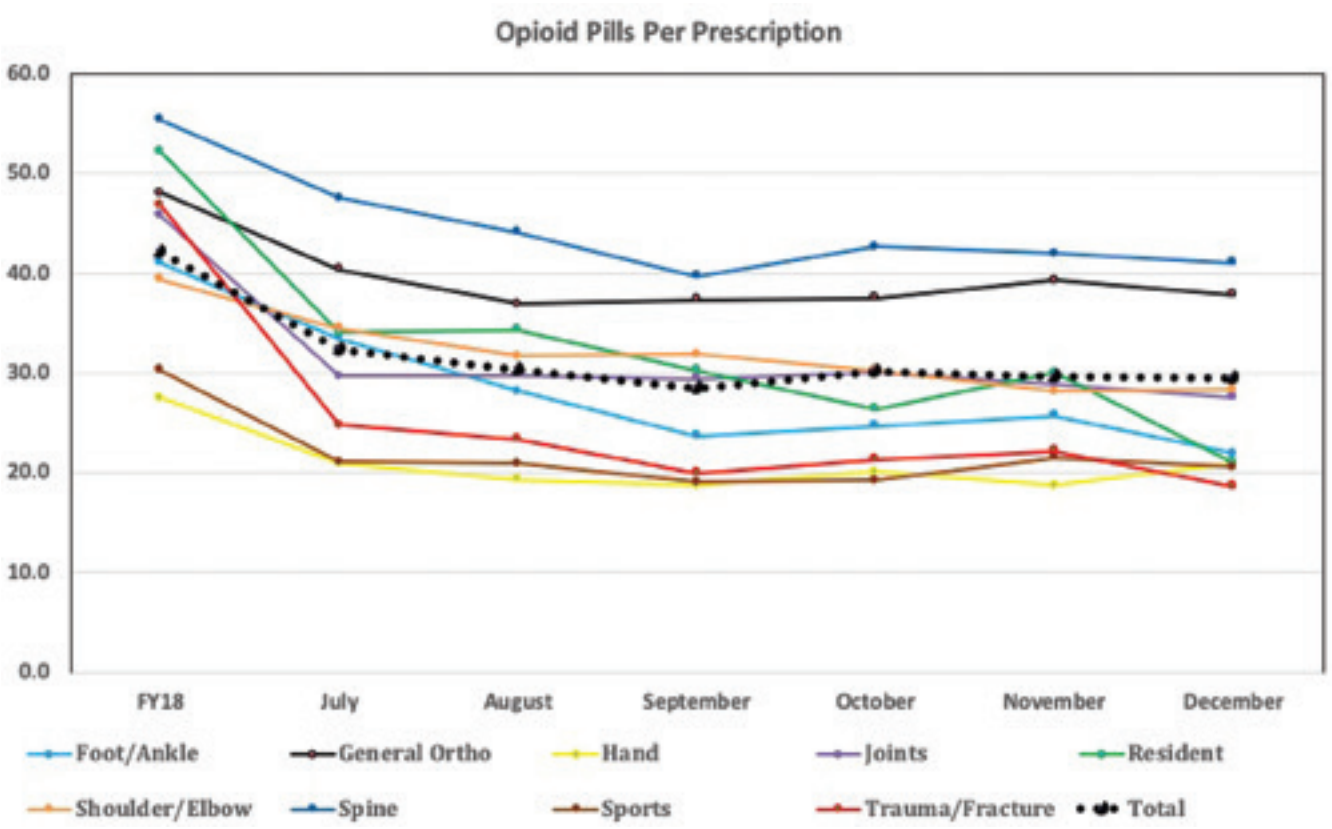


Figure 1. Average number of opioid pills per prescription for the entire fiscal year 2018 (FY18), and for each of the first six months of fiscal year 2019, starting with July 2018.

continued progress must be made in order to help decrease the burden of opioid use among patients and, indeed, to help our patients optimize pain response and control. This will be achieved through our department-wide commitment to the principle that quality, modern orthopaedic care demands a thoughtful, safe, and evidence-driven pain management regimen that serves both the individual patient and the community to the highest level.

References

1. Centers for Disease Control and Prevention: Prescription opioid data. National Center for Injury Prevention and Control, Division of unintentional Injury Prevention. (Updated October 19, 2018) https://www.cdc.gov/drugoverdose/data/prescribing.html. Accessed March 25, 2019.

2. Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SR: Characteristics of opioid prescriptions in 2009. *JAMA* 2011;305(13):1299-1301.

Faculty Achievements

Liane Miller, MD

Dr. Kristy Weber: First female AAOS President

It is with great excitement and pride that we announce the inauguration of our own Dr. Kristy Weber as the 87th President of the American Academy of Orthopaedic Surgeons (AAOS). Dr. Weber took office in March 2019 as the Academy's first female President and will serve until March 2020.

She has dedicated herself to guiding the future of orthopaedics and championing for diversity in the field having served on the board of directors of the AAOS, American Orthopaedic Association, Orthopaedic Research Society, and the Connective Tissue Oncology Society and served as past President of the Musculoskeletal Tumor Society and Ruth Jackson Society. She was also the recipient of the 2006 Kappa Delta Elizabeth Winston Lanier Award for her work in metastatic bone disease.

In her tireless advocacy for her patients, Dr. Weber also serves as chief of Orthopaedic Oncology in the Perelman School of Medicine, director of the Sarcoma Program in Penn Medicine's Abramson Cancer Center, and Vice Chair of faculty affairs in the Department of Orthopaedic Surgery at Penn.

In her inaugural address this March, Dr. Weber communicated her assessment of the current state of the Academy and provided a vision that was both ambitious and aspirational. She outlined a new strategic plan that will focus on "personalizing the member experience, especially in the area of digital learning, equipping members to thrive in the new value based environment, advancing the quality of orthopaedic care, and evolving the culture to become more innovative and diverse."

Dr. Weber made a final point during her address to confront the issues of bias, prejudice, and stereotyping within the field of orthopaedics, and acknowledged that much work remains to be done before the culture of this profession can be deemed inclusive of women and underrepresented minorities. She reminded the audience that "our differences should stimulate curiosity, not judgement" and asked that we all be mindful of the "unique qualities, experiences, and perspectives [we bring] to our practices, leadership roles, and interactions with others."

Despite the continued challenges and barriers we face as a field, we are encouraged that its future lies within the capable and progressive hands of Dr. Weber as she strives to create a more welcoming culture in our practices, institutions, and the Academy.

Figure 1: Dr. Kristy Weber and Dr. David A. Halsey, outgoing AAOS President, during the Opening Ceremonies at the 2019 Annual AAOS Meeting

Dr. L. Scott Levin: President of the American Society for Surgery of the Hand

On September 15th 2018, Dr. L Scott Levin was introduced as the incoming American Society for Surgery of the Hand (ASSH) President, during the organizations 73rd annual meeting in Boston. As the President, Dr. Levin will oversee the entire ASSH Council and work to further the objectives of the organization's strategic vision and mission to advance the science and practice of hand and upper extremity surgery.

Board certified in both Orthopaedic and Plastic Surgery, Dr. Levin also serves as the chairman of the Department of Orthopaedic Surgery at Penn, Professor of Plastic Surgery, founding member of the Penn Orthoplastic Limb Salvage Center, director of Penn Medicine's Hand Transplant Program and director of the CHOP Pediatric Hand Transplant Program, and the Paul B. Magnuson Professor of Bone and Joint Surgery. These experiences and achievements have made him well-suited for the presidential position.

The ASSH was founded shortly after World War II by a group of 35 military hand surgeons who met to discuss the care and treatment of service members with hand and upper extremity injuries. Today, the organization has over 3,800 international members from orthopedic, plastic surgery and general surgery backgrounds.The ASSH has a strong focus of advocacy for both patients and practitioners through collaboration, education, and clinical care—a legacy that Dr. Levin will no doubt continue to promote during his time as President He will serve in this role until September 2019.

Dr. Fred Kaplan: Winner of the Grand Hamdan International Award for Medical Sciences

The department is delighted to acknowledge the incredible work and dedication of Dr. Frederick S. Kaplan in his pursuit of cure Fibrodysplasia Ossificans Progressiva (FOP). Dr. Kaplan is the Isaac and Rose Nassau Professor of Orthopedic Molecular

Medicine and Chief of the Division of Molecular Orthopedic Medicine at the Perelman School of Medicine and has made tremendous strides in understanding the pathology and potential treatment opportunities for FOP.

On December 12th, 2018, he was presented with the Grand Hamdan International Award for Medical Sciences by H.H. Sheikh Hamdan bin Rashid al Maktoum, Deputy Ruler of Dubai, United Arab Emirates, Minister of Finance, and the Patron of the Award. This award highlights those within the profession who are dedicated to the alleviation of the sufferings of humanity through research and exemplary service.

Cartilage Symposium

Liane Miller, MD

On September 7th and 8th, 2018, the University of Pennsylvania Department of Orthopaedic Surgery was thrilled to host the 8th annual Penn Orthopaedics 2018 Cartilage Repair Symposium. The symposium is geared toward orthopaedic surgeons, non-operative sports medicine physicians, physical therapists, athletic trainers, nurses, and physician assistants to present the latest techniques in cartilage repair. With a focus on basic science, the symposium also attracts the best scientists and engineers to present their cutting edge work. Organized by James L. Carey, MD, MPH, and Robert L. Mauck PhD, the symposium topics for discussion included basic science and biology of cartilage, translational considerations for cartilage repair, and the latest surgical and clinical techniques for cartilage repair and rehabilitation, as well as an opportunity to engage in hands-on training in the most advanced cartilage repair techniques in the Human Tissue Laboratory at the University of Pennsylvania. Invited faculty included Tom Minas, MD, MS, Director of the Cartilage Repair Center in West Palm Beach, who discussed pushing the boundaries in repair of "high risk" chondral lesions. The symposium concluded with the surgical skill session, moderated by Miltiadis Zgonis, MD, where participants were able to observe and trial many currently available cartilage repair techniques. Under the leadership of Dr. Carey and Dr. Mauck, the symposium continues to grow in popularity and promises to be a gathering of the foremost cartilage repair specialists for years to come.

Figure 1. Word cloud created by Dr. James Carey demonstrating the most frequent faculty and speaker attendees, with larger font corresponding with higher number of symposiums attended.

Penn Center for Musculoskeletal Disorders Symposium

Liane Miller, MD

Under the direction of Dr. Lou Soslowsky, PhD, the Penn Center for Musculoskeletal

Disorders (PCMD) held their annual Scientific Symposium on November 7th,2018 in the Smilow Rubenstein Auditorium of the University of Pennsylvania. Designed to showcase and support the academic pursuits of PCMD members, the Symposium drew a large number of participants and visitors to celebrate the work being done by the researchers at Penn.

The morning began with a session headed by new members, moderated by Ling Qin,

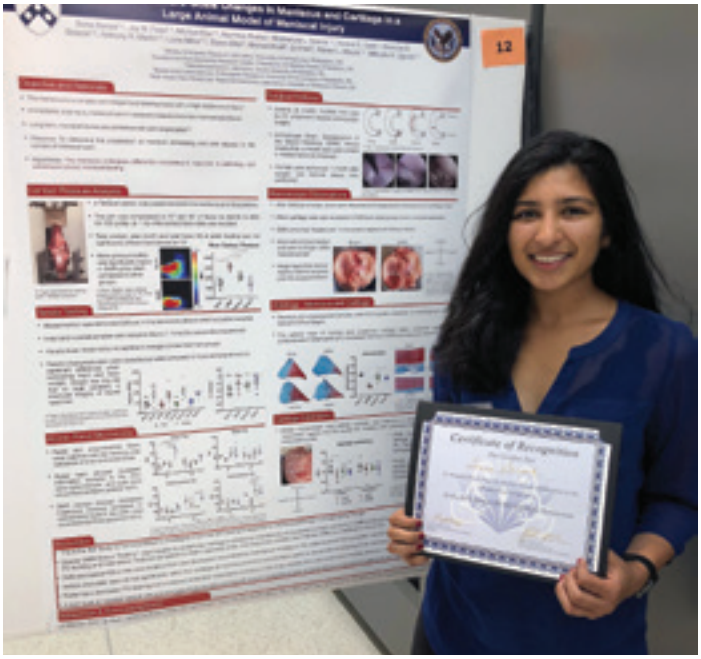
PhD. Speakers included Jordan Raney, PhD (3D Printing Bioinspired Materials with Spacially-Controlled Fiber Alignment); Zoltan Arany, MD, PhD (From Pregnancy to Titin); and Paris Margaritis, DPhil. (The Hemophilia A Rat as a Model to Study Hemophilic Arthropathy).

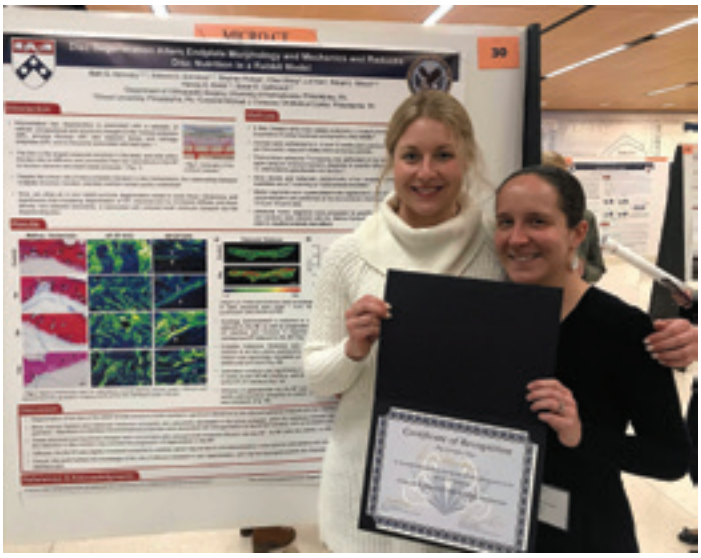
The morning continued with lectures by affiliate PCMD members, moderated by Lachlan Smith, PhD. Talks included "Orthopaedic Implants and Infections: Surfaces, Synovial Fluid, and the Joint Envioronment" by Noreen Hickok, PhD, of Thomas Jefferson University;"Peripheral Nerve Injury Adjunct Treatments for Classification" by John Elfar, MD, of Penn State Heath; and "Biomimetic Proteoglycans in Extracellular Matrix Regeneration" by Michele Marcolongo, PhD, from Drexel.

The lunch session coincided with poster presentations by all PCMD members, showcasing their work over the past year, which then led directly into the afternoon lecture session, moderated by Maurizio Pacifici, PhD.This session included talks by Pilot Grantees and included Dr. Harvey Smith discussing "Novel Quantitative Assessment and Treatment Strategies for the Degenerated Intervertebral Disc."

The afternoon session concluded with an address by the keynote speaker, Brendan Lee, PhD, and Robert and Janice McNair Endowed Chair in Molecular and Human Genetics at Baylor College of Medicine. Moderated by Kyu Sang Joeng, PhD, Dr. Lee discussed "Skeletal Dysplasias: Informing Skeletal Function and Homeostasis" where he provided a detailed look into what he and his team have accomplished at the forefront of bone research.

The symposium was then concluded with a final question and answer session with the keynote speaker followed by the announcement of poster award winners. The symposium was an enormous success, and promises to be a highly regarded function and point of pride for the Penn Center for Musculoskeletal Disorders in years to come.





PCMD Poster Award Winners

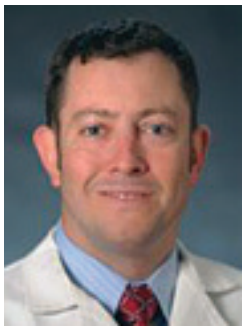
Orthopaedic Trauma Division Update

Samir Mehta, MD

Orthopaedic Trauma Faculty

Samir Mehta, MD

Jaimo Ahn, MD, PhD



Derek Donegan, MD

L. Scott Levin, MD, FACS

Anchored by a tremendous general surgery trauma service, expanded infrastructure at Penn Presbyterian Medical Center, and dedicated and determined housestaff and advanced practice providers, the Division of Orthopaedic Trauma strives to compete at a high level across all missions of the Health System and School of Medicine. The clinical program has continued to flourish at peripheral sites including Radnor and Cherry Hill. Thanks to the help of our administration and our clinical partners, the Division's Geriatric Hip Fracture program an idea nearly a decade in the making - has allowed for improved care of our patients with decreased time to OR, length of stay, and readmission rates.

In addition, the Division continues to explore and build relationships with Penn's newest partners Chester County Hospital, Lancaster General Hospital, and Princeton Hospital. Services that are provided to our sister hospitals as well as our regional orthopaedic community include complex fracture care, limb salvage, deformity correction, periprosthetic fracture reconstruction, and infection management. Our clinical program continues to utilize advanced technologies such as 3D printed implants, lengthening nails, and ring fixators. Our ability to provide care necessary to our patients in a 24/7/365 fashion would not be possible without the house staff, our nurse practitioner, our physician assistants, and the faculty who continue to take call on nights, weekends, and holidays.

Through the tireless efforts of our clinical research coordinators, the research program continues to expand. Several prospective funded studies are currently underway, including ones funded by industry examining the changes with suprapatellar nailing, the Department of Defense assessing infection control in open fractures, the REGAIN hip fracture trial and Pre-Operative Alcohol Skin Solutions in Fractured Extremities (PREPARE) study through PCORI, and better understanding the flora of open fractures through the AO Foundation. In addition, a generous grant from the Wyss foundation continues to support our work examining the biomarkers predicting fracture healing. Engaging in pragmatic trials allowing us to refine our approach to trauma and fracture care is a critical component of our work at Penn.

Ultimately, the orthopaedic trauma and fracture service is most proud of its continued dedication to resident education. The current complement on service includes a PGY1, two PGY2s, PGY3, PGY4, and PGY5. While there are occasional visiting fellows, these learners do not interfere with the education of the residents, who are the primary focus for the service. The residents continue to work hard on this service rewarded with opportunities in leadership, technical skill development, decision-making, and communication. Several teaching tools are utilized in the resident growth and development including critical and timely feedback, online education, written pre- operative plans, case-based teaching, and trauma conference.

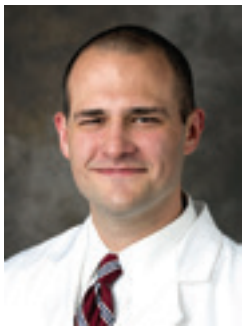
Spine Division Update

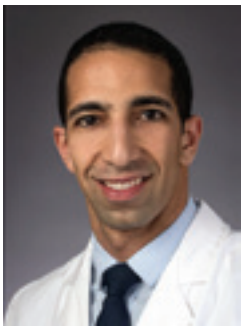
Harvey Smith, MD

Spine Faculty


Vincent Arlet, MD


Harvey Smith, MD


Andrew Milby, MD


Comron Saifi, MD


Michael Murray, MD

The academic year has been one of continued growth for the spine division.

Clinical Growth: Last year we on-boarded three spine surgeons, Drs. Milby, Murray, and Saifi. All three have demonstrated marked clinical and academic productivity; this is a testament to the depth of opportunities within the department. Dr. Milby has grown a significant practice at Penn Presbyterian Medical Center and Radnor, Dr. Saifi has established a new practice at Yardley, and Dr. Murray has established a rapidly growing practice at Chester County. In partnership with our neurosurgical colleagues, our division is sharing in the coverage of level 1 spine trauma at Penn Presbyterian Medical Center which has advanced our residents' educational experience.

Research: Our division continues to establish itself as a leader in both basic science and clinical spine research. Our translational research is conducted in partnership with the Translational Musculoskeletal Research Center at the VA and last year we published the first in vivo large animal tissue-engineered total disc replacement. Our clinical research division is led by Dr. Comron Saifi who is working on establishing an outcomes registry for our complex deformity patients as well as all adult spine patients. This is a large undertaking and he has made significant strides with marked academic output in terms of manuscripts, abstracts, and presentations. Dr. Murray's interest in minimally invasive (MIS) spine surgery has helped to establish a significant MIS presence at Chester County, and he is establishing a number of comparative effectiveness research projects demonstrating the value of MIS surgery which will be crucial for the academic analysis of bundled care scenarios and ensuring our ability to continue to introduce new technology. Dr. Milby this year assumed leadership as co-director of the Residency Program, a testament to the strength of his teaching and commitment to resident education and research.

Academic Productivity: Penn Ortho Spine has been represented in over 20 peer-reviewed publications, abstracts and presentations. Our faculty chair committees at North American Spine Society, have organized Instructional Course Lectures at national and international meetings. The Philadelphia Spine Summit meeting organized in partnership with Thomas Jefferson University is now entering its fifth year and is now one of the largest regional spine meetings.

Outreach Surgery: Under the leadership of Dr. Arlet Penn Spine maintains an ongoing outreach program in Trinidad managing complex spinal deformities; this program has received national and international recognition.

Spine Fellowship: Our spine fellowship is entering its third year of partnership with the Shriners Hospital of Philadelphia. Our complex spinal deformity fellowship is unique in that offers a combined adult and pediatric complex deformity experience.

Sports Medicine Division Update

Brian Sennett, MD

Sports Medicine Faculty


Brian Sennett, MD


James Carey, MD, MPH


John Kelly, MD


Miltiadis Zgonis, MD


Kevin McHale, MD

The Sports Medicine Division at Penn Orthopaedics has continued to grow and evolve over the past year. Dr. Rahul Kapur relocated to the University of Minnesota to be closer to family and will be missed after a decade of strong contributions to this division. However, with his departure, Dr. Kris Fayock has taken over as Fellowship Director for our Primary Care Sports Medicine Fellowship. Dr. Kate Temme has been appointed to the role of Assistant Fellowship Director and a second fellowship position has been established with a special focus on physical medicine and rehabilitation. The fellowships have blossomed under their leadership and Dr. Miltiadis Zgonis continues with his leadership as our Director of Sports Medicine Education. The primary care fellowship in sports medicine focuses on the non-operative treatments within sports medicine, as well as caring for the medical aspects of our University of Penn student-athletes. This includes sports-related concussion, core muscle injuries, running dysfunction, sports-related skin conditions, and screening for sudden cardiac death. The fellows work closely with our surgical colleagues, physical therapists, and athletic trainers to provide the best treatment plan for our patients and student-athletes.

In March 2019, the team assembled to host the sixth annual Throwing Symposium. This symposium has become an established outlet for education, discussion, and thought provocation with respect to the throwing athlete. It is a one-day conference dedicated to learning about the latest tools and techniques for enhancing performance and treating injuries in the throwing athlete. Through a series of panels, presentations and debates, wide range of topics are discussed to advance injury treatment and optimize performance for throwing athletes. The program chair is Dr. John D. Kelly IV and the course Co-chairmen are Kyle Schaeffer, ATC and Miltiades Zgonis, MD.

The athletic community continues to be served by the Penn Sports Medicine team. The running population was served by Penn Sports Medicine as John Vasudevan, MD served as medical director for the Tri-rock Philly Triathlon held in June, 2016, Alexis Tingan, MD continues to serve as the medical director for the Penn Relays and the Philadelphia Love Run Half-Marathon.

The Penn Athletics Sports Performance Program has continued to grow and expand. This program has been established as a collaborative effort between Penn Athletics and Penn Orthopaedics. During the past year, Dr. Andrea Wieland was brought on as an Associate Athletic Director in Sports Performance. Dr. Wieland is a licensed psychologist, who brings a wealth of experience in high performance environments, utilizing a "team around the team" approach. An Olympic athlete herself, a Division 1 coach, performance consultant to Special Operations soldiers, and business leaders, her most recent role was at IMG Academy in Bradenton, FL, as the Head of Mental Conditioning. Brian J. Sennett, MD, Chief of Sports Medicine, serves as the Head Team Physician for Penn Athletics and spearheads the medical aspects of the program.

The Penn Athletics Sports Performance Program seeks to holistically develops students to be the leaders of tomorrow while being physically, spiritually and emotionally well. Our goals include maximizing a best-in-class partnership with Penn Medicine to provide a state-of-the-art health, safety and sport performance environment for our student-athletes. From use of technology in assessing, educating and developing student-athletes in the areas of strength and conditioning, nutrition, mental health and mental performance, to injury prevention, accelerated return-to-play, and overall care by world-class medical specialists, a partnership with Penn Med presents a distinct and competitive advantage over our peer institutions.

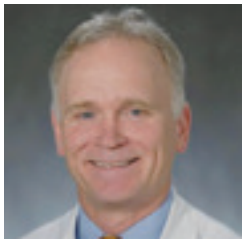
The Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment has continued to grow annually. The center is now recognized as one of the pre-eminent cartilage restoration centers nationally as it has become one of the top volume centers for both autologous chondrocyte implantation and meniscus transplantation surgeries. Dr. James Carey has been recently selected to serve as the lead Principal Investigator and Chairperson of the Clinical Steering Committee for the MACI Pediatric Study – PEAK (PEdiatric Autologous cultured chondrocytes treatment of cartilage defects in the Knee). In addition, Dr. Carey and the Penn Cartilage Center have been chosen to be a host and site, respectively, for the ICRS Traveling Fellows in September and October 2019. The Penn Center for Cartilage Symposium has also continued to grow annually. It has become an international course organized and run by Course Directors James L. Carey, MD, MPH and Robert L. Mauck, PhD. The course in 2018 was attended by a record 200 participants, including physicians, scientists, mid-level providers, nurses, veterinarians, physical therapists, athletic trainers, and students.

It has been an exciting year with more to come in this next academic year. On the horizon is the entire renovation of the Penn Sports Medicine Center, to be completed in 2020.

Hand Division Update

David Bozentka, MD

Hand Surgery Faculty


David Bozentka, MD


David Steinberg, MD


L. Scott Levin, MD, FACS


Benjamin Gray, MD


Robert Carrigan, MD


Apurva Shah, MD, MBA


Stephen Liu, MD

The hand and upper extremity service has had another exceptional year. The program continues to provide the highest quality service in its clinical and academic missions. The success of the section could have only occurred with teamwork and commitment of the entire group. We see this collaboration daily with the remarkable effort from our staff, residents and fellows. It has been exciting to watch the transition of the service with the continued integration with the plastic surgery service and association with our pediatric hand surgeons at CHOP and Shriner's Hospital.

This has been a busy year for our chairman L. Scott Levin MD as president of the American Society for Surgery of the Hand. His presidency has focused on promoting leadership, diversity and inclusion. The added commitment from the ASSH seems to only increase the energy he demonstrates on a daily basis.

Dr. Benjamin Gray MD has led a very productive clinical research program for the hand surgery section overseeing multiple externally funded studies. The group recently started enrolling patients to evaluate digital tomo-synthesis for the detection and case management of scaphoid and distal radius fractures with a comparison to MRI or computed tomography. In August, Mary Dooley joined the hand and upper extremity research team as our Clinical Research Coordinator. Mary is a welcome addition with a strong background in clinical research previously working in biomedical research at the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences. Mary has been instrumental in advancing the numerous ongoing research projects.

The hand transplant team successfully completed their fourth bilateral upper extremity transplant this year. The patient a quadra-membral amputee was similar to our last hand transplantation at Penn in that it involved a transatlantic coordination of the patient travelling from France. The patient is recovering well in her post-operative program.

The Surgical Simulation Committee of the American Society for Surgery of the Hand has created a curriculum to teach psychomotor skills outside the operating room for fellowship and residency programs. The curriculum, termed STEP (surgical training and education platform), was developed under the direction of Ranjan Gupta MD. The Penn in addition to Stanford, Wash U, Beth Israel, and Harvard are several sites chosen to develop construct validity. Residents, fellows and attending surgeons will be evaluated to establish normative data. Dr. Stephen Liu with the help of Brandon Haghverdian MD PGY-2 will lead the assessment at Penn.

Under the direction of David R. Steinberg MD, our two hand surgical fellows have continued the strong clinical and academic productivity of the fellowship. Brittaney Behar MD is our first legacy fellow as she is the daughter of Ellen Maitin MD a 1984 Penn Hand Fellow. Brittaney completed her plastic surgical residency at Penn State Hershey Medical Center under the direction of Shane T. Johnson MD a 2014 Penn Hand Fellow. Our second hand fellow, Tamara John MD completed her orthopaedic surgical residency training at Yale University School of Medicine and has accepted a position at Kaiser Permanente in Atlanta, Georgia.

The hand and upper extremity service could not function without the continued support from the superb advance practice providers and administrative assistants. Dr. Levin's service is supported by Christine McAndrew PA-C, Lorna Muramato and Emily Steffenino. At Pennsylvania Hospital, Dr. Gray works closely with Ashley Cleary PA-C, and Mindy Lawson. Dr. Bozentka is aided by Mylinh Nguyen PA-C and Jameelah Johnson. Dr. Steinberg is assisted by Meredith Stackhouse PA-C and Melissa Gonzalez while Dr. Liu is supported by Amanda Fleischut PA-C and Melissa Gonzalez. With this exceptional support and collaboration, the hand surgery section looks forward to another successful year.

Shoulder and Elbow Division Update

David Glaser, MD

Shoulder & Elbow Faculty

David Glaser, MD

G. Russell Huffman, MD, MPH

Andrew Kuntz, MD

It has been another outstanding year for the Shoulder and Elbow division of the Department of Orthopaedic Surgery in the Perelman School of Medicine at the University of Pennsylvania. With continued commitment to manage the most complex cases, the section's tertiary referral network has dramatically increased along with the complexity of cases. In 2018, the group performed over 11,000 visits and performed over 1000 surgical cases with revision shoulder arthroplasty and elbow surgery seeing increased volume.

Now in its third year, and in collaboration with our French colleagues, we offer our fellow an opportunity to visit world leaders in shoulder surgery. Greg Gomez followed Chad Myeroff (F'17), and Josh Rogozinski (F'18) spending three weeks visiting academic centers in Monaco and France. Director of our Fellowship, Russell Huffman continues to coordinate the next generation of academic surgeons, with our last several fellows joining teaching programs. Past fellow, Mohit Gilotra (F'15) won the 2018 ASES Charles Neer award and Chad is in academic practice at the University of Minnesota.

As director of research, Andy Kuntz is leading our research effort, with close collaboration with Louis Soslowsky and others in the McKay Research Laboratory. Together, we help form one of the largest shoulder research laboratories in the world. In addition to smaller grants, we now have three funded prospective clinical research studies in our division. One of the clinical research studies is a multi-center trial, which is the direct result and translational follow-up to basic science research performed in the McKay Lab. We have developed, in conjunction with Mike Hast in the Biedermann Lab, a new biomechanical testing apparatus and protocol currently being used to study reverse glenoid baseplate fixation.

Clinical studies include outcomes using multimodal pain control, transition to outpatient shoulder arthroplasty, and cost efficiency in delivering health care. The Penn shoulder and elbow faculty presented 8 abstracts at national meetings and gave 11 talks at international, national, regional and local meetings in 2018/19.

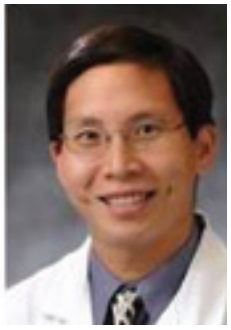
Arthroplasty Division

Arthroplasty Faculty

Charles Nelson, MD

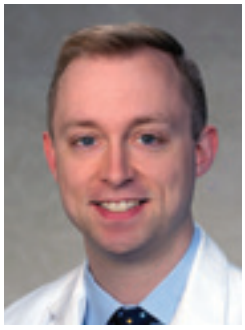
Craig Israelite, MD

Eric Hume, MD



Gwo-Chin Lee, MD

Neil Sheth, MD



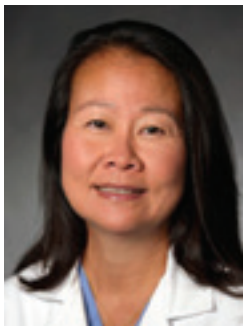
Christopher Travers, MD

Foot and Ankle Division Update

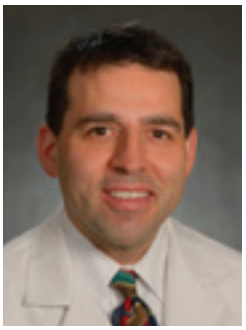
Keith Wapner, MD

Foot & Ankle Faculty

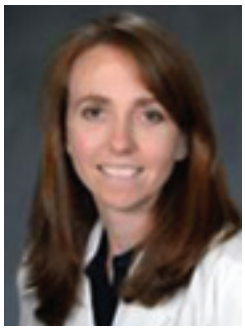
Keith Wapner, MD



Wen Chao, MD



Daniel Farber, MD



Kathryn O'Connor, MD, MSPT

The Foot and Ankle Division has had another productive year. Our current faculty includes Keith Wapner, Wen Chao, Kathryn O'Connor, and Daniel Farber. We continue to serve Center City and beyond with locations at the Farm Journal Building, PMUC, Cherry Hill, Radnor, and Exton and perform surgical procedures at Pennsylvania Hospital, Penn Presbyterian, the surgery center at PMUC, and at Chester County Hospital.

Dr. Keith Wapner has represented Penn Orthopaedics with presentations around the world and nationally. In addition to being Keynote Speaker at the Korean Foot and Ankle Society, where one of our former Penn foreign Fellows, Ho Sung Lee, MD was inducted as President, Dr. Wapner also spoke in China, Israel, and Qatar. He had an opportunity to honor his mentor, Dr. Roger Mann, and his innumerable contributions to the foot and ankle orthopaedic community in a tribute at the AOFAS Summer meeting in Boston. He will complete his six year tenure on the managerial board of the AOFAS Journal, Foot and Ankle International.

Dr. Daniel Farber leads the fellowship and research components of the division. Further, he serves on the AOFAS Education committee and is continuing work on a national accreditation pathway for foot and ankle fellowships in a cooperative venture between the AOFAS and AAOS. He also serves on the AAOS Resolutions committee and was an AAOS Leadership Fellows Program Mentor over the past year. Dr. Farber is the also Associate Editor for Review Articles for the Foot and Ankle Online Journal of the AOFAS. They have published a core group of essential review articles over the past year with two of those coming from Penn.

Dr. Wen Chao remains an Orthopaedic Consultant to the Pennsylvania Ballet. She serves on the Public Education Committee for the AOFAS. She is an active reviewer for the Foot and Ankle International and Foot and Ankle Orthopaedics.

Dr. Kathryn (Kate) O'Connor has rebuilt the foot and ankle education curriculum for the residents, runs the monthly foot and ankle resident and fellow cadaver lab and was awarded an AOFAS grant for her Achilles Research. She serves on the AOFAS Evidence Based Medicine Committee.

The division's research endeavors continue to expand. In addition to ongoing clinical studies on opioid use in foot and ankle surgery, Achilles tendonitis treatments and Achilles rupture treatments, we are involved in several national studies. These include completion of an ongoing study of the STAR ankle replacement, an investigation of the use of bone stimulators for acute operatively treated ankle fractures, and several others in development. The division is also involved in collaborative investigations with the department and of radiology and vascular surgery, looking at the use of weight bearing CT in hallux valgus and genetic markers for Charcot Arthropathy, respectively. We are working closely with Josh Baxter, PhD of Penn's Human Motion Laboratory exploring treatment of chronic Achilles pathology as well as acute Achilles ruptures. A recently completed study looks at the role Orthopaedic surgeons play in influencing patients' choice of footwear and will be a poster at this year's AOA meeting. Another study looking at the adequacy of radiographic images in foot and ankle literature was presented at this years AAOS meeting. Finally, we are nearing completion of a collaboration with the Biedermann lab and Mike Hast, PhD to explore the compression properties of a new plate for fusions of the hindfoot.

The division is actively collaborating with the McKay Lab and Lou Soslowsky, PhD investigating early return to activity after repaired and non-repaired Achilles ruptures with several publications. An ongoing investigation is exploring treatment options for simulated chronic Achilles ruptures in the rat model. There have been multiple studies completed in the McKay Lab over the past year on the effect of smoking on Achilles physiology and healing of ruptures.

Penn's Orthopaedic Foot and Ankle Division has had a successful year and looks forward to another year of growth with the anticipation of a new division chief as well as continuing to provide excellent patient care, service to the orthopaedic community and active research.

Orthopaedic Oncology Division Update

Kristy Weber, MD

Orthopaedic Oncology Faculty

Kristy Weber, MD, FACS

Robert Wilson II, MD

Orthopaedic Oncology at Penn: A basic, translational and clinical approach

The Orthopaedic Oncology clinical service at Penn is comprised of Dr. Kristy Weber and Dr. Robert Wilson who work as part of a multidisciplinary team of caregivers focused on patients of all ages with bone and soft tissue tumors. This includes the care of patients with benign and malignant primary tumors as well as patients with metastatic bone disease. The core team also includes Sarah Borgia, MHA, Administrative Coordinator, Kate Barrie, PA, and April Chambers, RN. Patients are seen 4 days per week with clinic locations at PCAM and Radnor. Surgeries are performed 2-3 days per week at HUP. Dr. Wilson also has a presence at the Philadelphia VA Hospital where he sees orthopaedic oncology patients in addition to patients needing hip or knee arthroplasty for non-oncologic reasons. Patients are also managed in the clinic and OR at CHOP along with Dr. Alex Arkader (orthopaedic oncology/ pediatric orthopaedics) and Amy Rapino, NP. A collaboration with the Philadelphia Shriners Hospital to evaluate and treat patients with bone or soft tissue tumors has continued this year. The Penn Orthopaedic Oncology Visiting Professor for 2019 is Dr. Ginger Holt, Program Director and Chief of Orthopaedic Oncology at Vanderbilt.

The multidisciplinary clinical team that treats patients with bone or soft tissue sarcomas meets weekly on PCAM South 12 for a clinical care videoconference to discuss the presentation and differential diagnoses of new patients as well as the ongoing multimodal therapy for existing patients. A Sarcoma leadership group meets monthly to work on quality initiatives and clinical pathways to improve the overall delivery of care to our patients. An initiative championed by Dr. Ronnie Sebro, MSK radiologist specializing in musculoskeletal tumors, has allowed an efficient process for image-guided needle biopsies for patients with bone and soft tissue tumors. Obstacles have been eliminated and now patients can get CT or ultrasound-guided biopsies without pre-procedure testing, often on the same day they are seen in tumor clinic.

Active marketing efforts continue at both Penn and CHOP to expand the reach of the orthopaedic oncology program in the region. Dr. Wilson continues his outreach to orthopaedic and oncology physicians and groups throughout Pennsylvania and New Jersey. In addition, with the addition of Lancaster General and Princeton to the Penn Health Network, we developed care pathways and personal connections to collaboratively diagnose and treat patients with bone and soft tissue tumors.

One of the features that stands out about the Penn Sarcoma program is the presence of a collaborative scientific team focused on new discoveries in sarcoma. The core sarcoma research team is growing and includes Karin Eisinger, PhD, Malay Haldar, MD, PhD, Celeste Simon, PhD, Irfan Asangani, PhD, Margaret Chou, PhD (CHOP), and Nicola Mason, PhD, BVetMed. Recently, we hired an established physician-scientist at CHOP to start July, 2019 named Patrick Grohar, MD. He is RO1 funded for translational work in Ewing sarcoma and will join our research team and see patients at CHOP. Great news to be celebrated this year is the securing of RO1 funding in sarcoma for Karin Eisinger (The role and regulation of Hippo pathway in sarcomagenesis) and Malay Haldar (Regulation of antigen-presenting cells in the tumor environment by retinoic acid). We have innovative clinical trials ongoing for patients with soft tissue sarcoma with the SARC trial combining pembrolizamab and IMRT as well as the immune trial targeting NY-ESO. Dr. Sebro's hypoxia imaging trial for sarcoma is also accruing patients.

Finally, philanthropic support from grateful patients is critical for our research efforts and we are thankful for their generosity. Our patient and family Sarcoma Advocacy group is in their 5th year of organization and planning to support sarcoma research at Penn Med/Penn Vet/CHOP. In 2018, over $110,000 was raised and nearly 1000 people attended the annual Walk/Run. This year the event is June 2, 2019 at Wilson Farm Park in Wayne, PA. More information can be found at www.stepstocuresarcoma.com/

Neuro-Orthopaedic Division Update

Keith Baldwin, MD, MPH, MSPT and David Spiegel, MD

Neuro-Orthopaedic Faculty

Keith Baldwin, MD, MPH, MSPT

David Spiegel, MD

A Holistic Approach to a Challenging Population

The Neuro Orthopedics service at Penn is a dynamic multidisciplinary service that cares for patients with complex orthopedic needs that span multiple traditional disciplines. The service is a "lifespan" service, caring for patients across the lifespan at both the Clinical Practices of the University of Pennsylvania, and the Children's Hospital of Philadelphia. Keith Baldwin, MD, MPH, MSPT is the chief of Neuro Orthopaedics and is one of a handful of orthopaedic surgeons nationally who cares for the spectrum of neuromuscular disorders in both adults and children. Dr. Baldwin works alonside Katie Walizer, PA and Ross Lenzi PA, to provide timely care to adults who have suffered a traumatic brain injury, spinal cord injury, multiple sclerosis, cerebral palsy and a variety of other conditions. This includes direct work with well-known rehabilitation services both inside and outside the system including Penn Good Shepard partners, Moss Rehabilitation, Magee Rehabilitation, and Bryn Mawr rehabilitation among others. On the Pediatric side, Dr. Baldwin works with David A. Spiegel MD to address the musculoskeletal needs in children with a variety of disorders such as Cerebral Palsy, Spina Bifida, Charcot Marie Tooth, Spinal Muscular atrophy, and others. They are supported by Kathy Abel CRNP, Emily Stegonshek CRNP, Andrea Harmony CRNP, and Jessica Staschak, who play a key role in serving this challenging population.

Treating neuromuscular disorders is a team sport, and the neuro orthopedic team is large. The service partners with many other services within Penn Orthopedics to provide cutting edge and high-level care by partnering in the last year with the Adult Reconstruction service, the Hand and Upper Extremity Service, the Ortho Plastics Service, and the Trauma Service. The adult Neuro Orthopedic Service was also invited to provide clinical training to a physiatry fellow last year. On the pediatric side the year was marked by the hiring of a new chief of Physical Medicine and Rehabilitation, Dr. Sally Evans, MD. We look forward to building the service further with Dr. Evans. Additionally, Laura Prosser PhD, PT, has spearheaded a mobile gait lab which provides innovative gait lab services which can be brought "on the go" for clinical evaluations.

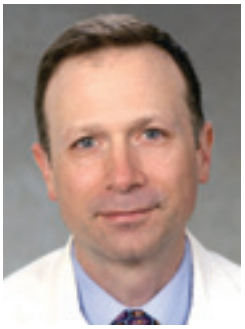
Outreach to outlying institutions has been highly successful. Penn has become the "go to" service for neuro orthopedic care for much of the surrounding area with referrals coming from all major rehabilitations in the area. Effort is ongoing to build a more regional and national presence on the adult and pediatric side. With regard to research on the international front, Drs Spiegel and Baldwin worked with colleagues from Nepal to publish a study utilizing a prospective cohort of children with Cerebral Palsy and compared them to a systematic review of patients in developed nations and found that less neurologic impairment resulted in greater functional disability. Additionally, the service identified a beneficial weight gain in patients with cerebral palsy following spinal fusion for neuromuscular scoliosis. This finding was further explored with the HARMS study group last year. Additionally, the service wrote chapters in neuro orthopedics for Orthopedic Basic Science, Chapmans Orthopedics and Physical Medicine Clinics of North America.

David Spiegel received the AAOS prestigious humanitarian award for his multi decade commitment to overseas work, which has allowed him to bring his expertise and clinical knowledge to children in Nepal, Pakistan and Iraq, as well as a knowledge of polio and late presenting cases of a variety of neuromuscular diseases to our residents and fellows here. The neuro orthopedic service at Penn continues to grow and provide one of a kind care that is not matched in the region.

Orthoplastic Division Update

Dr. Stephen Kovach III

Orthoplastic Faculty



Stephen Kovach III, MD

L. Scott Levin, MD, FACS

Multidisciplinary care of patients has become commonplace within modern medicine.The medical and surgical knowledge required to take appropriate care of patients is too vast for any one physician to master. The combination of the principles of Orthopaedic Surgery and Plastic Surgery or Orthoplastic surgery is the epitome of the multidisciplinary approach to patient care. Orthoplastic surgery harnesses the best aspects of each specialty and applies them to the care of the patient. The care of the orthopaedic patient encompasses meticulous fracture reduction and fixation, hand surgery, well executed arthroplasty, and tumor resection. Without special attention to the soft tissue envelope, each of these endeavors may be for naught. Whether it is microvascular coverage of a IIIB tibia fracture, prophylactic soft tissue coverage to allow for revision knee arthroplasty, or reconstruction of a musculoskeletal tumor defect to allow for limb salvage, the principles are the same: achieve the most functional outcome for the patient with the least risk and morbidity.

The idea of combining the beneficial aspects unique to each specialty in the care of the orthopaedic patient has served as the basis of Penn's Musculoskeletal Institute. At Penn, we have contributed to the evolution of microvascular perforator flaps to minimize patient morbidity, combined ringed fixators and free tissue transfer, used minimally invasive approaches to joint arthroplasty, and allowed for revision arthroplasty with prophylactic soft tissue augmentation. Perhaps the ultimate confluence of orthoplastic surgery has been the successful performance of 4 bilateral hand transplants. The coordination of care between orthopaedic and plastic surgery was paramount to the success of our vascularized composite allotransplantation program. Additionally, a new Targeted Muscle Re-innervation program has been started, with two TMR procedures performed in the acute amputation and revision amputation setting. Penn has remained fertile ground for the care of complex musculoskeletal patients, and orthoplastic surgery has blossomed as part of the Musculoskeletal Institute's dedication to improving care of patients.

In July 2018, the department officially launched the Penn Orthoplastic Limb Salvage Center (POLSC). This unique program, headed by Dr. L. Scott Levin, Dr. Stephen Kovach, and Dr. Samir Mehta, was initialed with the goal of preserving limb function for patients at risk for amputation or loss of limb function due to complex trauma, bone loss, soft tissue compromise, infection, vascular compromise, mal-union and non-union, or complicated sarcomas in a multi-disciplinary, collaborative environment.

Our goal continues to be to deliver the finest orthoplastic care to patients and to grow our individual programs within the Musculoskeletal Institute and Limb Salvage Center. We will continue to work together in a coordinated fashion to attract patients regionally, nationally and internationally. As Orthoplastic surgeons, we have a unique skill set and ability to work together for the betterment of patients and physicians alike.

Children's Hospital of Philadelphia Update

John Flynn, MD and Divya Talwar, PhD, MPH

Pediatric Faculty


John Flynn, MD


Jason Anari, MD


Alexandre Arkader, MD


Keith Baldwin, MD, MPH, MSPT


Patrick Cahill, MD


Robert Carrigan, MD


Benjamin Chang, MD, FACS


Richard Davidson, MD


Vincent Deeney, MD


Malcom Ecker, MD

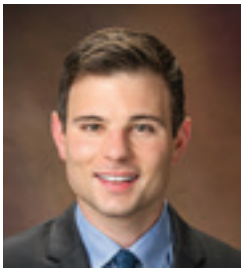

Theodore Ganley, MD


B. David Horn, MD


J. Todd Lawrence, MD, PhD


Bong S. Lee, MD


Ines Lin, MD


Christopher Renjilian, MD


Wudbhav Sankar, MD


Apurva Shah, MD, MBA


David Spiegel, MD


Kristy Weber, MD, FACS


Lawrence Wells, MD


Jennifer Winell, MD

Introduction

The Division of Orthopaedic Surgery at the Children's Hospital of Philadelphia (CHOP) had another successful and productive year of significant growth, accomplishment, and innovation. Upholding our mission and vision to provide the most comprehensive care to our patients, we have continued to expand our clinical, research, and teaching programs. In 2018, US News and World Report ranked the Division of Orthopaedics 2nd in the nation in pediatric orthopaedics.

In 2018, CHOP Orthopaedics continued the Nicholson Visiting Professorship, hosted major conference meetings and Food and Drug Administration (FDA) reviewers, started a FDA investigational drug trial and maintained a device trial, expanded our research coordinator team, obtained significant extramural funding from major funding agencies such as National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), National Science Foundation (NSF), and hired Quality Safety and Value initiatives advisor to improve the efficiency and value initiatives in orthopaedics.

Clinical Program

Our orthopaedics faculty continues to expand and is currently comprised of twenty-seven total providers, which consists of seventeen specially trained pediatric orthopaedic surgeons (twelve operative and five non-operative), five sports medicine-trained pediatricians, two active plastic surgeons, and three transition-to-adult care faculty. Our division welcomed a new faculty member, Dr. Jason Anari, MD (Figure 1) and Dr. Chris Renjilian, MD (Figure 2). Dr. Anari joins our program as new Attending Orthopaedic Surgeon and specializes in the treatment of spine and chest wall disorders in children. Dr. Renjilian is an Attending Physician and will on focus on sports injuries.

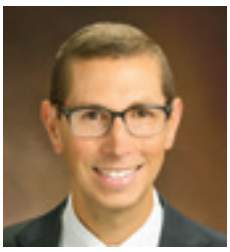


Figure 1. Jason Anari, MD

Figure 2. Chris Renjilian, MD

Education Program

CHOP Orthopaedics currently funds four one-year clinical fellowships and one one-year research fellowship. The 2018-2019 clinical fellows are Ishaan Swarup, MD (Figure 3); Brendan Williams, MD (Figure 4); Michael Hughes, MD (Figure 5); and Christopher Makarewich, MD (Figure 6). This year's research fellow is Dr. Daniel Weltsch, MD from Israel (Figure 7). While at CHOP Dr. Weltsch has focused his research efforts on between basic science projects related to cartilage regeneration and clinical research focused on pediatric trauma, neuromuscular conditions, and sports injuries.

Figure 3. Ishaan Swarup, MD

Figure 4. Brendan Williams, MD

Figure 5. Michael Hughes, MD

Figure 6. Christopher Makarewich, MD

Figure 7. Daniel Weltsch, MD

To celebrate the graduation of the 2017-2018 clinical fellows, the Division hosted the Nicholson Visiting Professor Program and Fellows Graduation & Reunion in June 2018. This year's Visiting Professor was Dr. James McCarthy, who is a professor for the Department of Orthopaedics Surgery at the University of Cincinnati as well as the director of Pediatric Orthopaedic Surgery and the Alvin L. Crawford chair in pediatric orthopaedics at Cincinnati Children's Hospital Medical Center. The program consisted of a mix of short lectures and discussions, a cocktail reception, and research and end-of-the-year remarks from the four fellows.

We continued to hold our Drummond Rising Star Visiting Professorship in October 2018. Current CHOP staff nominate visiting professors. The 2018 Drummond Rising Star Visiting Professor was Benton Heyworth, MD (Figure 8). Dr. Ben Heyworth, Assistant Professor in Orthopaedic Surgery at Harvard Medical School, visited us from Boston Children Harvard. He specializes in pediatric orthopaedic surgery, pediatric orthopaedic trauma, and arthroscopy/sports medicine injuries in the pediatric, adolescent and young adult populations. The Division also continued to host visiting scholars to provide them with an opportunity to observe clinical care of pediatric patients in a high volume, academic setting.

Figure 8. Benton Heyworth, MD

Research Program

Basic Science and Translational Research

This past year, our basic and translational medicine researchers led by Maurizio Pacifici, Ph.D. have made

impressive progress and generated novel, exciting, and far-reaching insights on key aspects of skeletal biology and growth and pediatric musculoskeletal pathologies. Our pediatric musculoskeletal research lab became much stronger with the recruitment of Dr. Fanxin Long (Figure 9) and Dr. Veronique Lefebvre (Figure 10). Our faculty members and their associates, including postdoctoral fellows, visiting scientists and research technicians, continued to tackle and fulfill the goals of several current NIH R01 grants and one Department of Defense (DOD) grant. These biomedical research projects aim to advance current understanding of basic cellular, biochemical and genetic mechanisms that regulate the behavior and function of skeletal forming cells. These basic and key insights and observations are used to predict what may subtend and lead to pediatric pathologies including Multiple Hereditary Exostoses (MHE), Fibrodysplasia Ossificans Progressiva (FOP) and Temporo-mandibular Joint dysfunction.

Figure 9. Fanxin Long

Figure 10. Veronique Lefebvre

Center for Thoracic Insufficiency Syndrome (CTIS) Frontier Translational Research Program

Through funding from the Frontier Program, the Division's Center for Thoracic Insufficiency Syndrome (CTIS) continued developing innovative projects in translational research. The CTIS program strives to develop novel imaging techniques, construct new metrics for clinical outcomes, and establish reliable evidence to support innovative surgical strategies and devices through its research. These efforts are made possible by the collaboration of a multidisciplinary team of specialists from clinical research, image processing, informatics, and basic sciences/biomechanics. Currently, the CTIS Basic Science Lab is developing an animal model of TIS that will provide a platform for testing novel devices. The animal surgeries and biomechanics testing will be performed at Penn Vet's New Bolton Center. In addition, the CTIS team recently engineered surgical instruments with a tensionometer to quantify the force generated by attending surgeons during VEPTR lengthening procedures.

CHOP lost a true giant in the field of orthopaedic surgery with the passing of Robert Campbell, MD, on July 29, 2018. The Campbell Center for Thoracic Insufficiency Syndrome will carry on Dr. Campbell's legacy and continue to grow, strengthened by the Frontier Program funding.

Genetic Research

CHOP Orthopaedics continues to work in collaboration with the Center for Applied Genomics (CAG), led by Dr. Hakon Hakonarson and Dr. Struan Grant, to compile a registry of DNA and RNA samples. These samples are obtained from patients and families with a variety of orthopaedic conditions including adolescent idiopathic scoliosis (AIS), osteochondritis dissecans (OCD) of the knee, and multiple hereditary exostoses (MHE). The team is investigating further genetic characterizations of the EXT1/EXT2 mutations harbored by each exostosis and identify second hit(s) across exostoses from the same patient. This pilot project represents the first biomedical research focused on MHE and will provide novel and broadly relevant information. The goal is to translate the findings to prognostic tools based on the severity of the disease and to identify therapeutic means to counter the effects of EXT1/EXT2 plus "second hit" mutations.

Orthopaedic Engineering

Dr. Saba Pasha, Director of Orthopedic Engineering, continues her research on the application of 3D imaging and computer simulation in surgical planning, use of predictive models in surgical decision-making, and the exploration of gait and motion analysis for a more personalized treatment. For her research, Dr. Pasha was awarded grants by POSNA and SRS.

With new emerging technology, such as the EOS x-ray imaging system, comprehensive information about a patient's condition is now readily available. Dr. Pasha's work utilizes advanced imaging and motion analysis to collect data on a range of conditions and patient populations.

Clinical Research

The Division of Orthopaedic Surgery is currently conducting 198 IRB-approved clinical research projects. This includes 80 prospective and observational studies. CHOP Ortho faculty are also members of a number of multicenter study groups, including the Harms Study Group (HSG), Research in Osteochondritis Dissecans of the Knee (ROCK), SCFE Longitudinal International Prospective Registry (SLIP), The Fox Pediatric Spinal Deformity Study (Fox PSDS), Pediatric ACL: Understanding Treatment Operations (PLUTO), Medial Epicondyle Outcomes Multicenter (MEMO) study and International Hip Dysplasia Institute (IHDI). Investigators within the division have been awarded funding from both internal and external sources to conduct these studies. In 2017, the Division published over 160 articles in major orthopaedic journals, including JBJS, JAMA Pediatrics, Annals of Internal Medicine, JPO, and CORR. Members across our division presented 148 presentations at international and national conferences last year alone.

The Division successfully continues to award the annual Benjamin Fox Fellowship Award for medical students who are interested in conducting a year of clinical research within orthopaedics. In July, Scott Lavalva (Perelman School of Medicine at the University of Pennsylvania), Blake Meza (Perelman School of Medicine at the University of Pennsylvania) and Ronit Shah (University of Toledo), were awarded with the fellowship (Figure 11-13).

Recognition and Achievements

Our faculty have assumed several leadership roles within the pediatric orthopaedic community over the past year.

Figure 11. Scott Lavalva

Figure 12. Blake Meza

Figure 13. Ronit Shah

Alexandre Arkader, MD was the international faculty "XXXVIII Congresso Annual Sociedad Argentina de Ortopedia y Traumatologia Infantil". Dr. Arkader continues to serve as a reviewer for Journal of American Academy of Orthopaedic Surgeons, Journal of Bone and Joint Surgery Essential Surgical Techniques, BMC Musculoskeletal Disorders and Journal of Children's Orthopaedics.

Keith Baldwin, MD, MSPT, MPH is the Associate Director of Orthopaedic Trauma in the Division of Orthopedic Surgery. Dr. Baldwin continued his term as president of the Orthopaedic Rehabilitation Association. He currently serves as a reviewer for a number of journals including the BMC Medical Education, BMC Musculoskeletal Disorders, Journal of Bone and Joint Surgery—American, and the American Academy of Pediatrics. He also serves as associate editor for Journal of Orthopedic Trauma and an editorial board member of the American Journal of Orthopedics, Current Orthopaedic Practice and World Journal of Orthopedics. Dr. Baldwin is an active member of CORTICES study group.

Patrick Cahill, MD continued his term as chair of the SRS research grants committee and is a member of POSNA's Quality, Safety, Value Initiative Committee. He continues to serve as an Associate Editor for Spine Deformity Journal and as a reviewer for the Journal of Bone and Joint Surgery

American and the Thrasher Research Fund. Dr. Cahill is an active member in the Harms Study Group, Children's Spine Study Group, and Fox Pediatric Spine Deformity study group, which are multi-center groups prospectively researching care improvements for complex pediatric spine deformities. He is now the Director for Center for Thoracic Insufficiency Syndrome.

Robert Carrigan, MD continues to serve on the AAOS CAQH Test Validation Committee, AAOS Appropriate Use Committee, and POSNA Resident Newsletter Committee. He also serves as a reviewer for Journal of Hand Surgery and Clinical Orthopaedics and Related Research.

Richard Davidson, MD has continued to serve as an associate editor for Foot & Ankle, International. He also serves as a reviewer for Clinical Orthopedics and Related Research and Advances in Orthopaedic Society.

B. David Horn, MD continues to serve as a reviewer for journals, such as Clinical Orthopaedics and Related Research (CORR), Pediatric Emergency Medicine, and Pediatrics.

Jack Flynn, MD, Chief of the Division of Orthopaedics, continues to serve his 10-year term as a Director of the American Board of Orthopaedic Surgery. Dr. Flynn is co-editor of Lovell and Winter's Pediatric Orthopaedics, Rockwood's Fractures in Children, Operative Techniques in Pediatric Orthopaedics. He is President of the Children's Spine Study Group and is active in the Harms Study Group, a multicenter collaboration of researchers studying care improvements for pediatric spine deformity surgery. In the past year, Dr. Flynn also was invited as the visiting professor at Nemours/duPont Hospital for Children, Seattle Children's Hospital, Johns Hopkins, University of Miami, University of Utah, St. Luke's Medical Center, and Riley Children's Hospital.

Theodore Ganley, MD is the Sports Medicine Director at CHOP, continued growth of clinical, research initiatives. Dr. Ganley has continued in several leadership roles with national organizations, such as the chairman for the POSNA Evidence Based Practice Committee, second vice president of the Pediatric Research in Sports Medicine (PRISM) group, co-founder and executive board member for the Research in Osteochondritis Dissecans of the Knee (ROCK) group, executive committee member for the American Academy of Pediatrics, advisory board member for the International Pediatric Orthopaedic Symposium, and program chair for the Philadelphia Orthopaedic Society. Along with his leadership roles, he continues to be actively involved in biomechanical studies utilizing cadaver specimens in collaboration with the Biedermann Lab for Orthopaedic Research and Human Motion Lab. Additionally, he is the site leader for the FDA clinical trial for studying the efficacy and safety of autologous cultured chondrocytes on porcine collagen membrane (MACI).

John Todd Lawrence, MD, PhD continued his collaborative work with Dr. Leo Han at Drexel University. Funded by the National Science Foundation, the project focused on conducting in vitro studies for a novel cartilage repair strategy. He also served as an international faculty member at the Salzburg Medical Seminar in Pediatric Orthopedics in Salzburg, Austria. Dr. Lawrence is an active member of sports medicine multicenter research groups such as PLUTO and he leads a 12-site study group called MEMO. He continues to serve as a reviewer for the American Journal of Sports Medicine (AJSM) and Journal of Shoulder and Elbow Surgery (JSES).

Wudbhav Sankar, MD is the Director of the Young Adult Hip Preservation Program at CHOP. Dr. Sankar currently serves as the chair of the POSNA Fellowship committee and co-director of the International Hip Dysplasia Institute. He remains active in several study groups including Academic Network of Conservational Hip Outcomes Research (ANCHOR), SCFE Longitudinal International Prospective Registry (SLIP) and International Perthes Study Group. Dr. Sankar is currently a reviewer for the Journal of Bone and Joint Surgery, Journal of Pediatric Orthopaedics, and an Editorial Board Reviewer of Techniques in Orthopaedics.

Apurva Shah, MD, MBA started his tenure as the current Director of Clinical Research. He continued to serve as co-PI on the POSNA Directed Research Grant entitled, "Improving value delivery in pediatric distal radius fracture care." The grant aims to asses practice pattern variation and compare treatment costs across institutions and low- and high-volume centers. Dr. Shah also received a new grant as co-PI from Orthopaedic Trauma

Association titled, "Opioid utilization after rotational ankle fractures". He continued to serve as team leader and traveled to Sigua Tepeque, Honduras for a pediatric hand surgery medical mission.

David Spiegel, MD continued his work with the Children's Hospital of Philadelphia Global Health Pilot Grant. He currently is the chair for International Scholars Program at the American Academy of Orthopaedic Surgeons (AAOS). In collaboration with Dr. Bibek Banskota in Nepal, Dr. Spiegel is conducting the longest follow-up in the world's literature of patients treated by the Ponseti method in a low-middle income country. Dr. Spiegel continued to be an active academic internationally, giving lectures in Iraq, Nepal and Pakistan.

Lawrence Wells, MD is the Associate Director of the Sports Medicine Performance Center at CHOP and Director of Quality, Safety, Value, and Patient Experience in the Division of Orthopaedic Surgery. Dr. Wells currently serves as the President of Board of Directors for the Philadelphia Orthopaedic Society

Chief's Corner: Academic Chief Update

Luke A. Lopas, MD, Kristin L. Buterbaugh, MD, and Nicole A. Zelenski, MD

As our tenure as academic chief residents come to a close, it is natural to reflect on the past year. First and foremost, we would like to thank Drs. Levin, Israelite, Ahn, and Milby for their support and mentorship. Thank you to the faculty, staff, and most importantly our co-residents for continuing to work diligently with us to continue to make Penn Orthopaedics a great place to work and train. While it is both impossible and unnecessary to completely overhaul the educational program in a single year, we hope that several of the initiatives we have focused on below have contributed to the continual and incremental improvement of the residency program and department as a whole.

One of our main initiatives was to revitalize a regular journal club program. This received broad support and participation amongst both residents and faculty. We chose to have two parallel types of journal clubs; 1) journal clubs focusing on how to read, critically analyze, interpret, and integrate data, and 2) journal clubs to cover both historical articles of importance and new and emerging literature in a specific subspecialty. The journal clubs focused on developing the skills to critically read the literature stemmed from a visit from Dr. Seth Leopold, the Editor in Chief of Clinical Orthopaedics and Related Research in the spring of 2018. Dr. Leopold was generous enough to provide a curriculum he has developed to systematically cover how to read and interpret articles of various types. In order to make this a more robust experience, Drs. Nicole Zelenski and Matthew Winterton applied for and received a grant to support resident journal clubs from the Journal of Bone and Joint Surgery. These funds have been important in making this a quality experience. So far, we have had numerous subspecialty journal clubs with significant investment and involvement from faculty. We would like to thank the faculty who have hosted and helped organize journal clubs for their dedication to our education.

Another area of focus for this year involved optimizing resident utilization of our research laboratories. Residents who are able to secure extramural funding are now able to schedule consistent and structured research time longitudinally throughout the year. As more of our residents take advantage of the many resources available to us, including but certainly not limited to the McKay, Biedermann, and Human Motion labs, the new initiative allows them to carry their work through to completion and publication.

Engaging with the international community provides substantial benefits for our department, trainees, and hopefully those abroad through not only the provision of medical care, but also through the robust and vibrant exchange of ideas. In addition to several of the faculty who are consistently involved in international work, we have sought to expand the opportunities for residents to participate in this work. Through the generous support of the Biedermann family, there is funding available for residents to travel to established sites abroad and participate in surgical mission trips. Two new overseas opportunities saw resident involvement this year. One took place in Azua, Dominican Republic, where two chief residents and Dr. Samir Mehta joined Community Empowerment and a group out of Rush University in Chicago for a trip to provide orthopaedic care to members of the local community who would otherwise not be able to afford or obtain care. The second involves a budding relationship with Dr. Louis Bahamonde of the University of Santiago, Chile. Dr. Bahamonde graciously offered to host two residents at the university hospital for two weeks, where the residents had opportunity to engage in patient care and learn from the diverse and talented faculty of the University of Santiago. It is our hope that the residents who are fortunate enough to have these experiences will give back to the fund, allowing future residents to participate in these impactful experiences as well.

Again this year, as in past years, our visiting professor program continues to be exemplary with educators coming not only from across the United States, but from around the globe. These visits provide the needed opportunity to expand our view outside of the microcosm of Penn Orthopaedics and learn from experts who often have performed seminal work or made truly outstanding contributions to the field.

It is hard to believe that our time as chief residents is nearing an end. It is our hope that throughout this year we were able to play a small part in continuing the tradition of excellence of our residency program. We look forward to the new heights that the program will undoubtedly continue to reach and want to thank everyone for their support. We wish the best for next year's chiefs.

Alumi Residents—Where are They Now?

Matthew Counihan, MD

Karen J. Boselli, MD

Fellowship: Shoulder, Elbow, and Sports Medicine at Columbia University

Current Employment: Concord Orthopaedics, Concord, NH

How has training at Penn impacted your practice?

Not a week goes by without telling a story of something from residency that impacted me personally or professionally. My training at Penn taught me critical thinking. I learned to challenge myself daily, yet know my limits. I also learned to treat every patient, no matter how difficult, with respect.

What have you learned in your first decade of practice?

The learning curve remains extremely steep. Ten years ago I thought that I knew all that I needed to start my career. In a sense, I did...but there is always a new challenge to face and nothing ever becomes "routine" in practice. I have learned to stay confident but extremely humble. I'm also extremely grateful that I chose a group with wonderful senior partners who continue to mentor me; they provide an incredible support system and a wealth of knowledge that you can only obtain from years in practice.

What advice would you give residents?

Take advantage of having some of the best mentors in the world available to you. Soak of every bit of knowledge they have to give, and don't hesitate to ask what you think may be a stupid question. If at first you feel humiliated for asking, you'll still be glad in the end that you know the answer. Spend less time worrying about having the knife in your hand, and more time memorizing every step and taking in every pearl that your attending has to give. You'll have plenty of time in fellowship and practice to continue to hone your technical skills, but only one chance to operate side by side with these brilliant surgeons.

Andrea L. Bowers, MD

Fellowship: Sports Medicine and Shoulder Surgery at the Hospital for Special Surgery

Current Employment: Burlington County Orthopaedic Specialists, Mt. Laurel, NJ

How has training at Penn impacted your practice?

I specifically chose to train at Penn because I ultimately wanted to practice near my hometown of Moorestown, NJ. I knew that the Penn pedigree would both open doors for local job opportunities and be recognized by patients as "brand name." I also appreciate that I have direct access to my Penn mentors for easy referrals for complex cases when necessary.

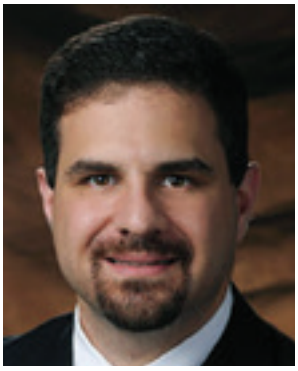
What have you learned in your first decade of practice?

Never be the first nor the last to adopt a new technology. Residency and fellowship provided a great foundation, but orthopaedics is always evolving, and it is critical to push your skill set beyond your comfort zone when necessary.

What advice would you give residents?

Take notes on EVERYTHING. Your attendings are dropping pearls of wisdom everywhere. You never know what your practice will look like down the road, and the more variety of cases you are willing to take on, the faster your practice and patient base will grow.

Gregory K. Deirmengian, MD



Fellowship: Hip and Knee Reconstruction, Rothman Orthopaedic Institute

Current Employment: Rothman Orthopaedic Institute, Philadelphia, PA

Harish S. Hosalkar, MD

Current Employment: Scripps Health, San Diego, CA

Jonas L. Matzon, MD

Fellowship: Hand Surgery, Curtis National Hand Center, Union Memorial Hospital

Current Employment: Rothman Orthopaedic Institute, Philadelphia, PA

SangDo Park, MD

Fellowship: Sports Medicine, Kerlan-Jobe Orthopaedic Clinic

Current Employment: St. Vincent Medical Center, Los Angeles, CA

How has training at Penn impacted your practice?

Training at Penn has allowed me to practice general orthopedics because it gave me a well-rounded curriculum. More importantly, my experiences at Penn have allowed me to develop many good habits and to be thorough in all matters related to patient care. I learned a lot of good habits from the attendings and my senior residents. This has carried over into allowing me to provide good care for my patients and to stay out of trouble.

What have you learned in your first decade of practice?

In my first decade of practice, I learned that nothing stays constant. Everything changes...the practice environment, business side of medicine, what we know of diseases, the surgical techniques, etc. I have to constantly adapt and learn various things. I also learned that practice of medicine is humbling. I did not always get the results I had wanted/anticipated. I tried my best to learn from my past experiences to become a better surgeon. Most importantly, I truly learned the significance of what we do as orthopedic surgeons. The bond that we form with our patients and the work we do for our patients are amazing. I did not realize this as a resident when more patients equals more burdensome work. I now feel very fortunate and privileged to be able to take care of each one of my patients.

What advice would you give residents?

Get exposed to as many different aspects of orthopedics as you can - you never know what kind of practice you will end up in. Scrub in as many cases as you can but also be eager to cover clinics - what you learn in clinics is just as important as what you learn in the OR. Learn from the surgical complications you see - you will get them as well and will need to learn how to identify and manage them.

Neil Sheth, MD

Fellowship: Adult Hip and Knee Reconstruction, Midwest Orthopaedics at Rush University

Current Employment: University of Pennsylvania, Philadelphia, PA

How has training at Penn impacted your practice?

My time at Penn was critical for my preparation for fellowship training where you have a very short period of time to demonstrate to your new mentors that you can operate. Training at Penn has adequately prepared me for every aspect of my career development.

What have you learned in your first decade of practice?

Learn as much as you can in residency and in fellowship maximize the amount of time you spend pre-operatively planning for cases. This allows you to do all of your thinking before a procedure the OR is not a place to think, it is a place to execute a well thought out plan.

What advice would you give residents?

Be thankful that you get to follow a very rigorous training program in order to provide excellent care. Orthopaedic

surgeons in most countries outside of the US do not have the privilege of training for as long as we do and don't have the same written and oral board requirements they are often turned out into practice well before they are ready. Take comfort in the fact that training at Penn allows you to be prepared for the future evidenced by the fact that for the past 5 years, 3-4 graduating residents have been offered a job at their fellowship. You learn how to operate in residency, not in fellowship fellowship is for fine tuning your decision making. Penn is an outstanding program to train.

Eric Ricchetti, MD

Fellowship: Shoulder and Elbow Surgery, Rothman Orthopaedic Institute

Current Employment: Cleveland Clinic, Cleveland, OH

Visiting Professor Series 2018-2019

October 11, 2018

Dr. Rush Fischer

Chief of Spine Section, Chrisitiana Care Health Services, Newark, DE
(written by Sachin Gupta)

The University of Pennsylvania Department of Orthopaedics was honored to welcome Dr. J. Rush Fisher, the Chief of Spine at Christiana Care Health Services. Dr. Fisher earned his bachelor's degree at Dartmouth College before attending the University of Pennsylvania School of Medicine. Following medical school, he then completed orthopaedic residency at Hospital of the University of Pennsylvania followed by the prestigious Henry Bohlman fellowship in reconstructive spinal surgery at Case Western Reserve University School of Medicine. He then taught as professor of orthopaedic surgery at the University of Kentucky School of Medicine. In 2002, Dr. Fisher co-founded the Christiana Spine Center in Newark, Delaware, where he has served as the chief of spine since 2007. He is a member of the American Academy of Orthopaedic Surgeons,American Medical Association, Medical Society of Delaware, North American Spine Society, and the Orthopaedic Trauma Association.

The morning began with an educational lecture regarding the twenty-year evolution of spinal care, highlighting the ever-changing nature of the spine world, and how techniques have improved drastically over the last several decades. Dr. Fisher also provided a thorough history regarding the past, present, and future of the Christiana Healthcare System. He discussed some of the daily tasks and meetings that he conducts, as head of the spine division, to ensure that everything runs smoothly on the spine service.

In addition, Dr. Fisher shared several informative spinal trauma cases prompting discussion from the faculty and residents alike.These cases illustrated the complexity of spinal trauma and deformity that he manages on a daily basis. Some of these cases helped detail the advances in spinal fixation techniques over time including development of sacropelvic fixation, use of wires followed by advancement to pedicle screws, and even the use of bisphosphonates.

To finish the morning's session, Dr. Fisher led a case-by-case discussion regarding complications, indications, and intricate surgical planning for procedures ranging from ACDF to multilevel thoracolumbar fusions for spinal deformity. With his experience and knowledge, he was able to provide insight into the principles of diagnosis and treatment of some very complex spine deformity cases. His visit was both an honor and a privilege for the department, and we look forward to continued collaboration in the future.

October 18, 2018

Dr. Andrew Spitzer

Co-Director Joint Replacement Program, Cedars-Sinai Orthopaedic Center, Los Angeles, CA
(written by Ryan D. DeAngelis)

Dr. Spitzer's career began on the West Coast, where he attended medical school at the University of California Los Angeles School of Medicine. He then went on to train in orthopaedic surgery at the Hospital of the University of Pennsylvania. Following his time spent here, he completed the esteemed joint arthroplasty fellowship at Brigham and Women's Hospital in Boston. Dr. Spitzer now serves as the Co-Director of the Joint Replacement Program at Cedars-Sinai Orthopaedic Center in Los Angeles, California.

Outside of the operating room, Dr. Spitzer pursues his research interests in hip and knee surgery implant design, blood management in total joint arthroplasty, thrombosis prevention, and the non-operative management of osteoarthritis in both the hip and knee. Dr. Spitzer also serves as a reviewer for some of the highest-impact orthopaedic research journals, including *The Journal of Bone and Joint Surgery*, *Journal of the American Academy of Orthopaedic Surgeons*, *Clinical Orthopaedics and Related Research*, *Journal of Knee Surgery*, and *Orthopedics*.

Dr. Spitzer's expertise in joint arthroplasty has garnered international recognition, which was further solidified after he became one of the select few of American orthopaedic surgeons to be named an honorary member of the Israel Orthopaedic Association. Since first becoming involved with the organization in 2003, Dr. Spitzer has made over a dozen trips to Israel. Given his long-term commitment to educating residents, fellows, and attending orthopaedic surgeons in both the operating room and classroom, the Israel Orthopaedic Association was honored to present him with this award in Tel Aviv.

Before beginning the morning's lectures, Dr. Spitzer briefly reflected on his own time spent sitting in the Agnew-Grice Auditorium and paid tribute to the wealth of knowledge he attained during his time as a Penn Orthopaedics resident. To begin his first lecture, Dr. Spitzer reviewed key demographic information regarding osteoarthritis of the knee and total knee arthroplasty, as well as patient satisfaction rates with total knee arthroplasty. He then discussed why total knees fail and highlighted the actual goals of a total knee arthroplasty. Dr. Spitzer continued by comparing and highlighting the data surrounding measured resection and gap balancing. Lastly, Dr. Spitzer reviewed his own approach to total knee arthroplasty using a mechanical axis gap balancing technique.

Dr. Spitzer's second lecture turned the audience's attention away from the operating room and focused on delaying a total knee arthroplasty. Here, Dr. Spitzer demonstrated how viscosupplementation is effective across the entire spectrum of osteoarthritis of the knee. This intervention serves to improve synovial fluid rheology, reduce inflammation, and may even help preserve cartilage. These injections ultimately decrease pain and in turn, delay the need for total knee arthroplasty. Dr. Spitzer closed his talk by highlighting how injection therapy bridges the gap between non-invasive measures and total knee arthroplasty.

Both lectures generated interactive, thought-provoking discussion amongst faculty and residents alike. The group then had the opportunity to work alongside Dr. Spitzer directly in a Sawbones total knee arthroplasty workshop where Dr. Spitzer demonstrated the techniques he discussed in his first lecture. The residents truly valued this experience, as it is extremely uncommon to have the opportunity to work so closely with an expert from another institution.

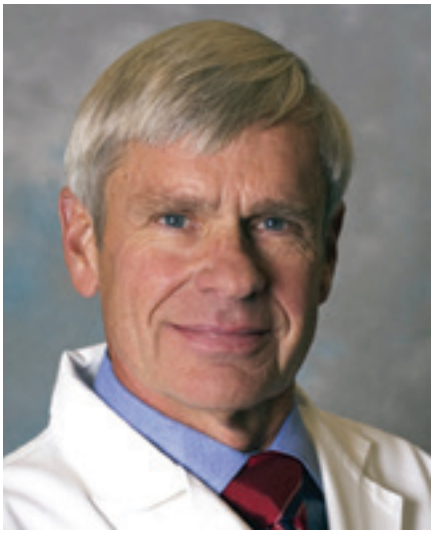
From Dr. Spitzer's insightful lectures, ensuing thoughtful discussion, and hands-on Sawbones lab, the morning was full of opportunity to further increase the department's knowledge in joint arthroplasty.

Figure 1. Dr. Spitzer and residents discussing total knee arthroplasty techniques in Sawbones lab

November 1, 2018: 19th Annual Dr. Ernest J. Gentchos Lectureship

Dr. Frederick Matsen III

Professor of Orthopaedic Surgery, University of Washington School of Medicine, Seattle WA and Couglas T. Harryman II Endowed Chair in Shoulder and Elbow Research
(written by Liane Miller)



Dr. Matsen earned his M.D. at Baylor University School of Medicine, followed by an internship at John Hopkins hospital and two year clinical associate position at the National Institutes of Health. He then completed his residency training in Orthopaedic Surgery at the University of Washington Medical Center in Seattle. He is a tenured full professor in the Department of Orthopaedics and Sports Medicine and the holder of the Douglas T. Harryman II Endowed Chair in Shoulder and Elbow Research at the University of Washington Medical Center.

Dr. Matsen is an internationally recognized expert in reconstructive shoulder surgery and pioneered the 'ream and run' procedure for patients desiring a high level of physical activity and wishing to avoid the potential risks of a plastic socket and bone cement in traditional shoulder arthroplasty.

His clinical interested include reconstructive shoulder surgery, major rotator cuff deficiencies, and complex revision shoulder surgery. Most importantly, he strives to provide individualized treatment to the specific needs of his patients in an evidenced-based practice. Not surprisingly, he has received recognitions in teaching and research from the University of Washington, as well as the American Orthopedic Association, the Association of Bone and Joint Surgeons, and the American Shoulder and Elbow Surgeons. With over 200+ peer reviewed publications to date, he is a true leader and innovator in his field.

During his lecture at Penn, Dr. Matsen provided a patient-focused discussion on his approach to patient care, highlighting the difference between what physicians do 'to' the patient versus what should be done 'for' the patient. He then examined a number of his own cases, and discussed how Orthopaedic Surgeons can learn from 'failures' in order to provide better, more appropriate care in the future.

Dr. Matsen's patient-centered focus and intellectual curiosity are a perfect complement to highlight the legacy of the annual Ernest J. Gentchos Lectureship. This lectureship is a proud tradition at Penn Orthopaedics, established in 2001 to honor the enormous contributions of our own Dr. Ernest Gentchos. As faculty at Penn, Dr. Gentchos advocated that superior patient care relies on studying one's patient, keeping an open mind, and challenging every idea. In addition to his countless academic achievements and clinical contributions, Dr. Gentchos carried his humanitarian passions outside the realm of medicine through his establishment of several endowed scholarships. On a yearly basis, Dr. Gentchos sponsors several medical school, college, and high school students, and maintains that the greatest gift you can give anyone is that of education. Always thirsting for knowledge, it is never out of the ordinary to see Dr. Gentchos reading a journal article or opening a textbook off of the shelf. His mantra of "What did you learn today?" serves as a reminder that we are forever students in the field of orthopaedics. The University of Pennsylvania Department of Orthopedics was truly fortunate to host Dr. Matsen for this lectureship.

November 29, 2018: Inaugural San Baw, MD Honorary Lecture in Orthopaedic Innovation Dr. Bartek Szostakowski

Royal National Orthopaedic Hospital, UK
(written by Lauren Boden)

The University of Pennsylvania Department of Orthopedic Surgery was honored to welcome Dr. Bartlomiej Szostakowski for its inaugural Dr. San Baw GM'58 Honorary Lecture in Orthopedic Innovation. Dr. Szostakowski works at the Department of Sarcoma, Soft Tissue and Bone Tumors at the Maria Sklodowska Curie Memorial Cancer Centre and Institute of Oncology in Warsaw, Poland. He is a graduate of the Medical University of Gdansk, Poland and completed a residency in trauma and orthopedics at the Infant Jesus Teaching Hospital in Warsaw. He was able to train in the UK with some of the most prestigious surgeons at the Royal National Orthopedic Hospital in Stanmore, where he holds post of the honorary research fellow.

Figure 1. Dr. San Baw…

This lectureship was established in memory of Dr. San Baw, a Penn Alumnus of the graduate school of medicine from Burma who helped pioneer the use of ivory hip prostheses for femoral neck nonunion and also developed a new technique for treating infantile pseudoarthrosis of the tibia. This lectureship was made possible by the generous contributions of Dr. San Baw's son, Professor Myint Zan. The University of Pennsylvania Department of Orthopedics was delighted to welcome Professor Myint Zan back to Philadelphia to participate in the inaugural lectureship.

Figure 2. Dr. Bartlomiej Szostakowski

In his lecture, titled "Dr. San Baw: A Son's Tribute", Professor Myint Zan gave a passionate account of Dr. San Baw's life story, from humble beginnings in Burma through his career as an orthopedic surgeon. With a spark in his eyes, Professor Myint Zan recounted his late father's journey to the United States and his subsequent contributions to orthopedics made possible by a strong work ethic and a creative mind. Although he may not have received as much press as other innovators and many of the original records of his contributions have been lost, his memory and eye for innovation will live on with this lectureship.

Dr. Bartlomiej Szostakowski became connected with Professor Myint Zan after a temporary interest in Dr. San Baw's career led to an email conversation. This conversation about medical history soon blossomed into a re-discovery of Dr. San Baw's orthopedic contributions. Because of their connection

Figure 3. Dr. Bartlomiej Szostakowski and Professor Myint Zan with Dr. Levin

and shared interest in sharing the story of Dr. San Baw, we had the pleasure of hosting Dr. Bartlomiej Szostakowski for the inaugural lecture, entitled "Dr. San Baw

The Forgotten Innovator in Orthopedic Biologic Reconstruction." Dr. Szostakowski emphasized the importance of using history to guide research. Reflecting on Dr. San Baw's work with ivory and the relatively low infection rates of his hip prostheses, he proposed potential modern implications for artificial recreation of ivory in the lab to improve current issues in orthopedic adult reconstruction.

The University of Pennsylvania Department of Orthopedics was truly fortunate to have Dr. Bartlomiej Szostakowski as the inaugural Dr. San Baw Honorary Lecture in Orthopedic Innovation, with a special introduction by Dr. San Baw's son, Professor Myint Zan.

December 13th, 2018

William Garrett, MD, PhD

Professor of Orthopaedic Surgery, Assistant Professor of Cell Biology, Duke University School of Medicine, Durham, NC
(written by David Falk)

A true clinician scientist hailing from Duke University Medical Center, Dr. Garrett is a leader in the field of sports medicine and an expert in ACL reconstruction. His impressive journey began with an undergraduate degree in chemistry from the University of North Carolina in Chapel Hill. He went on to participate in the NIH Medical Scientist Training Program (MSTP) program and obtained a PhD in Cell Biology and Anatomy as well as MD from Duke University. He then completed his Orthopaedic Surgery Residency at Duke in 1982, where he remained on faculty.

Dr. Garrett has since gone on to obtain numerous awards and honors, most notably AOA North American Traveling fellow, ABC traveling fellow, and the Kappa Delta Award. He is a past president of the American Orthopaedic Society for Sports Medicine, and has also been recognized with multiple teaching awards from the Duke Department of Orthopaedic Surgery.

Today, Dr. Garrett divides his time between his busy surgical practice and his work in the Michael W. Krzyzewski Human Performance Laboratory, affectionately known as the K-Lab. Through research focusing on knee and muscular injuries, Dr. Garrett has made significant contributions to the field of sports medicine in both the basic science and clinical realms.

Figure 1. From left to right Dr. Levin, Dr. Garrett, and Dr. Zgonis

Dr. Garrett delivered two highly educational lectures on ACL injuries and modes of reconstruction. He later discussed ACL reconstruction techniques, using his own research to demonstrate the benefits associated with anatomic placement of the ACL graft. Dr. Garrett humbly examined how his own surgical approaches have evolved over the years, and after reviewing his own technique to produce an anatomic graft he opened the floor for a thought-provoking question and answer session. Dr. Garrett's expertise and sense of humor were on full display as he fielded questions from residents and faculty. Dr. Milt Zgonis, who trained under Dr. Garrett while completing his sports medicine fellowship at Duke, shared additional anecdotes from their time in OR, further personalizing the highly educational experience.

His visit shed light on the unique career path of a clinician scientist and further strengthened the relationship between Duke and Penn Orthopaedics.

January 17, 2019 R. Bruce Heppenstall Lectureship

Dr. Seven Olson

Chief, Division of Trauma, Oncology, Pediatrics and Hip Preservation Professor, Department of Orthopaedic Surgery Duke University, Durham, NC
(written by Matthew Stein)

Dr. Olson is the current Chief in the Division of Trauma, Oncology, Pediatrics, and Hip preservation, and is a Professor in the Duke Department of Orthopaedic Surgery. He received his MD and residency training in Orthopaedic Surgery at University of Missouri-Columbia School of Medicine. His training continued with fellowships in Orthopaedic Trauma at University of California Davis Medical Center, and in Hip Reconstruction in France, Switzerland and Germany with Dr. Joel Matta, and Pelvic and Acetabulum Reconstruction at Good Samaritan Hospital in California. Dr. Olson began his practice at University of California Davis. He moved to Duke University in 2000 bringing both orthopaedic trauma and hip preservation

practices. Currently Dr. Olson is Director of the Orthopaedic Surgery Clinical Research Unit, and Division Chief for a group of 4 clinical sections including Oncology, Pediatrics, Trauma, and Hip Preservation. His clinical practice spans Orthopaedic Trauma, Hip Preservation, and Hip Reconstruction.

Figure 1. Dr. Olsen showing pelvic osteotomy cuts on a Sawbones pelvis model to the residents

While at Duke, in collaboration with the orthopaedic biomedical engineering lab, Dr. Olson helped develop the first in-vivo model of post-traumatic arthritis following articular fracture. This success led ultimately to receiving the Kappa Delta Award in 2015 for the role of inflammation in post-traumatic arthritis development. He is a prolific author with over 70 publications, and has served as President of the Orthopaedic Trauma Association. Dr. Olson has also won resident teaching awards at both University of California-Davis and Duke University.

His lecture was preceded by a special video welcome by Dr. Heppenstall himself, who was honored to have someone as distinguished as Dr. Olson here to speak at his lectureship.

Dr. Olson's first lecture focused on a traumatologists' perspective on hip preservation. We discussed his experience fixing acetabulum and pelvic fractures and how that experience has guided his views on hip preservation in both traumatic and atraumatic cases of hip pathology. His second lecture gave us an update on the current standards of hip fracture care, allowing a more in-depth view of the research he helped pioneer showing the role of inflammation in the development of post-traumatic arthritis.

Thereafter, Dr. Olson took the residents to the Human Tissue Lab to demonstrate his anterior and iliofemoral approaches to the hip and pelvis. His extensive knowledge of anatomy was immediately apparent and his exceptional dissection skills allowed a wonderful view of both the pelvic and hip anatomy. His expertise in education was evident and can only come from a life dedicated to teaching others.

January 24th, 2019

Luis Bahamonde, MD

Professor, Orthopaedic Surgery Program Director of Orthopaedics and Traumatology, University of Chile
(written by Brian Perez)

Dr. Bahamonde is currently the head of the Program of Orthopaedics and Traumatology at the University of Chile. He received his medical degree from the University of Chile where he also completed his residency in Orthopaedic Surgery in 1990. Dr. Bahamonde went on to complete a fellowship in Orthopaedic Oncology at the Insituto Ortopedico Rizzoli in Bologna, Italy. After completion of his training, he returned to his home country to work at the University of Chile.

Dr. Bahamonde delivered three captivating presentations during his visit. He began the day with a talk on distal press-fit fixation as an alternative treatment option over massive endoprosthetic reconstruction in Tumor and revision surgery, where the awe-inspiring cases he presented stimulated lively discussions amongst the faculty. In addition, Dr. Bahamonde's second talk on the management of femoral nonunions, was an interactive session with the residents in attendance that only foreshadowed the invaluable educational opportunity that was to take place in the Human Tissue Lab. Dr. Bahamonde, with the assistance of Dr. Mehta, presented a variety of his cases from Chile, which sparked discussions about treatment options and techniques in a question answer format between Dr. Bahamonde, Dr. Mehta, and the Orthopaedic Residents.

Figure 1. Dr. Bahamonde showcasing 3D printed models of patients with acetabular bone loss

Lastly, the residents were able to spend time with Dr. Bahamonde in the Human Tissue Lab. During this session, Dr. Bahamonde gave a talk on the free "periostized" fibular graft and the "Ice Cream Cone Prosthesis" for large pelvic defects. Following the insightful presentations, Dr. Bahamonde began the hands on portion of the day and brought in a 3D printed model of a pelvis for one of his upcoming cases. This allowed the residents to see first hand how he prepares for large complex cases. As the session progressed, Dr. Bahamonde walked multiple residents through the sawbones approach for

the "Ice Cream Cone Prosthesis". Following the sawbones, we enjoyed a captivating prosection of the iliofemoral approach to the acetabulum that is not commonly seen in our program further adding educational value.

Figure 2. Residents practicing placement of the Ice Cream Cone Prosthesis

Dr. Bahamonde generously presented much of his work and results from complex surgical reconstructions of lower extremity pathology in Chile. During his time, here we were able to discuss future collaborative plans and are eager to organize a special rotation for Penn Orthopaedic Surgery residents to work side by side with him in Chile.This could be the start of an exceptional international collaboration between Penn Ortho and the Orthopaedic Surgery and Orthopaedic Oncology Departments in the University of Chile.

Februrary 21st, 2019: Ralston Lecture

Dr. Lewis Zirkle, MD

President and Founder of SIGN Fracture Care International
(written by Joseph Koressel)

Dr. Lewis Zirkle graduated from Davidson College and Duke Medical school. In 1966, his first year of orthopaedic residency at Duke, Dr. Zirkle was drafted by the US Army and was deployed in Vietnam where he cared for the US military, Vietnamese military, and civilians. He remained in the US Army for the remainder of his orthopaedic training.

He continued his work overseas and found that many providers abroad simply do not have the equipment necessary to provide suitable patient care. During his lecture, Dr. Zirkle recounted a return visit to Vietnam where he found a man that had been in traction for 3 years following a distal femur fracture. Dr. Zirkle realized that these communities needed access to appropriate implants so they can treat their wounded.

Dr. Zirkle is the founder and president of SIGN fracture Care, which was officially incorporated as a nonprofit in 1999. The goal of SIGN is to design, educate, and provide appropriate implants to providers to treat trauma victims in developing countries. He discussed in depth the desisgn of the SIGN nail, an innovative implant system for treating fracture patients in under-sourced hospitals. This system is comprised of the traditional intramedullary nail which are held in place with interlocking screws, however, it is uniquely designed for use in facilities that do not have fluoroscopic or power equipment

During his visit to the University of Pennsylvania, Dr. Zirkle discussed the history and future of SIGN in orthopaedics, and the need for appropriate implants given traumatic injuries are rising in developing countries. Additionally, Dr. Zirkle and his team demonstrated how to use the SIGN nail system, and instructed the Penn orthopaedic residents in SIGN nail application in a sawbones lab.

March 21st, 2019: Stein Lecture

Amy Ladd, MD

Assistant Dean for Student Advising, Stanford University School of Medicine, Chief of Chase Hand & Upper Limb Center, Chief of the Children's Hand Clinic, Lucile Salter Packard Children's Hospital, Palo Alto, CA

Dr. Ladd graduated from Dartmouth College with an BA in History before receiving her MD from SUNY Upstate Medical University. She completed an Orthopaedic Surgery Residency at the University of Rochester, and then moved on to complete the Harvard Combined Hand Surgery Fellowship.

She was a fellow at L'Institut de la Main in Paris, France prior to joining the Stanford University faculty in 1990. Dr. Amy Ladd is the Elsbach-Richards Professor of Surgery, Assistant Dean for Medical Advising at Stanford University, the orthopaedic vice-chair of Academic Affairs, and hand fellowship director. Dr. Ladd is the immediate past-Chair of the AAOS Board of Specialties and past President of the Ruth Jackson Society.

Dr. Ladd's hand surgery practice includes both adults and children. Her research focuses on deciphering human motion of injury, disease, and deformity. In addition to research, she holds eight innovation patents and trademarks that encompass treatments for wrist fractures, thumb arthritis, and promotes musculoskeletal health awareness. Dr. Ladd's advocacy to promote pipeline education and mentorship complements community and national orthopaedic initiatives. She is an passionate supporter for promoting women and other underrepresented minorities in orthopaedics, as well as examining gender and cultural differences and similarities across medicine, and better understanding our unconscious biases.

In a similar vein, Dr. Ladd's lecture at Penn started as an interactive session discussing the impact of bias in science, Orthopaedic Surgery and society in general. Prior to her lecture, Dr. Ladd sent out a few recent articles for review that broached this topic to spur discussion, and she encouraged us all to take the Implicit Association tests (https://implicit.harvard.edu/implicit/takeatest.html), in order to get a sense of our own implicit, uncounsciuous biases.

Figure 1. Dr. Ladd and residents reviewing upper extremity anatomy in the Human Tissue Lab

Dr. Ladd concluded her time here with us by leading a dissection session in the Human Tissue Lab with the residents and fellows. Her extensive knowledge of anatomy was immediately apparent as she demonstrated a number of surgical approaches, making sure to point out anatomical landmarks and dangers to be aware of. After reviewing the various approaches, we then proceeded to further dissect out tendons, ligaments, arteries and nerves in order to better understand the surrounding anatomy.

Current Residents

Clinical Year 5 Resident Spotlight

Jenna A. Bernstein, MD

Hometown: Fairfield, CT
Undergraduate: Cornell University
Medical School: University of Connecticut School of Medicine
Residency Highlights: Operating with my co-residents and sterile hand holding
Future Directions: Adult Reconstruction Fellowship at NYU/ISK

Kristin Buterbaugh, MD

Hometown: Pittsburgh, Pennsylvania
Undergraduate: Northwestern University
Medical School: Icahn School of Medicine at Mount Sinai
Residency Highlights: operating with my co-chiefs, international surgical trip in the Dominican Republic, being trauma chief (trauma team beanies)
Future Directions: fellowship in hand and upper extremity surgery at Indiana Hand to Shoulder center

Jose A. Canseco, MD, PhD

Hometown: Mexico City, Mexico
Undergraduate: Rice University
Medical School: Harvard Medical School / Massachusetts Institute of Technology
Future Directions: The Rothman Orthopaedic Institute/Thomas Jefferson University Spine Fellowship, Research/Clinical 2-year track

Jonathan R. Dattilo, MD

Hometown: Cincinnati, OH
Undergraduate: Northwestern University
Medical School: Johns Hopkins University School of Medicine
Residency Highlights: Making secret trauma man-cave with Dan Gittings that no one else ever found, nerding out filming surgeries with Josh Rozell and Matt Winterton
Future Directions: Adult Reconstruction Fellowship at Anderson Orthopaedic Research Institute (Alexandria, VA)

James M. Friedman, MD*

Hometown: Durham, NC
Undergraduate: Duke University
Medical School: Duke University School of Medicine
Residency Highlights: Co-resident friendship, faculty mentorship
Future Directions: UCSF for sports fellowship

Cody D. Hillin, MD, MS*

Hometown: Glenwood Springs, CO
Undergraduate: University of Rochester
Medical School: Baylor College of Medicine
Residency Highlights: Working in the trenches/OR with co-residents
Future Directions: Indiana Hand to Shoulder Fellowship

Luke A. Lopas, MD

Hometown: Sturgeon Bay, Wisconsin
Undergraduate: University of Wisconsin-Madison
Medical School: University of Wisconsin School of Medicine & Public Health
Residency Highlights: Surgical mission trip to the Dominican Republic. Operating with my co-residents. The privilege of learning from outstanding mentors. The small, often mundane, but memorable moments that compromise the things I'll never forget.
Future Directions: Orthopaedic Trauma Fellowship in Tampa, Florida. After that I hope be a happy, healthy, and busy orthopaedic traumatologist in an academic, level 1 trauma center

Nicole A. Zelenski, MD

Hometown: Madison, Wisconsin
Undergraduate: Bryn Mawr College
Medical School: Duke University School of Medicine
Residency Highlights: sterile hand holding, international trip to Chile, the undying support of Niko
Future Directions: Mayo Clinic for Hand Surgery Fellowship

*Indicates Resident is in the 6-year Research Track

Clinical Year 4 Residents

Blair S. Ashley, MD*

Undergraduate:
The College of William and Mary

Medical School:
University of Pittsburgh School of Medicine

Ryan Charette, MD

Undergraduate:
University of Connecticut

Medical School:
University of Connecticut School of Medicine

Rikesh Gandhi, MD

Undergraduate:
Boston College

Medical School:
Duke University School of Medicine

Daniel Gittings, MD*

Undergraduate:
Providence College

Medical School:
Boston University School of Medicine

Mark Hasenauer, MD

Undergraduate:
Boston College

Medical School:
New York Medical College

Matthew Sloan, MD, MS

Undergraduate:
University of Massachusetts

Medical School:
University of Massachusetts Medical School

Andrew Tyler, MD, PhD

Undergraduate:
Harvard University

Medical School:
University of Texas at Dallas Southwestern Medical School

Matthew Winterton, MD

Undergraduate:
Brigham Young University

Medical School:
Perelman School of Medicine University of Pennsylvania

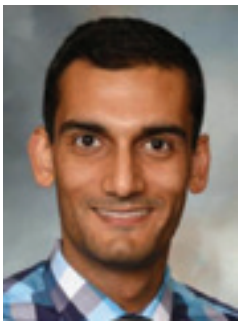
*Indicates Resident is in the 6-year Research Track

Clinical Year 3 Residents

Gerald Andah, MD

Undergraduate:
University of Pennsylvania

Medical School:
Perelman School of Medicine University of Pennsylvania



Adnan Cheema, MD*

Undergraduate:
University of Missouri-Kansas City

Medical School:
University of Missouri-Kansas City School of Medicine

Michael Eby, MD, MS*

Undergraduate:
University of Pennsylvania

Medical School:
Georgetown University School of Medicine

Chelsea Hendow, MD, MS

Undergraduate:
Univ. of CA—Los Angeles

Medical School:
New York Medical College

Christina Nypaver, MD

Undergraduate:
Univ. of Notre Dame

Medical School:
Loyola Univ.—Chicago Stritch School of Medicine

Christopher Scanlon, MD, MS

Undergraduate:
Univ. of So. Carolina—Columbia

Medical School:
Drexel University College of Medicine

Kimberly Stevenson, MD, MS

Undergraduate:
Univ. of Delaware

Medical School:
Georgetown University School of Medicine

Matthew Webb, MD

Undergraduate:
Harvard College

Medical School:
Yale School of Medicine

Research Year

Matthew Counihan, MD, MS*

Undergraduate:
Univ. of Richmond

Medical School:
Drexel University College of Medicine

Liane Miller, MD*

Undergraduate:
Univ. of CA—Santa Barbara

Medical School:
Univ. of CA—San Francisco School of Medicine

*Indicates Resident is in the 6-year Research Track

Clinical Year 2 Residents

Perez Agaba, MD

Undergraduate:
Indiana University at Purdue University

Medical School:
Duke University

Sarah Blumenthal, MD

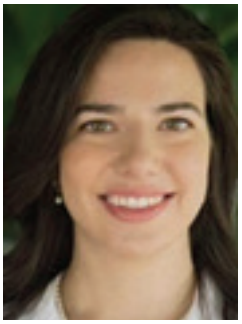
Undergraduate:
Harvard University

Medical School:
University of California–Los Angeles

Kelsey Bonilla, MD*

Undergraduate:
Rutgers University

Medical School:
Perelman School of Medicine at University of Pennsylvania



Agnes Dardas, MD, MSc

Undergraduate:
Harvard University

Medical School:
Washington University in St. Louis

George Fryhofer, MD, MTR*

Undergraduate:
Harvard University

Medical School:
Perelman School of Medicine at University of Pennsylvania

Brandon Haghverdian, MD

Undergraduate:
University of California–Irvine

Medical School:
University of California–Irvine

Eric Pridgen, MD, PhD

Undergraduate:
University of Delaware

Medical School:
Stanford University

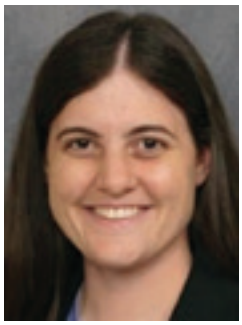
Ivan Zapolsky, MD, MS

Undergraduate:
Tulane University

Medical School:
Tulane University

*Indicates Resident is in the 6-year Research Track

Clinical Year 1 Residents



Lauren Boden, MD

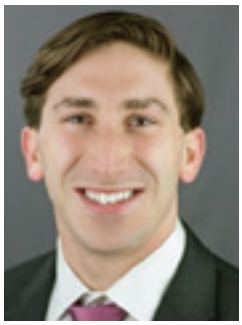
Undergraduate:
Pomona College

Medical School:
Emory University

Ryan DeAngelis, MD

Undergraduate:
The College of New Jersey

Medical School:
Cooper Medical School of Rowan University



David Falk, MD

Undergraduate:
University of Michigan

Medical School:
George Washington University

Sachin Gupta, MD*

Undergraduate:
George Washington University

Medical School:
George Washington University

Joseph Koressel, MD

Undergraduate:
University of CA - Davis

Medical School:
Weill Cornell

Brian Perez, MD

Undergraduate:
Rutgers University

Medical School:
Albert Einstein

Viviana Serra Lopez, MD, MS

Undergraduate:
Mass. Inst. of Technology

Medical School:
University of Puerto Rico

Matthew Stein, MD, MS*

Undergraduate:
Univ. of Maryland

Medical School:
Georgetown University

*Indicates Resident is in the 6-year Research Track

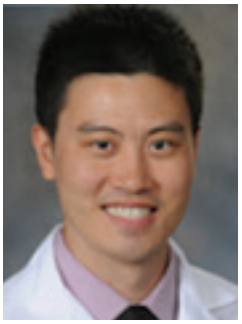
Current Fellows

August 1, 2018–July 31, 2019

Brittany Behar, MD
Hand Surgery

Tamara John, MD
Hand Surgery

Perry Evangelista, MD
Adult Reconstructive Orthopaedics



David Sun, MD
Adult Reconstructive Orthopaedics

Gregory Gomez, MD
Adult Reconstructive Orthopaedics / Shoulder & Elbow Surgery

Ryan Plyler, MD
Sports Medicine

Christopher Richard, MD
Sports Medicine

Karim Mahmoud, MD
Foot & Ankle
(Non-Accredited)

Sreenivasulu Metikala, MD
Foot & Ankle
(Non-Accredited)

Christopher Catapano, DO
Spine Surgery
(Non-Accredited)

Sajeel Khan, MD
Spine Surgery
(Non-Accredited)

Corporal Michael J. Crescenz Philadelphia VA Medical Center Update

David Steinberg, MD

Acting Chief of Orthopaedic Surgery Department, VAMC

During 2018, we saw some faculty transitions and expansion of clinical services, which will allow us to better serve our veterans. We welcomed Dr. Vincent Moretti as a fulltime joint reconstruction surgeon. He received degrees in biomedical engineering & medicine at Northwestern University, then spent a year as a Clinical Research Fellow at Penn. Vince returned to Chicago for his orthopaedic residency at the University of Illinois, and then travelled back to Philadelphia for an Adult Reconstruction Fellowship at the Rothman Institute, followed by two years as an assistant professor in the Orthopaedic Department at Drexel University. He adds a new perspective & approach to total joint arthroplasty, in addition to providing some general orthopaedic & trauma coverage. He is helping to revamp the veterans' total joint experience, bringing with him lessons learned during his fellowship, such as facilitating expanded perioperative care & post-operative therapy in an effort to reduce length of stay for our patients.

Dr. Marlene DeMaio has stepped down as Chief of Orthopaedics and has assumed an exciting new role at the VAMC. While she remains a Clinical Professor of Orthopaedics at the Perelman School of Medicine, she has moved to the Rehab Medical Service to be Co-Director, with Carla Scanzello, of the Osteoarthritis Clinic, which will provide a multi-disciplinary approach to OA. She is also working with Women's Health to develop a Women's Musculoskeletal Conditions Service. Both of these efforts support the VA's Whole Health Initiative. It will help with more appropriate and efficient referrals to orthopaedics. With her continued dedication to resident education, Dr. DeMaio is working with Dr. Edna Schwab, Chief Education Officer, on training programs for surgeons and new VA providers. This transition will help the VA with new programs for patients, providers, and trainees in a different capacity. Dr. DeMaio has been inducted as the new president of the Ruth Jackson Society. (Three past presidents have also had Penn connections: Drs. Mary Ann Keenan, Helen Horstmann, and Kristy Weber, Figure. 1).

With Dr. DeMaio's transition, David Steinberg has assumed the role of Acting Chief of Orthopaedic Surgery, in addition to his responsibilities as Chief of Hand Surgery. He runs a weekly hand clinic, and is working with Dr. Levin & VA administration to develop a regional hand center covering Eastern Pennsylvania, New Jersey & Delaware.

We continue to offer other subspecialty services to our veterans, including joint arthroplasty (Drs. Eric Hume, Joe Bernstein, Robert Wilson, & Vince Moretti), spine (Drs. Andrew Milby & Harvey Smith), foot & ankle (Dr. Kate O'Conner), trauma (Dr. Jaimo Ahn), orthopaedic oncology (Dr. Wilson) & shoulder (Dr. Andy Kuntz). Dr. Bernstein continues in his multiple roles as student & resident educator, staffing clinic, and performing general orthopaedic surgery. All of the faculty staff general orthopaedic as well as specialty clinics four days a week. From January 1 to December 31, 2018, 6046 visits were recorded for the outpatient Orthopaedic Surgery Clinic. We would not be able to provide comprehensive orthopaedic care to our patients without the dedication of our residents, hand fellows, our two exceptional orthopaedic physician assistants, Mitchel "Chip" Staska, MP-C and John Wheeler, PA-C, our nurses Kathleen Sweeney, RN and Catherine Linowski, RN MSN, and the other clinic staff. We offer surgical services five days weekly, and performed over 368 operative procedures last year. Under Dr. DeMaio's leadership, the orthopaedic service made major improvements in patient safety, new total joint order set, improved coding, and improved length of stay.

Figure 1. Past Presidents of the Ruth Jackson Society along with Dr. DeMaio, the new Ruth Jackson Society President.

Our faculty, residents and Penn's scientists, engineers & research staff continue to forge new paths through the partnership between the McKay Orthopaedic Laboratory and the PVAMC Translational Musculoskeletal Research Center. Drs. Smith (completing his Career Development Award this year), Bernstein, Kuntz, Esterhai, Ahn & Steinberg, working alongside Drs. Mauck, Soslowsky & Dodge, are investigating many facets of the musculoskeletal system, including repair & regeneration of tendon, meniscus, cartilage, & the intervertebral disc.

In addition to patient care and research, the orthopaedic program at the VAMC promotes the third pillar of academic medicine, education. In addition to clinical and surgical training of residents, hand fellows and students, we are expanding our educational efforts. This includes weekly resident conference with Dr. Kuntz, quarterly Chairman's rounds with Dr. Levin, the pending acquisition of an arthroscopic simulator, and new programs, such as an integrated curriculum with Penn, being developed by Dr. DeMaio.

Pennsylvania Hospital

Neil Sheth, MD

Chief of Orthopaedic Surgery, Pennsylvania Hospital

Pennsylvania Hospital (PAH) has a rich history in Philadelphia as the nation's first hospital. Founded in 1751 by Benjamin Franklin and Dr. Thomas Bond, the hospital was intended as a safe haven for the care of the "sick-poor and insane of Philadelphia." Located in the heart of South Philadelphia, its brand name draws thousands of patients annually to receive their care at the corner of 8th and Spruce Streets.

Residents are typically in the operating room three to four days per week, with dedicated clinic time in multiple sub-specialties. The foot and ankle resident and spine chief resident are at PAH hospital full time, while residents from the arthroplasty and sports medicine services spend part of their week operating and staffing clinic in the Cathcart building. In a continuing commitment to resident education, conferences are now video conferenced from PMUC. With a rigorous, structured curriculum, specialty specific conferences include spine and foot and ankle.

The administration at Pennsylvania hospital continues to be extremely supportive of the expanded presence of orthopaedic faculty and residents. The hospital system has increased the number of physician extenders, doubled the OR block time for the department, and increased physical space for clinical work and administrative duties. Their continued support is critical as the orthopaedic volume continues to grow, allowing PAH to maintain its reputation in the region as a first-class hospital. PAH was ranked 23rd in US News and World Report for 2018-2019, specifically for Total Hip Arthroplasty.

The Department of Orthopaedic Surgery at the University of Pennsylvania now staffs seventeen attending surgeons from various sub-specialties to populate the orthopaedic clinic in the Cathcart Building and the Farm-Journal Building. Among the sub-specialties represented are adult hip and knee reconstruction, foot and ankle, hand/plastic surgery, neuro-orthopaedics, shoulder and elbow, spine/deformity, sports medicine, and trauma. Notable for this past year, Dr. Christopher Travers joined Penn after completing his Adult Reconstruction Fellowship at PPMC and PAH. In addition, Linda Lee has joined the spine service as a Physician Assistant for Dr. Comron Saifi.

With the continued increase in operative volume, PAH continues to be staffed by a PGY-1, PGY-2, PGY-5 and Adult Reconstruction Fellow at all times, complemented by a team of nurse practitioners and physician extenders that assist with patient clinical care and floor work. Over the past academic year, the Orthopaedic Intern is now spending a portion of the week on the Foot and Ankle Service, as well as assisting the PAH team with patient care issues on the floor. The PGY-2 resident is now dedicating a portion of the week to Sports Medicine under the guidance of Dr. Miltiadis Zgonis. Starting in August 2019, the Adult Reconstruction service will have 3 Fellows, spending 4 months each at PPMC, PAH and Virtua.

With the continually changing healthcare environment, we continue to grow the outpatient total joint arthroplasty program which started two years ago. The plan is for there to be a dedicated rapid recovery section of the hospital. This service is to be extend to Tuttleman which has experienced a significant increase in operative volume over the past two years. In addition, we plan to offer a robotics platform at PAH in the near future. Pennsylvania Hospital is poised to be successful in the region as we continue to evolve.

Figure 1. Surgical Amphitheater at Pennsylvania Hospital (constructed in 1804).

Penn Center for Musculoskeletal Disorders Update

Louis J. Soslowsky, PhD

Founding Director of the Penn Center for Musculoskeletal Disorders

The Penn Center for Musculoskeletal Disorders (PCMD) was initiated in 2004 with a goal to bring musculoskeletal researchers across campus together at the University of Pennsylvania. In 2006, the National Institute of Arthritis and Musculoskeletal Skin Diseases of the NIH funded our center grant proposal at which time we became one of five such NIH-recognized Centers in the country (www.med.upenn.edu/pcmd). In 2011, this Center grant was renewed for another five years and was the only one of the three up for renewal that was re-funded that year. Through the review by the NIH, Penn scored a perfect "ten" and was hailed as "exceptional" by the review panel! In 2016, we received another "exceptional" score, highest ranked in the country, by the NIH review panel and were renewed for another five years. We are the longest running such center in the country.

The overall goal of this Center is to promote cooperative interactions among investigators, accelerate and enrich the effectiveness and efficiency of ongoing research, foster new collaborations and new research, and ultimately, translate our research efforts into better and new therapies for musculoskeletal disorders. The central theme of the Center continues to be "Musculoskeletal Tissue Injury and Repair". This theme is broad (as it includes all musculoskeletal tissue types, such as bone, cartilage, disc, ligament, meniscus, muscle, and tendon), focused (as takes advantage of commonalities in approaches across tissue types), and clinically significant (as it fosters development of assays, procedures and knowledge in pre-clinical animal and human models of translational relevance). It is important to note that our PCMD is not a "bone center" nor is it a "muscle center". Rather, it is truly a "musculoskeletal center" and has emerged as the recognized home for musculoskeletal research across the Penn campus and as a technical and intellectual resource for the broader Philadelphia musculoskeletal research community. Thus, the primary overall aims of this Center are to enhance and advance the research productivity of investigators in musculoskeletal tissue injury and repair by:

1. Providing innovation within critical resource core facilities in areas that cross disciplines, length scales, and hierarchies. These core facilities are microCT Imaging, Biomechanics, and Histology
2. Developing a pilot and feasibility grant program for investigators, with direct mentorship, whereby new approaches, ideas, and collaborations can be developed prior to seeking extramural funding
3. Developing educational and research enrichment programs spanning tissue types, research approaches, and paradigms, through which members can learn from national leaders and from each other. High quality musculoskeletal research is currently being conducted by many groups at Penn.

While many bring sophisticated approaches to bear on musculoskeletal problems, few groups have the required expertise and facilities to perform high quality and specialized assays in their own labs. Furthermore, most investigators are not aware of approaches utilized, and results obtained, in other tissues that may have direct relevance on their research questions. Ultimately, close cooperation, communication, and collaboration among researchers across musculoskeletal tissue types and from a wide variety of disciplines will significantly enhance the research of our members. The Center will provide opportunities to integrate multi-disciplinary techniques to determine mechanisms for tissue function, injury, degeneration, repair, and regeneration, with the ultimate goal of advancing the diagnosis, treatment, and prevention of diseases and injuries of the musculoskeletal system.

The Center currently has a membership of more than 193 faculty across five schools at Penn (Perelman School of Medicine, School of Engineering and Applied Science, School of Veterinary Medicine, School of Dental Medicine, and School of Arts and Sciences). We also now have faculty members for more than 13 Philadelphia-area institutions as we expand the reach and impact of our Center. For more information on the PCMD, please visit our website at www.med.upenn.edu/pcmd.

McKay Orthopaedic Research Laboratory Update

Robert L. Mauck, PhD and Louis J. Soslowsky, PhD

The McKay Orthopaedic Research Laboratory of the Department of Orthopaedic Surgery in the Perelman School of Medicine continues to explore important problems in musculoskeletal research. The research facility, including labs and offices, occupies over 22,000 sq. ft. of newly renovated space on the 3rd Floor of Stemmler Hall (Figure 1). There are more than 120 full- and part-time staff and trainees now in the labs. McKay is an active, thriving research and educational community committed to advancing basic and translational musculoskeletal research.

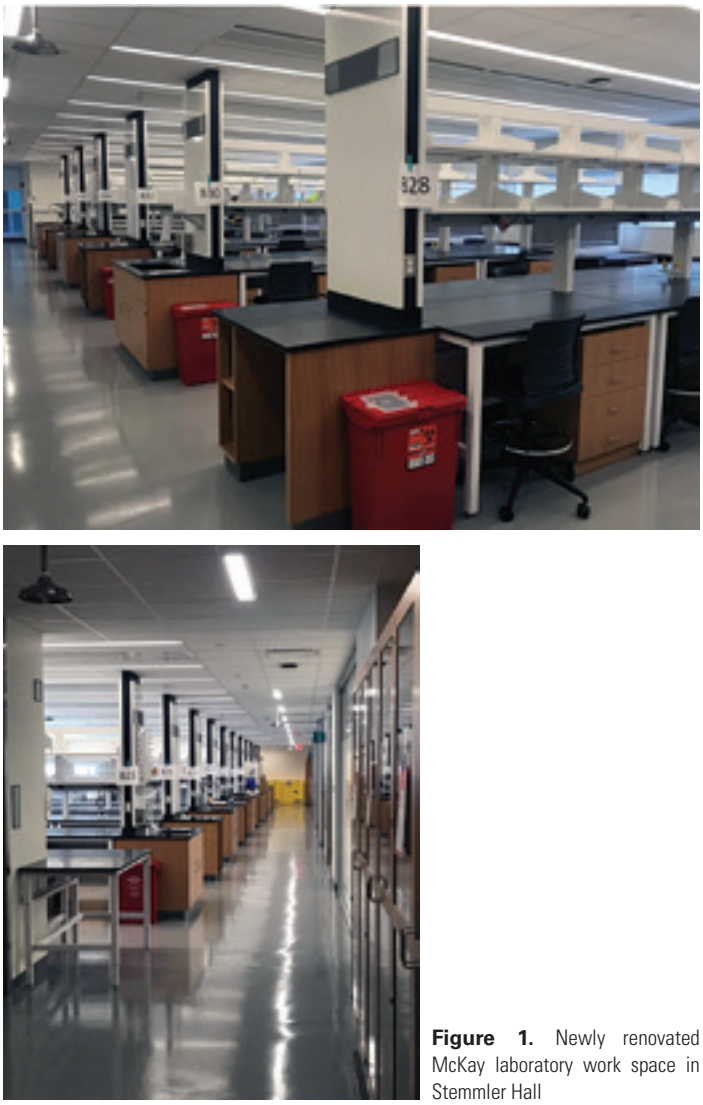


Figure 1. Newly renovated McKay laboratory work space in Stemmler Hall

The Mckay labs have just completed a transformation both in terms of physical space and faculty. Our home, Stemmler Hall, underwent a >$120 million dollar renovation, completed in early 2019, which resulted in a fully modernized facility in which to grow our laboratory space, faculty, and research and training endeavors. We moved into our new space in November 2018. Last year, we were delighted to welcome Dr. Joel Boerckel, PhD, an expert in bone mechanobiology and Dr. Kyu Sang Joeng, an expert in disease models of bone and tendon, as our newest tenure track faculty members. We are also very excited that Dr. Lachlan Smith was recently promoted to Associate Professor with tenure. We are also now actively recruiting for an endowed chair faculty position, and hope to grow our ranks further in the very near future.

Currently, the lab has an annual research budget from extramural grants, gifts, and endowments > $14,124,397 and continues to rank within the top 5 orthopaedic programs in the country in terms of funding from the National Institutes of Health (NIH) with a 2018 ranking of #4. This past year has seen a very impressive and continued rise in new grant activity amongst the faculty. We were also excited that Sherry Liu was awarded the Kappa Delta Award at the 2019 American Academy of Orthopaedic Surgeons Meeting, Eileen Shore was named a Fellow of the American Society for Bone and Mineral Research (ASBMR), Robert Mauck was named a Fellow of International Orthopaedic Research (FIOR), and Lou Soslowsky was awarded the H.R. Lissner Medal from the American Society of Mechanical Engineers (ASME), the highest honor of that society.

We have had several new grants (>$25,000) awarded last year, representing the breadth and diversity of research undertaken by our faculty. These include:

- Dr. **Robert Mauck**
- "Evaluation of Cartilage Tissue Engineering Strategies by IR Imaging"
- a new R01 in collaboration with Temple University
- Dr. **Lou Soslowsky**
- "Collagen XI and XI/V regulatory mechanisms in assembly of tendon hierarchical structure and acquisition of mechanical properties in development and injury response"
- a new R01 from the National Institutes of Health
- Dr. **Foteini Mourkioti**
- "Telomeric protein requirements in cardiac dystrophy"
- a new grant from the Muscular Dystrophy Association
- Dr. **Eileen Shore** and Dr. **Robert Mauck**
- "Mechanobiology of Progenitor Cells in Heterotypic Ossification"
- a new R01 from the National Institutes of Health

In addition to the above-mentioned new grants this year, each of the McKay Laboratory faculty remains well-funded

through existing research grants not identified in this new grants list.

Further, there were several new industry grants and clinical trials (>$25,000) initiated by both basic science and clinical faculty this year. These include:

- Dr. **Scott Levin**
- "Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient Reported Outcome Metrics and the Candidate Screening Process", a new grant from the Department of Defense
- Dr. **Gwo-Chin Lee**
- Retrospective study to evaluate patients/ clinical factors related to positive response from hyaluronic acid injections
- from Ferring Pharmaceuticals, Inc.
- Dr. **Samir Mehta**
- "Diagnosis of Orthoapedic Trauma Related Infections at the Intersection of the Transcriptome and Microbiome"
- in collaboration with Virginia Commonwealth University
- Dr. **Samir Mehta**
- "PREPARE: Pragmatic Randomized trial Evaluating Pre-operative Alcohol skin solutions in Fractured Extremities"
- in collaboration with the University of Maryland

Growing musculoskeletal research in the Department of Orthopaedic Surgery and across the Penn campus has been a primary objective for our program, and this effort has been particularly fruitful in the past year. This spring will mark the 40th year of operation of the McKay labs, and we are excited to celebrate this occasion with all of you at the upcoming Ortho Alumni Weekend and McKay 40th Celebration. In the last decade alone, we have grown in terms of lab faculty (71% increase), lab personnel (95% increase), lab space (110% increase), and research expenditures (141% increase). With our 40 years of leadership, training, and scientific contributions to musculoskeletal research, we are excited for what the future will bring.

What's New at the PVAMC Translational Musculoskeletal Research Center?

George R. Dodge, Ph.D. and Robert L. Mauck, Ph.D.

Aches and pains are a part of daily life and normal aging. However, musculoskeletal (MSK) conditions can also arise as a direct consequence of military service, with associated trauma and accidents. In fact, MSK diseases and related disabilities are more prevalent in Veterans than in the general population. Furthermore, while improvements in armor and "in theater" medical care has introduced incredible life-saving technologies, an increasing number of our wounded soldiers return home with damaged limbs and joints. Also, as with any population, when veterans age, there is an increasing tendency to develop arthritis and various degenerative joint diseases, each of which can significantly compromise quality of life. In response, the Department of Veterans' Affairs has focused research efforts to improve our understanding of the function of MSK tissues and injuries that occur to them, with the goal of developing novel technologies to enhance tissue repair, regeneration, and ultimately function.

In keeping with this goal, the last several years have witnessed a dramatic growth in VA-sponsored MSK research across the nation, with one of the largest increases occurring at our Corporal Michael Crescenz VA Medical Center (CMC VAMC) in Philadelphia. Physician investigators, basic scientists, and engineers at the CMC VAMC, together with colleagues from the University of Pennsylvania, are currently carrying out research projects focused on the injury and repair of MSK tissues, including tendons, ligaments, disc, bone, meniscus, and cartilage. Additional studies are underway to develop new technologies that may one day aid in the replacement of these tissues and ultimately improve function and quality of life. In keeping with this research focus, the CMC VAMC established the Translational Musculoskeletal Research Center (TMRC) in 2013. This Center brings together investigators from Orthopaedic Surgery, Rheumatology, Physical Medicine and Rehabilitation, Neurosurgery, and Bioengineering all under one roof, in >9,000 sq. ft. of newly renovated research space. Drs. George Dodge and Robert Mauck co-direct this enterprise with input, advice, and support from a joint PVAMC/Penn TMRC Advisory Committee.

The goal of the TMRC is to develop a focused, internationally recognized research center at the CMC VAMC and to emerge as a VA Center of Excellence, bringing new resources and regenerative technologies to all service members, past and present. To date, more than 30 VA-based physicians, scientists, bioengineers, and research staff have co-localized to the newly renovated, state-of-the-art research space at the CMC VAMC Medical Research Building. Current VA funding to these investigators has increased to >$2 million in direct costs per year. In addition, the VA has committed more than $6.5 million in equipment to outfit this facility, including state-of-the-art devices such as vivo micro-CT, fluoroscopy, atomic force microscopy and nano-indentation, super-resolution, confocal, multiphoton, and light-sheet imaging. Overall, the TMRC is on an upward trajectory, with a vibrant multi-disciplinary team of investigators and significant new funding directed towards making possible new discoveries in musculoskeletal repair and regeneration. The TMRC is committed to our goal of translating this research into life changing improvements in patient care and quality of life for both Veterans and the general population.

The Biedermann Lab: Current Research Trajectory and Future Directions

Michael Hast, PhD

Director, Biedermann Lab for Orthopaedic Research

Since its opening in 2015, the Biedermann Lab has sought to characterize the macroscopic biomechanical interactions between connective tissues, bone, and orthopaedic implants. We have con-ducted a variety of biomechanical experiments that span across a variety of injuries and subspecialties. These efforts have resulted in abstracts and full-length publications that include but were not limited to: tendon and ligament biomechanics[1–4], trauma implant performance[5–10], osteoporotic fracture and fixation[11,12], and other orthopaedic applications[13–15].

Our group focuses on implant compliance, which, among other pathologies, has direct clinical implications with respect to osteoporotic fracture reconstruction. Several publications from the Biedermann Lab demonstrate the importance of implant compliance. For example, one of our first studies revealed that fatigue life is codependent upon stable locking of the screws, and the im-plant's ability to bend elastically[8]. We have also shown that location of the implant may have direct implications with respect to fixation strength and fatigue life[11].

Our research focus has resulted in several sponsored projects with industrial partners. In a recent study with Zimmer Biomet, we found that cement augmentation can significantly change initial compliance of a reconstruction, but these changes made no significant improvement in fatigue life. In a separate study, funded by Integra Life Sciences, we examined the compliance of reverse total shoulder implants. We found no changes between compliant and stiff groups before initial implant loosening; however, stiffer implants significantly delayed the onset of catastrophic failures. Results from these two studies are uniquely different, which underscores the importance of examining research questions in this niche on an application-specific basis. Aside from the aforementioned studies, the Lab has also been supported by the following sources: AOFAS, AOTNA, The Bach Fund, DePuy Synthes, The McCabe Fund, NIAMS, OREF, and Stryker Orthopaedics.

Results from our work are beginning to directly impact clinical practice. For example, our "don't miss high" finding in proximal humerus locking plate location has begun to change clinical practice. This study provides critical evidence that buttressing (not perforating) poor quality bone stock with surgical screws provides improvements in fixation strength and fatigue life. This finding has recently been confirmed in a clinical study[21], while findings from another study have directly led to an actively funded clinical trial at Penn.

It is clear that the forward momentum of the lab is strong, our national recognition is on the rise, and the future holds great promise to change the current paradigms associated with osteoporotic fracture fixation. None of this would be possible without the Biedermann family's generous contribution. We look forward to making this this already successful collaboration even more successful in the coming years.

Instron machine set-up at the Biedermann Lab for Orthopaedic Research

WORKS CITED

1. Baxter JR, Hast MW. Plantarflexor metabolics are sensitive to resting ankle angle and optimal fiber length in computational simulations of gait. Gait Posture 2019;67:194–200. doi:10.1016/j.gaitpost.2018.10.014.

2. Baxter JR, Farber DC, Hast MW. Plantarflexor fiber and tendon slack length are strong de-terminates of simulated single-leg heel raise height. *J Biomech* 2019. doi:10.1016/j.jbiomech.2019.01.035.

3. Schmidt EC, Chin M, Aoyama JT, Ganley TJ, Shea KG, Hast MW. Mechanical and Micro-structural Properties of Native Pediatric Posterior Cruciate and Collateral Ligaments. *Or-thop J Sports Med* 2019;7:2325967118824400. doi:10.1177/2325967118824400.

4. Schmidt EC, Chin M, Aoyama JT, Ganley TJ, Shea KG, Hast MW. Mechanical and Micro-structural Properties of Pediatric Anterior Cruciate Ligaments and Autograft Tendons Used for Reconstruction. *Orthop J Sports Med* 2019;7:2325967118821667. doi:10.1177/2325967118821667.

5. Mehta S, Chin M, Sanville J, Namdari S, Hast MW. Use of an Additional Nonlocking Screw in Olecranon Fracture Osteosynthesis Changes Failure Mechanism. *Orthopedics* 2019;42:e74–80. doi:10.3928/01477447-20181120-01.

6. Pulos N, Yoon RS, Shetye S, Hast MW, Liporace F, Donegan DJ. Anteroinferior 2.7-mm ver-sus 3.5-mm plating of the clavicle: A biomechanical study. *Injury* 2016;47:1642–6. doi:10.1016/j.injury.2016.06.002.

7. Bachner EM, Schmidt EC, Chin M, Namdari S, Baxter JR, Hast MW. Parameterization of proximal humerus locking plate impingement with in vitro, in silico, and in vivo tech-niques. *J Shoulder Elbow Surg* 2019. doi:10.1016/j.jse.2018.11.062.

8. Namdari S, Mehta S, Tierney A, Hast MW. Locking Cap Designs Improve Fatigue Properties of Polyaxial Screws in Upper Extremity Applications. *J Orthop Trauma* 2017;31:275–80. doi:10.1097/BOT.0000000000000780.

9. Rozell JC, Chin M, Donegan DJ, Hast MW. Biomechanical Comparison of Fully Threaded Solid Cortical Versus Partially Threaded Cannulated Cancellous Screw Fixation for Lisfranc Injuries. *Orthopedics* 2018;41:e222–7. doi:10.3928/01477447-20180103-03.

10. Hast MW, Hanson BG, Baxter JR. Simulating contact using the elastic foundation algo-rithm in OpenSim. *J Biomech* 2019;82:392–6. doi:10.1016/j.jbiomech.2018.11.025.

11. Mehta S, Chin M, Sanville J, Namdari S, Hast MW. Calcar screw position in proximal hu-merus fracture fixation: Don't miss high! *Injury* 2018;49:624–9. doi:10.1016/j.injury.2018.02.007.

12. Rajapakse CS, Kobe EA, Batzdorf AS, Hast MW, Wehrli FW. Accuracy of MRI-based finite element assessment of distal tibia compared to mechanical testing. *Bone* 2018;108:71–8. doi:10.1016/j.bone.2017.12.023.

13. Gittings DJ, Fryhofer GW, Hast MW, Steinberg DR, Levin LS, Gray BL. The Saline Load Test is Effective at Diagnosing Traumatic Arthrotomies of the Wrist. *Tech Hand Up Extrem Surg* 2019. doi:10.1097/BTH.0000000000000233.

14. Jacobs IN, Redden RA, Goldberg R, Hast M, Salowe R, Mauck RL, *et al.* Pediatric laryn-gotracheal reconstruction with tissue-engineered cartilage in a rabbit model. *The Laryn-goscope* 2016;126 Suppl 1:S5-21. doi:10.1002/lary.25676.

15. Hast MW, Piazza SJ. Position of the quadriceps actuator influences knee loads during sim-ulated squat testing. *J Biomech* 2018;73:227–32. doi:10.1016/j.jbiomech.2018.03.024.

16. Incidence and Economic Burden of Osteoporosis-Related Fractures in the United States, 2005–2025 - Burge - 2007 - *Journal of Bone and Mineral Research* - Wiley Online Library n.d. https://onlinelibrary.wiley.com/doi/full/10.1359/jbmr.061113 (accessed March 4, 2019).

17. Alt V, Miclau T. Osteoporotic fractures

18. The Biological Perspective. *Injury* 2016;47:S1–2. doi:10.1016/S0020-1383(16)30001-8.

19. Singer A, Exuzides A, Spangler L, O'Malley C, Colby C, Johnston K, *et al.* Burden of Illness for Osteoporotic Fractures Compared With Other Serious Diseases Among Postmenopau-sal Women in the United States. Mayo Clin Proc 2015;90:53–62. doi:10.1016/j.mayocp.2014.09.011.

20. Day: Population projections of the United States,... - Google Scholar n.d. https://scholar.google.com/scholar_lookup?hl=en&publication_year=1996&author=JC+Day&title=Population+Projections+of+the+United+States+by+Age%2C+Sex%2C+Race%2C+and+Hispanic+Origin%3A+1995+to+2050 (accessed March 4, 2019).

21. Vokó Z, Gáspár K, Inotai A, Horváth C, Bors K, Speer G, et al. Osteoporotic fractures may impair life as much as the complications of diabetes. *J Eval Clin Pract* 2017;23:1375–80. doi:10.1111/jep.12800.

22. Padegimas EM, Zmistowski B, Lawrence C, Palmquist A, Nicholson TA, Namdari S. Defin-ing optimal calcar screw positioning in proximal humerus fracture fixation. *J Shoulder El-bow Surg* 2017;26:1931–7. doi:10.1016/j.jse.2017.05.003.

Human Motion Lab Update

Josh Baxter, PhD

Director, Human Motion Lab

2018 was a great year in the Human Motion Lab! After developing strong collaborations with clinicians and researchers at Penn, we've had 12 research studies accepted for publication in peer-reviewed journals and 15 abstracts and have presented 9 abstracts and scientific conferences. Our lab is focused on understanding the links between musculoskeletal structure and injury with patient function and outcomes. To do this, we have integrated medical imaging, motion capture, functional testing, computational modeling, and cadaveric experiments to rigorously test clinically important questions.

The Human Motion Lab has active projects with promising young clinicians and researchers at Penn Medicine. In collaboration with the Human Motion Lab, several projects were developed into grant applications and have secured funds:

- Dr. Josh Baxter—Applying machine leaning algorithms to predict tendon health using ultrasound imaging
- Dr. Kathryn O'Connor—Correlating tendon diastasis with functional outcomes in acute Achilles tendon ruptures
- Dr. Rikesh Gandhi—The development of a low-cost hand-tracking sensor to measure hand motion
- Dr. Comron Saifi—Validation of a functional screening for patients with spinal deformity

Patient movement biomechanics that were once challenging to characterize, can now be accurately quantified in the Human Motion Lab at Penn Medicine. Located within the clinics of the Department of Orthopaedic Surgery, the Human Motion Lab's mission is simple: support decision making with objective and quantitative measurements of patient biomechanics. The 1,200 square foot lab is fully instrumented with motion capture, strength testing, muscle analysis, and ultrasonography equipment to study a wide array of musculoskeletal pathologies. These resources allow our researchers to work closely with musculoskeletal providers to identify key indicators of injury and treatment outcomes.

Thanks to the Human Motion Lab being located in the Department of Orthopaedic Surgery clinics at Penn Medicine University City, we are able to prospectively study patients as part of their routine visits to see their treating physician. We are currently studying the effects of treatment on patients following Achilles tendon ruptures. Working closely with Dr. O'Connor, we have discovered that the calf muscles change their shape after tendon rupture. Importantly, the magnitude of this change in muscle shape in strongly correlated with the amount of power deficits measured 3 months after injury. With these important findings, we are developing a follow-up study to determine the clinical treatments that minimize these changes in muscle structure. To help understand these links between muscle-tendon structure and function, we developed a computer simulation where we tested how changing the muscle and tendon affected patient function. Working with Drs. Farber and Hast, we confirmed our clinical findings that muscle changes are responsible for functional deficits, which are unique in the fact that these Achilles tendon injuries lead to changes in muscle. These computational simulation findings were published in the Journal of Biomechanics.

The Human Motion Lab is focused on establishing itself as a leader in the field of Achilles tendon health. Using motion capture, ultrasonography imaging, and musculoskeletal modelling we are beginning to explain the biomechanical factors that explain functional outcomes in these patient cohorts. With strong collaborations around the Department of Orthopaedic Surgery, we are excited for the future of the Human Motion Lab.

Penn Orthoplastic Limb Salvage Center Update

Meghan Wilson, RN

The Penn Orthoplastic Limb Salvage Center (POLSC) has taken off after its official program launch in July 2018. This unique program is headed by Dr. L. Scott Levin, Dr. Stephen Kovach, and Dr. Samir Mehta. Similar subspecialties are not only rare across the nation, but also not formally combined. The POLSC is a niche collaboration between orthopedics and plastic reconstructive surgery with the incorporation of complex microvascular surgical techniques.

The number one goal of the program is to preserve limb function to patients at risk for amputation or loss of limb function due to complex trauma, bone loss, soft tissue compromise, infection, vascular compromise, mal-union and non-union, or complicated sarcomas. There is an individual multi-team collaboration for each case to ensure there is adequate healthy tissue coverage to maintain wound closure and avoid infections, while also correcting boney injuries. This includes treatments such as vascularized free muscle and bone grafts, limb lengthening, and tendon and nerve transfers.

Since the official launch of POLSC, community outreach has been increasing, bringing in more patients looking for limb salvage evaluation. Awareness of the program has led to increased internal, as well as external referrals from other healthcare organizations in the surrounding areas. We are promoting ourselves as an additional resource to those health care centers who do not have access to the skilled techniques we can offer here at Penn. There has also been an increase in public awareness that has led to individual patients finding us online and through word of mouth.

The program's clinical staff is also growing with the addition of two new clinical roles. In December, the POLSC has added a full-time registered nurse to assist in these complex patient cases to manage their care and promote the program. There will also be a dedicated orthoplastic and limb salvage fellow starting in August of 2019. The fellow will learn different surgical approaches for managing bone trauma, soft tissue trauma, infection, tendon injury and transfers, acquired conditions, and microsurgery (including nerve repair and reconstruction, free soft tissue transfer, vascularized bone grafts, upper extremity replantation/ allotransplantation, and brachial plexus surgery). The addition of these two clinical roles will lead to the growth of the POLSC with hopes to develop dedicated limb salvage clinic time slots. These combined roles will increase continuity in the complex care these patients require.

The program extends beyond these complex reconstructive cases. Another component of POLSC includes the Total Aesthetic Limb Lengthening & Extremity Reconstruction (TALLER). Headed by Dr. Samir Mehta, The TALLER program is one of only a handful in the world and is ideal for people who want a discreet, less-invasive way to increase their height. TALLER involves using the advanced NUVASIVE technology which stimulates bone growth with an internal fixation and the assistance of an external magnetic devise patients can use at home daily to lengthen their lower extremities. This technique is already being used with great success within POLSC to treat patients who have suffered significant bone loss and require bone lengthening, usually in addition to a free vascularized bone autograft.

Additionally, POLSC includes our forearm vascularized composite allograft (VCA) recipients in our hand transplant program. So far, all transplant patients we have done at Penn have received bilateral hand transplants with 100% success. This program encompasses a large team that spends countless hours evaluating, preparing, and caring for recipients of hand transplants. These are life-long patients who will continue to be under our care from here on out. This continues to be a very active program as we are constantly evaluating, listing, and treating these patients.

POLSC will continue to grow and develop, leading the nation on the forefront of what microvascular surgery can accomplish. The annual Penn Flap course will continue to increase training residents and fellows, who will go on to discover more ways to restore limb function through microvascular surgery. Using a multidisciplinary approach, we ensure the patient is treated as a whole and restore dignity and function back to our patients.

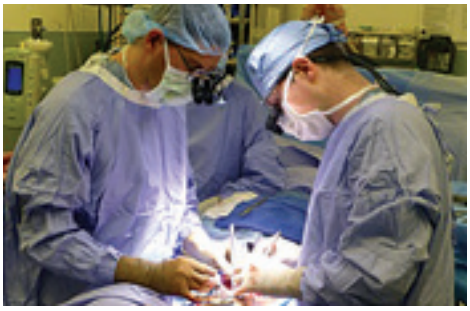


Figure 1. Dr. Stephen Kovach preforms a microvascular procedure for limb salvage.

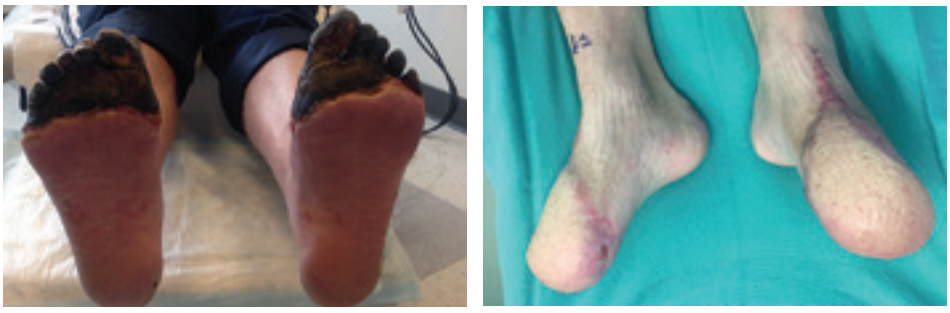


Figure 2. Images depicts before and after of a microvascular salvage procedure; Patient underwent a debridement of all necrotic tissue, then a lateral arm microvascular flap composed of skin, soft tissue and blood vessels was harvested and transferred to both feet. This microanastomosis (microsurgical attachment) of flap vessels to the recipient vessels was performed using the operating microscope.

Clinical Research Update

Annamarie D. Horan, MPA, PhD

Director of Clinical Research, Orthopaedic Surgery and Anesthesia & Critical Care

Annamarie Horan, PhD, Director of Clinical Resarch, Orthopaedic Surgery and Anesthesiology & Critical Care.

Samir Mehta, Chief, Division of Orthopaedic Trauma, Medical Director, Orthopaedic Clinical Research.
Associate Professor of Orthopaedic Surgery

Penn Orthopaedics Clinical Research continues to grow and evolve in response to the needs of our patient population, the availability of technology, and the innovative drive and reputation of our faculty. Each subspecialty has grown substantially and almost every Division has an assigned CRC. Some Division specific highlights for the year are noted. It has been a very exciting year and space does not permit full itemization. We hope that you appreciate the outstanding effort put forth by our faculty and staff highlighted in the following summaries.

The **Adult Reconstruction** faculty celebrates major accomplishments this year. Dr. Gwo-Chin Lee began work on an extramurally funded, investigator initiated, retrospective cohort study. The study, sponsored by Ferring Pharmaceuticals, investigates *Patient and Clinical Factors Related to Positive Response From Hyaluronic Acid Injections*. Dr. Lee also serves as Principal Investigator (PI) on four prospectively enrolling industry sponsored studies with Smith & Nephew (NCT03056534), KCI USA (NCT03274466), Recro Pharma, Inc. (NCT03434275) and United Orthopedic Corp. (NCT02761499). Dr. Lee also collaborates with colleagues at the Rothman Institute on an unfunded project to investigate *The Utility of Next-generation Sequencing for the Diagnosis of Periprosthetic Joint Infection* (NCT03200470). Dr. Neil Sheth has started his first industry sponsored study with Medacta to evaluate their Masterlock® Hip device and has also secured funding from Medacta in parallel for an investigator initiated retrospective review of the transition from posterior approach primary Total Hip Arthroplasty (THA) to anterior approach THA. We are also introducing Dr. Christopher Travers as a new PI at Pennsylvania Hospital. Dr. Travers assumed the responsibility for two of Dr. Kamath's studies upon his departure. Easily the biggest news in Adult Reconstruction Clinical Research is the initiation of the Mymobility study. *A Prospective Multicenter Longitudinal Cohort Study of the Mymobility®* Platform (NCT03737149) seeks to enroll 600 patients at Penn Orthopaedics, and 10500 across all sites, to determine if mobile application-guided education and exercise, paired with accurate and sensitive activity monitoring captured from consumer wearables, can provide a viable (and potentially improved) alternative to current standard of care physical therapy for hip and knee arthroplasty. Dr. Craig Israelite is the PI for this study at Penn Orthopaedics, Drs. Charles Nelson and Eric Hume are sub-Investigators. Both Dr. Nelson and Hume have active Clinical Research portfolios of their own. Dr. Nelson is the PI on the PCORI co-sponsored PEPPER Study (NCT02810704). Dr. Hume is the PI for two DePuy sponsored post-marketing approval Ceramic-on-Ceramic Total Hip Replacement Studies (NCT02096211 and NCT01657435) and he also s Joint Replacement Registry (AJRR).

Dr. Al Mukaddam, CRC in training.

Dr. KaplanMarcoon, CRC in training.

FOP Clinical Research has enjoyed multiple successes this year. The Clementia Pharmaceuticals sponsored research program to study Palovarotene, a RARy-specific agonist, as the first therapeutic intervention against Fibrodysplasia Ossificans Progressiva continued with the addition of a Phase 3 study, NCT03312634. A second industry sponsor, Regeneron Pharmaceuticals, has joined the fight against FOP with the initiation of the LUMINA-1 Trial, NCT03188666. The LUMINA-1 Trial will test REGN2477 vs placebo over a 6 month dosing period followed by a 6 month follow up open-label treatment period. The study will assess the safety and tolerability of the investigational product in the target population and will attempt to measure the change from baseline in heterotopic ossification (HO) in patients as measured by 18-NaF uptake by PET and CT. Dr. Frederick Kaplan is the Global PI for the Clementia Program and the Global Study Advisor for the Regeneron Study. Dr. Mona Al Mukaddam is the Penn PI for all FOP Clinical Research. We are extremely hopeful that the combined efforts of these ongoing and planned studies will result in a therapy that will have minimal side effects and will restore these patients to a mobile lifestyle.

On other fronts, Dr. Kaplan's lifetime of selfless and relentless pursuit of a cure for FOP was recognized this year through the reception of the Grand Hamdan International Award - Musculoskeletal Disorders. This award is focused on those who are dedicated to the alleviation of the sufferings of humanity through research and exemplary service. For more information please visit http://www.hmaward.org.ae/archive.php?termid=67

With the initiation of the GE Healthcare sponsored VolumeRad observational study, NCT03856450, (Dr. David Steinberg, PI) **Hand Surgery** leads the Department in the metric that every faculty member in the Division is the PI on at least one extramurally funded study. Dr. David Bozentka is the local PI of *A Multicenter, Prospective, Randomized, Subject and Evaluator Blinded Comparative Study of Nerve Cuffs and Avance Nerve Graft Evaluating Recovery Outcomes for the Repair of Nerve Discontinuities (RECON*), NCT01809002, which is sponsored by Axogen Corporation. Dr. Benjamin Gray is the local PI of the *Protect Neuro Trial Post Marketing Surveillance Prospective Cohort Evaluation of Neurocap®* In *The Treatment of Symptomatic Neuroma*, NCT02993276, sponsored by Polyganics BV. Dr. L. Scott Levin is the co-Global PI of the RECON study with Dr. Jonathan Isaacs, and Dr. Levin is the North American PI of the Polyganics study. Dr. Levin has himself secured an impressive amount of extramural research support in the past year. His dedication to Vascularized Composite Allotransplantation (VCA) surgery has resulted in the success of his partnering-PI relationship with the University of Delaware's Dr. David Tulsky and Dr. Scott Tintle of Walter Reed National Military Medical Center and Penn Orthopaedics. Together, Drs. Levin, Tintle, and Tulsky have been awarded a Department of the Army grant entitled, *Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient Reported Outcome Metrics and the Candidate Screening Process*. This project will carefully and thoughtfully examine the entire process of VCA candidate selection, surgery, and post-operative outcomes to establish *de novo* multimodal candidate guidelines for this growing surgical subspecialty.

In other Divisions the activity from previous years is carrying forward with expansion on the horizon. **Shoulder & Elbow** has three active industry studies under Dr. Andrew Kuntz as PI. Two of these are sponsored by Integra Lifesciences and one is sponsored by Orthofix. Dr. Kuntz is fielding another study for the upcoming year as is Dr. Huffman. Both pending studies are from new sponsors. Dr. Harvey Smith has been transferring his skills and leadership in bench science to serve as the PI in the DePuy Vivigen study, NCT02814825. Dr. Smith is also courting other studies and sponsors for the **Spine Division**. Dr. Robert Wilson in **Orthopaedic Oncology** is initiating human subjects research as well. We look forward to working with him and supporting his activity.

Sports Medicine clinical research now includes a NIAMS/PCORI co-sponsored trial through Vanderbilt University Medical Center, under the local leadership of Dr. John Kelly to study *Operative Versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears (ARC),* NCT03295994, with an overall target enrollment of 800 subjects and 12 month follow-up. Dr. James Carey is the Global and Local PI of the Vericel Corporation sponsored PEAK study, NCT03588975, entitled *A Study of MACI in Patients Aged 10 to <17 Years With Symptomatic Chondral or Osteochondral Defects of the Knee (PEAK).* The objective of this study is to compare the efficacy and safety of MACI® vs arthroscopic microfracture in the treatment of patients aged 10 to <17 years with symptomatic articular chondral or osteochondral defects of the knee. Dr. Carey is also the local PI of the *HyaloFAST Trial for Repair of Articular Cartilage in the Knee (FastTRACK),* NCT02659215, sponsored by Anika Therapeutics, Inc., which evaluates the safety and efficacy of Hyalofast® scaffold with bone marrow aspirate concentrate (BMAC) compared to microfracture in the treatment of symptomatic cartilage defects of the knee. He also serves as the site PI of the ROCK Registry. Dr. Zgonis has recently initiated work on his investigator initiated study to examine *T1Rho as a Surrogate for Cartilage Overload in Patellofemoral Malalignment* that was funded through the Penn Center for Precision Medicine.

Foot & Ankle has undergone a few transitions this year as long time PI of the STAR Ankle study (NCT01284283) Dr. Keith Wapner passed the baton to Dr. Kathryn O'Connor. Dr. O'Connor also received and is executing her own study with Dr. Josh Baxter to *Correlate Tendon Diastasis with Functional Outcomes in Achilles Tendon Ruptures*, for which she won a McCabe Award. Dr. Dan Farber remains the PI of the DJO *CMF Bone Stimulation as Adjunct to Surgical Treatment of Ankle Fractures* (NCT02688855) and this study will be expanding to Presbyterian Medical Center to include the Ortho Trauma Faculty in order to boost recruitment.

After a short period of maintenance and minor contraction, **Orthopaedic Trauma** is gearing up to launch several new funded studies. Last year, we told you about the PCORI sponsored REGAIN Trial (NCT02507505) (PI: Mark Neuman, MD), an ongoing $12M *42*-site multicenter trial to investigate the role of anesthesia delivery on functional outcomes after hip fracture surgery in the elderly. REGAIN incorporates a well-integrated team of Orthopaedic Surgery Faculty (Drs. Mehta co-I, Donegan, and Ahn) with faculty from Anesthesiology & Critical Care (Drs. Neuman, Elkassabany, and others) and is pressing hard to meet its enrollment goal of 1600 evaluable subjects; 1188 subject have been randomized to date (50 at Penn) and this study is already the largest to ever compare general vs spinal anesthesia in any indication. Next up for Ortho Trauma is another PCORI co-sponsored study with McMaster University that is directed through the University of Maryland entitled *Pre-operative Alcohol Skin Solutions in Fractured Extremities (PREPARE)* NCT03523962. The

PREPARE study will compare the most common alcohol-based pre-operative antiseptic skin solutions used during extremity fracture surgery: DuraPrep vs ChloraPrep. Randomization will be cycled by time at each site and 8000 subjects will be followed for up to 12 months for primary and secondary endpoints. Other similarly sized studies in the Ortho Trauma queue include a grant from the AO Foundation to investigate the *Intersection of the Transcriptome and Microbiome,* this study will be starting to enroll imminently and will expand on previously published work.

At this time, it is important to recognize the **Staff**. We congratulate those who worked with us previously and who have moved on to other opportunities. At this writing, we have recently said farewell to Rupa Chowdary and note that Alyssa Perez de Corcho will be departing our team. Both of these individuals worked well with us and have moved on professionally. John Flacco who served as a CRC for Adult Reconstruction has been accepted to Medical School and will be starting in the fall of 2019. Aliaksei Basatski, formerly of Penn Orthopaedics has transitioned into a Project Manager role in Penn Anesthesiology & Critical Care (ACC). We welcome Sarah Bart to FOP, Kelly Clark to Ortho Trauma, Dr. Mary Dooley to Hand, Zahida Halimi to ACC, and Aaron Tatad to Spine. We also congratulate those on our team who recently passed the ACRP exam to become Certified Clinical Research Coordinators (CCRCs): Alyssa Perez de Corcho and Beth Howard.

FY 19 Clinical Research Team

Figure 1 Top row, Sarah Bart (FOP), Evan Bannister (Shoulder & Elbow), Aliaksei Basatski (ACC), Rupa Chowdary (ACC), Rebecca Churchill ((Temp), Kelly Clark (Ortho Trauma). Middle Row, Olivia Colarullo (PAH), Dr. Mary Dooley (Hand), John Flacco (Adult Recon), Zahida Halimi (ACC), Beth Howard (Sports Medicine), Renee Jurek (FOP), Helena Moses (Adult Recon). Bottom Row, Alyssa Perez de Corcho (PAH), Kamlesh Rai (FOP), Aron Schwartz (ACC), Shawn Simmons (Sports Medicine), Cody Sylvester (Temp), Aaron Tatad (Spine), Katherine Toder (FOP).

Thank you to all the named and unnamed staff and faculty on our team, the residents, fellows, and other clinical support staff, and especially the leadership of Penn Orthopaedics and Anesthesiology & Critical Care for their ongoing support of our highly active team. Specifically, we thank the Chairs, Drs. Levin and Fleisher, the Vice-Chairs for Research, Drs. Soslowsky and Eckenhoff as well as the Chief Operating Officers, Neil Ravitz and Dennis Harris for your ongoing guidance and support in every way throughout the year.

Human Tissue Lab Update

Lorianne Kish-Burdsall

The Human Tissue Laboratory,"HTL" opened its doors in August of 2011 under the direction of

Dr. L.Scott Levin., chair of the division of Orthopaedic Surgery at the University of Pennsylvania.The original mission of the lab was to provide an opportunity for residents and surgeons to practice and explore the vast arenas of surgery, review anatomy and learn new approaches and techniques as they are developed that ultimately lead to better patient results and recovery. While the mission has not changed, it has expanded to include assisting authors of medical anatomy books, hosting international courses and workshops to inspire young minds. Since 2011, the human tissue lab has hosted hundreds of courses, comprised of internal training courses and industry partnered events. Departments from all areas of Penn Medicine now use the facility as this type of training is invaluable. The HTL and the teachings of the Penn faculty is what sets the Penn residency program apart from all others in the world.The administration of the HTL continues to reinvest in the lab with improvements, additions and upgrades to equipment. Currently the lab has two full time staff members to ensure availability 7 days a week, day or evening. Penn is proud to offer the same quality experience as is available in a commercial lab.The 14 station HTL offers an HD overhead camera for the lead surgeon, OR quality surgical lights, live streaming capabilities, flat screens for participant viewing, arthroscopy towers, specimen holders, a full complement of arthroscopic trays, a full-size C Arm, peg board positioners, hand held power saws and drills, ancillary instrumentation, disposables, scrubs, locker room and a sterilizing dishwasher. Again this year, the HTL volume and genre of educational events has expanded.The HTL will continue to reinvest in its equipment to enhance the experience of the attendees.

Orthopaedic Administration Update: Navigating a Time of Change

Neil Ravitz, MBA

Chief Operating Officer
Chief Administrative Officer, Musculoskeletal Service Line

Heraclitus, the Greek philosopher, has been quoted as saying "change is the only constant in life." It seems like there is no truer place for that saying than in American healthcare and as such, we continue to see an enormous amount of change at Penn Medicine and in the Department of Orthopaedics. That change takes on many different shapes and sizes, but one thing for sure is that it is constant.

One of the largest changes to impact the American healthcare delivery system this year happened when Medicare moved Total Knee Arthroplasty (TKA) off of the "inpatient only list," meaning that TKAs could be done and reimbursed as an outpatient procedure. Long gone are the days of patients staying in the hospital for a week for knee replacements. In fact, patients at Pennsylvania Hospital and Presbyterian Medical Center routinely are just staying one or two nights after surgery. The pressure placed on the healthcare system by Medicare was soon followed by other insurance providers. This pressure challenges us to think about our patient selection criteria and our systems of care to help support the patients and deliver care within the constraints of payment. Working closely with nursing colleagues on early mobilization and with physical therapy on how to safely discharge a patient are now regular occurrences within the Adult Reconstruction division. As these changes and pressures happen, it forces us to relook at how we deliver care.

We also have seen a tremendous shift from society in reaction to the opioid epidemic in the United States. It has forced us to look closely as individuals and as a department on our opioid prescribing habits. Both Dr. Levin and I are so proud of the way that the physicians, advanced practice providers, residents, and fellows have embraced this work. Over the last 18 months, the department has reduced opioid prescribing by more than 46%. That prescribing represents a significant reduction in the number of pills that are being prescribed into our communities and demonstrates our department's ability to continue to deliver care safely and effectively in this changing environment.

Technology represents another aspect of change in both our personal and professional lives, and we feel that here in the department. We recently started a clinical research study in collaboration with an implant vendor and Apple which is designed to capture patient data post-operatively, while at the same time delivering patient education to them via their iWatch. What seemed futuristic just a decade ago is now happening right here in the department. Whether it is our electronic health record or text alerts that a hip fracture patient has arrived in the emergency room, we will continue to adapt to changes in technology.

We also had two new clinical faculty members join the Department in the past year. Dr. Christopher Travers joined the Adult Reconstruction division in September of 2018 after completing a residency at Tufts and then a fellowship in Adult Reconstruction here in Penn Orthopaedics. His practice is focused on all forms of adult reconstruction. He is seeing patients at Pennsylvania Hospital and in Cherry Hill, NJ and has quickly built a busy practice. Dr Stanley Michael also joined the faculty this past year joining Dr Kevin McHale down at Cape Regional Hospital. He is also a member of the Adult Reconstruction division and joined us after practicing at Temple University for many years. Welcome to both of them!

Each of these examples represent changes in our world. Regardless of the size of change though, each one requires us to look at what we are doing here in the department. It forces us to change and navigate through the stability we seek. The fortunate thing for the Department of Orthopaedics is that we have a tremendous team of professionals working side by side with each other. Physicians, administrators, nurses, physician assistants, residents, fellows all working together is what enables us to navigate this change. Your dedication to patient care and your desire to help Penn Medicine and Penn Orthopaedics be the very best is what makes us strong. Thank you for all you do!

Advancing & Integrating Care Across the Health System

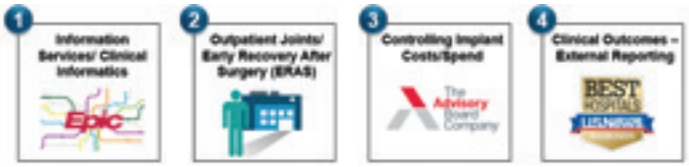
Sean Looby, MHA

Director, Service Line & Network Integration, Musculoskeletal & Rheumatology

The Musculoskeletal and Rheumatology (MSKR) service line continues to evolve in driving advancements and integration across the health system. These efforts are pursued through the work of the multidisciplinary disease teams, other health system wide initiatives, and individual pursuits to improve care at each of the Penn Medicine acute care hospitals. As the health system continues to grow, the potential for focused efforts to drive integration among and between hospitals and physicians throughout the system grows with it. In proactive recognition of this opportunity, we held the Major Lower Joint (MLJ) System Integration Summit in March 2019.

As the first of its kind, the Summit brought together administrative and clinical leadership from the five system hospitals performing joint replacements to focus on opportunities for the advancement and integration of joint arthroplasty care throughout our hospitals and service areas. Representing the largest portion of total orthopedic surgical volume across Penn Medicine (over 6,000 cases annually), and facing various changing dynamics impacting where and how care is provided and paid for, joint arthroplasty offers opportunities and challenges ripe for this type of focused effort. The goals of the Summit were to bring stakeholders together to share information and provide education, gain insights into opportunities and challenges, and provide a forum for collaboration among teams across hospitals and markets.

The Summit was well attended, with over 75 total attendees, including 20 surgeons. In addition to a keynote speech, a panel discussion, and an update on clinical research opportunities, the bulk of the time was spent in breakout sessions focusing on four key areas:



It was a productive day with an abundance of both best practices and challenges shared. Given that each of our hospitals serve different patient populations, have different capacity and resource constraints, and have various other inherent differences, the discussions and opportunities identified were a mix of those impacting all system hospitals and those related to specific hospitals. This format allowed stakeholders to understand and appreciate the different obstacles faced by their peers at other hospitals, while recognizing the benefit and value of standardizing and integrating various aspects of care across the health system.

As with most efforts of this nature, the follow-up and action plan is where the rubber meets the road. MSKR service line leadership has taken the lead in setting a path forward and developing a framework for pursuing identified opportunities, with a mix of both system-level and hospital-level ownership of improvement initiatives. As the demand for joint replacement services continues to grow with the aging population, and payers and consumers increasingly seek and reward high quality, cost efficient care, it is these types of initiatives that will help position us for continued success.

As we think more broadly across the MSKR service line, we must continue to identify and create opportunities for collaboration to leverage and spread the novel work being done throughout the system, while allowing our hospitals and physicians to achieve the value and reap the benefits of being part of the MSKR service line and broader health system. We look forward to working closely with stakeholders across the health system to continue to identify and implement innovative approaches to improve care for the patients we serve.

Orthopaedic Advanced Practice Provider Update

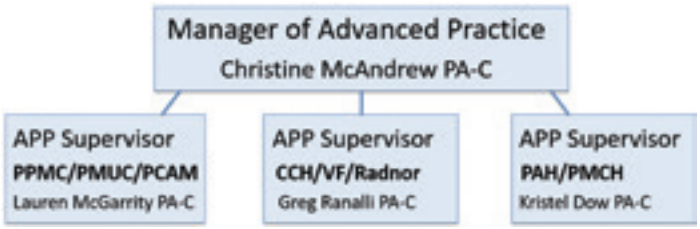
Christine McAndrew, PA-C

'Advanced Practice Provider'(APP) is a general title used to describe individuals who have completed the advanced education and training that qualifies them to (1) manage medical problems and (2) prescribe and manage treatments within the scope of their training. Some specific types of APPs include clinical nurse specialists, nurse practitioners, and physician assistants. APPs are well positioned and increasingly recognized for their ability to drive value across healthcare.

Within the department of Orthopaedic Surgery we have had extensive growth within our APPs over the last ten years or so. Back in 2002 the first three advanced practice providers were hired into the department. Over the next ten years the APPs doubled in size. From 2012 until present day the APP growth has risen to 36 advanced practice providers across all sub divisions and geographic locations. The ratio is just about 1:1; supervising physician: APP.

Our APP's have had a tremendous impact on patient care within Penn Orthopaedics. They are on the front lines making significant strides to improve clinical care here at Penn Medicine. They have increased access to care, support an increasing clinical demand, and manage continuity and continuum of care. They drive safety, quality, cost and satisfaction to our patients. The majority of our APPs all run independent sessions which range from post-operative patients, return and new patients; as well as minor procedures. They also do the majority of the history and physicals and prepare the patients for surgery. Each year we have seen an increase in total visits by our APPs. In FY18 they saw a total of 3,491 new patients and 17,182 established patients.

In October of 2018 we implemented a new APP Leadership structure. Under the new configuration we have an APP Supervisor at each hospital: PPMC, PAH and CCH. The APP supervisors work under the direction of the APP Manager to provide clinical and operational management for the APPs aligned to their regional assignments, while maintaining their clinical responsibilities and in support of departmental missions. Our goal is to continue to expand the individual development of our APPs and open lines of communication to reach our common objective of improved patient care.



In January of 2019 the department opened the Orthopaedic Extended Hours of Cherry Hill which is primarily physician assistant run and supported by Dr. Samir Mehta as attending physician. Hours of operation are Tuesday 4-8PM and Saturday 9-1PM. Appointments can be made ahead of time or walks ins are available. This has not only opened access to care but also allows for additional hours beyond the "normal" business hours. It allows us to streamline care to ensure that patients are getting in to the correct surgeon or practitioner and in a timely manner.

In summary, the advanced practitioners of Orthopaedic surgery are highly valued members of the clinical care team. I would like to take this opportunity to personally congratulate the advanced practitioners on their achievements and thank them for their endless dedication and commitment to the department and patients.

Figure 1. Some of the many APPs after a meeting at Pennsylvania Hospital

AN FDA-APPROVED OPTION FOR PATIENTS WITH ARTICULAR CARTILAGE DEFECTS OF THE KNEE **AVAILABLE ONLY IN THE U.S.**

AUTOLOGOUS CHONDROCYTE DELIVERY, **SIMPLIFIED**

maci®

autologous cultured chondrocytes on porcine collagen membrane

MACI builds on over 20 years success with Articular Cartilage Implantation (ACI)[1]
Utilizing a unique biocompatible membrane, MACI offers potential benefits over traditional ACI through minimal incision, simplified delivery, and suture-free fixation for the treatment of articular cartilage defects of the knee.

INDICATION

MACI® (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product that is indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the adult knee, with or without bone involvement.

MACI is intended for autologous use and must only be administered to the patient for whom it was manufactured. The implantation of MACI is to be performed via an arthrotomy to the knee joint under sterile conditions.

The amount of MACI administered is dependent upon the size (surface in cm2) of the cartilage defect. The implantation membrane is trimmed by the treating surgeon to the size and shape of the defect, to ensure the damaged area is completely covered, and implanted cell-side down.

Limitations of Use

Effectiveness of MACI in joints other than the knee has not been established.

Safety and effectiveness of MACI in patients over the age of 55 years have not been established.

IMPORTANT SAFETY INFORMATION

MACI is contraindicated in patients with a known history of hypersensitivity to gentamicin, other aminoglycosides, or products of porcine or bovine origin. MACI is also contraindicated for patients with severe osteoarthritis of the knee, inflammatory arthritis, inflammatory joint disease, or uncorrected congenital blood coagulation disorders. MACI is also not indicated for use in patients who have undergone prior knee surgery in the past 6 months, excluding surgery to procure a biopsy or a concomitant procedure to prepare the knee for a MACI implant.

MACI is contraindicated in patients who are unable to follow a physician-prescribed post-surgical rehabilitation program.

The safety of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of present malignant or dysplastic cells during the culturing process or implantation is possible.

Patients undergoing procedures associated with MACI are not routinely tested for transmissible infectious diseases. A cartilage biopsy and MACI implant may carry the risk of transmitting infectious diseases to healthcare providers handling the tissue. Universal precautions should be employed when handling the biopsy samples and the MACI product.

Final sterility test results are not available at the time of shipping. In the case of positive sterility results, health care provider(s) will be contacted.

To create a favorable environment for healing, concomitant pathologies that include meniscal pathology, cruciate ligament instability and joint misalignment, must be addressed prior to or concurrent with the implantation of MACI.

Local treatment guidelines regarding the use of thromboprophylaxis and antibiotic prophylaxis around orthopaedic surgery should be followed. Use in patients with local inflammations or active infections in the bone, joint, and surrounding soft tissue should be temporarily deferred until documented recovery.

The MACI implant is not recommended during pregnancy. For implantations post-pregnancy, the safety of breast feeding to infant has not been determined.

Use of MACI in pediatric patients (younger than 18 years of age) or patients over 65 years of age has not been established.

The most frequently occurring adverse reactions reported for MACI (≥5%) were arthralgia, tendonitis, back pain, joint swelling, and joint effusion.

Serious adverse reactions reported for MACI were arthralgia, cartilage injury, meniscus injury, treatment failure, and osteoarthritis.

VERICEL

For more information, please see Highlights of Prescribing Information about MACI, or visit MACI.com

1. Saris D, Price A, Widuchowski W, et al. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: Two-year follow-up of a prospective randomized trial. Am J Sports Med. 2014;42(6):1384-94.

maci

autologous cultured chondrocytes on porcine collagen membrane

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MACI safely and effectively. See full prescribing information for MACI.

MACI® (autologous cultured chondrocytes on porcine collagen membrane)

Cellular sheet for autologous implantation

Initial U.S. Approval: 2016

RECENT MAJOR CHANGES

Dosage and Administration, shaping the MACI implant (2.2) 06/2017

INDICATIONS AND USAGE

MACI® is an autologous cellularized scaffold product indicated for the repair of symptomatic, single or multiple full-thickness cartilage defects of the knee with or without bone involvement in adults. (1)

Limitations of Use

- Effectiveness of MACI in joints other than the knee has not been established.
- Safety and effectiveness of MACI in patients over the age of 55 years have not been established.

DOSAGE AND ADMINISTRATION

For autologous implantation only.

- Contact Vericel at 1-800-453-6948 or www.MACI.com regarding training materials for surgical implantation of MACI. (2)
- The amount of MACI implanted depends on the size (surface area in cm^2) of the cartilage defect. (2.1)
- MACI should be trimmed to the size and shape of the defect and implanted with the cell-side down. (2.2)

DOSAGE FORMS AND STRENGTHS

Each 3 x 5 cm cellular sheet (MACI implant) consists of autologous cultured chondrocytes on a resorbable porcine Type I/III collagen membrane, at a density of at least 500,000 cells per cm^2. (3)

CONTRAINDICATIONS

- Known history of hypersensitivity to gentamicin, other aminoglycosides, or products of porcine or bovine origin. (4)
- Severe osteoarthritis of the knee. (4)
- Inflammatory arthritis, inflammatory joint disease, or uncorrected congenital blood coagulation disorders. (4)
- Prior knee surgery (within 6 months), excluding surgery to procure a biopsy or a concomitant procedure to prepare the knee for a MACI implant. (4)
- Inability to cooperate with a physician-prescribed post-surgical rehabilitation program. (4)

WARNINGS AND PRECAUTIONS

- Safety of MACI in patients with malignancy in the area of cartilage biopsy or implant is unknown. Expansion of malignant or dysplastic cells present in biopsy tissue during manufacture and subsequent implantation may be possible. (5.1)
- Because patients undergoing procedures associated with MACI are not routinely tested for transmissible infectious diseases, cartilage biopsy and MACI implant may carry risk of transmitting infectious diseases. (5.2)
- Local inflammation or active infection in the bone, joint, and surrounding soft tissue, meniscal pathology, cruciate ligament instability, and misalignment should be assessed and treated prior to or concurrent with MACI implantation. (5.3)
- Final sterility test results are not available at the time of shipping. (5.4)

ADVERSE REACTIONS

The most frequently occurring adverse reactions (≥5%) reported for MACI were arthralgia, tendonitis, back pain, joint swelling, and joint effusion. (6)

Serious adverse reactions reported for MACI were arthralgia, cartilage injury, meniscus injury, treatment failure, and osteoarthritis. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Vericel at 1-800-453-6948 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch for voluntary reporting of adverse reactions.

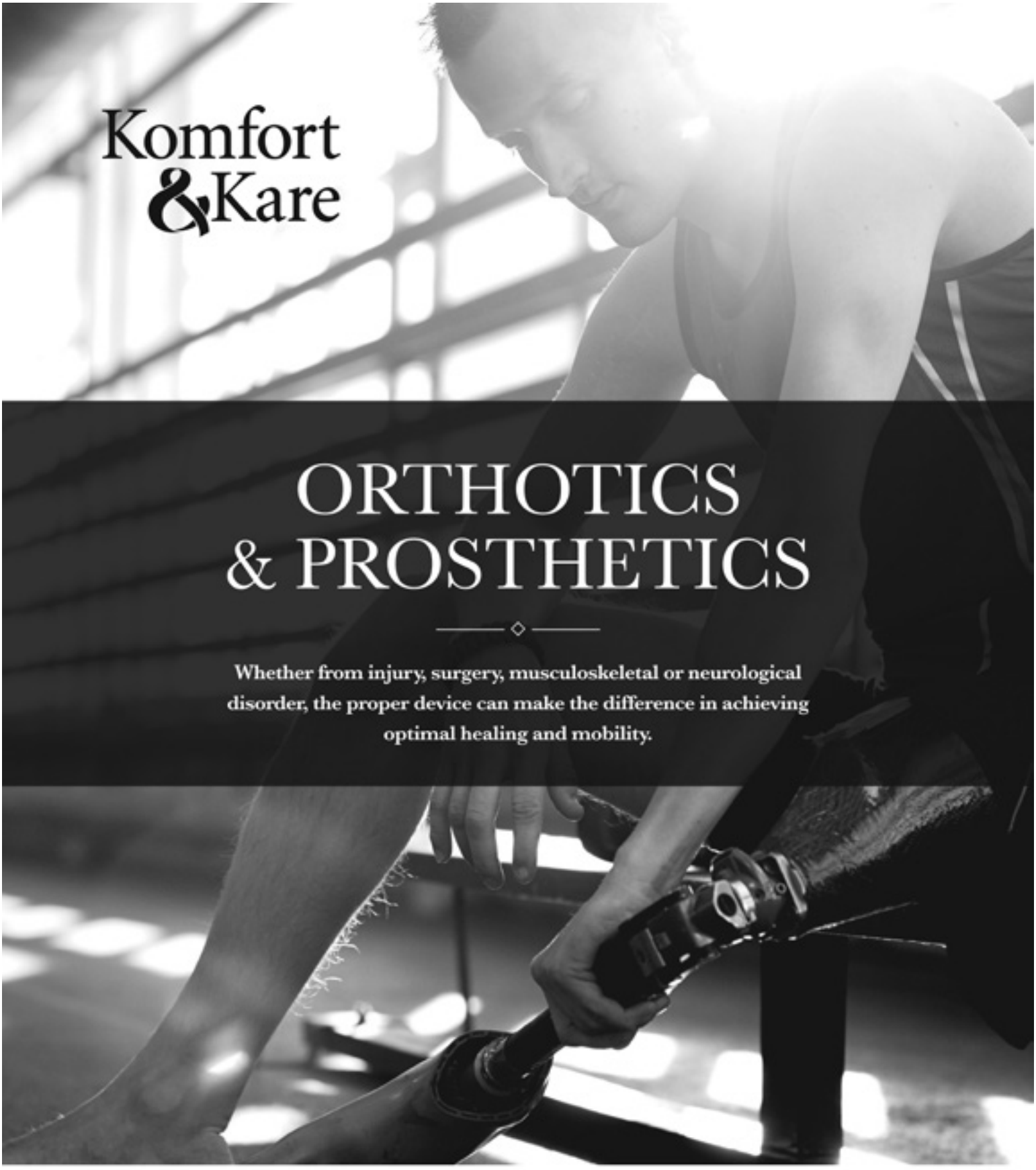
USE IN SPECIFIC POPULATIONS

Pregnancy: Because MACI implantation requires invasive surgical procedures, use in pregnancy is not recommended. (8.1)

See 17 for PATIENT COUNSELING INFORMATION Revised: 06/2017

VERICEL

For more information, please see Full Prescribing Information on MACI.com



Komfort &Kare

ORTHOTICS & PROSTHETICS

Whether from injury, surgery, musculoskeletal or neurological disorder, the proper device can make the difference in achieving optimal healing and mobility.

424 N. White Horse Pike
Magnolia, NJ 08049
856.854.3100

205 Tuckerton Road
Medford, NJ 08055
856.854.3100

3 Myers Drive
Building A, Suite 202
Mullica Hill, NJ 08062
856.854.3100

230 W. Washington Square
5th Floor
Philadelphia, PA 19106
215.829.6955

266 W. Lancaster Ave
Suite 300B
Malvern, PA 19355
610.981.4782

KOMFORTKARE.COM

University of Pennsylvania Orthopaedic Journal

2019 Clinical and Basic Science Research

The following sections highlight clinical and basic science research conducted at the University of Pennsylvania in the field of Orthopedics, including work from the Department of Orthopaedic Surgery, The McKay Laboratory for Orthopaedic Research, Children's Hospital of Philadelphia, the Philadelphia Veterans Affairs Translational Musculoskeletal Research Center, The Biedermann Laboratory for Orthopaedic Research, and the Human Motion Lab. In addition to research, each clinical section is preceded with a "Tips and Tricks" article highlighting case reports or surgical techniques for education and to display the breadth of musculoskeletal disease seen and treated in our hospital system.

Clinical Research Sections:

Trauma

Spine

Sports

Hand

Pediatrics

Shoulder and Elbow

Arthroplasty

Foot and Ankle

Oncology

Orthoplastics

Basic Science Research Sections:

Bone

Cartilage

Tendon

Trauma Tips & Tricks: Cortical Replacing Screws for Reducing Proximal-Third Tibial Shaft Fractures

Agnes Z. Dardas, MD, MSc
Samir Mehta, MD

Background

Extramedullary proximal tibial shaft fractures provide numerous challenges to orthopaedic surgeons with respect to appropriate reduction that re-establishes length, alignment, and rotation. This is due to numerous factors including thinner cortices, spongier metaphyseal bone, the proximal flared shape of the tibia, and soft-tissue deforming forces. Numerous intra-operative reduction and fixation techniques have been reported including external fixation, percutaneous plate fixation, open reduction internal fixation, intramedullary nails, and any combination of the above as an initial reduction and subsequent permanent fixation technique. Intramedullary nails provide an ideal fixation method due to their load-sharing ability, thereby allowing early mobilization. However, achieving coronal and sagittal alignment presents a challenge for otherwise-uncomplicated proximal third tibial shaft fractures due to the size mismatch of the wide metaphyseal proximal tibia and significantly smaller intramedullary nail diameter with reports of malreduction in 58 to 84% of fractures having undergone intramedullary nailing.[1,2] This often results in an apex anterior deformity due to the proximal and anterior pull of the extensor mechanism and valgus malalignment.

First described by Kretek et al, cortical replacing ("blocking") screws provide a supplementary technique to addressing malalignment.[3] Also known as "Poller" screws, referring to metal-shaped objects that are used to block or re-direct road-traffic,[4] they essentially serve the same purpose during placement of intramedullary nails for proximal tibial shaft fractures by re-directing the guidewire and subsequently the nail in such a manner that corrects the deforming forces. Additionally, when left in situ, they provide increased biomechanical construct stability and resistance to continued deforming forces post-operatively by providing a three-point internal mold.[5,6] Below, we review tips and tricks to implementing this technique in order to successfully reduce proximal tibial shaft fractures during intramedullary nail fixation.

Preoperative Assessment

As with any proximal tibia fracture, pre-operative assessment should start with good history taking, including prior injury or congenital deformity to the limb, and physical exam, including a high suspicion for developing compartment syndrome, sustaining a neurovascular injury due to the anatomic proximity of the peroneal artery and nerves, or presenting with an open fracture due to the subcutaneous position of the tibia anteriorly. Obtain appropriate orthogonal radiographs of the tibia (Figure 1A, 1B), knee, and ankle. Supplementary views can include the "twin peaks" and "flat plateau" views to better assess intra-articular extension. If there is concern for intra-articular extension and the appropriate resources, proceed with a CT scan.

Initial stabilization can occur with a short leg splint and knee immobilizer to ensure that neither the respective proximal or distal ends act as a fulcrum for further deformity. Alternatively, a long leg splint may be applied.

Intramedullary fixation may be contraindicated in Gustilo-Anderson type II or III open fractures due to need for repeat debridements and higher risks of development of osteomyelitis; an external fixation construct may be more appropriate initially in such cases.

Surgical Technique

The patient is placed supine on a radiolucent table with a bump under the ipsilateral hip so that the patella faces toward the ceiling. Cortical replacing screws can be used with any nail insertion technique. However, a suprapatellar approach with a radiolucent foam ramp placing the knee in 10-20 degrees of flexion provides among the easiest intra-operative set-ups as it reduces deforming forces by relaxing the extensor mechanism and removing gravity, and provides easier fluoroscopic assessment by positioning the limb parallel to the floor and elevating it from the contralateral limb for easier lateral views. For the purposes of this review, the blocking screw technique will be highlighted with a suprapatellar approach.

Mark the incision from one finger breadth above the superior pole of the patella to 2-3cm proximally. Incise down through the quadriceps tendon to bone in line with the fibers. Using blunt finger dissection, free up adhesions in the suprapatellar pouch and insert the soft-tissue guide. Confirm via fluoroscopy the starting

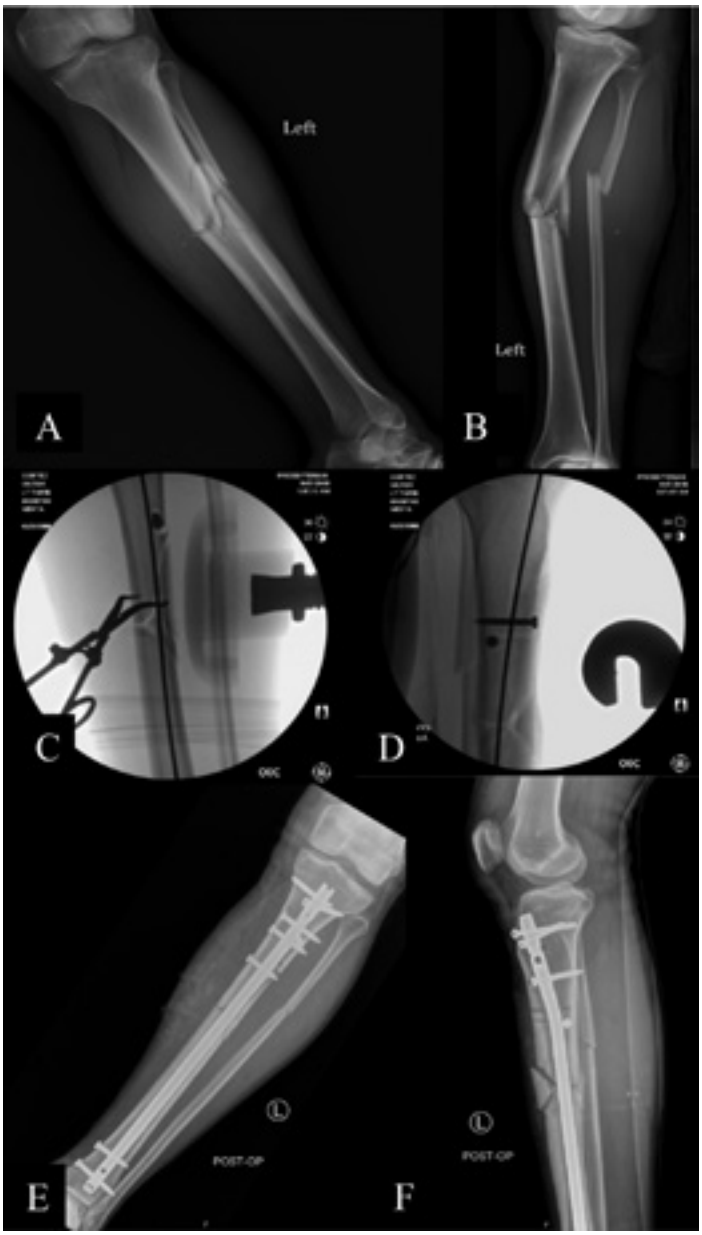


Figure 1. Radiographs demonstrating the use of cortical replacing screws for improving intra-operative reduction of a proximal- third tibial shaft fracture during insertion of an intramedullary nail. **(A)** AP radiograph of a proximal-third tibial shaft fracture with valgus mal-alignment; **(B)** Lateral radiograph of a proximal-third tibial shaft fracture with apex-anterior deformity; **(C)** Intra-operative fluoro with reduction of the fracture using clamps; **(D)** Intra-operative fluoro with a guidewire passing after placement of posterior and lateral cortical replacing screws; **(E)** Post-operative AP radiograph of a proximal-third tibial shaft fracture after intermedullary nailing using cortical replacing screws; **(F)** Post-operative lateral radiograph of a proximal-third tibial shaft fracture after intermedullary nailing using cortical replacing screws.

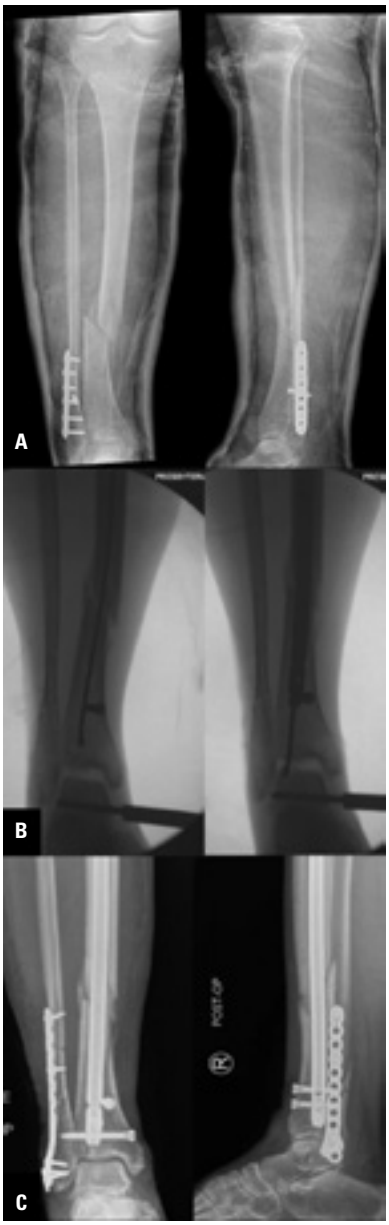


Figure 2. Radiographs demonstrating the use of cortical replacing screws for improving reduction of a distal-third tibial shaft fracture, another location of bone width-nail diameter mismatch. **(A)** AP and lateral radiographs of the initial distal-third tibial shaft fracture with lateral translation; **(B)** Intra-operative fluoros with a guidewire and nail passing after placement of a medial cortical replacing screw; **(C)** Post-operative AP and lateral radiographs of the distal-third tibial shaft fracture after intermedullary nailing using cortical replacing screws.

point as medial to the lateral tibial spine and at the junction between the anterior cortex and anterior articular surface of the tibia with a trajectory parallel to the anterior cortex. Place a guidewire within the soft-tissue guide and provisional advance past the level of the tibial tubercle to confirm appropriate placement. Secure the soft-tissue guide to the femur or tibia using a large-diameter wire to protect the patellofemoral joint. This will maintain the cannula allowing for easy passage of instruments. Use an opening reamer to open the proximal tibial cortex. Assess the deformity present at this time and make note of the concave sides on AP and lateral fluoroscopy as this will be where the cortical replacing screws should be placed. Reduce the fracture with closed or open techniques (Figure 1C). Insert a coronal and saggital blocking screw in the proximal fragment at least 1 cm away from the fracture line as needed. An interlocking screw or a large diameter screw ($\geq$ 4.5mm) is recommended as there have been reports of smaller screws bending or breaking with subsequent reaming. Alternatively, a Schantz pin may be initially placed during reaming to reduce deformity to the reamer and subsequently replaced with a screw just prior to final nail insertion (Figure 1D). Introduce a ball-tipped guidewire down the length of the tibia and reassess reduction. These steps may be repeated multiple times until the reduction is deemed satisfactory.

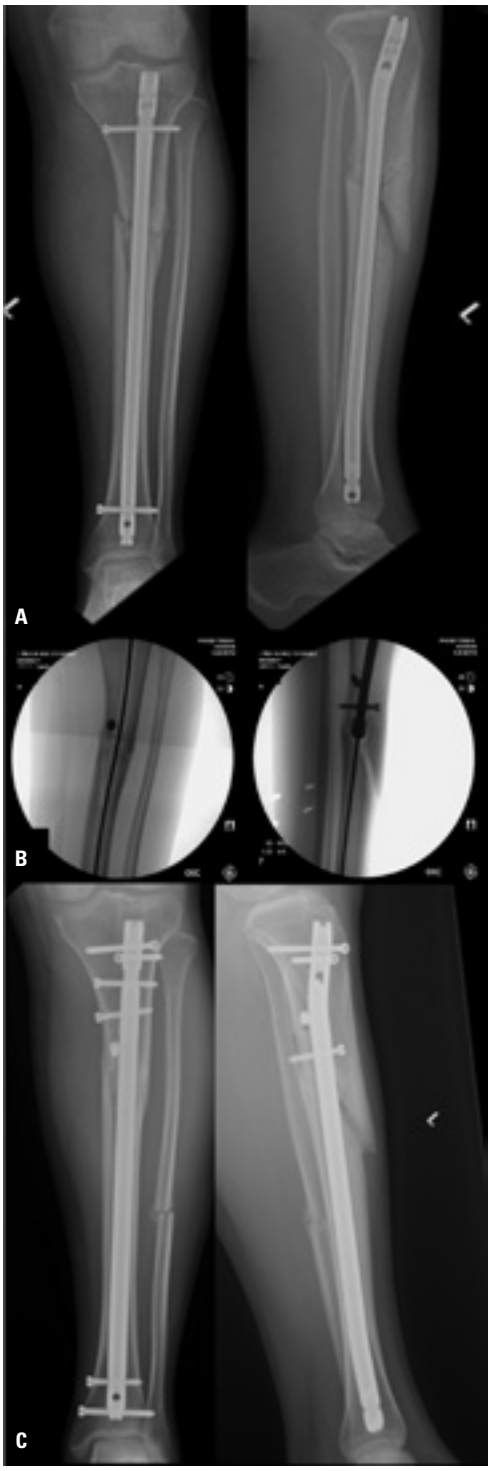


Figure 3. Radiographs demonstrating the use of cortical replacing screws for improving reduction of a proximal-third tibial shaft fracture non-union with varus mal-alignment. **(A)** AP and lateral radiographs at time of initial evaluation; **(B)** Intra-operative fluoros with a guidewire and reamer passing after placement of medial and posterior cortical replacing screws; **(C)** Post-operative AP and lateral radiographs three months post-operatively.

Proceed with sequential reaming and placement of the nail and its interlocking screws in a standard fashion (Figure 1E, 1F).

Post-Operative Care

The standard post-operative protocol can be followed after this reduction technique without modification including weight-bearing as tolerated and initiation of physical therapy post-operative day 1.

Final Considerations

In short, the use of cortical replacing screws as outlined above is meant to serve as one tool out of many available in the Orthopaedic surgeon's skillset for reducing proximal-third tibial shaft fractures. It can also be applied to other sites where intramedullary nails are used in the setting of a bone width-nail diameter mismatch (Figure 2) and in cases of mal-union and non-union corrections (Figure 3) at these sites.

From a technical standpoint, actual execution in the OR may not be as easy as outlined due to imperfect fluoroscopic views, pre-operatively unrecognized fracture comminution, or imperfect technical execution. Furthermore, other characteristics of the fracture may make it more amenable to a different reduction technique such as an existing external fixator or clamping through an open fracture site. Even in such cases, though, cortical replacing screws can be used to continue to hold the alignment after the fracture has already been reduced.

The use of cortical replacing screws as a way to obtain and maintain reduction is far better than accepting a mal-reduction of the tibia with significantly reported improvements from 59-84% incidence of tibial mal-union in cohorts reduced without cortical replacing screws to 1-6% incidence of tibial mal-union in separate study cohorts using this technique.[1,2,7,8]

References

1. Freedman EL, Johnson EE. Radiographic analysis of tibial fracture malalignment following intramedullary nailing. *Clin Orthop.* 1995; 315:25–33.

2. Lang GJ, Cohen BE, Bosse MJ, *et al.* Proximal third tibial shaft fractures. Should they be nailed? *Clin Orthop.* 1995; 315:64–74.

3. Krettek C, Stephan C, Schandelmaier P, *et al.* The use of Poller screws as blocking screws in stabilising tibial fractures treated with small diameter intramedullary nails. *J Bone Joint Surg Br.* 1999 Nov; 81(6):963-8.

4. Shahulhameed A, Roberts CS, Ojike NI. Technique for precise placement of poller screws with intramedullary nailing of metaphyseal fractures of the femur and the tibia. *Injury.* 2011 Feb; 42(2):136-9.

5. Krettek C, Miclau T, Schandelmaier P, *et al.* The mechanical effect of blocking screws ("Poller screws") in stabilizing tibia fractures with short proximal or distal fragments after insertion of small-diameter intramedullary nails. *J Orthop Trauma.* 1999 Nov; 13(8):550-3.

6. Stedtfeld HW, Mittlmeier T, Landgraf P, *et al.* The logic and clinical applications of blocking screws. *J Bone Joint Surg Am.* 2004; 86A(Suppl. 2):17–25.

7. Ricci WM, O'Boyle M, Borrelli J, *et al.* Fractures of the proximal third of the tibial shaft treated with intramedullary nails and blocking screws. *J Orthop Trauma.* 2001 May; 15(4):264-70.

8. Kulkarni SG, Varshneya A, Kulkarni S, *et al.* Intramedullary nailing supplemented with Poller screws for proximal tibial fractures. *J Orthop Surg.* 2012; 20(3):307-311.

Characterizing the Mechanical Effects of Bone Substitute Material and Far-Cortical Locking Techniques in Proximal Humerus Fracture Reconstructions: A Cadaveric Study

Michael W. Hast, PhD[1]
Matthew Chin, BS[1]
Elaine C. Schmidt, MS[1]
Jennifer Sanville[1]
G. Karl Van Osten, MD [2]
Samir Mehta, MD[1]

1 Department of Orthopaedic Surgery University of Pennsylvania, Philadelphia, PA

2 Department of Orthopaedic Surgery North Mississippi Medical Center

Introduction

Proximal humerus fractures are one of the most common fractures in the elderly population.[1] When surgical intervention is required, locking plate fixation is employed to provide support for the reconstructed bone as it heals. This technique is more susceptible to failure when bone quality is poor, and failure rates remain as high as 40% in some studies.[2] It has been posited that implant fixation may be improved in two ways. First, a far cortical locking (FCL) technique can be used to transfer energy away from the fragile humeral head and into the more robust shaft. In this case, the screw holes on the lateral side of the humerus are oversized, which permits controlled motion between the humeral head reconstruction and the humeral shaft (Figure 1). Second, bone substitute material (BSM) can be employed to reinforce the humeral head. Here, a bone substitute is injected through cannulated screws in an attempt to provide reinforcement to the native bone stock. It is understood that FCL "softens" the reconstruction and BSM "stiffens" it; however, it is unknown how these changes affect the fatigue life of the repair. Therefore, the purpose of this study was to make comparisons of the biomechanical properties of these techniques and to determine which fixation is most effective in reducing implant failure given the current highly excessive failure rates. We hypothesized that a combination of both techniques (ALL) will significantly improve the fatigue life of the implant.

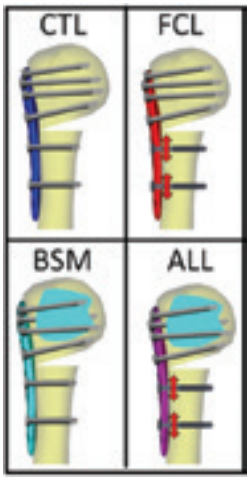


Figure 1. Computer-aided drawings illustrating the 4 groups tested in this experiment. The red arrows indicate motion provided by FCL screws and the cyan blob in the humeral head indicates BSM.

Methods

This study was performed on sixteen matched pairs of fresh frozen cadaveric upper extremities (5M, 11F, mean age: 80.2 years). Lumbar DEXA scans were performed on donors to confirm that all specimens had osteopenia or osteoporosis on at least one vertebral body (mean min T-score:-2.96). Skeletonized humeri were osteotomized at the neck with a 30° wedge to represent a simple two-part fracture. Specimens were equally divided into CTL (traditional locking plate fixation), FCL, BSM, and ALL groups (n=8). Implants (Periarticular Proximal Humeral Locking Plate, Zimmer Biomet) were fixated per manufacturer guidelines by fellowship trained orthopaedic surgeons (SM and KVO). In the case of BSM and ALL groups, two locked screws in the humeral head were replaced with cannulated screws, and up to 5cc of BSM (N-Force, Zimmer Biomet) was injected. After implantation, BSM and ALL groups were vacuum sealed and placed in a 98.5° F water bath for 24 hours to allow the calcium phosphate to cure. Non-destructive, quasi-static torsional (internal/external rotations) and axial (0°, +20°, −20° of abduction) stiffness tests were performed in a universal test frame (ElectroForce 3550, TA Instruments), similar to previous studies.[3,4] For fatigue testing, specimens were positioned at 0° of abduction and underwent a protocol that monotonically increased the magnitude of compressive loading by 0.25 N/cycle until failure. Relative displacement between the humeral head and shaft was calculated with optical 3-D motion tracking recordings (Optitrack, Natural Point, Inc.). One-way ANOVAs (α=0.05) were performed to determine differences between the 4 groups (SigmaStat 4.0, Systat Software, Inc.).

Results

BSM exhibited significant differences between FCL and ALL in internal rotation torsional stiffness (Figure 2). Significant differences in 0° neutral and 20° adduction axial stiffness were seen between CTL and FCL, FCL and BSM, and BSM and ALL. In addition, there was a significant difference between CTL and

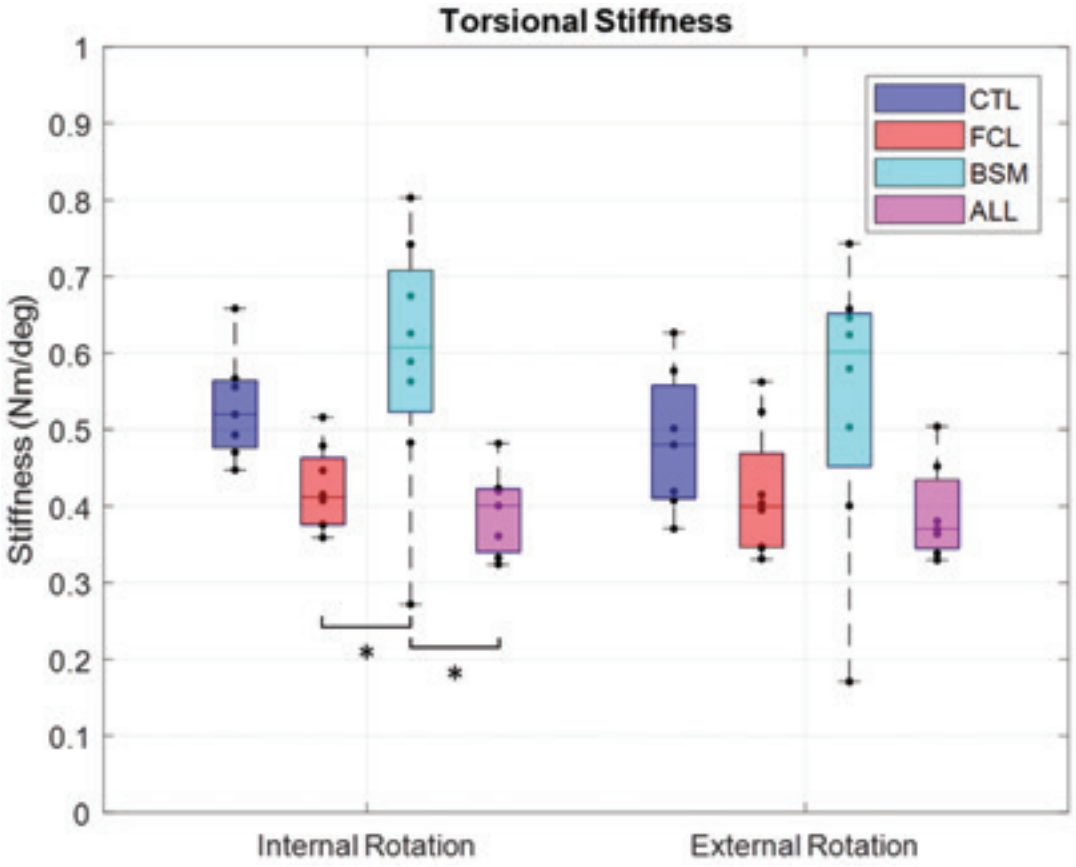


Figure 2. Plots of torsional stiffness in internal and external rotation. Significant differences between groups are marked with *.

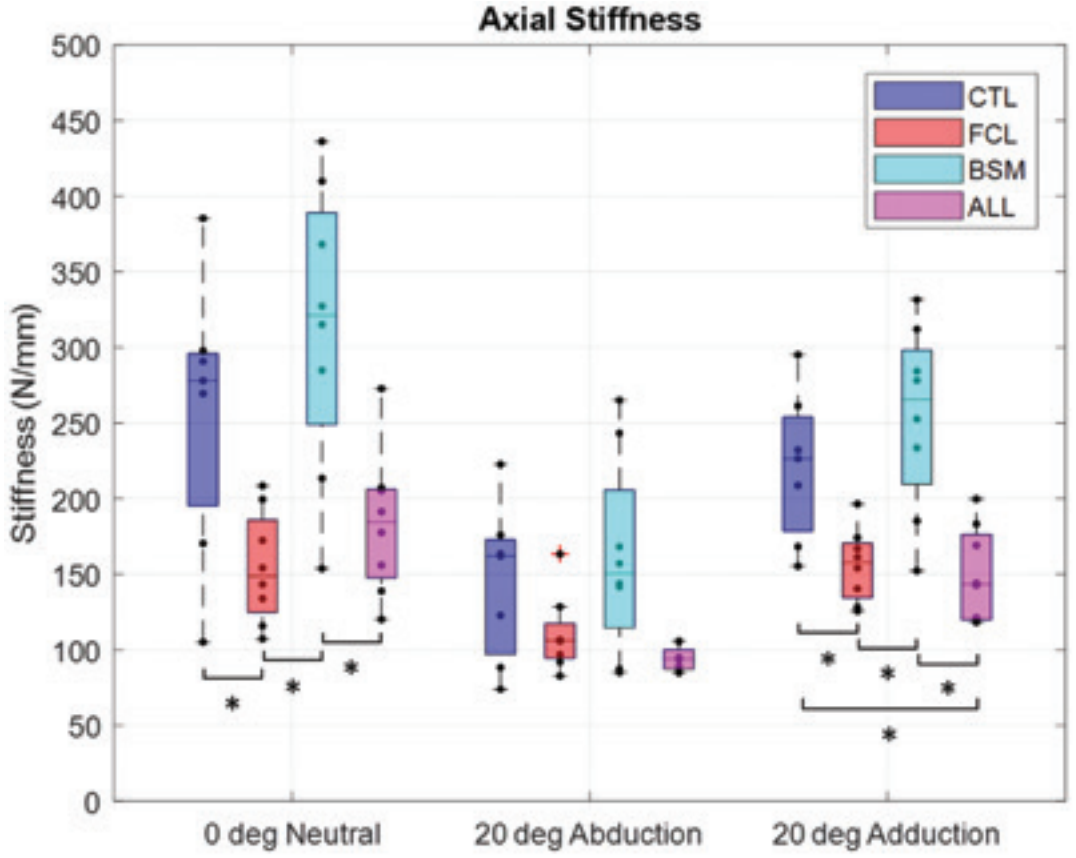


Figure 3. Plots of axial stiffness during 0 deg, −20 deg, and +20 degree tests. Significant differences between groups are marked with *.

ALL in 20° adduction axial stiffness.There were no statistically significant differences for number of cycles survived until 3 mm of permanent deformation, as measured by 3-D motion capture (CTL 2051±501; FCL 1859±626; BSM 2284±811; ALL 2049±338).

Discussion

As expected, the quasi-static torsional and axial tests suggest that BSM improves construct stiffness, while FCL and ALL provide lower stiffnesses. Results from the pooled data from this experiment suggest that the techniques used in the four groups provide similar implant fatigue life, which was contrary to our hypothesis. There are several limitations to this study that may be confounding the results. The screws used in this study were the same length for all specimens, which may have resulted in variable qualities of initial fixation. Additionally, variation in human anatomy and bone mineral density led to large data variability, which is inherent in cadaveric research. Future analyses will be performed on matched pairs of specimens to further assess the effects of these surgical techniques in a more controlled setting, and clinical trials should be pursued to further investigate this issue.

Significance

This study shows that use of FCL and BSM by surgeons may directly change the mechanics of proximal humerus fracture repairs with locking plates, but the impact these changes have on fatigue life remains unclear.

Acknowledgements

This study was funded by Zimmer Biomet

References

1. Lee SH, Dargent-Molina P, Bréart G, *et al.* Risk factors for fractures of the proximal humerus: results from the EPIDOS prospective study. *J Bone Miner Res.* 2002 May; 17(5):817-25.

2. Owsley KC, Gorczyca JT. Fracture displacement and screw cutout after open reduction and locked plate fixation of proximal humeral fractures [corrected]. *J Bone Joint Surg Am.* 2008 Feb; 90(2):233-40. Erratum in: *J Bone Joint Surg Am.* 2008 Apr; 90(4):862.

3. Mehta S, Chin M, Sanville J, *et al.* Calcar screw position in proximal humerus fracture fixation: Don't miss high! *Injury.* 2018 Mar;49(3):624-629.

4. Lescheid J, Zdero R, Shah S, *et al.* The biomechanics of locked plating for repairing proximal humerus fractures with or without medial cortical support. *J Trauma.* 2010 Nov; 69(5):1235-42.

Cost Comparison of Sliding Hip Screw (SHS) and Cephalomedullary Nails (CMN) for the Treatment of Stable Intertrochanteric Hip Fractures

Logan Brock, BS
Nicole Zelenski, MD
Ryan Charette, MD
Samir Mehta, MD

Purpose

There are 250,000 hip fractures in the U.S. annually with an expected increase to 500,000 by 2040. Geriatric hip fractures are associated with high morbidity and mortality as well as high rate of disability among patients. Additionally, national costs of hip fractures are estimated to approach 16 billion by 2040. Currently, stable intertrochanteric hip fractures can be successfully treated with either an extramedullary implant (sliding hip screw, SHS) or an intramedullary implant (cephalomedullary nail, CMN) however CMN implants are significantly more expensive. In the setting of the projected increasing cost of hip fractures in the US, and the rising importance of value, the purpose of this study is to compare the cost of care between patients who undergo treatment with a CMN versus SHS after stable intertrochanteric hip fracture.

Methods

All research was carried out in accordance with protocols approved by the Institutional Review Board of the University of Pennsylvania. A retrospective cohort was created using ICD-9-CM codes for all fractures of proximal femur (sub-capital, femoral neck, intertrochanteric or subtrocanteric) from 2010-2013 in patients over the age of 65. Exclusion criteria were polytrauma, prior hip fracture sustained within one year, pathologic fracture or non-operative management. A chart review of 84 patients was performed which included basic demographic information (Table 1). Hospital financial data for this cohort was examined as reported for medicare reimbursement. Statistical analysis was performed using t-test for parametric and chi-squared for non-parametric data.

Results

There were no significant differences between the IMN and SHS groups with regard to age, sex, BMI, or ASA score. Length of stay, number of consults, rate of discharge to home, 30 day readmission, 90 day mortality were not significantly different between groups. There were no statistically significant differences between IMN patients and SHS patients with regard to direct cost, contribution margin, or profit. Total direct costs for both groups were over $20,000 for the hospitalization.

Conclusions

We found no difference in any variable between patients treated with SHS vs. IMN except a higher amount of transfusion in patients treated with CMN. Although a cephalomedually device costs significantly more, this was not reflected in overall cost at our institution.

Table 1. Patient Demographics & Cost

	SHS	CMN	p-value
Age (years)	79	81	0.57
Sex (% female)	60%	69%	0.40
BMI	23.6	22.8	0.54
ASA	3.0	2.8	0.55
Time from admission to OR (% <48hrs)	73%	69%	0.71
Units RBCs	0.9	1.9	0.02
Length of stay (days)	8.3	8.0	0.76
Consults (number)	1.3	1.5	0.62
Discharge to home (%)	18.5%	20.8%	0.81
30-day readmission (%)	17.3%	22.7%	0.59
90-day mortality (%)	6.3%	14.3%	0.28
OR Time (min)	92.0	94.0	0.87
EBL (mL)	155	153	0.94
Direct cost ($)	22,324	19,881	0.18
Indirect cost ($)	8,443	8,433	0.99
Contribution margin ($)	15,321	16,001	0.64
Profit ($)	-1,313	-4,373	0.13

Parameterization of Proximal Humerus Locking Plate Impingement with In Vitro, In Silico, and In Vivo Techniques

Emily Bachner, BS[1]
Elaine C. Schmidt, MS[1]
Matthew Chin, BS[1]
Surena Namdari, MD[2]
Josh R. Baxter, PhD[1]
Michael W. Hast, PhD[1]

1 Department of Orthopaedic Surgery
University of Pennsylvania

2 Department of Orthopaedic Surgery
Thomas Jefferson University

Introduction

Locked plating of displaced proximal humerus fractures is common, but rates of complications remain high.[1] Subacromial impingement of the plate is a frequent complication that can compromise range of motion, cause pain, and lead to revision surgery. Computational assessments of implant impingement have proven to be effective in arthroplasty procedures, but this space has yet to be sufficiently explored in proximal humerus fixation. The goal of this study was to utilize a multidisciplinary approach to elucidate the relationships between common surgical parameters, anatomical variability, and the likelihood of plate impingement.

Methods

Phase 1 - Cadaveric Experimentation

A controlled *in vitro* experiment was conducted to simulate impingement (Figure 1). Four cadaveric upper extremities (2M, 2F, mean age: 66.75 years) were used in this experiment. Shoulder joints were isolated and LCP Periarticular Proximal Humerus Plates (DePuy Synthes) were implanted per manufacturer protocols. Specimens were imaged with fluoroscopy and measurements were made for humeral head diameter, acromial tilt, and acromial slope. Motion capture retroreflective marker clusters were rigidly attached to the implant and scapula to track anatomic motion. A thin-film pressure sensor (i6900, Tekscan) was used to detect subacromial impingement. A custom-built jig was used to create simulated arm abduction, controlled by a universal testing frame (ElectroForce 3550, TA Instruments). A simple two body OpenSim model was created to calculate scapulohumeral joint angles using the inverse kinematics algorithm. Timed data from the pressure sensor measurements were synchronized with inverse kinematics output to identify shoulder joint angles during impingement.

Figure 1. Graphical depictions of the three phases of the experiment.

Phase 2 - Computational Simulations

A dynamic *in silico* musculoskeletal model was developed to simulate changes to implant geometry, surgical techniques, and acromial anatomy that may cause impingement. The locking plate was altered from a neutral position (−10 to +10 mm), and plate thickness was also changed (native bone to +5.0 mm thickness). Acromial tilt and acromial slope were changed between 20-35°.The model used a fixed ball joint to represent the shoulder.To simulate translation of the humeral head during motions, the center of rotation was moved to several discrete locations (neutral to +5.0 mm proximal). The 720 unique models simulated thoracohumeral abductions from 0-180°. The abductions were performed at 23 cross-body adduction angles, ranging from −90° to 130° in 10° increments. Incidence of simulated contact between the plate and acromion was detected with the on-board elastic foundation contact algorithm.

Phase 3 - In vivo measurements

With institutional review board approval and written informed consent, eight healthy subjects (4M, 4F, mean age 21.5 years) performed 9 activities of daily living. Upper extremity kinematics were recorded using a 12-camera motion capture system and reflective markers. Using a boot-strapping technique, 95% confidence intervals for cross-body adduction angle, abduction, and internal rotation were calculated for each ADL. Results were superimposed on Phase 2 results.

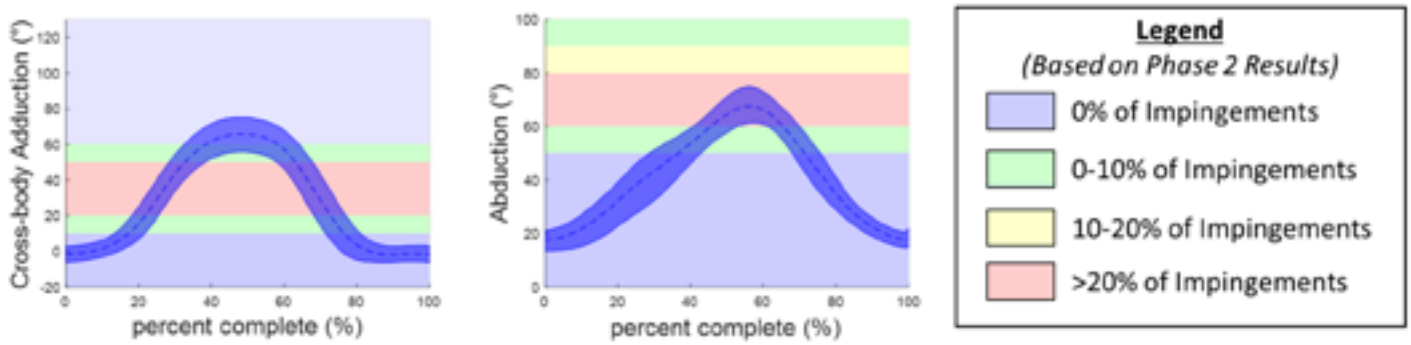


Figure 2. Plots of joint angles during a hair combing activity. The blue clouds represent 95% confidence intervals, based on in vivo data collection, and the colored bands in the background represent the likelihood of impingement in the in silico model.

Results

Impingement was measured at 73.3±14.5° abduction in the cadaveric model and 92.0±34.0° with computational simulations. Overhead activities involving 20-50° of cross-body adduction paired with 60°−80° abduction, similar to combing one's hair, were most likely to cause impingement (Figure 2). Simulation outputs demonstrated that superior implant placement, increases in plate thickness, superior translation of the humeral center of rotation, and increases in acromial tilt all increased the likelihood of impingement.

Discussion

The *in vitro* and *in silico* models used in this study produced results that very closely matched those from previous studies.[2-4] Differences can be attributed to the use of scapulohumeral angles in the cadaveric model, while thoracohumeral angles were used in the *in silico* and *in vivo* models. It is tempting to believe that the higher abduction angles observed in the computational model indicate a later onset of impingement. Interestingly, the opposite is true. When the scapular rhythm is accounted for, impingement occurs when the arm is positioned at approximately 118° of thoracohumeral abduction. This over-approximation in the cadaveric model is likely due to a lax capsule, which may have caused the humeral head to move posteriorly relative to the glenoid. This study has several limitations, as changes to the model's bone geometry may alter simulation results and ADLs measured in a young healthy population may not fully characterize post-operative ranges of motion.

Clinical Relevance

This study improves the biomechanical understanding of locking plate-subacromial impingement with a combination of in *vitro*, *in vivo*, and *in silico* models. It also provides valuable information to allow clinicians and rehabilitation specialists to better predict patient outcomes and better guide rehabilitation.

References

1. Clavert P, Adam P, Bevort A, *et al.* Pitfalls and complications with locking plate for proximal humerus fracture. *J Shoulder Elbow Surg.* 2010 Jun; 19(4):489-94.

2. Graichen H, Bonél H, Stammberger T, *et al.* Sex-specific differences of subacromial space width during abduction, with and without muscular activity, and correlation with anthropometric variables. *J Shoulder Elbow Surg.* 2001 Mar-Apr; 10(2):129-35.

3. Hughes PC, Green RA, Taylor NF. Measurement of subacromial impingement of the rotator cuff. *J Sci Med Sport.* 2012 Jan; 15(1):2-7.

4. Tasaki A, Nimura A, Nozaki T, *et al.* Quantitative and qualitative analyses of subacromial impingement by kinematic open MRI. *Knee Surg Sports Traumatol Arthrosc.* 2015 May; 23(5):1489-97.

Mechanical Behavior of Additive Manufactured Proximal Humerus Fracture Fixation Plate: Experimental Study on Unstable 3-Part Fractures with Osteoporosis

Maryam Tilton, BS[1]
April Armstrong, MD, MSc[2]
Jennifer Sanville[3]
Matthew Chin, BS[3]
Michael W. Hast, PhD[3]
Gregory S. Lewis, PhD[2]
Guha Manogharan, PhD[1]

1 Department of Mechanical and Nuclear Engineering, Pennsylvania State University

2 Department of Orthopaedics and Rehabilitation, Pennsylvania State University

3 Department of Orthopaedic Surgery, University of Pennsylvania

Introduction

Proximal humerus fractures are among the most frequent fractures within the osteoporotic patient population. If the fracture is displaced and surgical intervention is required, locking plates are often used to provide mechanical stability. It is thought that design features of these implants, such as fixed-angle screw trajectories and locking screw heads, improve the mechanical stability of the proximal humeral head. However, complications including varus collapse, loss of fixation, screw cutout, and impingement due to plate misalignment continue to be major challenges in this treatment approach with failure rates exceeding 10%. Additive manufacturing (AM) techniques, commonly referred to as 3-D printing, provide a unique opportunity to expand the design space for these plates besides offering personalized solutions for the most challenging cases in a quick and efficient manner. This study was designed to compare the initial fixation provided by a conventional locking plate and two AM implants including a novel design in which a strut provides medial support to the humeral head. It was hypothesized that the AM implants would have the capacity to recapitulate the fixation parameters provided by currently used implants, and that the addition of a strut will provided much-needed medial column support to the humeral head.

Methods

The experiment was designed to quantify the initial fixation properties of locking plates in the presence of an osteoporotic 3-part comminuted proximal humerus fracture. A total of 9 osteoporotic synthetic humeri (4th Gen Composite Humerus, 10 pcf, Sawbones) were used in this study. Three types of implants were used: (i) conventional locking plates (3.5 mm LCP Proximal Humerus, DePuy Synthes) (CTRL, n=3); (ii) AM-made reversed engineered (to mimic CTRL) plates (RE, n=3); and (iii) novel design concept in which a solid medial strut is added to the conventional plate design (MS n=3) (Figure 1). RE and MS groups were fabricated via laser powder bed fusion technique using Stainless Steel 316L virgin powder with layer thickness of 60 µm and powder size distribution of 40-63 µm. Simulations of unstable 3-part fractures (AO 11-B3.2) were created with the aid of custom-built jig and reconstructions were performed by a senior surgeon (AA). Nondestructive quasi-static torsion and compression (-20°, 0°, 20° abduction) tests were performed in accordance with a previously established protocol. Fatigue tests were performed with monotonically increasing sinusoidal cyclic loads, where the peak load magnitude was increased by at every cycle. Relative displacement between bone fragments were recorded with 3D motion tracking techniques.

Results

There were no significant differences between groups with regard to quasi-static torsional and axial stiffness. The MS group significantly decreased the motion between the P1 and P3 fragments during quasi-static compression testing ($p < 0.05$, Figure 1A). The CTRL and RE groups exhibited similar stiffnesses and provided similar resistance to fragment

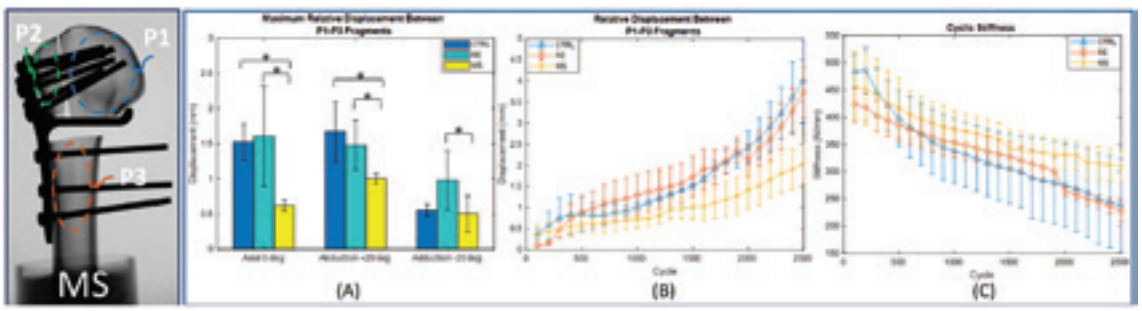


Figure 1. Example of the prepared construct; **(A)** Maximum relative displacement result for non-destructive testing (an asterisk (*) indicates $p < 0.05$); **(B)** Relative displacement during fatigue testing; **(C)** Stiffness during the fatigue test. (Mean Standard Error)

migration throughout cyclic testing. In contrast, MS group with the novel medial support design showed significantly improved stiffness and more resistance to fragment migration throughout the fatigue test ($p<0.05$, Figure 1B-C).

Discussion

This study systematically evaluated the effectiveness of AM locking fracture fixation plates with respect to mechanical stability. Results suggest that reverse-engineered AM implants behaved similar to traditional forged locking plates with identical geometry. These outcomes may increase the confidence in AM locking plates and expand the design space for personalized implants in shorter manufacturing cycle. The addition of a medial strut in the AM design led to improved long-term stiffness of the construct and reduced the motion of the proximal head during fatigue testing. These findings may offer an alternative solution for medial support fixation in complex comminuted fractures. Additional design modifications, such as porous medial support in the place of conventional solid structures, can be readily made with AM processes, and would allow for bone ingrowth at the comminution site. This study was limited to 3-part comminuted fracture and conducted on synthetic bones. A cadaveric study will be conducted for additional validation.

Clinical Relevance

This study provided a new alternative design and fabrication technique for medial fixation of unstable comminuted proximal humerus fractures and showed significant reduction in the varus angulation by maintaining satisfactory mechanical stability.

Estimating Micromotion in Distal Femur Fracture Reconstructions: A Lightweight Computational Framework

Michael W. Hast, PhD
Elaine C. Schmidt, MS
Samir Mehta, MD
Josh R. Baxter, PhD

Department of Orthopaedic Surgery, University of Pennsylvania

Summary

Controlled micromotion between bone fragments is a vital component of fracture healing. The functional stiffness of a distal femur locking platesis altered by implant geometry, material, and bridge span (the distance between screws crossing the fracture line). Loads applied to the implant are directly affected by the location of the fracture along the femur. Surgeons currently rely upon anecdotal experience to create dynamic reconstructions that encourage bone healing. This paper outlines a lightweight computational modelling technique that estimates implant deflection during walking. The algorithm accounts for changes in fracture location, bridge span, and material properties of the implant. Preoperative utilization of this modelling paradigm could potentially improve a surgeon's "best guess" to optimize the mechanical environment for callus formation to occur.

Introduction

Distal femoral fractures are debilitating injuries that typically require surgical intervention to repair. Bridge plating of distal femoral fractures is an inexact science, with high reoperation rates.[1] The purpose of this study was to develop a lightweight computational algorithm capable of estimating displacements between bone fragments. We developed a paradigm using a musculoskeletal model in conjunction with uniform beam theory assessments to make estimations of implant deflections and interfragmentary displacements. We hypothesized that this model would provide reasonable approximations of implant deflection with minimal computational time.

Methods

A musculoskeletal model of a walking 50th percentile male was used in the study (Figure 1A).[2] The right femur was split and reconstructed with a weld joint between 50-90% of the length of the femur. Muscle forces during walking were estimated using the on-board static optimization algorithm. Joint reaction forces and moments were calculated at the weld joint (Figure 1B). Estimations of plate bending were performed using Euler–Bernoulli uniform beam theory (Figure 1C).[3] Implants were represented as simply supported stainless steel or titanium rectangular bars (W: 18mm x H: 4mm) with lengths between 20-180mm. Loads and moments determined from the dynamic simulations were applied at the midpoint. Maximum deflections were calculated for every trial and results were summarized.

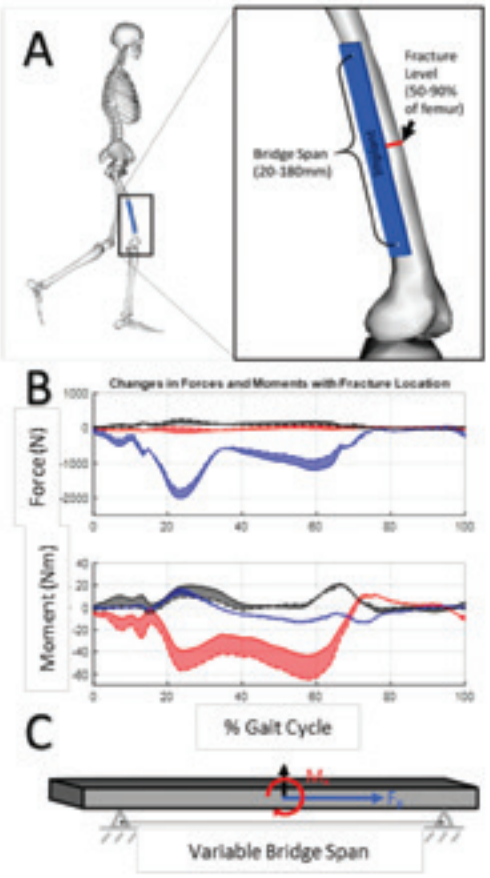


Figure 1. Summary of the methods used in the experiment, involving **(A)** a musculoskeletal model with variable fracture locations; **(B)** variable range of forces and moments applied to the mid-point of the implant; **(C)** application of loads and moments to a uniform beam.

Results and Discussion

The estimated plate deflections were nonlinear and ranged between 0.01–3.57 mm. Plate deflections were slightly lower than an existing finite element model[4] that assessed bridge spans between 20-180mm. Stainless steel simulations had an RMSE of 0.32mm, while titanium simulations had an RMSE of .33mm. Assessments took less than one minute of

computational time on a PC with an i7 3.6GHz processor and 16 GB of RAM.

Conclusions

Estimations of deflection were close to finite element solutions, and exceed the "best guess" of a clinician. Future work will validate this model with benchtop testing and will include variations in body mass and activities of daily living. This paradigm could be used quickly and efficiently to guide patient-specific surgical techniques towards an idealized bridge span.

References

1. Ricci WM, Streubel PN, Morshed S, *et al.* Risk factors for failure of locked plate fixation of distal femur fractures: ananalysis of 335 cases. *J Orthop Trauma.* 2014 Feb; 28(2):83-9.

2. Delp SL, Anderson FC, Arnold AS, *et al.* OpenSim: open-source software to create and analyze dynamic simulations of movement. *IEEE Trans Biomed Eng.* 2007 Nov; 54(11):1940-50.

3. Avallone EA, Baumeister T, Sadegh AM. Marks' Standard Handbook for Mechanical Engineers. 11th ed. New York, NY: The McGraw-Hill Companies; 2007.

4. Elkins J, Marsh JL, Lujan T, *et al.* Motion predicts clinical callus formation: construct-specific finite element analysis of supracondylar femoral fractures. *J Bone Joint Surg Am.* 2016 Feb; 98(4):276-84.

Direct and Indirect Costs of Ankle Fracture Fixation Between Two Surgical Departments

Elizabeth Duckworth, BA[1]
Kimberly Stevenson, MD[2]
Samir Mehta, MD[1,2]
Derek Donegan, MD, MBA[1,2]

1 Perelman School of Medicine, University of Pennsylvania

2 Department of Orthopaedic Surgery, University of Pennsylvania

Background

Ankle fractures are the most common fracture of the foot and ankle treated at trauma hospitals in the United States. In 2011, professional fees and hospital charges for operative treatment of ankle fracture totaled $50.3 million.[1] The purpose of this study was to determine if there is a difference in the direct and indirect costs of surgical fixation of ankle fractures between orthopaedic surgeons and podiatrists at our tertiary care academic medical center.

Methods

We analyzed cost, volume, length of stay, collections, and contribution margin data for surgical treatment of ankle fracture in both the inpatient and outpatient settings by the orthopaedic surgery and podiatry departments during the fiscal years 2016-2018. Based on these data we compared projected costs, collections, and contributions margins across a five-year period with the procedure being performed by a single department (orthopaedics only, podiatry only).

Results

Total costs per case fell by 16% in the orthopaedic surgery department and 8% in the podiatry department over the three-year period. The podiatry department spent an average of $1,261 (45%) more per case than the orthopaedic surgery department, which was driven by increased average supply costs. Both departments had decreased total costs and significantly decreased direct costs ($p = 0.0056$ orthopaedic surgery, $p = 0.033$ podiatry) in the outpatient setting. The orthopaedic surgery department also had significantly decreased total costs in the outpatient setting ($p = 0.0091$).

Conclusion

The orthopaedic surgery department performed a higher volume of cases at a lower cost per case than the podiatry department. These cost savings were driven by decreasing direct costs and lower supply costs. Our results suggest treatment of ankle fracture cases by the orthopaedic surgery department alone is economically advantageous.

References

1. Belatti DA, Phisitkul P. Economic burden of foot and ankle surgery in the US Medicare population. *Foot Ankle Int.* 2014; 35: 334-340.

U·P·O·J

Classical Beam Theory Provides Reasonable Estimates of Interfragmentary Motion in Dynamic Simulations of Distal Femur Fracture Reconstructions

Josh R. Baxter, PhD
Elaine C. Schmidt, MS
Samir Mehta, MD
Michael W. Hast, PhD

Introduction

Distal femoral fractures are debilitating injuries that typically require surgical intervention to repair. Proper healing requires secondary callus formation, which is promoted by axial interfragmentatry motions but inhibited by shear displacements.[1] Locking plates are often used to address these injuries, and surgeons can attempt to tune the stiffness of the reconstruction with bridge-plate fixation techniques. It is known that increasing the distance between the two closest screws on a plate, "bridge span" (Figure 1) will decrease the stiffness of the repair. Bridge plating in distal femoral fracture reconstruction is an inexact science, which is evidenced by a recent clinical study that had a 19% re-operation rate.[2] Benchtop experiments and finite element models have been developed to characterize the interfragmentary motions associated with bridge-plate reconstructions of the distal femur, but these experiments are costly, time consuming, and often only quantify the mechanics of the repair during a single pose under static or quasi-static load. To date, it is thought that patient-specific preoperative assessment of the mechanical environment for callus formation remains impractical.

The purpose of this study was to develop a computational musculoskeletal model that could provide estimations of the forces and moments that are experienced at the fracture site during a dynamic task. With this information in hand, we utilized simplified representations of locking plates (using uniform beam theory) to make estimations of the interfragmentary displacements associated with a specific subject and activity. We hypothesized that this rudimentary model may provide reasonable approximations of implant deflections and relative displacements between bones.

Methods

Loading biomechanics at the fracture site were simulated using a musculoskeletal model of a 50th percentile male during the stance phase of walking.[3] A transverse fracture of the distal femur was virtually created by adding additional coordinate systems to the right femur of the model. This fracture was iteratively created between 50-90% (1% increments) the distance from the proximal to distal length of the femur (Figure 1). To account for the lateral placement of surgical plates, the 'fracture' coordinate system was placed on the lateral cortex of the femur. Muscle forces were estimated using a static optimization algorithm to generate the joint loads necessary to produce the motion of walking. These muscle forces were then combined with ground reaction forces to estimate the loading biomechanics at the lateral surface of the fracture site, a surrogate measure of the loads that would be experienced at the mid-point of the locking plate implant.

Estimations of plate bending were performed using Euler–Bernoulli beam theory.[4] Implants were represented as rectangular bars with a cross section of 18mm × 4mm. Material properties were assigned as either stainless steel (316L; E = 193GPa) or medical grade titanium (Ti6Al4V; E = 113.8GPa). Bridge spans, or working lengths of the beams, were varied between 20-180mm in 10mm increments. The fixation on both ends of the beam were assumed to be simply supported. Axial loads, shear loads, and in-plane moments (determined from the dynamic simulations) were applied to the beam at the midpoint. Maximum displacements were calculated for every trial and results were summarized.

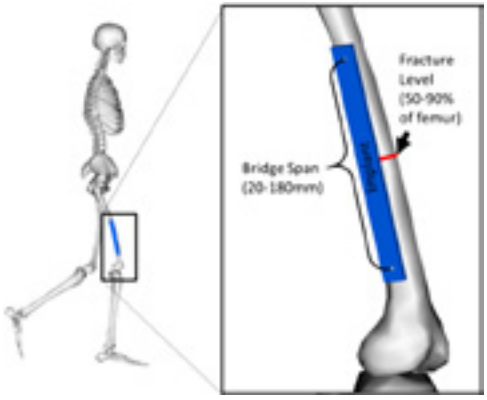


Figure 1. Representative images from the musculoskeletal model showing a subject during stance. Changes to the level of the femoral fracture, implant material, and bridge span led to differences in implant deflection.

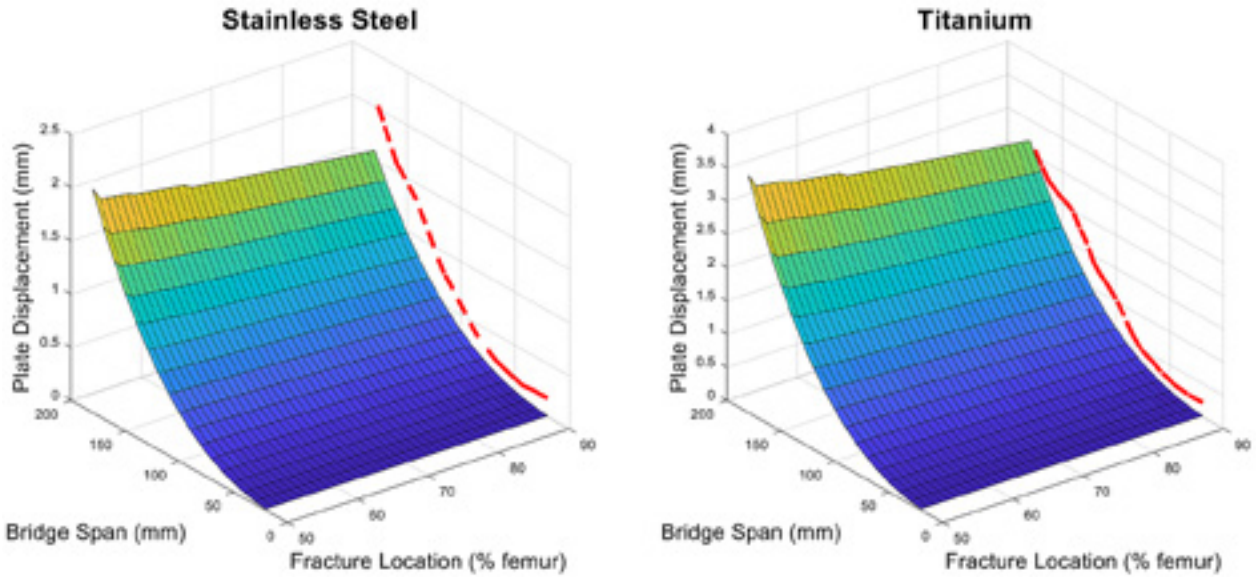


Figure 2. Outputs of the simulations for stainless steel (left) and titanium (right) beams. The red dashed lines represent outputs from a previous finite element study [CIT]. Root mean squared errors between simulations and the previous study are shown above.

Results

The estimated plate displacements increased in a non-linear fashion as a function of bridge span (Figure 2). The magnitudes of displacements were distinctly different for the stainless steel and titanium plates. Specifically, the stainless steel plates had a maximum deflection of 2.10 mm in the simulation that utilized a 50% fracture location and a bridge span of 180mm (Figure 2A). The titanium plate simulations had a maximum deflection of 3.57mm in the same scenario. When simulations outputs were compared to an existing finite element model[5] that related transverse deflection of distal femoral locking plates (~90% fracture location) to bridge span during standing, the stainless steel simulations had an RMSE of 0.32mm, while the titanium simulations had an RMSE of 0.33mm. Assessment of all 1394 individual simulations of gait took less than one minute of computational time on a PC with an i7 3.6GHz processor and 16 GB of RAM.

Discussion

This patient-specific dynamic model provides a fast but coarse estimation of implant deflections. Given the number of assumptions that were made, the outputs provide fairly reasonable approximations of implant deflections and provide insight into interfragmentary motions. The current model only represents a walking motion of a 50th percentile male, but results would change with alterations to body mass, activity, and implant material, and implant cross-sectional geometry. Because preoperative gait assessment after a distal femoral fracture is not possible, a library of simulation results could provide surgeons with a lookup table (based on body mass, activity level, implant geometry, and fracture location) to determine an appropriate bridge span. This framework could be readily adapted to assess locking plate behavior on other bones of the body.

Clinical Relevance

Preoperative utilization of this modeling paradigm could potentially improve a surgeon's "best guess" to optimize the mechanical environment for callus formation to occur.

References

1. Goodship AE, Kenwright J. The influence of induced micromovement upon the healing of experimental tibial fractures. *J Bone Joint Surg Br.* 1985 Aug; 67(4):650-5.

2. Ricci WM, Streubel PN, Morshed S, *et al.* Risk factors for failure of locked plate fixation of distal femur fractures: ananalysis of 335 cases. *J Orthop Trauma.* 2014 Feb; 28(2):83-9.

3. Delp SL, Anderson FC, Arnold AS, *et al.* OpenSim: open-source software to create and analyze dynamic simulations of movement. *IEEE Trans Biomed Eng.* 2007 Nov; 54(11):1940-50.

4. Avallone EA, Baumeister T, Sadegh AM. Marks' Standard Handbook for Mechanical Engineers. 11th ed. New York, NY: The McGraw-Hill Companies; 2007.

5. Elkins J, Marsh JL, Lujan T, *et al.* Motion predicts clinical callus formation: construct-specific finite element analysis of supracondylar femoral fractures. *J Bone Joint Surg Am.* 2016 Feb; 98(4):276-84.

Spine Tips & Tricks: Increasing Sacropelvic Fixation with the "Four Rods" Technique in Parkinson's-Related Camptocormia

Andrew Tyler, MD, PhD
Vincent Arlet, MD

Department of Orthopaedic Surgery
University of Pennsylvania

Introduction

Operative care of significant spinal deformity and instability frequently requires pelvic instrumentation in order to maintain the desired correction. However, spinopelvic constructs are exposed to substantial cantilever forces at the base of the spine that are at a higher risk of failure if the surgeon does not account for these additional stresses. Several methods have been used to overcome this obstacle, each with their own advantages and disadvantages. Here we describe a case report demonstrating the use of the "four rods" technique of spinopelvic instrumented fusion[1] in a patient with Parkinson's-related camptocormia with painful spinal sagittal imbalance. This method allowed for spinal fixation that not only decreased the patient's painful symptoms but also facilitated early upright ambulation while minimizing the risk of construct failure.

Case Report

The patient is a 57 year old male with a history of nonoperatively treated adolescent idiopathy scoliosis and Parkinson's disease well-controlled with pharmacologic therapy who presented to clinic complaining of lower back pain and stiffness as well as bilateral radicular pain radiating to the buttock (right side worse than left) with worsening symptoms in the past year. Prior nonoperative therapies, including physical therapy, optimization of his Parkinson's medication regimen, and spinal facet injections, were ineffective in relieving his pain. On examination, the patient had no evidence of lower extremity myelopathy with no pathologic

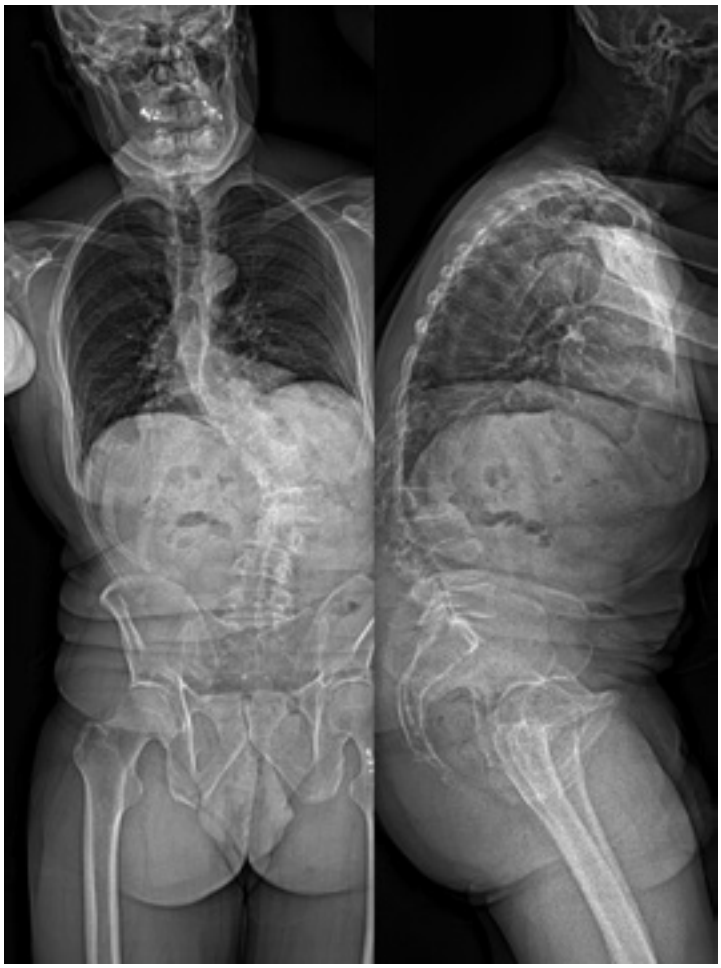


Figure 1. Preoperative radiographs (AP and lateral) demonstrating significant deformity.

reflexes and had a negative straight leg raise bilaterally. He had clinically evidence of scoliosis with decrease in interval between the ribs and pelvis on the right to 5 cm, a shoulder imbalance with the right slightly inferior, and a loss of lumbar lordosis when viewed from the side. He was also found to have camptocormia (from the Greek for "bent trunk"), a condition defined by extreme forward flexion of the thoracolumbar spine that may worsen during walking or standing but completely disappears when the patient lays supine. Originally described as a psychogenic disorder in soldiers returning from World War I[2], it has more recently been associated with Parkinsonism and other movement disorders.[3] Preoperative imaging demonstrated a 17° right sided thoracic curve from T5-T11 and a 25° left sided lumbar curve from T11-L5 with moderate-to-severe neuroforaminal narrowing at the L2/L3 level. Therefore, after a long discussion with the patient, a plan was made to proceed with surgical intervention involving instrumented posterior spinal fusion from T3 to pelvis with Smith-Peterson osteotomies at T12/L1, L1/L2, L2/L3, and L3/L4 in order to correct the sagittal imbalance. Given the length of the construct and the low level of the osteotomies, spinopelvic fusion the "four rods" technique was deemed appropriate and necessary.

For the procedure, the patient placed under general anesthesia. Neuromonitoring leads were placed for intraoperative evaluation at which point the patient was arranged prone on an open top radiolucent table with a "break" in the center to allow for manipulation of the curvature during surgery. The patient was prepped and sterilely drapped in the typical fashion. On the approach, significant hemorrhage well-controlled with Floseal was noted. Although the patient was given tranexamic acid prior to incision, this bleeding was believed to be due to the patient's neuromuscular disorder leading to lack of vasoconstriction of the vasculature. Once hemostasis was achieved, the "four rods" technique was implemented. Polyaxial lumbosacral pedicle screws were inserted bilaterally at the L1, L2, L3, L4, L5, and S1 level after which four pelvic screws including bilateral anatomic pelvic and S2/iliac screws were placed. Screw fixation was then extended up to the T3 level with transverse process hooks at the T3

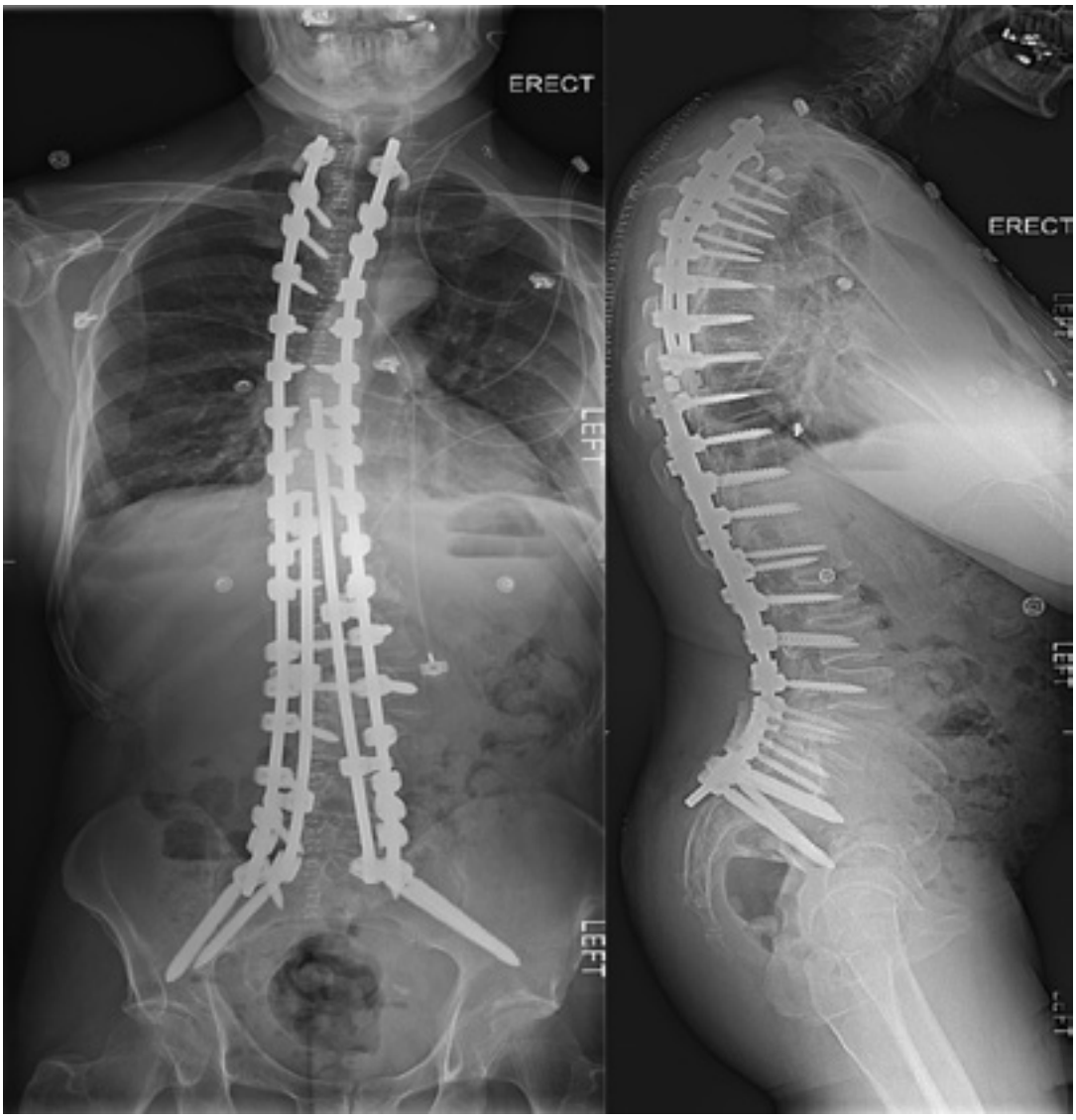


Figure 2. Postoperative radiographs (AP and lateral) demonstrating the "four rods" technique of spinopelvic fusion.

level for additional support. All screws were then individually checked under fluoroscopy and with motor evoked potentials (MEPs) to ensure they were fully contained within the pedicles and avoiding nerve root injury. At this point Smith-Peterson osteotomies were performed at the T12/L1, L1/L2, L2/L3, and L3/L4 levels to afford -20° of lordosis. Rods were then measured and bent to maintain the corrected sagittal balance. Bilateral single rods were placed from the T3 to pelvis levels with additional bilateral rods crossing the lumbopelvic junction from T11 to pelvis on the right and T9 to pelvis on the left. The correction was again checked under fluoroscopy and the wound was irrigated. Posterolateral fusion was performed from T3 to sacrum with local bone graft, cancellous allograft, and bone morphogenetic protein (BMP). A layered closure was then performed over a drain. Blood loss was estimated to be 2500 mL, and the patient received 750 mL albumin, 4000 mL of crystalloid, 6 units of Cell Saver, 2 units of RBCs, 1 unit of FFP, and 1 unit of platelets. Postoperatively he was placed on a phenylephrine drip for blood pressure support which was discontinued due to reflexive bradycardia. He required a further 2 units of RBCs on postoperative day 1 with midodrine to continued hypotension which responded appropriately; midodrine was discontinued. The patient was made weightbearing as tolerated and progressed well with physical therapy but given his baseline Parkinson's disease was recommended for placement in an acute rehabilitation facility to which he was discharged on postoperative day 5.

Discussion

Spinopelvic fixation is often necessary for complete correction of significant sagittal alignment deformities, especially long fusions extending to the sacrum or those requiring corrective osteotomies.[4] However, this coincides with the area defined by McCord et al[5] as the lumbosacral pivot point, identified on sagittal radiographs as the posterior superior corner of the S1 vertebra. As such, enormous cyclical dynamic forces are exerted at this interval as patients attempt to stand upright and walk postoperative. This frequently leads to construct failure, pseudarthrosis, and continued painful symptoms and as such demands supplemental rigid support. Several options have historically been described for lumbosacral and spinopelvic fixation include sacral sublaminar devices, S1 and S1 pedicle screws, sacral alar screws, iliosacral screws, Jackson intrasacral rod technique[6], Galveston iliac fixation[7], and iliac screw fixation.[4] However, while these methods have shown success in the past, many require extensive dissection laterally leading to an increase in potential space and the possibility of hematoma formation in order to properly achieve the desired effect.

The "four rods" technique described originally by Shen et al is a variation on iliac screw fixation that does not require further dissection beyond that of a typical posterior approach to the spine and sacrum.[1] As the name indicates, four rods are placed across the lumbopelvic junction in order to maximize the strength of the construct. The rods are designated as either "medial" or "lateral" and are supported by polyaxial screws in the lumbar spine and pelvis. In order to create the required channels to allow for four parallel rods in the constrained space of the posterior spine the lumbar screws are placed in alternating Roy-Camille "straight ahead" or Magerl "lateral-to-medial converging" orientations. This positions the screw heads either more medial or more lateral, respectively, and allows for rods to be place parallel without significantly increased the profile of the construct. In addition, four total pelvic screws (2 into each iliac wing) are placed in a Galveston-like orientation, aiming toward the anterior inferior iliac spine, although in the case currently described an S2/iliac screw was used given the anatomy of the patient. Rods are then bent accordingly and locked into the polyaxial screws to achieve the desired spinal curvature.

There are disadvantages to the "four rods" technique. In order to disperse the forces across the construct and avoid screw pullout the supplement rods typically are extended from the pelvis proximally to at least the L2 level, which may be more cephalad than other techniques. However, crosslinking the rods to the ipsilateral and/or contralateral rods can reduce this risk and potentially decrease rod length. In addition, construct prominence may be an issue unless the screws (particularly those in the pelvis) are properly recessed to avoid symptomatic hardware.

Overall, the "four rods" technique represents a relatively accessible method of increasing distal construct stability when extending fixation across the lumbosacral junction and allows for early independent motion, thereby decreasing the risk of postoperative morbidity typically associated with such procedures. Given the relative ease of conceptualizing the design as well as the incorporation of common operative techniques in spinal surgery, the "four rods" method should find more widespread use in cases involving spinopelvic fixation.

References

1. Shen FH, Harper M, Foster WC, *et al.* A novel "four-rod technique" for lumbo-pelvic reconstruction: theory and technical considerations. *Spine (Phila Pa 1976)* 2006; 31: 1395-401.

2. Sandler SA. Camptocormia; a functional condition of the back in neurotic soldiers. *Arch Neurol Psychiatry* 1946; 55: 158-60.

3. Melamed E, Djaldetti R. Camptocormia in Parkinson's disease. *J Neurol* 2006; 253(Suppl 7): 16.

4. Moshirfar A, Rand FF, Sponseller PD, *et al.* Pelvic fixation in spine surgery. Historical overview, indications, biomechanical relevance, and current techniques. *J Bone Joint Surg Am* 2005; 87(Suppl 2): 89-106.

5. McCord DH, Cunningham BW, Shono Y, *et al.* Biomechanical analysis of lumbosacral fixation. *Spine (Phila Pa 1976)* 1992; 17: 235.

6. Jackson RP, McManus AC. The iliac buttress. A computed tomographic study of sacral anatomy. *Spine (Phila Pa 1976)* 1993; 18: 1318-28.

7. Allen BL, Ferguson RL. The Galveston experience with L-rod instrumentation for adolescent idiopathic scoliosis. *Clin Orthop Relat Res* 1988; 229: 59-69.

Evaluation of a Human-Scale Tissue Engineered Intervertebral Disc in a Large Animal Model

Sarah E. Gullbrand[1,2]
Beth G. Ashinsky[1,2,3]
Edward D. Bonnevie[1,2]
Dong Hwa Kim[1,2]
Lachlan J. Smith[1,2]
Dawn M. Elliott[4]
Thomas P. Schaer[1]
Harvey E. Smith[1,2]
Robert L. Mauck[1,2]

1 University of Pennsylvania, Philadelphia, PA

2 Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA

3 Drexel University, Philadelphia, PA

4 University of Delaware, Newark, DE

Introduction

Intervertebral disc degeneration is commonly associated with back and neck pain, and current surgical treatments for end-stage degeneration (i.e., fusion), do not restore spine function. Replacement of the degenerative intervertebral disc with a living, tissue engineered construct has the potential to restore normal structure and function to the spine.[1] Towards this end, we developed endplate-modified disc-like angle ply structures (eDAPS) that recapitulate the native structure and function of the disc. These implants combine a cell seeded hydrogel nucleus pulposus (NP) and an electrospun poly(ε-caprolactone) (PCL) annulus fibrosus (AF) with acellular PCL foam endplates.[2,3] We previously showed in a rat tail disc replacement model that eDAPS implants functionally mature *in vivo*, recapitulating many of the characteristics of the native disc.[4] The rat tail is a fraction of the scale of the human intervertebral disc, however, and so translation of this technology towards clinical use will require evaluation of human-sized implants in a larger animal model. We anticipate that the first human application of the eDAPS implant may be in the human cervical spine, and so here evaluate the structure, composition, and mechanical function of the eDAPS after 4 and 8 weeks *in vivo* in a goat cervical disc replacement model.

Methods

eDAPS sized for the goat and human cervical disc space (9 mm height, 16 mm diameter) were fabricated as previously described [5] and seeded with allogeneic goat (caprine) bone-marrow derived mesenchymal stem cells. eDAPS were cultured for a total of 13-17 weeks in a chemically defined media with TGF-β3 prior to implantation. With IACUC approval, 9 male large frame goats underwent a surgical procedure to implant the eDAPS at the C2-C3 level of the cervical spine. Implanted motion segments were immobilized with an anterior cervical plate to ensure construct retention. Animals were euthanized at 4 weeks (n=4) or 8 weeks (n=3) for analyses. In the 8 week group, quantitative T2 mapping was performed. Following MRI, the eDAPS implanted motion segment and the adjacent native cervical motion segment were isolated and subjected to 20 cycles of compression, where the applied compressive stress was equivalent to that in the human cervical discs due to the weight of the head (0 to −25 N, 0.084 MPa). eDAPS implanted motion segments were then fixed, decalcified and processed through paraffin for histology. Histologic analyses were conducted on samples from the 4 and 8-week groups. Sections were stained with alcian blue (proteoglycans) and picrosirius red (collagens). Second harmonic generation imaging (SHG) was also utilized to visualize organized collagen at the eDAPS-vertebral body interface. Significant differences ($p<0.05$) in quantitative outcomes were assessed via Kruskal-Wallis with a Dunn's multiple comparison test.

Results

eDAPS composition and structure were maintained at or above pre-implantation levels after 4 weeks *in vivo* (Figure 1A, B). After 8 weeks *in vivo*, there was an increase in collagen matrix deposition within the PCL endplates and the annulus fibrosus, accompanied by slight reductions in proteoglycan staining within the NP region compared to 4 weeks. SHG images also revealed the deposition of organized collagen within the initially acellular PCL endplates, resulting in nascent integration of the eDAPS with the vertebral bodies at 4 weeks that further matured after 8 weeks (arrows, Figure 1B). T2-weighted MRIs demonstrated improved signal intensity within the eDAPS after 8 weeks *in vivo,* compared to pre-implantation levels, suggestive of improved construct water content (Figure 1C). Compressive mechanical testing showed significant maturation of eDAPS mechanical properties from pre-implantation values after 8 weeks *in vivo* (Figure 2A). While toe and linear region moduli (Figure 2B) of the eDAPS implanted motion segments trended higher than native goat cervical disc moduli, the transition and maximal strains (Figure 2C) were significantly reduced from pre-implantation levels at 8 weeks, and were not significantly different from the native cervical motion segment.

Discussion

In this study, we demonstrate the feasibility of a total disc replacement with a human-scale, tissue engineered disc in a large animal

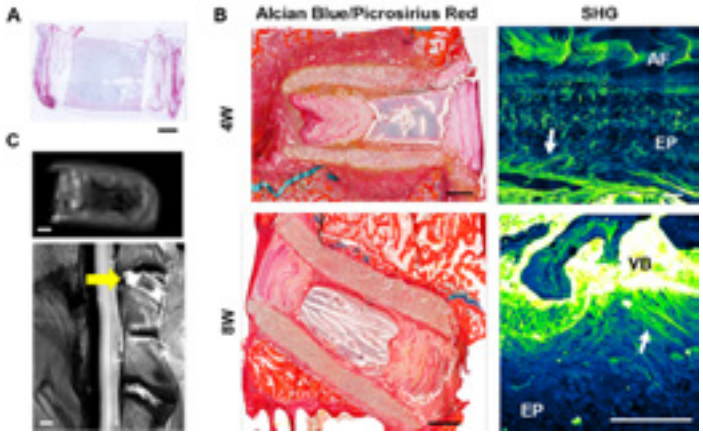


Figure 1. (A) Alcian blue and picrosirius red stained histology of eDAPS prior to implantation, scale = 2mm. **(B)** Histology (scale = 2mm) of whole eDAPS and SHG images (scale = 200μm) of the EP-vertebral body interface 4 and 8 weeks post implantation. (C) T2 weighted MRI of eDAPS before (top, scale = 2mm) and after (bottom, scale = 5mm) 8 weeks of implantation.

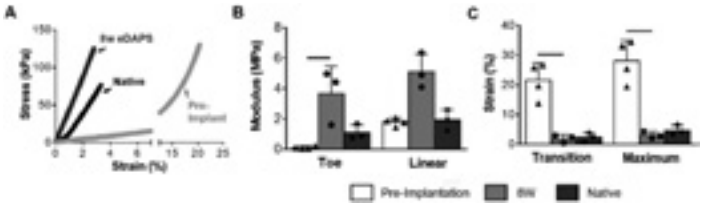


Figure 2. (A) Representative compressive stress-strain curves for each experimental group. **(B)** Toe and linear region moduli, and **(C)** transition and maximum strain for each experimental group. Bars denote significance, $p<0.05$.

model. Composition in the EP and AF regions of the eDAPS generally matured with increasing duration of implantation as the eDAPS progressively integrated with the native spine, while NP composition was maintained or slightly reduced from pre-implantation levels. Significant improvements in eDAPS compressive mechanical properties were observed after implantation, reaching near native levels after 8 weeks. Ongoing and future work is focused on further translating the eDAPS towards clinical use by optimizing the NP region for improved *in vivo* performance, implanting eDAPS for longer durations within the goat cervical spine, and exploring the effects of fixator removal to restore physiologic loading to the construct *in vivo*.

Significance

This work demonstrates for the first time the function of a human-scale tissue engineered disc following *in vivo* implantation in a large animal model. Development and translation of tissue engineered total disc replacements has the potential to significantly expand treatment options for symptomatic disc degeneration, restoring structure and function via a living implant.

References

1. Bowles RD, Gebhard HH, Härti R, *et al.* Tissue-engineered intervertebral discs produce new matrix, maintain disc height, and restore biomechanical function to the rodent spine. *Proc Natl Acad Sci USA* 2011; 108(32): 13106-11.

2. Nerurkar NL, Sen S, Huang AH, *et al.* Engineered disc-like angle-ply structures for intervertebral disc replacement. *Spine (Phila Pa 1976)* 2010; 35(8): 867-73.

3. Martin JT, Gullbrand SE, Kim DH, *et al.* In vitro maturation and in vivo integration and function of an engineered cell-seeded disc-liked angle ply structure (DAPS) for total disc arthroplasty. *Sci Rep* 2017; 7(1): 15765.

4. Gullbrand SE, Kim DH, Bonnevie E, *et al.* Towards the scale up of tissue engineered intervertebral discs for clinical application. *Acta Biomater* 2018; 70: 154-64.

Inflammatory Cytokine Expression in a Goat Model of Intervertebral Disc Degeneration

Chenghao Zhang[1,2]
Sarah E. Gullbrand[1,2]
Thomas P. Schaer[1]
Dawn M. Elliott[3]
George R. Dodge[1,2]
Robert L. Mauck[1,2]
Neil R. Malhotra[1]
Lachlan J. Smith[1,2]

1. University of Pennsylvania, Philadelphia, PA
2. Corporal Michael J. Crescenz Philadelphia VA Medical Center, Philadelphia, PA
3. University of Delaware, Newark, DE

Introduction

Intervertebral disc (IVD) degeneration is strongly implicated as a leading cause of low back pain. Persistent, localized inflammation within the disc nucleus pulposus (NP) and annulus fibrosus (AF) is considered to be a key mediator of disc degeneration, and is associated with downstream catabolic enzyme activity and extracellular matrix destruction. Disc inflammation is characterized by expression of cytokines including IL-1β, IL-6 and TNF-α, amongst others, with expression levels positively correlated with severity of degeneration.[1]

There is currently a lack of validated preclinical animal models of disc degeneration that recapitulate clinically-relevant, persistent inflammatory cytokine expression. Our lab recently described a goat model of disc degeneration, in which different doses of chondroitinase ABC (ChABC) were used to reproducibly induce a spectrum of clinically-relevant structural, biomechanical and histological degenerative changes.[2]The objective of this study was to further enhance the clinical-relevance of this model by establishing whether these degenerative changes are associated with tissue-level expression of key inflammatory cytokines.

Methods

With IACUC approval, 9 goats underwent a surgical procedure to induce degeneration of the lumbar intervertebral discs. Using an open, lateral, retroperitoneal transpsoatic approach, L1-2, L2-3 and L3-4 lumbar discs were randomized to receive either subtotal nucleotomy (n=4) or injection of 200μL of either 0.1U, 1U or 5U ChABC via a 22G spinal needle (n=4 per dose). The L4-L5 (n=4) disc received a sham saline injection, and the T13-L1 or L5-L6 discs served as intact controls. Animals were euthanized 12 weeks after surgery, and lumbar spines harvested. Intervertebral discs with bony endplates intact were isolated, fixed in formalin, decalcified, and processed for paraffin histology. Mid-sagittal sections were double stained with either Alcian blue (glycosaminoglycans) and picrosirius red (collagen), or hematoxylin and eosin. Severity of degeneration was established via semi-quantitative histological grading.[2] Immunohistochemistry was performed to investigate relative expression of IL-1β, IL-6 and TNF-α in the NP and AF. Sections were counterstained with hematoxylin and imaged using bright field microscopy.Antibody reactivity and specificity was validated using goat cells pretreated with lipopolysaccharide. Expression levels were quantified by determining the percentage of positive vs. total cells in the NP and AF (average of 3 regions per disc). Differences in expression levels between intervention groups were established using Kruskal-Wallis tests with post-hoc Dunn's tests ($p<0.05$). Linear correlations between expression levels and histological grade were also evaluated.

Results

Multiple comparisons tests revealed significant effects of intervention type on expression levels of IL-1β, IL-6 and TNF-α in both the NP and AF (Figure 1). TNF-α expression was highest for 1U ChABC discs (both NP and AF), and significantly elevated compared to controls (Figures 1 and 2). IL-1β and IL-6 expression were both highest in the NP and AF of 5U ChABC discs, and significantly elevated compared to control, saline and nucleotomy. No cells (NP or AF) stained positive for any cytokines in any control discs. There were moderate, positive correlations between expression levels and overall histological grade for all three cytokines, which were significant with the exception of TNF-α in the AF (Figure 3).

Discussion

Inflammation is a defining feature of human disc degeneration and is a key mediator of tissue breakdown and painful innervation. Anti-inflammatory therapies such as catabolic cytokine inhibitors [3,4] have the potential to slow the degenerative cascade and provide a microenvironment more conducive to stem cell-based disc regeneration; however, the absence of a preclinical animal model that effectively recapitulates physiological inflammation represents an impediment to effective translation of such therapies. In this study, we provide evidence that an established goat model of disc degeneration is characterized by elevated expression of IL-1β, IL-6 and TNF-α, three cytokines that are well-established mediators of human disc degeneration. Specifically, we

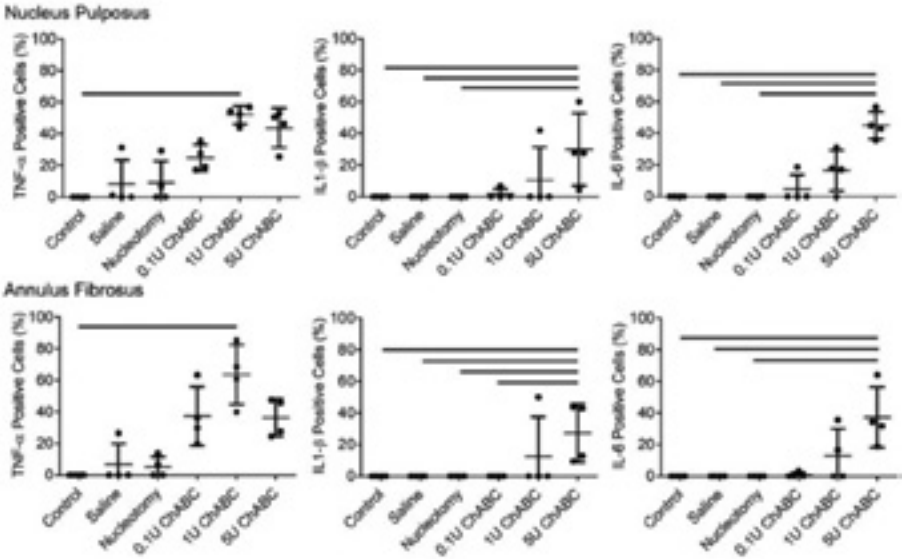
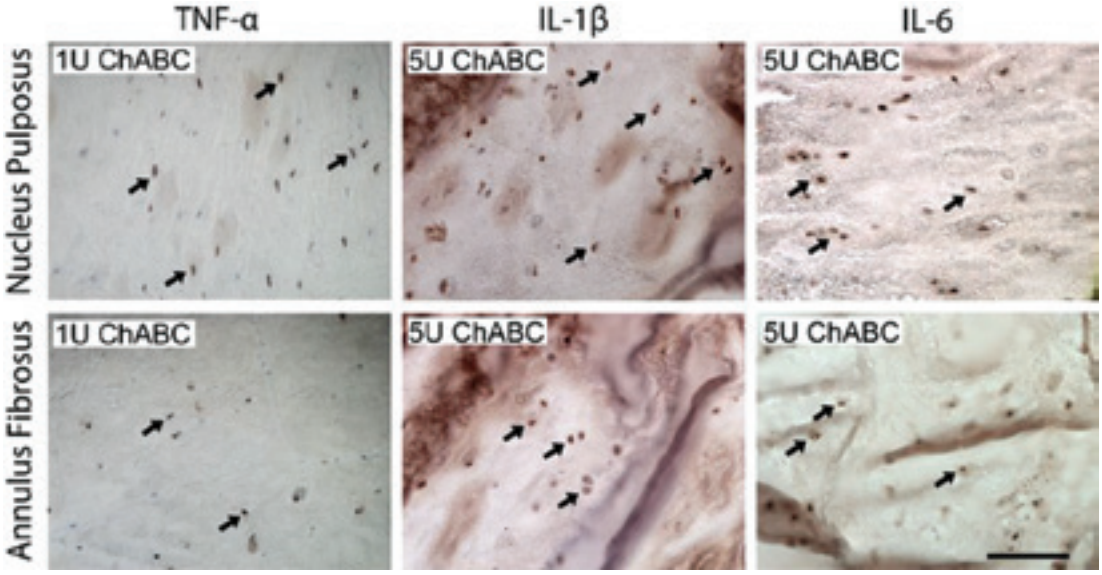


Figure 1. Quantification of expression levels of TNF-α, IL-1β and IL6 by cells in the NP and AF of goat discs 12 weeks following initiation of degeneration using different techniques. Bar indicate significant differences between groups ($p<0.05$). Mean ± SD.



Figures 2. Representative images showing positive expression of TNF-α, IL-1β and IL-6 by NP and AF cells (arrows = examples) in degenerate goat intervertebral discs. Scale = 100μm.

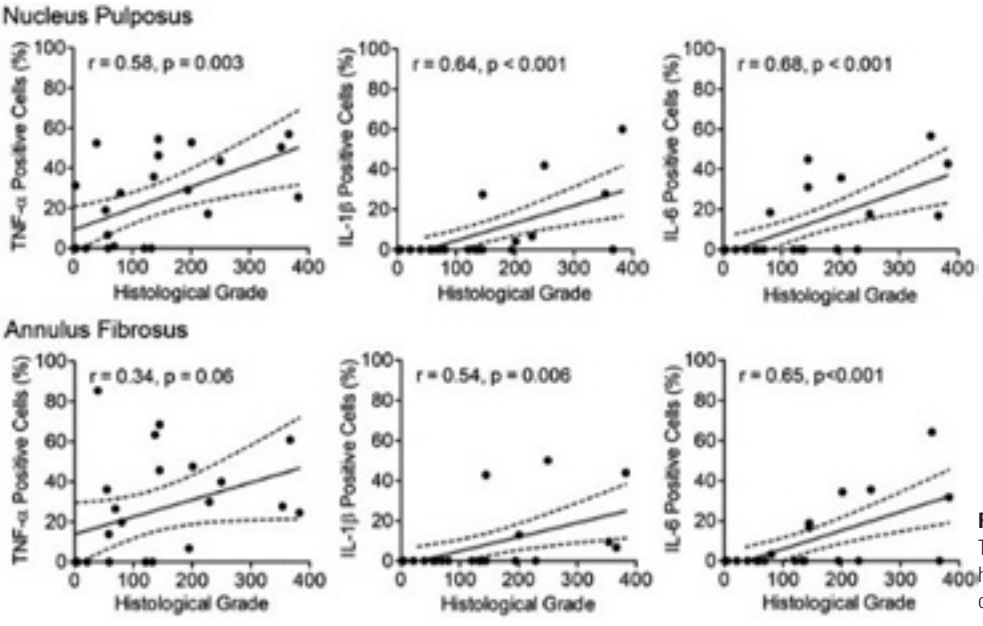


Figure 3. Linear correlations between expression of TNF-α, IL-1β and IL-6 by NP and AF cells, and the overall histological grade of goat discs 12 weeks following initiation of degeneration. Dotted lines = 95% confidence intervals.

found that cytokine expression was significantly elevated in moderately and severely degenerate discs (1U and 5U ChABC), suggesting that these discs may provide the most suitable models for evaluating anti-inflammatory therapies. Ongoing studies will seek to establish corresponding expression of downstream catabolic enzymes and pain mediators, and our long term goal is to leverage this model to evaluate anti-inflammatory therapies for disc degeneration.

Significance

Anti-inflammatory therapies represent a promising treatment strategy for painful disc degeneration. The animal model described here provides a platform for preclinical evaluation of such therapies and progressing them towards clinical use.

References

1. Risbud MV and Shapiro IM. Role of cytokines in intervertebral disc degeneration: pain and disc content. *Nat Rev Rheumatol* 2014; 10(1): 44-56.

2. Gullbrand SE, Malhotra NR, Schaer TP, *et al.* A large animal model that recapitulates the spectrum of human intervertebral disc degeneration. *Osteoarthritis Cartilage* 2017; 25(1): 146-56.

3. Gorth DJ, Mauck RL, Chiaro JA, *et al.* IL-1ra delivered from poly(lactic-co-glycolic acid) microspheres attenuates IL-1ß-mediated degradation of nucleaus pulposus in vitro. *Arthritis Res Ther* 2012; 14(4): R179.

4. Sainoh T, Orita S, Miyagi M, *et al.* Single intradiscal administration of the tumor necrosis factor-alpha inhibitor, Etanercept, for patients with discogenic low back pain. *Pain Med* 2016; 17(1): 40-5.

Non-Invasive Imaging of Therapeutic Cells Delivered Percutaneously to the Mouse Intervertebral Disc

Chenghao Zhang
Sun H. Peck
Justin R. Bendigo
Yian Kai A. Lau
Neil R. Malhotra
Lachlan J. Smith

Departments of Neurosurgery and Orthopaedic Surgery
University of Pennsylvania

Introduction

Intervertebral disc degeneration is strongly implicated as a cause of low back pain, and cell-based therapies hold significant promise for disc regeneration.[1] While large animal models are a requisite preclinical step prior to clinical translation of cell-based disc therapies, mouse models represent an important intermediate *in vivo* platform, as genetic manipulation permits mechanistic studies of cell-mediated regeneration. The small size of the mouse disc, however, poses technical challenges with respect to surgical technique and, consequently, experimental reproducibility. Our group recently described a percutaneous needle-injury model of moderate severity disc degeneration in the mouse caudal spine suitable for evaluating cell-based regenerative therapies.[2] As a prerequisite for using this model in studies of cell-based disc regeneration, the objectives of the current study were to: 1) establish a technique for percutaneous delivery of therapeutic cells to the mouse caudal disc; and 2) validate a technique for non-invasive quantitative tracking of injected cells.

Methods

With institutional IACUC approval, mesenchymal stem cells (MSCs) were isolated from the bone marrow of adult C57BL/6 mice using established techniques[3], expanded through 3 passages, and labeled with cell tracker red (Thermo Fisher). Using standard aseptic technique and under general anesthesia, and ~2-5x10^4 MSCs were suspended in saline were injected percutaneously into the nucleus pulposus (NP) of 3 caudal discs (C7-8, C9-10 and C11-12) of 5 adult male C57BL/6 mice (15 discs total) using a 33G needle under fluoroscopic guidance. Mice were euthanized at 1, 3, 5, 7 and 14 days post-injection. As a negative control, 1 additional mouse received injection of unlabeled MSCs into 3 caudal discs, while another served as an un-injected control, both euthanized after 1 day. Immediately following euthanasia, intact tails were imaged using an IVIS Spectrum (Perkin Elmer) imaging system. Mean fluorescence intensity was calculated for each injected disc for a 4mm diameter region of interest centered on the point of peak fluorescence intensity. Whole discs were isolated via sharp dissection and stained with Hoechst to visualize cell nuclei. Discs were then imaged through their complete thickness in the axial plane using confocal microscopy to assess both total cells (blue fluorescence) and injected cells (red fluorescence) in the NP. The NP boundary was identified using Photoshop (Adobe) and the relative area occupied by injected (red) cells was then determined using ImageJ (NIH) on a z-projection image. Linear correlation between the mean fluorescence intensity for each disc as determined via IVIS imaging, and NP area occupied by injected cells determined via confocal microscopy was evaluated ($p<0.05$).

Results

All animals successfully underwent surgery and survived to the study endpoints. MSCs labeled with cell-tracker could be detected using IVIS imaging (Figure 1) at all time points post injection, with mean fluorescence intensities for injected discs ranging from 0.50 to 6.02 $\times$ 10^7. No fluorescence signal was evident for either discs injected with unlabeled MSCs, or un-injected control discs (Figure 1). Confocal imaging clearly demonstrated the presence of injected MSCs in the NP (red fluorescence; Figure 2). The area occupied by injected MSCs ranged from 3.0 to 33.5% of the total NP area. There was a moderate, significant correlation between mean fluorescence intensity of injected MSCs measured non-invasively using IVIS imaging, and area occupied by injected MSCs measured using confocal microscopy ($r = 0.65$, $p = 0.008$; Figure 3).

Discussion

The small size of the mouse intervertebral disc makes surgical delivery of cells extremely challenging. The percutaneous technique applied here does not require an open incision and therefore minimizes local inflammation and scar tissue formation that could confound results. The non-invasive imaging technique validated here to track cells post-injection can be used to account for a variable number of cells injected by establishing a baseline against which longitudinal changes in cell survival and localization can be compared. Further, non-invasive imaging that does not require animal sacrifice may facilitate a reduction in animals

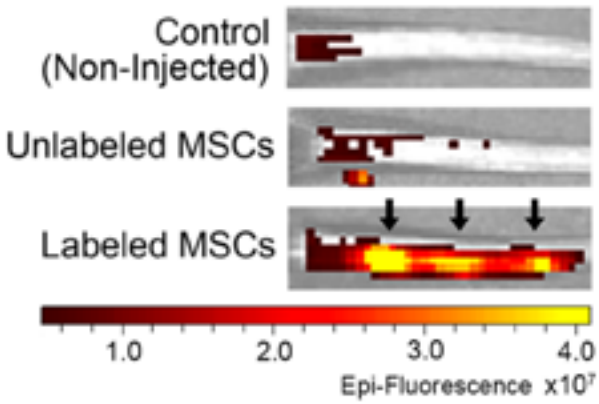


Figure 1. Non-invasive assessment of cell tracker-labeled MSCs delivered to the C7-8, C9-10 and C10-11 (arrows) mouse caudal intervertebral discs using the IVIS imaging system 1 day post-injection. No fluorescent signal is evident for control (non-injected) discs or discs injected with unlabeled MSCs.

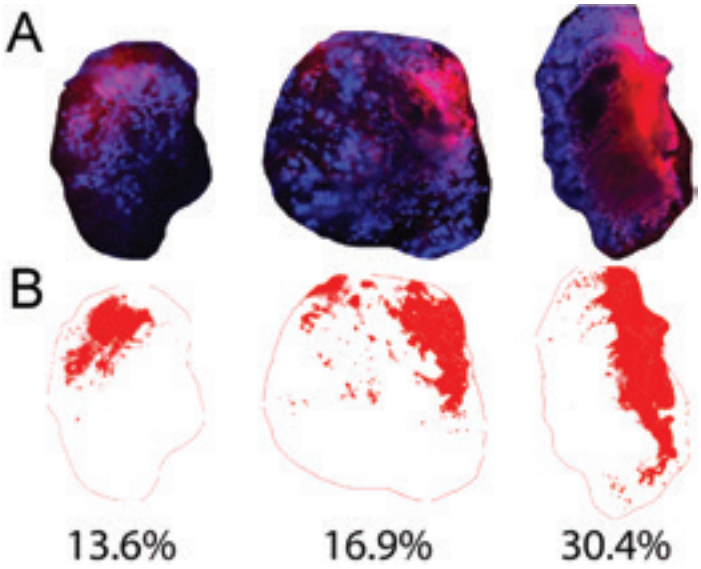


Figure 2. Nucleus pulposus area occupied by MSCs as determined by confocal microscopy of whole, isolated mouse intervertebral discs. **A.** Representative confocal images showing all cells (Hoechst, blue) relative to injected MSCs (cell tracker, red). **B.** Relative area occupied by injected cells determined using ImageJ.

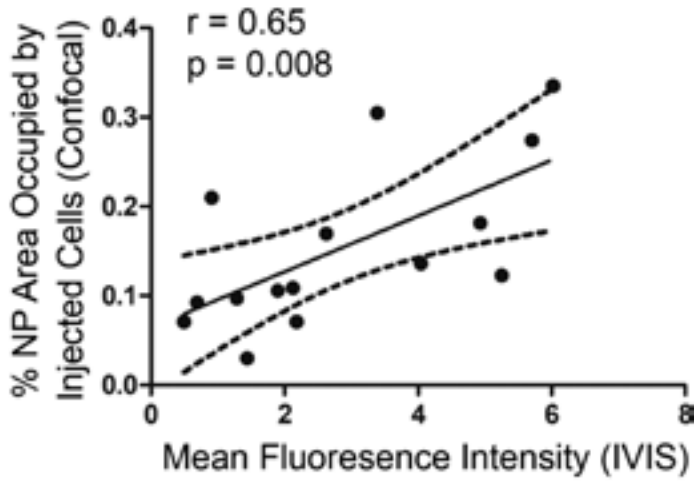


Figure 3. Correlation between mean fluorescence intensity of injected MSCs measured non-invasively using IVIS imaging, and NP area occupied by injected MSCs measured using confocal microscopy.

required for *in vivo* experimentation. Ongoing studies will apply these techniques to evaluate the regenerative effects of therapeutic cell types including MSCs and notochordal progenitor cells.

Significance

This study establishes techniques for percutaneous delivery of therapeutic cells to the mouse intervertebral disc and for subsequent non-invasive imaging of those cells.These techniques can be applied to conduct mechanistic studies of cell-based intervertebral disc regeneration in mice.

References

1. Tong W, Lu Z, Qin L, *et al.* Cell therapy for the degenerating intervertebral disc. *Transl Res* 2017; 181: 49-58.

2. Piazza M, Peck SH, Gullbrand SE, *et al.* Quantitative MRI correlates with histological grade in a percutaneous needle injury mouse model of disc degeneration. *J Orthop Res* 2018; 36(10): 2771-9.

3. Soleimani M and Nadri S. A protocol for isolation and culture of mesenchymal stem cells from mouse bone marrow. *Nat Protoc* 2009; 4(1): 102-6.

Sports Tips and Tricks: Endoscopic Fasciotomy for Exertional Compartment Syndrome

Matt Webb, MD[1]
Brian Sennett, MD[1]

1 Department of Orthopaedic Surgery
University of Pennsylvania

Introduction

Exertional Compartment syndrome is a condition characterized by reversible ischemia of the muscles of compartment due to exercise. The cause of exertional compartment syndrome has not been definitively identified, but fascial herniations and decreased capillary density have been implicated (1). Second to medial tibial stress syndrome, exertional compartment syndrome is the second most common exercise induced leg syndrome, and it is estimated that one out of eight young patients with exercised-provoked leg pain suffers from chronic exertional compartment syndrome (2). The syndrome is characterized by severe aching or burning pain and a feeling of tightness that is located in the leg compartments with exercise (3). Symptoms are reproduced by exercise and patients can often predict how long the symptoms will last. The pain can also be associated with paresthesias of the dorsum of the foot or first webspace. The results of invasive dynamic compartment pressure measurement are essential to the diagnosis of exertional compartment syndrome (4). Pathologically elevated muscle compartment pressures are defined as resting (pre-exercise) compartment pressure >15 mmHg, immediate (1 minute) post-exercise pressure >30, 5 minutes >20, or 15 minutes >15 (5). If conservative therapies including rest, anti-inflammatory medications, activity modification, alteration of running technique, and physical therapy fail then fasciotomy is considered the therapy of choice (5).

It is important to review the risks and benefits of surgery so that the patient can make an informed decision before proceeding with surgery. For some patients, activity modification may be preferable to surgery when weighed against the expected outcomes and the risks inherent to surgery. For example, scarring is important to many patients, and some recreational athletes may prefer to change their sporting activities rather than sustain permanent visible scars on their legs. Using an endoscopic approach scarring and the risk of wound problems can be minimized, but the small incisions are still necessary.

Case Example

In this case, the patient is a 20 year old male collegiate squash player who experienced bilateral leg pain with exercise and competition. Compartment syndrome pressure measurements were obtained pre-operatively and revealed elevated pressures consistent with exertional compartment syndrome in the anterior and lateral compartments of both legs. Due to the patient's active lifestyle and lack of improvement with a conservative approach it was recommended that he proceed with fasciotomies of the affected compartments.

The description of endoscopic fasciotomies is as follows and was utilized in the care of this patient.

The patient is positioned supine. Following satisfactory induction of general anesthesia, both legs are prepped and draped in the usual sterile fashion. A conforming gauze bandage soaked in betadine can be used to create a luggage tag to suspend the legs by the great toes and second toes from a candy cane stirrup positioner during surgical skin preparation. Following prepping and draping, the leg is exsanguinated using an Esmarch rubber bandage. The tourniquet is then inflated to 325 mm Hg.

With respect to surgical incisions, the tibial crest is marked along its length and the lateral malleolus is outlined. To access the anterior and lateral compartments two 3cm longitudinal incisions are created on the anterolateral leg. The distal is centered 12.5 cm proximal to the lateral malleolus and 5cm lateral to the tibial crest. The proximal incision is made 12 cm proximal to the first and 6cm lateral to the tibial crest. The incisions are made in line with each other to improve cosmesis (Figure 1).

The superficial peroneal nerve emerges from the lateral compartment at approximately the level of this distal incision. Through this incision the superficial peroneal nerve can be readily identified and protected. Using a scalpel the skin is incised and the dissection is carefully continued to the level of the fascia using Metzenbaum scissors. Care is taken to avoid injury to the superficial peroneal nerve. At this level the intermuscular septum that divides the anterior compartment from the lateral compartment is often visible. The Metzenbaum scissors are used to raise flaps superficial to the fascia.These full-thickness flaps are created large enough for sufficient visualization of the anterior and lateral compartments, but their size is limited to minimize the creation of subcutaneous dead

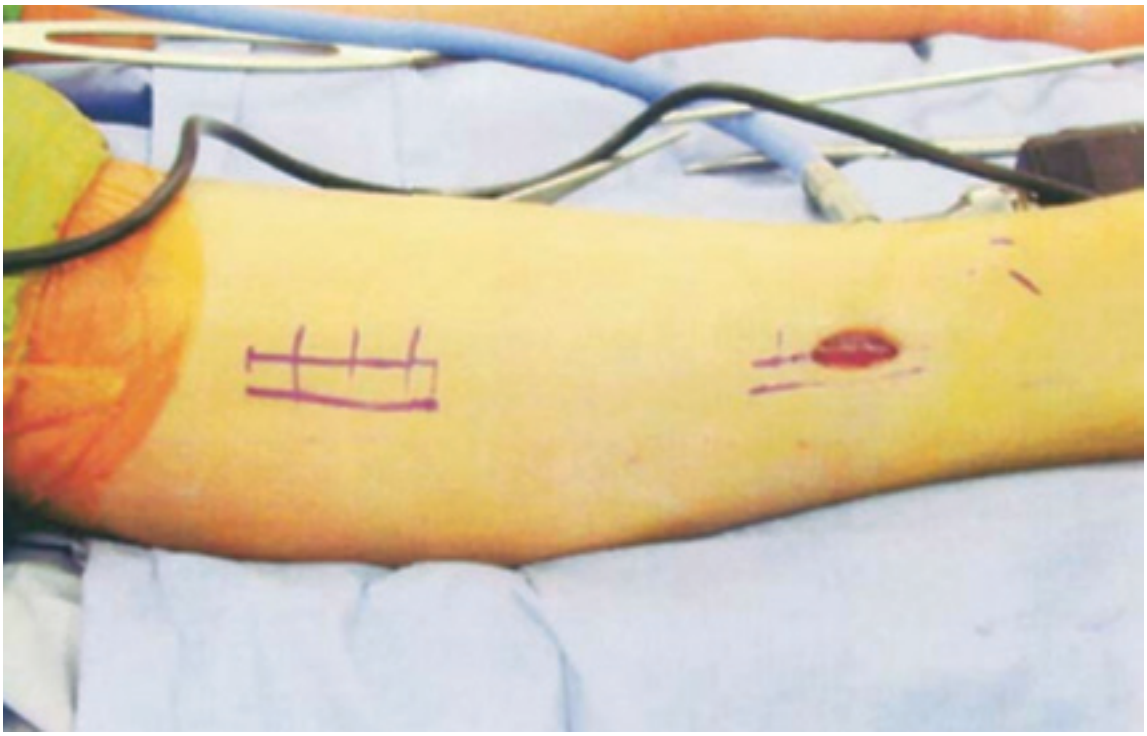


Figure 1. The distal incision is centered 12.5 cm proximal to the lateral malleolus and 5cm lateral to the tibial crest. The proximal incision is made 12 cm proximal to the first and 6cm lateral to the tibial crest. The incisions are made in line with each other to improve cosmesis.

space. Using a scalpel, a longitudinal rent of approximately 1 cm in length is created in in each compartment.

The endoscope will then be introduced to continue the dissection subcutaneously. A plastic Yankauer suction device is manually straightened. The Yankauer will be used to elevate tunneled flaps in the line of intended subcutaneous fasciotomies. The long blade of an Army/Navy retractor is introduced deep to the flap with the blade directed distally and centered over the rent in the fascia of the anterior compartment. The Yankauer is introduced deep to the blade of the retractor and a tunneled subcutaneous flap is created directly over the anterior compartment. The fasciotomy is continued distally with Metzenbaum scissors until it can no longer be directly visualized. Then an assistant holds the retractor while the endooscope is introduced deep to the blade of the retractor and the Metzenbaum scissors are used to carefully continue the fasciotomy under endoscopic visualization (Figure 2).

Superficial vessels and nerve branches are often encountered and in most cases they can be elevated, isolated, and avoided while continuing the fasciotomy. This preserves cutaneous sensation and limits postoperative hematoma. The light source is visible through the skin and dissection is not continued past the lateral malleolus. In a similar fashion, the Yankauer is used to create a subcutaneous tunnel and under endoscopic visualization the proximal aspect of the anterior compartment fasciotomy is extended proximally. The distal and proximal aspects of the lateral compartment fasciotomy are also carefully extended. During release of the anterior to lateral compartment, the superficial peroneal nerve can often be visualized with the endoscope. The endoscope light source is visible through the skin. Approximately 6 cm proximal to the distal incision the marker is used to mark spots to indicate the proximal extents of the anterior and lateral compartment fasciotomies created through the distal incision.

The proximal skin incision is created in a similar manner as the distal incision. Through the proximal skin incision rents are created over the anterior and lateral compartments and subcutaneous tunnels are created with the Yankauer and directed toward the marks that indicate the proximal extent of the fasciotomies. The proximal fasciotomies can then be created and connected with the proximal extents of the distal

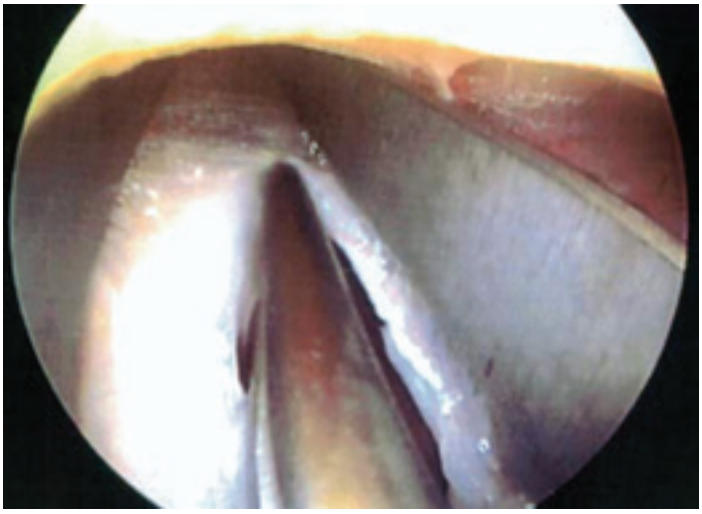


Figure 2. The fasciotomy is continued with Metzenbaum scissors until it can no longer be directly visualized. Then an assistant holds the retractor while the endoscope is introduced and the Metzenbaum scissors are used to carefully continue the fasciotomy under endoscopic visualization. Here a long forceps is used to retract while the fascia over the anterior compartment is incised with Metzenbaum scissors.

fasciotomies to create complete fasciotomies of the anterior and lateral compartments. The proximal fascia is often more robust than the distal fascia and superficially an oblique fibrous layer is often appreciated in the proximal third of the leg. On the deep aspect of the fascia a translucent layer of fascia is sometimes encountered and if it is not appreciated and incised it may result in incomplete fasciotomy and persistent symptoms. Oftentimes muscle under pressure will bulge through the completely incised fascia (Figure 3). This bulging appearance is not always apparent and may be more common in patients with elevated resting and pre-exercise compartment pressures. When this muscle bulging is visualized, however, it is indicative of complete fasciotomy. A single-incision endoscopic fasciotomy technique has also been described (6). A cadaver study compared single-incision endoscopic technique to double incision technique and found 83% and 81% release of the anterior and lateral compartments via single incision compared to 99% and 96% release via dual incision technique (7).

Although exertional compartment syndrome of the posterior compartments is much less common than compartment syndrome of the anterior and lateral compartments, the posterior compartments can be released through a separate incision along the medial border of the anterior aspect of the tibia. A 5 cm incision is created just medial to the palpable medial border of the tibia and the fascia of the superficial posterior compartment is incised under direct visualization. The proximal aspect of this incision is located even with the distal aspect of the lateral proximal incision. The fasciotomy of the superficial posterior compartment is then extended under endoscopic visualization in both a posteroproximal direction and posterodistal direction. to create and trapezoidal shaped fasciotomy. The deep posterior compartment is then released with access through the superficial compartment adjacent to the medial tibia. Care is taken to protect the saphenous vein as it is located just medial to the incision.

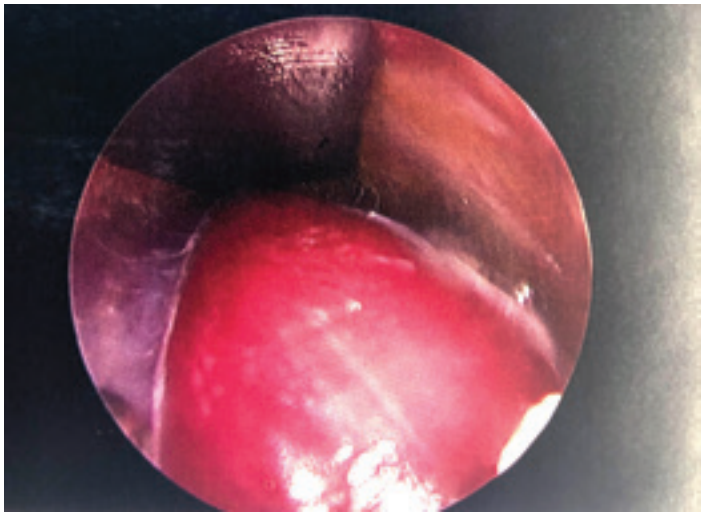


Figure 3. At times, muscle under pressure will bulge through the completely incised fascia. This bulging appearance is not always apparent and may be more common in patients with elevated resting and pre-exercise compartment pressures. When this muscle bulging is visualized, however, it is indicative of complete fasciotomy of a compartment with an elevated resting pressure.

After complete fasciotomies of all involved compartments are completed, the tourniquet is deflated and hemostasis is achieved. The incisions are closed with 3-0 nylon sutures. Horizontal mattress sutures are utilized to minimize skin tension while preserving perfusion. Finally, sterile dressing are applied. The patient may bear weight as tolerated and follows up in 1-2 weeks for wound check and suture removal. Physical therapy is initiated two weeks following surgery with gradual progression back to athletic activities.

References

1. Frapoint MJ, Adamson GJ. Chronic exertional compartment syndrome. *J A, Acad Orthop Surg* 2003. Jul-Aug; 11(4): 268-76

2. Qvarfordt P, Christenson JT, Eklof B, Ohlin P, Saltin B. Intramuscular pressure, muscle blood flow, and skeletal muscle metabolism in chronic anterior tibial compartment syndrome. *Clin Orthop Relat Res* 1983; (179): 284-290

3. Winkes MB, Hoogeveen AR, Houterman S, Giesberts A, Wijn PF, Scheltinga MR. Compartment pressure curves predict surgical outcome in chronic deep posterior compartment syndrome. *Am J Sports Med* 2012; 40: 1899-1905

4. Pedowitz RA, Hargens AR, Mubarak SJ, Gershuni DH. Modified criteria for the objective diagnosis of chronic compartment syndrome of the leg. *Am J Sports Med* 1990; 18: 35-40

5. Brennan Jr. FH, Kane SF. Diagnosis, treatment options, and rehabilitation of chronic lower leg exertional compartment syndrome. *Curr Sports Med Rep* 2003; 2: 247-250

6. Stein DA, Sennett BJ. One-portal endoscopically assisted fasciotomy for exertional compartment syndrome. *Arthroscopy* 2005; Jan;21(1):108-12.

7. Leversedge FJ, Casey PJ, Seiler JG, Xerogeanes JW. Endoscopically assisted fasciotomy: Description of technique and in vitro assessment of lower-leg compartment decompression. *Am J Sports Med* 2002; 30:272-278.

Anterolateral and Anterior Cruciate Ligament Reconstruction in the Young Athlete: When Should Both Be Considered?

Scott M LaValva, BA[1,2]
Theodore J Ganley, MD[1,2]

1 Department of Orthopaedic Surgery
Children's Hospital of Philadelphia

2 Perelman School of Medicine
University of Pennsylvania

Introduction

Anterior cruciate ligament (ACL) ruptures have grown increasingly problematic in pediatric athletes, owing largely to an amplified competition level, increased single-sport specialization, and year-round play.[1–3] While reconstruction of the ACL generally offers excellent results[4], the re-rupture rate remains highest in young and active patients.[5] As surgeons strive to optimize the outcomes of ACL reconstruction in this high-risk population, the anterolateral ligament (ALL) has gained significant attention over the last decade as many hypothesize that residual rotational instability from unaddressed injuries to the supporting anterolateral structures may be contributing.[6]

The ligament's original description was in 1879 by Paul Segond, who hypothesized that the present-day "Segond fracture" was an avulsion fracture of the lateral tibia due to increased tension on a "pearly, resistant, fibrous band" now dubbed the ALL.[7] More recent anatomic studies have strengthened the idea that the ligament is a distinct entity deep to the iliotibial band, most often arising proximally from the lateral femoral epicondyle and inserting between the fibular head and the Gerdy tubercle.[8] Though the ligament has now been relatively well-described in the adult, less is known about the pediatric ALL, though two recent pediatric-specific cadaveric investigations have revealed an identification rate of 12.5% and 64% of specimens, respectively.[9,10] The objective of this article is to appraise and apply the existing literature on the ACL and ALL to provide our indications for performing a combined reconstruction procedure in the young athlete.

Question

When is it appropriate to consider performing a combined ACL and ALL reconstruction in young athletes as opposed to ACL reconstruction alone?

Discussion

Several recent biomechanical studies have demonstrated that the ALL appears to play an important role as a restraint against internal rotation of the tibia, especially at increased knee flexion angles.[11] However, data reporting long-term clinical outcomes is relatively lacking. Thus, in the absence of high-quality, prospective data to guide surgical decision-making, many surgeons elect to perform a combined ACL/ALL reconstruction in patients with the greatest risk of graft rupture, for which the specific indications vary widely from surgeon to surgeon. The following are scenarios in which we would consider augmenting an ACL reconstruction with a combined ALL reconstruction in the young athlete.

Revision ACL Reconstruction

The cause of ACL graft ruptures following initial reconstruction is often multifactorial. In fact, patients who suffer a first-time ACL rupture are actually at a greater risk of contralateral ACL tear compared to ipsilateral graft rupture.[12] Nonetheless, patients who suffer a re-tear with no readily apparent cause may have residual rotational laxity at the knee to blame. While ACL-only reconstruction provides outstanding correction against anterior tibial translation, a small percentage of patients can experience residual post-operative rotatory instability, ultimately leading to increased graft tension and possible failure.[13] Thus, we strongly consider performing a combined ACL/ALL reconstruction in revision cases where a cause of graft failure is not apparent.

Generalized ligamentous laxity

Patients with ligamentous laxity carry a heightened risk for several ligamentous injuries, especially of the ACL.[14] A prospective study in 2017 showed that patients with hypermobility—as determined by a modified Beighton score—who underwent ACL reconstruction suffered a graft failure rate of 24.4% compared to only 7.7% of those without hypermobility.[15] Furthermore, the hypermobile patients also reported inferior subjective and functional outcome scores following ACL reconstruction. Ultimately, we believe that patients with evidence of hyperlaxity with a Beighton score of > 6 or knee hyperextension of > 15 degrees may benefit from the additional stability afforded by an ALL reconstruction, especially for those involved in high-level pivoting sports.

High-Grade Pivot Shift

The goal of the pivot shift test is to reproduce the original mechanism of injury by simulating dynamic valgus and internal rotation, ultimately to assess the rotational stability of the knee.[16] The presence of a grade 2 or 3 pivot shift is suggestive

of significant rotational instability which may be insufficiently addressed with an ACL reconstruction alone, and has thus been shown to increase the risk of re-rupture.[13] Furthermore, in patients with a grade 3 pivot shift, up to 73% may have radiographic evidence of injury to the anterolateral structures, compared to only 20% of patients with a grade 1 pivot shift.[17] In these patients, an ALL reconstruction may provide an effective means to restore the apparent rotational stability of the knee.

Elite, Year-Round, Pivoting Sport Athlete

Athletes involved in sports which require constant pivoting and dynamic valgus are at the greatest risk for ACL ruptures and graft failure.[18,19] Accordingly, patients with high-level participation in soccer, football, basketball, or lacrosse may benefit greatly from a combined ACL/ALL reconstruction. In a recent large study of young athletes involved in pivoting sports, the addition of an ALL reconstruction was associated with a 2.5 – 3.1 times lower rate of graft failure compared to ACL reconstruction alone.[20] Thus, in the patient with a first-time ACL rupture who plans to return to a high level of competition in a high-risk sport, the addition of an ALL reconstruction may provide supplementary support against the dynamic valgus position.

Increased Posterior Tibial Slope

Radiographic parameters may also provide important information regarding re-rupture risk as well. Previous studies have demonstrated a direct correlation between increasing lateral posterior tibial slope and the magnitude of anterior translation of the tibia relative to the femur.[21] Consistent with this finding, an increased posterior tibial slope has been shown to increase both the risk of native-ACL rupture and also graft failure in ACL-reconstructed knees.[21,22] Specifically, the odds ratio for graft failure with 4 and 6 degree increases in tibial slope angle was 2.4 and 3.8, respectively.

Radiographic Evidence of ALL Disruption [Future]

The consistent and reliable identification of the intact ALL via MRI has been well demonstrated in adults and less so in skeletally immature patients.[23] However, the use of imaging modalities to reliably detect an ALL injury and subsequently guide clinical decision-making remains in its infancy. Nonetheless, we expect that future investigations will bolster the ability to accurately and reliably detect an ALL injury in the setting of an acute ACL rupture, which may provide more targeted indications for ALL reconstruction in the future.

Conclusions

The anterolateral ligament has garnered a substantial amount of interest within the sports medicine community as of late, though highest-level, evidence-based surgical literature in pediatric patients is currently lacking since descriptions of procedures for this structure remain in their infancy.At our high-volume center, we consider performing a combined anterior cruciate ligament and anterolateral ligament reconstruction in patients with the highest risk of graft rupture, namely those with a history of graft rupture, generalized ligamentous laxity or knee hyperextension, a high-grade pivot shift, increased posterior tibial slope, or the expectation of continued participation in high-level pivoting sports.

References

1. Beck NA, Patel NM, Ganley TJ. The pediatric knee: Current concepts in sports medicine. *J Pediatr Orthop Part B*. 2014.

2. Swenson DM, Collins CL, Best TM, *et al*. Epidemiology of knee injuries among U.S. high school athletes, 2005/2006-2010/2011. *Med Sci Sports Exerc*. 2013.

3. Jayanthi N, Pinkham C, Dugas L *et al.* Sports Specialization in Young Athletes: Evidence-Based Recommendations. *Sports Health*. 2013.

4. Ramski DE, Baldwin KD, Ganley TJ *et al.* Anterior cruciate ligament tears in children and adolescents: A meta-analysis of nonoperative versus operative treatment. *Am J Sports Med*. 2014.

5. Wiggins AJ, Grandhi RK, Schneider DK, *et al.* Risk of Secondary Injury in Younger Athletes after Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2016.

6. Kraeutler MJ, Welton KL, Chahla J, *et al.* Current Concepts of the Anterolateral Ligament of the Knee: Anatomy, Biomechanics, and Reconstruction. *Am J Sports Med*. 2018.

7. Segond, PF. Recherches cliniques et experimentales sur les epanchements sanguins du genou par entorse. *Prog Med*. 1879.

8. Weber AE, Zuke W, Mayer EN, *et al*. Lateral Augmentation Procedures in Anterior Cruciate Ligament Reconstruction: Anatomic, Biomechanical, Imaging, and Clinical Evidence. *Am J Sports Med*. 2018.

9. Shea KG, Polousky JD, Ganley TJ *et al.* The anterolateral ligament of the knee: An inconsistent finding in pediatric cadaveric specimens. *J Pediatr Orthop*. 2016.

10. Shea KG, Milewski MD, Ganley TJ *et al.* Anterolateral Ligament of the Knee Shows Variable Anatomy in Pediatric Specimens. *Clin Orthop Relat Res*. 2017.

11. Parsons EM, Gee AO, Spiekerman C *et al.* The biomechanical function of the anterolateral ligament of the knee. *Am J Sports Med*. 2015.

12. Magnussen RA, Meschbach NT, Kaeding CC, *et al.* ACL graft and contralateral ACL tear risk within ten years following reconstruction a systematic review. *JBJS Rev*. 2015.

13. Sonnery-Cottet B, Daggett M, Fayard JM, *et al*. Anterolateral Ligament Expert Group consensus paper on the management of internal rotation and instability of the anterior cruciate ligament - deficient knee. *J Orthop Traumatol*. 2017.

14. Ramesh R, Von Arx O, Azzopardi T *et al.* The risk of anterior cruciate ligament rupture with generalised joint laxity. *J Bone Joint Surg Br*. 2005.

15. Larson CM, Bedi A, Dietrich ME, *et al.* Generalized Hypermobility, Knee Hyperextension, and Outcomes After Anterior Cruciate Ligament Reconstruction: Prospective, Case-Control Study With Mean 6 Years Follow-up. *Arthrosc - J Arthrosc Relat Surg*. 2017.

16. Musahl V, Hoshino Y, Ahlden M, *et al.* The pivot shift: A global user guide. *Knee Surgery, Sport Traumatol Arthrosc*. 2012.

17. Song GY, Zhang H, Wang QQ *et al.* Risk Factors Associated with Grade 3 Pivot Shift after Acute Anterior Cruciate Ligament Injuries. *Am J Sports Med*. 2016.

18. Gans I, Retzky JS, Jones LC *et al.* Epidemiology of Recurrent Anterior Cruciate Ligament Injuries in National Collegiate Athletic Association Sports: The Injury Surveillance Program, 2004-2014. *Orthop J Sport Med*. 2018.

19. Gornitzky AL, Lawrence JT, Ganley TJ *et al.* Sport-Specific Yearly Risk and Incidence of Anterior Cruciate Ligament Tears in High School Athletes: A Systematic Review and Meta-analysis. *Am J Sports Med*. 2016.

20. Sonnery-Cottet B, Saithna A, Cavalier M *et al.* Anterolateral Ligament Reconstruction Is Associated with Significantly Reduced ACL Graft Rupture Rates at a Minimum Follow-up of 2 Years: A Prospective Comparative Study of 502 Patients from the SANTI Study Group. *Am J Sports Med*. 2017.

21. Dare DM, Fabricant PD, McCarthy MM, *et al.* Increased lateral tibial slope is a risk factor for pediatric anterior cruciate ligament injury: An MRI-based case-control study of 152 patients. *Am J Sports Med*. 2015.

22. Christensen JJ, Krych AJ, Engasser WM *et al.* Lateral Tibial Posterior Slope Is Increased in Patients with Early Graft Failure after Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2015.

23. Hartigan DE, Carroll KW, Kosarek FJ *et al.* Visibility of Anterolateral Ligament Tears in Anterior Cruciate Ligament–Deficient Knees With Standard 1.5-Tesla Magnetic Resonance Imaging. *Arthrosc - J Arthrosc Relat Surg*. 2016.

Macro- and Micro-Scale Changes in Meniscus and Cartilage in a Large Animal Model of Meniscal Injury

Sonia Bansal, BS[1,2]
Jay M. Patel, PhD[1,2]
Michael Eby, MD MS[1,2]
Kevt'her Hoxha, BS[3]
Mackenzie L. Sennett,[1,2]
Kamiel S. Saleh, BS[1]
Brendan D. Stoeckl, MSE BSE[1,2]
Anthony R. Martin, BSE[1,2]
Liane M. Miller, MD[1,2]
Dawn M. Elliott, PhD[4]
Michael W. Hast, PhD[5]
Lin Han, PhD[3]
Miltiadis H. Zgonis, MD[1,2]
Robert L. Mauck, PhD[1,2]

1 McKay Orthopedic Research Laboratory
University of Pennsylvania

2 Translational Musculoskeletal Research Center
CMC VA Medical Center

3 NanoBiomechanics Laboratory
Drexel University

4 Multi-Scale Fiber-Reinforced Tissue Biomechanics Laboratory
University of Delaware

5 Biedermann Laboratory for Orthopaedic Research
University of Pennsylvania

Introduction

The meniscus is a complex and integral load-bearing tissue in the knee[1] that is commonly injured.[2] Depending on the type of injury, the ability of the meniscus to transfer and distribute loads is reduced to varying degrees. For example, with tears of the enthesis (root tears), free meniscal excursion occurs with joint loading, the mechanical equivalent meniscus removal (meniscectomy).[3] Indeed, small animal (mouse and rat) models have used destabilization of the medial meniscus (DMM) to instigate controlled joint degeneration.[4] Even with smaller surgical excisions to treat radial or circumferential tears in the inner zone, the joint degrades over the longer term,[5,6] as evidenced by the early onset of OA in humans. While degeneration of the articular cartilage is well established in small animal models of meniscus destabilization, and in human cohorts after meniscus surgery, progression of disease in the meniscus itself is not well studied, especially in larger animal models. Thus, the purpose of this study was to investigate how meniscus injury in a large animal model instigates pathologic remodeling of the meniscus itself and the joint as a whole, at the macro- and micro-scale.

Methods

Juvenile (6 month old) Yucatan minipigs (n=12) underwent bilateral arthroscopic surgery and received two of the following four injuries to the medial meniscus—sham, DMM, a vertical longitudinal tear (1/3 arc length, red-white zone), or a radial tear (50% of meniscus width) (n=6/group). Animals were euthanized at one month and joints harvested for a series of macro- and micro-scale analyses. For macro-scale tests, intact joints were compressed to 1× body weight (400 N) at 15° of flexion using a custom rig and universal test frame. Pressure sensors (TekScan #6900-110) were inserted into the joint to measure load transfer through the medial compartment [3]. Next, tissues were imaged for macroscopic changes to the meniscus and for cartilage wear (using India ink)[7]. Subsequently, medial menisci were harvested and sectioned (16 micron thickness, vertical plane, anterior and posterior horns) for atomic force microscopy (AFM)[8]. Additional sections were subjected to histological analysis of proteoglycan (PG) content (Safranin O/Fast Green)[9]. Osteochondral cylinders were isolated from the medial tibial compartment and indented using a 2 mm spherical indenter to determine cartilage mechanical properties in the region covered by the meniscus[10]. These samples then underwent microCT scanning followed by decalcification and paraffin processing for analysis of proteoglycan content (Safranin O/Fast Green)[11]. Histological outcomes were graded using the OARSI scoring method[7] by four blinded observers.

Results

Sham operated menisci showed no macroscopic changes. Most vertical tears were no longer visible at 1 month, while radial tears were readily apparent. DMM menisci showed some healing with evidence of fibrous tissue at the anterior horn (Figure 1A). However, this scar tissue was not mechanically competent, as the mean contact pressure was significantly higher in DMM joints compared to other groups (Figure 1B). Menisci from sham limbs showed more intense staining for PGs compared to DMM menisci, with slight reductions in staining intensity radial and vertically defected menisci (Figure 2A). AFM analysis revealed an increase in the indentation modulus of radial fibers in the inner zone of the anterior horn with radial defects, as well as a decrease in circumferential fiber modulus in the outer zone of the posterior horn with DMM (Figure 2B). While no macroscopic signs of wear were visible on the tibial cartilage surface, PG staining was markedly reduced in DMM (Figure 3A) and slightly reduced in radial and vertical samples. OARSI scoring revealed changes in all groups, with significance for radial and vertical samples (Figure 3B). Cartilage indentation modulus was significantly decreased for DMM samples, and trended lower for vertical and radial samples (Figure 3C). There were no changes in the subchondral bone for any group at this time point (data not shown).

Discussion

This is the first study, to our knowledge, to investigate meniscal remodeling in a minimally invasive (arthroscopic), large animal surgical model of meniscus injury. Despite the fibrous "healing" of the DMM in this model, load transfer to the underlying cartilage remained altered at 1 month post-surgery, with increases in contact

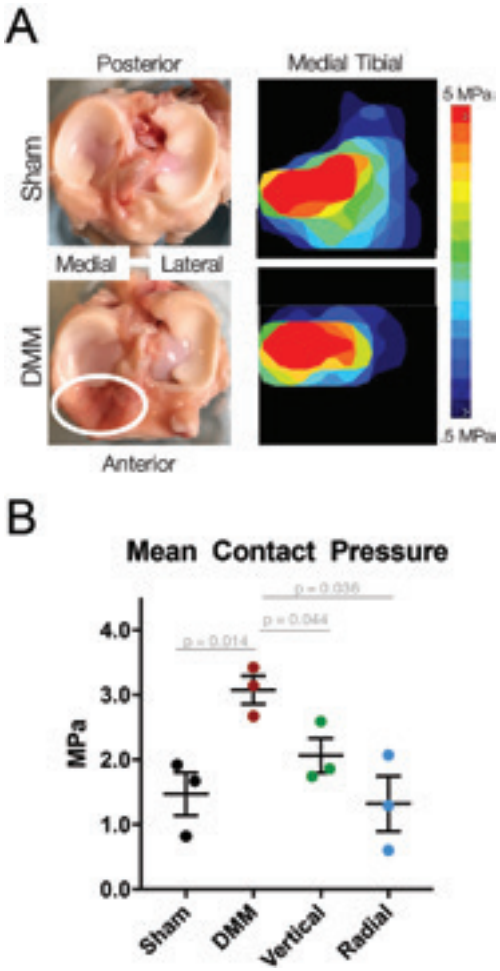


Figure 1. Macroscopic images **(A)** of sham (upper left) and DMM (lower left) operated menisci, showing fibrous attachment formation in the DMM meniscus (white circle). Representative contact pressure maps shown from peak contact load point (right). Quantification of mean contact pressure **(B)** for all operative groups.

pressure and decreases in cartilage PG staining and indentation modulus. This is consistent with outcomes from open surgical procedures in small[4,12] and large animal[13] models of DMM in the literature. Meniscus remodeling was also evident at this time point for DMM samples. Specifically, the PG content of the inner anterior horn was reduced, as was the indentation modulus of circumferential fibers in the outer posterior horn. This suggests that unloading caused by DMM results in remodeling of the meniscus. Vertical and radial tears did not alter load transmission at this time point, but both resulted in signs of cartilage degeneration (according to OARSI scoring) and radial tears increased micromechanics of the radial tie fiber network in the anterior horn of the meniscus. Future work will increase the sample size and extend the study duration to detail the temporal progression of meniscal injury-induced remodeling of the meniscus (and joint as a whole) at both the micro- and macro-scales in this large animal model. Understanding the progression of joint disease after meniscal injury in a large animal model will improve surgical decision making and inform novel repair strategies.

References

1. **Makris**+ 2011
2. **Mordecai**+ 2014
3. **Bedi**+ 2010
4. **Glasson**+ 2007
5. **Roos**+ 1995
6. **Lohmander**+ 2007
7. **Little**+ 2010
8. **Li**+ 2018
9. **Pauli**+ 2011
10. **Meloni**+ 2017
11. **Sennett**+ 2018
12. **Doyran**+ 2017
13. **Waller**+ 2017

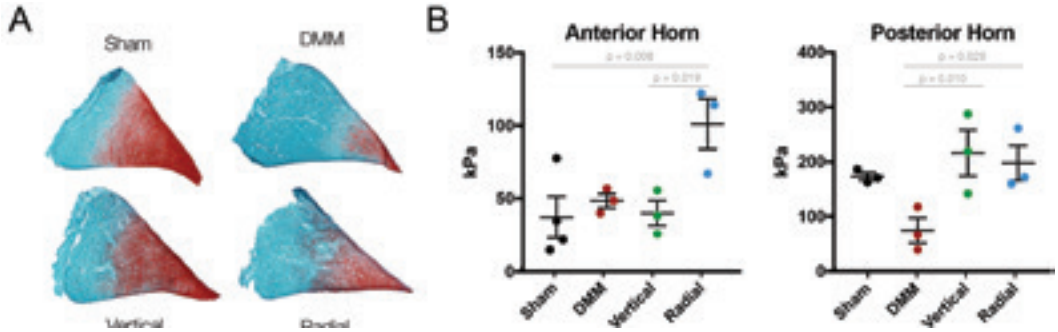


Figure 2. Histological staining **(A)** of radial vertical sections from the anterior horn of the meniscus. Staining done with Safranin O / Fast Green for proteoglycan content. AFM indentation modulus **(B)** of the Anterior Horn, inner zone radial fibers (left) and Posterior Horn, outer zone circumferential fibers (right).

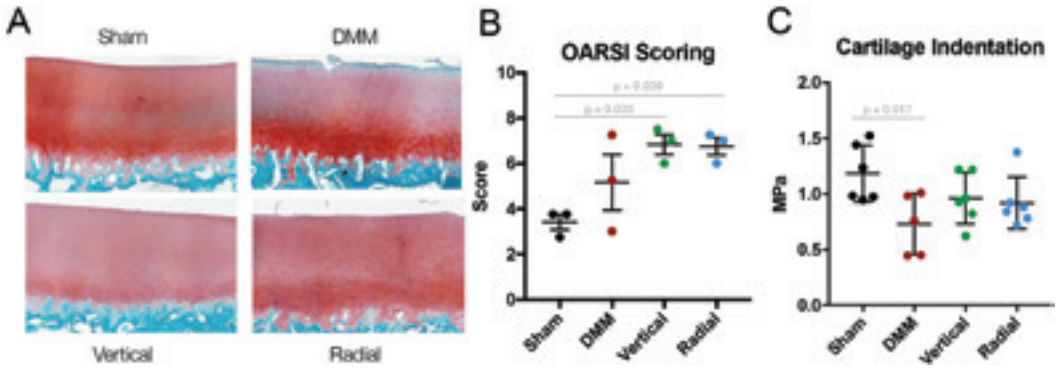


Figure 3. Histological staining **(A)** of osteochondral sections from each surgical group. Staining done with Safranin O / Fast Green for proteoglycan content, scale bar = 500 microns. Scoring **(B)** by four blinded observers using OARSI guidelines for large animals. Cartilage indentation modulus **(C)** for each group.

Reverse Total Shoulder Arthroplasty: Impressive Recent Increase in Utilization

Alex M Beschloss, BA [1]
John D Kelly IV, MD [2]

[1]Perelman School of Medicine
University of Pennsylvania

[2]Department of Orthopaedic Surgery
University of Pennsylvania

Introduction

Reverse total shoulder arthroplasty (rTSA) is a surgical procedure performed to manage certain pathologies that affect the glenohumeral joint. Unlike an anatomical shoulder replacement, the "cup" is placed into the proximal head of the humerus and the metal ball is fixed to the glenohumeral socket. Reverse total shoulder arthroplasty (rTSA) has become an increasingly utilized procedure for patients with a wide variety of shoulder pathology. In spite of a considerable complication rate, reverse total shoulder arthroplasty has experienced a large increase in utilization between 2011 and 2014.[1] Largely due to the relative success of the reverse shoulder implant in treating rotator cuff arthropathy—since FDA approval in 2004– indications for this procedure have been expanded to include many other diagnoses: including proximial humeral fractures and glenohumeral arthritis. Given the increasing focus on health care utilization and value-based care, it is essential to understand the volume and value of rTSA procedures performed in the United States. The purpose of this manuscript is to describe the utilization, current patient demographics, and economic data associated with reverse total shoulder arthroplasty (rTSA) procedures performed in outpatient centers across the United States.

Methods

The National Inpatient Sample comprises a 20% weighted sample of discharges from US hospitals (excluding rehabilitation and long-term acute care hospitals) and represents 96% of the US population. The NIS database was queried for Reverse Total Shoulder Arthroplasty in the United States for incidence, mean length of stay (LOS), mean age, mean hospital charge, mean hospital costs, national bill, national costs, sex, payer type, hospital teaching status, and hospital owner type. These data were queried between 2011 to 2014.

Results

Between 2011 and 2014, 114,650 reverse total shoulder arthroplasty surgeries were performed. In 2011, 21,155 surgeries were performed. This increased by 180% to 38,180 in 2014.The incidence (per 100,000 individuals) over this same timeframe increased by 176% from 6.8 to 12. Over this period, there was a mean of 28,663 surgeries performed per year.

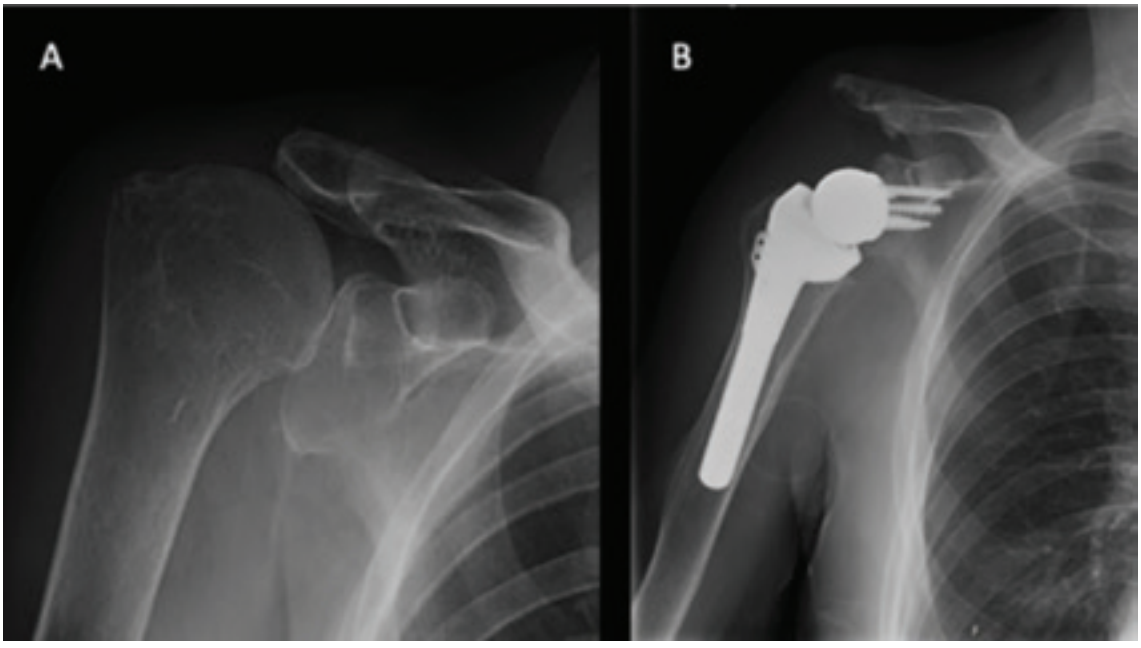


Figure 1: Reverse Total Shoulder Arthroplasty. (A) A radiograph of rotator cuff tear arthropathy; (B) A radiograph of reverse shoulder arthroplasty. (Surgeon: John Kelly)

Table1. Demographic and Economic Data of patients who receive rTSR

	2011	2012	2013	2014
Total Number	21,155	24,465	30,850	38,180
Incidence Per 100,000	6.8	7.8	9.8	12
Hospital Charge	$64,813	$66,086	$68,480	$70,820
Hospital Cost	$19,196	$20,124	$20,091	$19,724
National Bill	$1,356,197,540	$1,551,620,170	$2,002,124,985	$2,580,087,647
Mean Age	71.9	72.6	72.5	72.7
Mean LOS	2.6	2.5	2.4	2.4
Payer Type				
%Medicare	79%	78%	80%	76.5%
% Medicare	1%	2%	2%	2%
% Private	15%	16%	14%	16%
Hospital Ownership				
% Gov. Owned	13%	9%	9%	10%
% Non Profit	15%	15%	16%	15%
% For Profit	14%	15%	16%	15%
Teaching Status				
Urban Teaching		49%	48%	63%
Urban Non-Teaching		39%	42%	23%
Rural		9%	11%	11%

The mean hospital charge for rTSA, defined by the mean amount that the hospital charged for a specific procedure, was $64,813 in 2011, and increased by 9.3% to $70,820 in 2014. The mean hospital cost, which represents the mean cost of production of a specific procedure, was $19,196 in 2011 and increased by only 2.8% to 19,724 in 2014.The cost-charge difference—as defined by the difference between mean hospital charge and cost—increased significantly from $45,617 to $51,096 in 2014; this reflects a 12.0% increase. The aggregate charge, also called the national bill, is the sum of all charges for all hospitals for all rTSA performed in the US. This increased from nearly $1,356,197,540 in 2011 to $2,580,087,647 in 2014—a 90% increase.

The mean age of patient was 72.4 years and the mean length of stay was 2.5 days post-surgery. Over this period, 36% of patients were male and 64% of patients were female. 78.3%, 1.7% and 15% of patients were insured with Medicare, Medicaid or private insurance, respectively. 10% of these procedures were performed at government owned hospitals. 75% of these procedures were performed at private, not for profit hospitals, and 15% occurred at private, for profit hospitals.

Discussion

There been an explosive, 180%, increase in the utilization of rTSR surgery in the United States between 2011 and 2014.This has been accompanied with a 10% increase in the amount that hospitals charge, an only 2.8% increase in the cost of the for this surgery over this time period.This increase in the amount that hospitals charge could be partially driven by the inherent large cost of the implant itself, which Coe et al report to cost approximately $12,000—which is 61% of the hospital cost of the procedure in 2014.[1]

This increase in both cost and utilization is particularly concerning because of a notable complication rate for the surgery which is naturally associated with increased costs as well.[2,3] In 2011, Walch et al found the complication rate to be 19%.[4] In 2007, Wall et a found the complication rate to be unacceptably high, at 68%.[5] In 2016, Barco, et al reported that the complication rate for primary rTSA was 15%, a lower, however still substantial rate. Typical complications of rTSA include: instability, infection, notching, loosening, nerve injury, acromial and scapular spine fracture, and component disengagement.[6]

Since FDA approval of rTSR in 2004, it has been used for an increasing number of "off label" indications for which it has not been officially improved.[7] The sizable increase in utilization of this procedure demands close inspection of how much value rTSA affords patients, especially in comparison to lesser invasive alternatives, such as partial arthroscopic rotator cuff repair or superior capsular reconstruction.[8]

The limitations of this study are primarily due to the intrinsic nature of utilizing a large patient database. The NIS database does not include physician based-fees, however the hospital-specific cost-to charge ratios have been validated by the Agency for Healthcare Research and Quality. Since the NIS is based on ICD-9 billing codes, any inaccuracies in a hospital's billing record will be reflected in the data in the NIS.

In summary, rTSR has an increasing utilization rate, hospital charge and a both high and increasing complication rate. In addition to this, demographic information about the rTSR patient population was identified. The goal of this study was not to determine the cause of these observed trends, but to identify these trends and relate them to one another.

Conclusions

These data show an increase in utilization and hospital charge for this procedure-which is particularly concerning when considering the high and increasing complication rate. Understanding this economic data in addition to the demographic data of the patient population is the first step to allowing the medical community to make better decisions to provide improved value-based-care with respect to rTSR.

References:

1. Coe M.P, Greiwe R, Joshi R *et al.* The cost-effectiveness of reverse total shoulder arthroplasty compared with hemiarthroplasty for rotator cuff tear arthropathy.

2. Zumstein M.A, Pinedo K, Old, P Boileau. Problems, complications, reoperations and revisions in reverse total shoulder arthroplasty. *J Shoulder Elbow Surg.*2010, pp.12-22

3. Healy M, Mullard A. Hospital and Payer Costs Associated with Surgical Complications. *JAMA Surgery.* 2016;151(9):823-830

4. Sershon RA, Walch G, Bacle G, Lädermann A, Nové-Josserand L, Smithers CJ Do the indications, results, and complications of reverse shoulder arthroplasty change with surgeon's experience? *J Shoulder Elbow Surg.* 2012 Nov; 21(11):1470-7

5. Wall B., Nové-Josserand L., O'Connor D.P, *et. al.* Reverse total shoulder arthroplasty: a review of results according to etiology. *J Bone Joint Surg Am.* 2007;89(7):1476–1485.

6. Barco R, Savvidou OD, Sperling JW, *et al.* Complications in reverse shoulder arthroplasty. *EFORT Open Rev* 2016;1:72-80.

7. Van Thiel GS, Lin EC, ***et. al.*** Clinical outcomes of reverse total shoulder arthroplasty in patients aged younger than 60 years. *J Shoulder Elb Surg.* 2014;23(3):395–400

8. Mihata, Teruhisa, et al. "Clinical results of arthroscopic superior capsule reconstruction for irreparable rotator cuff tears." *Arthroscopy: The Journal of Arthroscopic & Related Surgery* 29.3 (2013): 459-470.

What's New in Tibial Spine Fractures? A Review of the Literature from 2017 to 2019

Blake C Meza, BS[1,2]
Julien T Aoyama, BA[1]
Sprikena Nako[1]
Theodore J Ganley, MD[1]

1 Department of Orthopaedics
Children's Hospital of Philadelphia

2 Perelman School of Medicine
University of Pennsylvania

Introduction

Tibial spine, or tibial eminence, fractures most often occur in children and adolescents, though cases have been reported in adults as well.[1-5] Traditionally, the highest risk activity for tibial spine fracture was considered to be a fall from a bicycle, though following the popularization of recreational sports, non-contact injuries in soccer, rugby, and skiing have become more common.[2,6] Regardless of sport type, the underlying mechanism remains similar to an ACL tear, namely excessive knee flexion with external rotation of the tibia and resultant excessive axial loading of the joint.[7,8]

The Meyers and McKeever classification,[7] later modified by Zaricznyj,[9] clusters tibial spine fractures by severity and displacement and helps guide management. Non-displaced (Type I) fractures are typically managed non-operatively with cast immobilization, while the management of partially displaced (Type II) fractures is more controversial. Operative management is indicated for completely displaced (Type III) or comminuted (Type IV) fractures. Surgical correction can be done arthroscopically or openly with a variety of fixation methods, ranging from cannulated screws[10,11] to suture anchors[12,13] to Kirschner wires.[14]

With an incidence of 3 per 100,000,[15] much of the evidence regarding the management and long-term outcomes of tibial spine fractures comes from case reports or retrospective case series, leading authors to call for retrospective, multicenter or prospective studies.[16-18] These studies would allow orthopaedic surgeons to better evaluate treatment options, however, conducting these studies takes time. The goal of this review was to determine what progress has been made in the research on tibial spine fractures over the past two years.

Methods

We performed a literature review of PubMed for articles published between January 1, 2017 and March 6, 2019 using the search terms "tibial spine fracture," tibial eminence fracture," "tibial spine avulsion," or "tibial eminence avulsion." Articles were reviewed to determine their categorization and level of evidence according to the Journal of Bone and Joint Surgery's (JBJS) Levels of Evidence chart. Articles were also characterized by study type of Research, Technique, or Review.

Results

The search yielded 39 publications: 26 original research studies, 8 technique articles, and 5 reviews. Research studies were predominantly of lower level evidence with zero Level I and only two Level II studies published since 2017 (Figure 1). Technique articles were primarily from Egypt (n=3) and the United States (n=3), with France, Japan, and China each producing one Technique article during the review period as well. Review articles came from the U.S. (n=3), France (n=1), and India (n=1).

Discussion

Techniques

Over the past two years, much of the newly published literature on tibial spine fractures has focused on arthroscopic surgical techniques. The benefits of arthroscopic approaches include inspection of the cartilage, ligaments, and menisci for concomitant injuries, less post-operative pain and need for hospitalization compared to the more invasive open approaches.[18,19] Many of the articles were case reports of novel techniques, though the largest case series included 27 operative patients.[20]

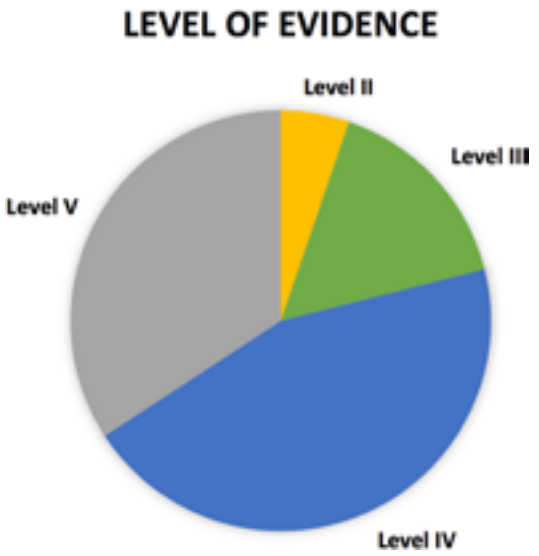


Figure 1. JBJS Levels of Evidence of Literature Published on Tibial Spine Fractures since 2017. One Level II study was diagnostic. One Level III study was prognostic. The remainder were therapeutic studies.

Regardless of technique, the principles of surgical management remain the same: ensure optimal tensioning of the ACL to prevent future injury and ideal fixation of the fracture without disrupting the physis.[18,21] Traditional arthroscopic fixation of tibial spine fractures has involved either suture-based or screw-based methods of fixation.[22] Recently, some authors have proposed novel techniques, including looped cerclage wires for compression of comminuted fractures[19] and a self-tensioning knotless, absorbable suture technique that obfuscates the need for distal fixation.[23] Others have proposed using bioabsorbable nails[24] and resorbable magnesium screws[25] for fixation, and demonstrated minimal deficits in range of motion or complications at long-term follow-up. Alternatively, some authors have adopted devices originally intended for arthroscopic fixation of acromioclavicular (AC) joint.[26,27] These suspension sling devices typically require drilling through the avulsed fragment and leaving hardware in the joint, however, Aboalata et al. published their new four-point fixation technique that avoids these risks.[27]

Recent variations of suture-based methods have included utilizing a single tibial tunnel,[28] a combination of suture anchors and EndoButtons,[29] and suture fixation over a bony bridge.[30] Gamboa et al. have demonstrated success with a suture lever reduction technique, in which they drill a tunnel underneath, rather than into, the avulsed fragment, thus eliminating the need for provisional fixation.[31] Similar to the method proposed by DeFroda, Pandey et al developed a novel technique of tying two non-absorbable sutures over a bony bridge by using an intravenous cannula needle as a suture passer. At final follow-up, all twelve patients with Type III and fourteen with Type IV tibial spine avulsion fractures exhibited complete range-of-motion and no knee instability.[32]

Original Research

Beyond new techniques, recently published literature has also included multicenter studies on the incidence of concurrent meniscal injuries,[33,34] the largest retrospective study on the epidemiology of tibial spine fractures,[35] and a cadaveric biomechanical study comparing suture-based, screw-based, and suture anchor methods of fixation.[22] In 54 patients studied, Feucht et al found that nearly 40% of those undergoing surgical treatment for tibial spine fractures have meniscal injuries, with those who are older or more advanced in their Tanner staging being more likely to have concomitant meniscal injury. As the only prospective study published in the past two years, they found that 90% of injuries were to the lateral meniscus, and that just two tear types (longitudinal posterior horn and root detachment of the anterior horn) accounted for 50% of all tears.[33] Among the retrospective studies, the largest, with a sample size of 163, describes rates of meniscal entrapment and associated injuries, however, as a case series it is not able to provide comparative analyses of treatment or outcomes.[34]

Two additional retrospective case series analyzed the epidemiology of tibial spine fractures and rates of concurrent ACL injury.[35,36] Axibal et al found that organized sports-related injuries were a more common cause of tibial spine fractures than bicycle injuries in 122 patients studied (36% vs. 25%). Younger patients were more likely to have displaced (Type III) fractures, but there were no other significant predictors of Meyers and McKeever classification.[35] In an earlier study, the same authors identified concomitant ACL injuries in 25 of their 129 patients (19%), with higher rates in older male patients. Interestingly, they noted that pre-operative MRI had low sensitivity (0.09) in identifying ACL injury compared to intra-operative evaluation.[36] Another group compared outcomes between tibial eminence fractures and ACL tears in controls matched based on age, sex, skeletal maturity, and preinjury activity level and found that those with tibial eminence fractures had higher rates or arthrofibrosis and residual laxity, but did return to sport sooner and had similar rates of subsequent ACL injury.[37]

Finally, comparisons of fixation methods were investigated in 24 cadaveric knees.[22] Li et al showed that a modified suture fixation technique using neckwear knots and the suture bridge technique were superior to traditional suture or screw-based fixation in terms of ultimate failure load and fragment displacement, respectively. In the future, similar biomechanical studies should be conducted in humans to better evaluate the clinical implications of these findings.

Over the past two years, progress has been made in research on tibial spine fractures with many new published techniques, the largest epidemiology study to date, and two multicenter studies evaluating concurrent injury rates. Continued collaborative efforts through prospective, multicenter studies will be necessary to determine which surgical approaches and methods of fixation are best.

References

1. Kellenberger R, von Laer L. Nonosseous lesions of the anterior cruciate ligaments in childhood and adolescence. *Progress in pediatric surgery* 1990;25:123-31.

2. Aderinto J, Walmsley P, Keating JF. Fractures of the tibial spine: epidemiology and outcome. *Knee* 2008;15(3):164-7.

3. Loriaut P, Moreau PE, Loriaut P, *et al.* Arthroscopic treatment of displaced tibial eminence fractures using a suspensory fixation. *Indian J Orthop* 2017;51(2):187-91.

4. Menge TJ, Chahla J, Mitchell JJ, *et al.* Avulsion of the anterior lateral meniscal root secondary to tibial eminence fracture. *Am J Orthop* 2018;47(5).

5. Patterson SP, Christiansen GB, Daffner RH. Avulsion fracture of the tibial eminence in an adult with a unique mechanism of injury. *Radiology case reports* 2018;13(4):843-7.

6. Ahmad CS, Stein BE, Jeshuran W, *et al.* Anterior cruciate ligament function after tibial eminence fracture in skeletally mature patients. *Am J Sports Med* 2001;29 (3):339-45.

7. Meyers MH, McKeever KF. Fracture of the intercondylar eminence of the tibia. *J Bone Joint Surg Am* 1959;41-a(2):209-20.

8. Gronkvist H, Hirsch G, Johansson L. Fracture of the anterior tibial spine in children. *J Pediatr Orthop* 1984;4(4):465-8.

9. Zaricznyj B. Avulsion fracture of the tibial eminence: treatment by open reduction and pinning. *J Bone Joint Surg Am* 1977;59(8):1111-4.

10. Senekovic V, Veselko M. Anterograde arthroscopic fixation of avulsion fractures of the tibial eminence with a cannulated screw: five-year results. *Arthroscopy* 2003;19(1):54-61.

11. Berg EE. Pediatric tibial eminence fractures: arthroscopic cannulated screw fixation. *Arthroscopy* 1995;11(3):328-31.

12. Vega JR, Irribarra LA, Baar AK, *et al.* Arthroscopic fixation of displaced tibial eminence fractures: a new growth plate-sparing method. *Arthroscopy* 2008;24 (11):1239-43.

13. Kim JI, Kwon JH, Seo DH, *et al.* Arthroscopic hybrid fixation of a tibial eminence fracture in children. *Arthrosc Tech* 2013;2(2):e117-20.

14. Furlan D, Pogorelic Z, Biocic M, *et al*. Pediatric tibial eminence fractures: arthroscopic treatment using K-wire. *Scand J Surg* 2010;99(1):38-44.

15. Hargrove R, Parsons S, Payne R. Anterior tibial spine fracture - an easy fracture to miss. *Emerg Nurse* 2004;12(3):173-5.

16. Adams AJ, Talathi NS, Ganley TJ, *et al.* Tibial spine fractures in children: evaluation, management, and future directions. *J Knee Surg* 2018;31(5):374-81.

17. Gans I, Baldwin KD, Ganley TJ. Treatment and management outcomes of tibial eminence fractures in pediatric patients: a systematic review. *Am J Sports Med* 2014;42(7):1743-50.

18. Osti L, Buda M, Soldati F, *et al.* Arthroscopic treatment of tibial eminence fracture: a systematic review of different fixation methods. *Br Med Bull* 2016;118(1): 73-90.

19. Abdelhamid MM, Bayoumy MA, Elkady HA, *et al.* Arthroscopic reduction and fixation of tibial spine avulsion fractures by a stainless steel wiring technique. *Arthrosc Tech* 2017;6(6): e2289-e94.

20. Shin CH, Lee DJ, Choi IH, *et al.* Clinical and radiological outcomes of arthroscopically assisted cannulated screw fixation for tibial eminence fracture in children and adolescents. *BMC MusculoSkelet Disord* 2018;19(1):41.

21. Strauss EJ, Kaplan DJ, Weinberg ME, *et al.* Arthroscopic management of tibial spine avulsion fractures: principles and techniques. *J Am Acad Orthop Surg* 2018;26(10): 360-7.

22. Li J, Yu Y, Liu C, *et al.* Arthroscopic fixation of tibial eminence fractures: a biomechanical comparative study of screw, suture, and suture Anchor. *Arthroscopy* 2018;34(5): 1608-16.

23. Bley JA, Pomajzl RJ, Smith PA. Knotless arthroscopic reduction and internal fixation of a displaced anterior cruciate ligament tibial eminence avulsion fracture. *Am J Orthop* 2017;46(4): 203-8.

24. Momaya AM, Read C, Steirer M, *et al.* Outcomes after arthroscopic fixation of tibial eminence fractures with bioabsorbable nails in skeletally immature patients. *J Pediatr Orthop B* 2018;27(1):8-12.

25. Gigante A, Setaro N, Rotini M, *et al.* Intercondylar eminence fracture treated by resorbable magnesium screws osteosynthesis: a case series. *Injury* 2018;49 Suppl 3:S48-s53.

26. Loriaut P, Moreau PE, Loriaut P, *et al.* Arthroscopic treatment of displaced tibial eminence fractures using a suspensory fixation. *Indian J Orthop* 2017;51(2):187-91.

27. Aboalata M, Almohandes A, Abunar O, *et al*. The Adjustable Locking Suspension Sling Technique for Fixation of the Tibial Eminence Fracture in Adolescents. *Arthrosc Tech 2018;7* (5):e491-e7.

28. Elsaid ANS, Zein AMN, ElShafie M, *et al.* Arthroscopic single-tunnel pullout suture fixation for tibial eminence avulsion fracture. *Arthrosc Tech* 2018;7(5):e443-e52.

29. Zhang Q, Yang J, Zhao G, *et al.* A new technique for arthroscopic reduction and fixation of displaced tibial intercondylar eminence fractures, using suture anchor and EndoButton system. *J Orthop Surg* 2017;25(1).

30. DeFroda SF, Hodax JD, Shah KN, *et al.* Tibial eminence fracture repair with Double Hewson suture passer technique. *Arthrosc Tech* 2017;6(4):e1275-e9.

31. Gamboa JT, Durrant BA, Pathare NP, *et al.* Arthroscopic reduction of tibial spine avulsion: suture lever reduction technique. *Arthrosc Tech* 2017;6(1):e121-e6.

32. Pandey V, Cps S, Acharya K, *et al.* Arthroscopic suture pull-out fixation of displaced tibial spine avulsion fracture. *J Knee Surg* 2017;30(1):28-35.

33. Feucht MJ, Brucker PU, Camathias C, *et al.* Meniscal injuries in children and adolescents undergoing surgical treatment for tibial eminence fractures. *Knee Surg Sports Traumatol Arthrsoc* 2017;25(2):445-53.

34. Rhodes JT, Cannamela PC, Cruz AI, *et al.* Incidence of meniscal entrapment and associated knee injuries in tibial spine avulsions. *J Pediatr Orthop* 2018;38(2):e38-e42.

35. Axibal DP, Mitchell JJ, Mayo MH, *et al.* Epidemiology of anterior tibial spine factures in young patients: a retrospective cohort study of 122 cases. *J Pediatr Orthop* 2019;39(2):e87-e90.

36. Mayo MH, Mitchell JJ, Axibal DP, *et al.* Anterior cruciate ligament injury at the time of anterior tibial spine fracture in young patients: an observational cohort study. *J Pediatr Orthop* 2017.

37. Melugin HP, Desai VS, Camp CL, *et al.* Do tibial eminence fractures and anterior cruciate ligament tears have similar outcomes? *Orthop J Sports Med* 2018;6(12).

Hand Tips and Tricks: Treatment of a Volar Coronal Shear Lunate Fracture with Midcarpal Instability

Viviana Serra López, MD, MS
David Falk, MD
Brittany Behar, MD
Daniel Gittings, MD
David Steinberg MD

Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA.

Introduction

Traumatic fractures of the lunate are rare, with an incidence ranging from 0.5% to 6.5% of all carpal bone fractures.[1,2] Different mechanisms have been described, including impaction fractures into the radial fossa as a result of wrist hyperextension with ulnar deviation, or an axial load that drives the capitate into the lunate.[1,3] Fractures may also be associated with instability of the radiocarpal or midcarpal joint. Left untreated, these fractures may lead to degenerative changes or avascular necrosis of the lunate. Displaced fractures should be treated with ORIF,[4] whereas extra-articular non-displaced fractures may be treated conservatively.[1]

We report the case of a 44 year old female who sustained a coronal volar shear lunate fracture associated with midcarpal instability following an assault.

Case Report

History and presentation

A 44 year old right hand dominant female presented to the emergency department (ED) with a closed left coronal volar shear lunate fracture with volar dislocation of the distal carpal row and median nerve paresthesias after being assaulted (Figure 1). The patient underwent closed reduction of the dislocated distal carpal row in the ED. Median nerve paresthesias resolved after the reduction maneuver. In addition to x-rays, a post-reduction computed tomography (CT) scan was obtained for preoperative planning for fixation of the lunate fracture (Figure 2). The patient was scheduled for surgical fixation as an outpatient.

Operative Course

The patient underwent surgical treatment five days after her initial injury. A volar approach to the lunate through the carpal tunnel was used to decompress the median nerve and access the lunate volar shear fracture fragment. The volar lunate fragment had an intact capsular attachment that was anatomically reduced and provisionally fixed with a Kirschner wire. A cannulated 2.4 mm headless screw definitively fixed the fracture with absolute stability (Figure 3). A dorsal spanning bridge plate from the radius to the third metacarpal provided supplemental fixation to offload the lunate and maintain the reduction of the midcarpal joint (Figure 4). The wounds were then irrigated and closed with nylon sutures and a volar splint was applied for comfort.

Postoperative course

One week post operatively, fluoroscopic imaging demonstrated maintenance of the anatomic reduction and stable fixation. Two weeks post operatively, the patient's wounds were well healed and sutures were removed. The patient was transitioned to a short arm cast. Seven weeks post operatively, the patient underwent removal of her dorsal plate. Examination under anesthesia at that time did not reveal carpal instability (Figure 5). Thirteen weeks after the initial fixation, radiographs demonstrated

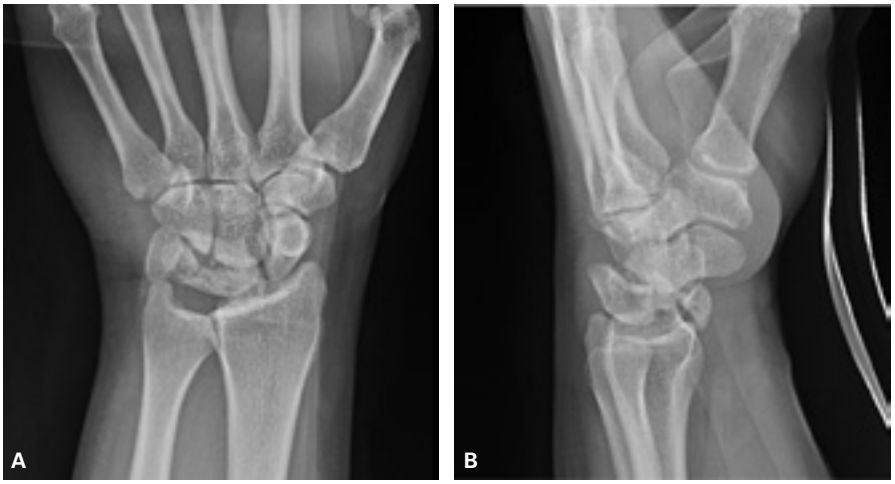


Figure 1. X-rays of the initial injury. **(A)** PA and **(B)** lateral views of the left wrist.

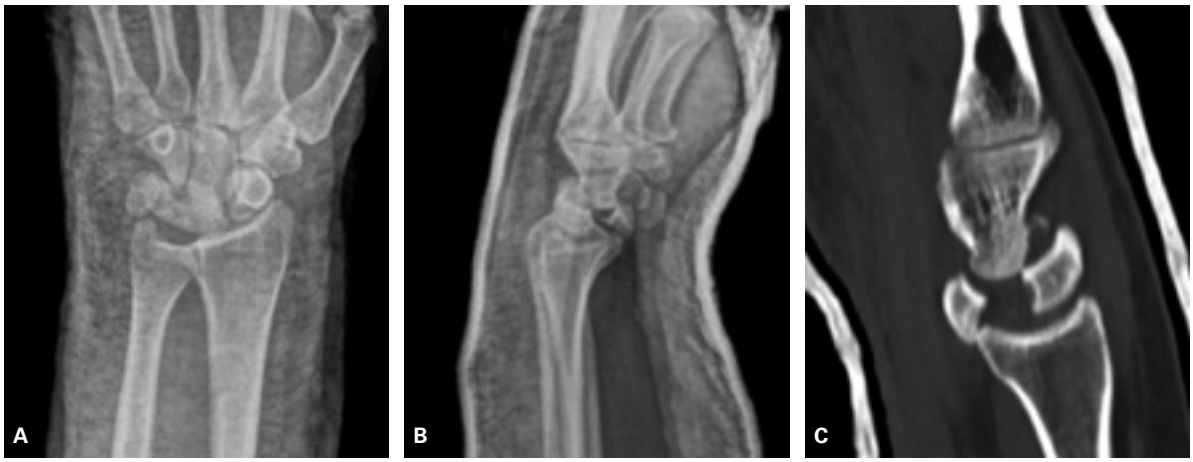


Figure 2. Images obtained following closed reduction and splinting. **(A)** PA and **(B)** lateral views of the left wrist. **(C)** Sagittal cut from CT scan.

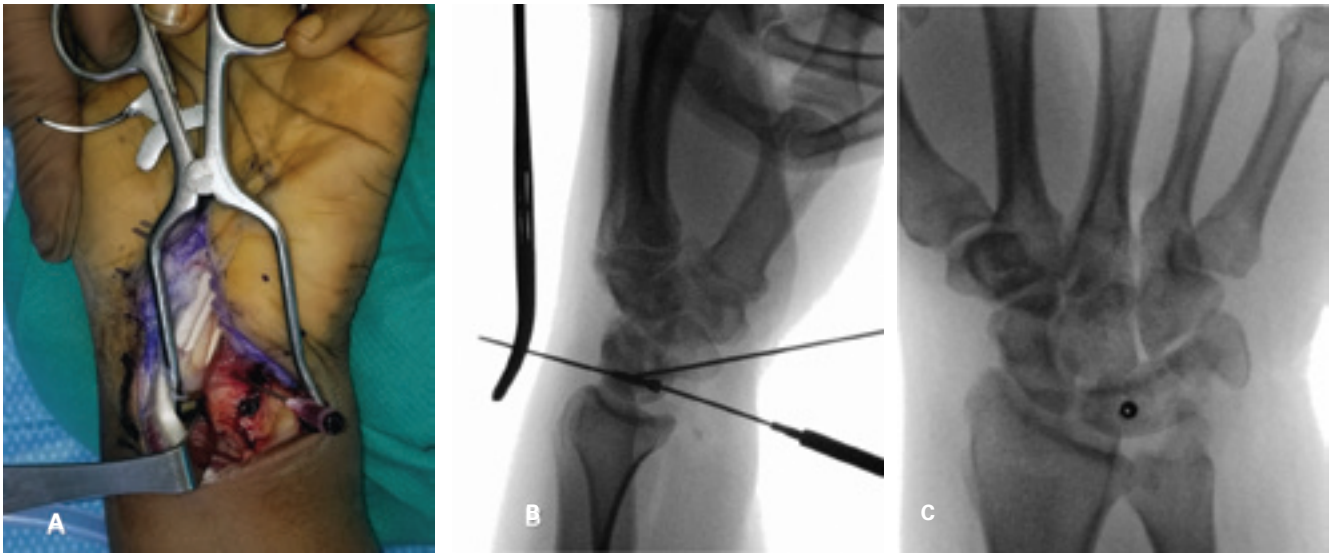


Figure 3. Intra-operative images demonstrating the approach. **(A)** Volar approach via the carpal tunnel. An 18G needle was used to localize the volar fracture fragment **(B)** Intraoperative fluoroscopy demonstrating cannulated screw applied volarly over a Kirschner wire. **(C)** AP view showing fracture reduction with the cannulated screw.

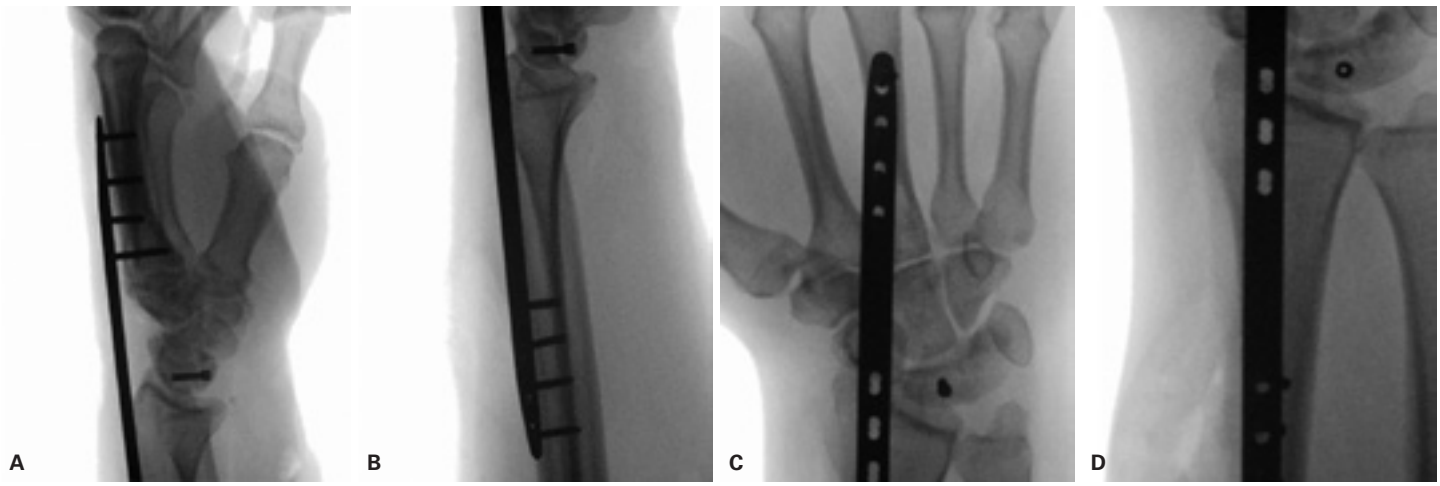


Figure 4. Fluoroscopic images obtained after fixation with a cannulated screw and dorsal spanning bridge plate. **(A)** Distal and **(B)** proximal lateral views. **(C)** Distal and **(D)** proximal AP views.

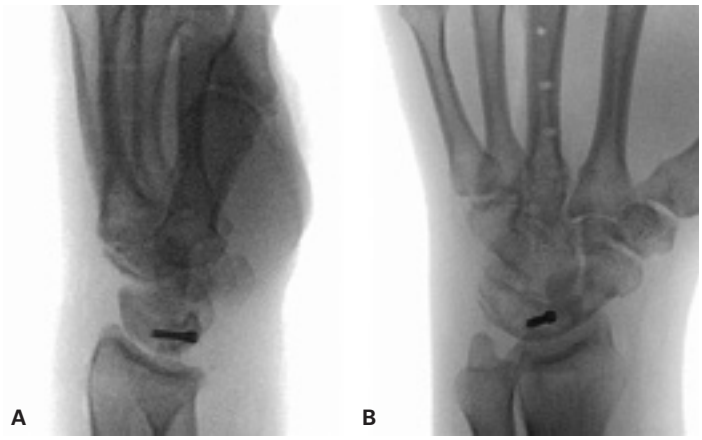


Figure 5. Fluoroscopic image obtained intraoperatively after removal of the dorsal bridge plate seven weeks after the initial fixation. **(A)** Lateral and **(B)** oblique views of the left wrist.

maintenance of the reduction with stable fixation and no signs of lunate avascular necrosis.

Discussion

We report a case of a traumatic lunate fracture with a volar shear fragment and midcarpal instability. In this patient, a volar approach through the carpal tunnel was performed and stable fixation was achieved with a cannulated headless screw and supplemental dorsal bridge plate. In a case report of an isolated lunate fracture without ligamentous injury, open reduction and internal fixation with microscrews via the same approach resulted in satisfactory fixation at follow-up.[5] Open reduction and internal fixation of the lunate has also shown no evidence of malunion in a series of patients with Kienbock disease with an average follow-up time of seven years.[6]

Conclusions

Lunate fractures are uncommon, complex injuries that are difficult to treat. They may be treated with an anatomic open reduction and internal fixation with good results.

References

1. Shunmugam M, Phadnis J, Watts A, Bain GI. Lunate fractures and associated radiocarpal and midcarpal instabilities: A systematic review. *J Hand Surg Eur Vol.* 2018.
2. Teisen H, Hjarbaek J. Classification of fresh fractures of the lunate. *J Hand Surg Am.* 1988.
3. Lee SK. Fractures of the Carpal Bones. In: *Green's Operative Hand Surgery.* ; 2017:588-652.
4. Pan T, Lögters TT, Windolf J, Kaufmann R. Uncommon carpal fractures. *Eur J Trauma Emerg Surg.* 2016.
5. Hsu AR, Hsu PA. Unusual Case of Isolated Lunate Fracture Without Ligamentous Injury. *Orthopedics.* 2011.
6. Chou J, Bacle G, Ek ETH, Tham SKY. Fixation of the Fractured Lunate in Kienböck Disease. *J Hand Surg Am.* 2019.

Low Profile Volar Rim Plates do not Prevent Flexor Pollicus Longus Tendon Wear Compared to Distally Placed Conventional Plate

Nicole A. Zelenski, MD[1]
Elaine Schmidt, BA[1]
Daniel Gittings, MD[1]
David Steinberg, MD[1]
Michael Hast, PhD[2]

1 Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA

2 Biedermann Lab for Orthopaedic Research, Philadelphia, PA

Hypothesis

A standard variable angle volar plate (VA-LCP) distal to the watershed line can be used to treat distal radius fractures with a small volar rim fragment; however, this technique may lead to inflammation, tendon wear, and ultimately rupture.[1] Low profile plates have been specifically designed to address this issue but the clinical efficacy of these implants is still unknown. We hypothesized that low profile volar rim plates would decrease contact pressure, reduce tendon-wear, and improve tendon mechanical properties relative to distally placed standard plates.

Methods

9 matched pairs of fresh-frozen cadaveric upper extremities were used in this study. Three groups were compared: 1) VA-LCP implants proximal to watershed line (VA-LCP); 2) VA-LCP implants distal to the watershed line (VA-LCP Distal); and 3) low profile volar rim plates (Volar Rim). N = 6 per group. A mass of 1 kg was hung from the thumb, and specimens were cyclically loaded by actuating the flexor pollicis longus (FPL) tendon. A thin-film pressure sensor was placed between the plate and FPL tendon and maximum contact loads were measured over the course of 10 cycles. Specimens were then cyclically loaded for 10,000 cycles. FPL tendons were harvested, photographed, and graded for wear by 5-blinded observers on a Likert scale. Uniaxial tensile testing was performed. Stress relaxation, ultimate strain, and ultimate tensile strength were recorded while stiffness and Young's modulus were determined by calculating the slopes of the linear portions of the force-displacement and stress-strain curves, respectively.

Results

Contact pressure was significantly higher in VA-LCP Distal (Median 7.6N, $p = .006$) and Volar Rim (Median 3.9N, $p = .016$) relative to VA-LCP plates (Median 0.11N) (Figure 1). Tendon-wear was also significantly increased in VA-LCP Distal (Mean 3.0, SD 0.9, $p = 0.024$) and Volar Rim plates (Mean 3.0, SD 0.7, $p = 0.015$) relative to VA-LCP plates (Mean 2.0, SD 0.5) (Figure 2). There was no significant difference in contact pressure or tendon-wear between distally placed VA-LCP and volar rim plate.There was no significant difference in mechanical properties between any of the groups.

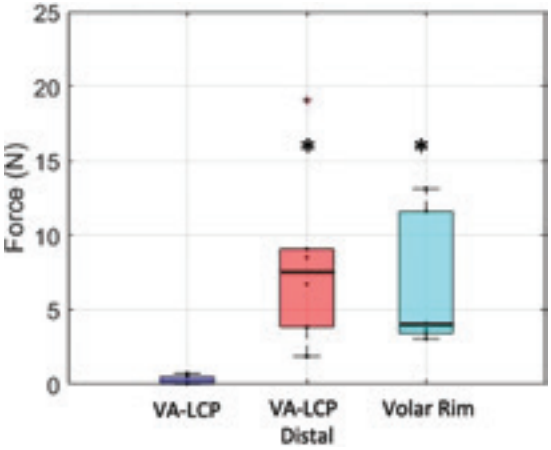


Figure 1. Median average maximum normal contact force between FPL tendon and plate increased significantly in VA-LCP placed distal to watershed line and volar rim plate when compared to VA-LCP placed proximal to the watershed line. Box represents 25%, bars represent 75%. **Indicates $p<0.05$ by Tukey Test.*

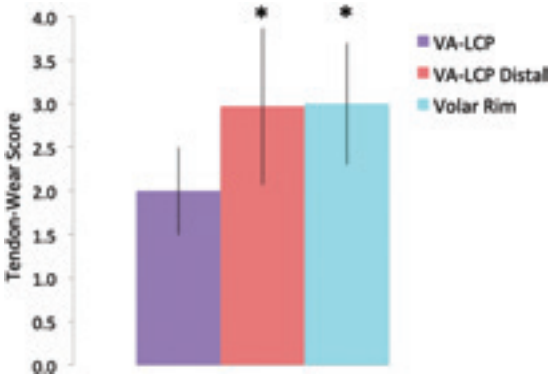


Figure 2. Mean tendon-wear score in distally placed VA-LCP and volar rim plate increased significantly when compared to appropriately placed VA-LCP. **Indicates $p<0.05$ in two tailed t-test when compared to VA-LCP group.*

Summary Points

- Plates placed distal to the watershed line including low profile rim plates have high contact pressure and high tendon-wear
- Low profile plates do not decrease contact pressure, grade of FPL tendon-wear or mechanical properties in tendons

- Although volar rim plates allow for fixation of smaller volar fragments, they do not have improved tendon-wear properties and may contribute to FPL tendon rupture if not removed.

References

1. Soong M, Earp BE, Bishop G, Leung A, Blazar P. Volar locking plate implant prominence and flexor tendon rupture. J Bone Joint Surg Am. 2011;93(4):328e335.

Design and Implantation of an Engineered Porcine Accessory Carpal Osteochondral Unit

Brendan Stoeckl, MS[1, 2]
Hannah Zlotnick, BS[1, 2, 3]
Megan Farrell, PhD[1]
Liane Miller, MD[1, 2]
Thomas Schaer, VMD[4]
Michael Hast, PhD[1]
Robert Mauck, PhD[1, 2, 3]
David Steinberg, MD[1, 2]

1 Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA

2 Translational Musculoskeletal Research Center, CMC VAMC, Philadelphia, PA

3 Department of Bioengineering, Philadelphia, PA

4 Comparative Orthopaedic Research Laboratory, School of Veterinary Medicine, Kennett Square, PA

Introduction

Trapeziometacarpal (TMC) osteoarthritis (OA) is one of the most common conditions affecting middle and older aged adults.[1] Conservative treatments often fail in the long term, and many patients will eventually require destructive surgical intervention, involving removal of all or part of the trapezium and replacement with tendon, fascia, or an artificial implant.[2] While effective at reducing pain, these procedures compromise grip strength and, in some cases, result in subsidence and disFigurement of the hand.[2] Efforts to replace articular cartilage (and bone) with living, functional tissue have matured substantially over the last two decades,[3] as has technology for generating constructs that can match the anatomical complexity and geometry of native articulating surfaces.[3,4] For these technologies to progress toward translation, appropriate large animal models are required. In our previous work, we identified the porcine accessory carpal (AC) as a potential model for TMC OA, given its similar shape, size, mechanics, and chemical composition, and we designed a tissue engineered implant for the articulating surface of the AC.[5, 6] Here, we further explore the loading patterns of this joint as a function of flexion, refine the design of our proposed implant, and evaluate the feasibility of its implantation in the Yucatan minipig forelimb.

Methods

CT images of the forelimb of a skeletally mature Yucatan minipig were obtained and 3D models of the bones were segmented in ITK-SNAP.[7] A musculoskeletal model was generated in OpenSim, and the relative motion of the AC and its contact forces were evaluated through passive range of motion. Three adult minipig forelimbs were obtained from unrelated studies. In each, an incision was made and a TekScan iScan 6900 pressure sensor was placed into joint space between the accessory carpal and the ulnar carpal. The carpus was moved through a range of angles from 90 degrees to full extension while contact forces were measured. To reduce the bony component of the implant while simultaneously increasing surface area for potential cell ingress and bony integration, our previous implant was redesigned. Two different surgical fixation designs were evaluated—a "cross" keel and a single "keel" design (Figure 1A). Simplified mock-ups of the cross keel and single keel fixation methods were created in Solidworks (Dassault Systèmes), and a finite element analysis was performed (Figure 1B). The keel was rigidly fixated and a 3N load was applied to the lateral face of the implant, with the materials assigned a bulk modulus of 3MPa. Positive molds of the keel design were 3D printed out of an ABS-like photopolymer (Figure 2B). To fabricate elastomeric negative molds, Sylgard 184 (polydimethylsiloxane, PDMS) was prepared at a 10 parts monomer to 1 part curing agent ratio, poured over the 3D printed designs, degassed, and allowed to cure at 40°C overnight. Poly(ε-caprolactone) (PCL) was dissolved in chloroform at 20% wt/vol and mixed with NaCl crystals sieved to ~106 μm, and Zirconium nanoparticles were included for radioopacity. The slurry was poured into the mold and the solvent was evaporated. The units were demolded and the salt was leached. We next performed a proof-of-concept surgery on an adult minipig forelimb. We made an incision

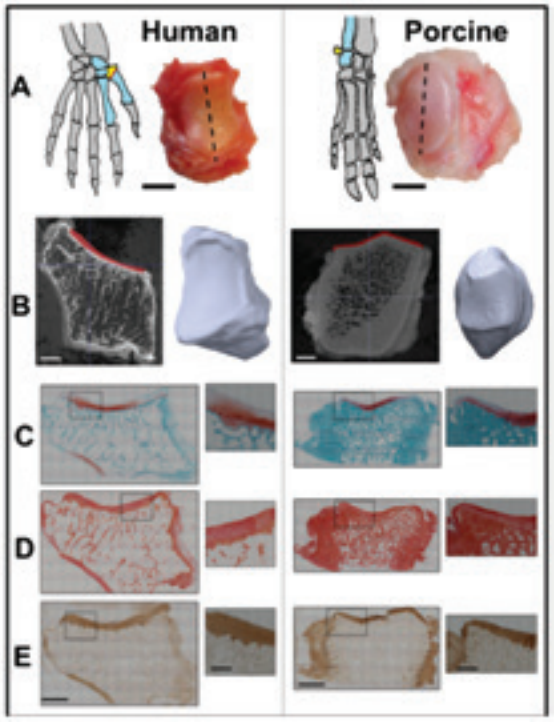


Figure 1. (A) Solidworks models of three different AC implant designs: peg, cross, and keel; **(B)** Finite element model of cross (top) and keel (bottom) implant designs. Von Mises stress is on the left and strain is on the right.

into the joint and rotated the articulating surface of the AC into view. We used a reciprocating saw followed by an osteotome to remove the surface of the AC and a 2mm burr followed by a curette to create a slot in the remaining bone, matching the keel on the implant. The construct was held in place with two 1mm Ø by 8mm long bicortical screws oriented normally to the plane of the keel. Fluoroscopy and MicroCT were performed to evaluate positioning of the implant. Images were segmented using ITK-SNAP and visualized in Meshlab (ISTI).

Results

In the OpenSim model, the contact force remained ~0 as the carpus was extended until ~20 degrees flexion. At this point, force increased and reached a peak of 67N at full extension (Figure 3C). In the *ex vivo* experiment (Figure 3D), the force across the joint remained close to zero until 15 degrees of flexion, and then rose rapidly to a maximum of 29.1±10.5N at 0 degrees (Figure 3E). The contact area and stress followed the same pattern (Figure 3F-G). The AC implant design from our previous work had a volume of 423 mm^3 and an integrating surface area of 129.3 mm^2. Two new designs—the cross keel and single keel, had volumes of 380.75mm^3 and 355.65mm^3 and integrating surface areas of 240.5mm^2 and 215.6mm^2, respectively (Figure 1A). FE modeling showed that the centroid of the implant displaced by 0.18 mm in the cross keel design and 0.22mm in the single keel design (Figure 1B). Neither experienced local strains over 7%. We chose the single keel design for implantation (Figure 2A). Using a 3D printed positive mold, we produced a PDMS negative mold (Figure 2B) which was used to create a porous PCL implant (Figure 2C). This was readily implanted into a cadaveric minipig forelimb (Figure 2D) and was visible fluoroscopically (Figure 2E) and on μCT (Figure 2F).

Discussion

In this study, we expanded on our previous work[5,6] by further characterizing the biomechanical environment

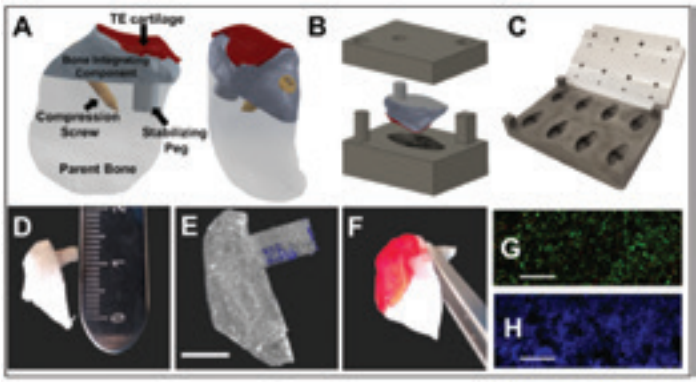


Figure 2. (A) Design of composite implant with keel, bicortical screws, parent bone, and TE cartilage surface (in red); **(B)** ABS positive mold (top) and PDMS negative mold (bottom) used to create PCL implant **(C)**; **(D)** Implantation of PCL construct; **(E)** Fluoroscopic visualization of implant *in situ*; **(F)** μCT and 3D rendering of AC implant *in situ*.

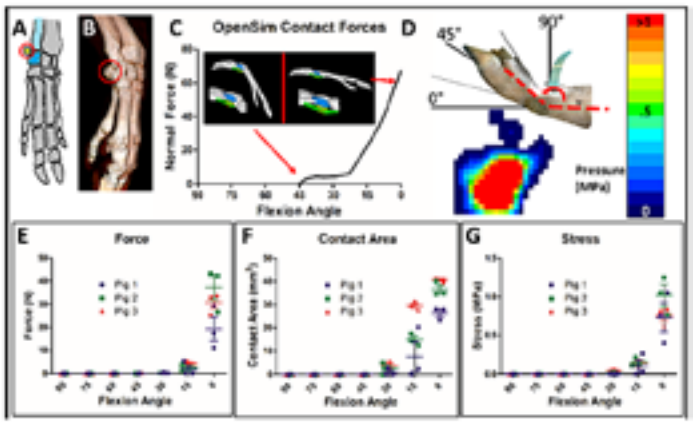


Figure 3. (A) Diagram of porcine AC (yellow) and its articulation with the ulnar carpal (blue) and ulna (light blue); **(B)** μCT rendering with AC identified; **(C)** Plot of contact forces computed in OpenSim model; **(D)** Example TekScan pressure map of the AC contact; **(E-G)** Plots of force, contact area, and stress with respect to flexion angle computed with TekScan.

experienced by the AC in the Yucatan minipig, refining the design of our implant, improving the fabrication process, and finally implanting an engineered AC into a minipig forelimb. The loading pattern measured *ex vivo* matched that predicted via OpenSim. These models and data show that the AC is essentially unloaded except when the carpus is fully extended. This means that when implanted into a living animal, the construct will only experience loads when the animal is standing, or in the stance phase of ambulation. We chose the single keel implant design because it offered a reduced volume to be filled in with bone, while increasing the surface area over which boney integration could occur. It was not appreciably less stable than the cross design in FE simulations, and practically speaking, allowed for a much easier surgical approach to implantation. Next steps are to evaluate the long-term function of a cell seeded osteochondral implant (with a stem cell-laden hydrogel cap to form a cartilage layer) in a living animal.

Significance

This study refined the design, fabrication, and implantation of an engineered porcine AC, furthering the goal of total biologic resurfacing of this joint as an analog for the treatment of TMC OA in humans.

References:

1. Becker et al., CORR, 2013.
2. Wajon et al., Cochrane Database, 2015.
3. O'Connell et al., J Knee Surg, 2012.
4. Saxena et al., Tissue Eng, 2016.
5. Stoeckl et al., ORS 2018.
6. Stoeckl et al., ORS 2019.
7. Yushkevich et al., Neuroimage, 2006.

Pediatrics Tips & Tricks: Management of Pediatric Capitellar Fractures

Brandon Haghverdian MD[1]
Apurva S. Shah MD[1,2]
Alexandre Arkader MD[1,2]

1 Department of Orthopaedic Surgery University of Pennsylvania, Philadelphia, PA

2 Department of Orthopaedic Surgery Children's Hospital of Philadelphia, Philadelphia, PA

Introduction

Isolated fractures of the capitellum humeri are infrequent in pediatric patients, representing less than 1% of elbow fractures in children and adolescents.[1] The management of capitellar fractures in adults has been previously well-described with surgical options for displaced fractures including osteosynthesis, fragment excision, and prosthetic replacement.[2] The evaluation and treatment of capitellar fractures in children, however, has received less attention, resulting in frequently-missed injuries and delays in diagnosis. Even when promptly treated, displaced capitellar fractures often yield poor radiographic and functional outcomes including early arthritis, osteonecrosis, limited range of motion, and mechanical symptoms. These potential complications have therefore prompted recent efforts to better classify pediatric capitellar injuries with an aim towards guiding treatment and optimizing functional outcomes.

Classification

The most widely-used classification system for adult capitellum fractures is attributed to Bryan and Morrey, although it employs prior eponymous descriptions of classic fracture patterns.[3] Type-I fractures (Hahn-Steinthal) involve anterior shear fractures of a large osseous piece of the capitellum.Type-II (Kocher-Lorenz) are shear fractures of the articular cartilage involving minimal to no subchondral bone. Type-III fractures (Broberg-Morrey) are multifragmentary, severely comminuted fractures of the capitellum. In 1996, McKee introduced a fourth classification to include anterior coronal shear fractures involving both the capitellum and trochlea.[4]This system is often criticized for its subjective nature and failure to guide management.

In 2017, Murthy *et al.* introduced a classification scheme unique to pediatric patients based on their observation of 37 children and adolescents with capitellum fractures (Figure 1).[5] Type-I fractures were most

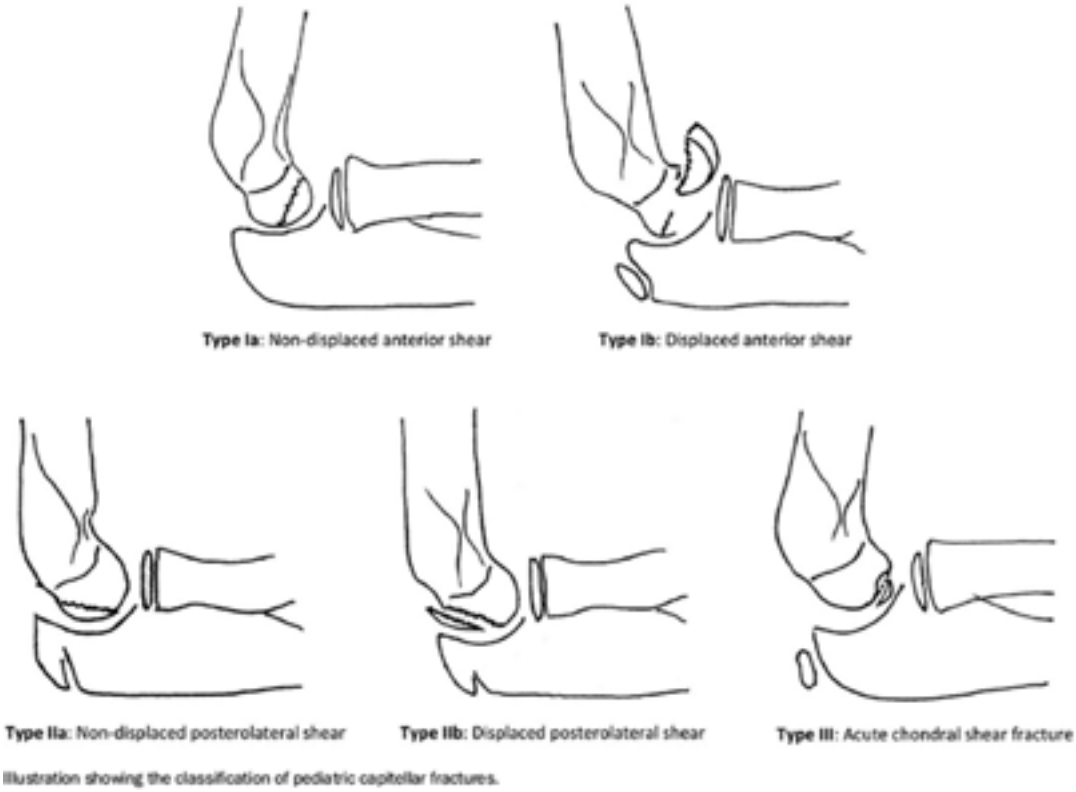


Figure 1. Abstracted from: Murthy, P.G., Vuillermin, C., Naqvi, M.N., Waters, P.M., Bae, D.S., 2017. Capitellar Fractures in Children and Adolescents: Classification and Early Results of Treatment. J Bone Joint Surg Am 99, 1282–1290.

common (incidence = 68%), representing anterior shear injuries of the capitellum, with or without involvement of the lateral crista of the trochlea, similar in description to the adult type-I (Hahn-Steinthal) fracture scheme. Type-II fractures (incidence = 24%) were posterolateral shear injuries. Type-III fractures (incidence = 8%) were acute chondral shear injuries. Each fracture type was further subdivided depending on the degree of displacement (nondisplaced = "a," displaced = "b"). Given its specificity towards the pediatric population, we will reference this classification system in the remainder of this article.

Evaluation

The evaluation of capitellum fractures is prompted in a child or adolescent with acute traumatic elbow symptoms. These injuries are frequently difficult to visualize on plan radiographs, particularly type-II and type-III fracture patterns. A large fracture fragment may be apparent on a lateral radiographic, however on the anteroposterior (AP) view it may be obscured by the underlying distal humeral metaphysis. The inclusion of oblique views is therefore recommended in the initial evaluation of traumatic elbow pain without clear evidence of an injury on the standard AP-lateral radiographs. In capitellar fractures, the postulated mechanism of injury is compression or shear by the radial head. Associated injuries to the radial head or neck are therefore common, estimated to be as high as 31%.[6] Patients with confirmed fractures of the capitellum may benefit from evaluation with magnetic resonance imaging (MRI) or computed tomography (CT) to better define the fracture pattern and plan surgical treatment. Given the high rates of radiographically-occult capitellar fractures and the potentially devastating outcomes resulting from missed injuries, we recommend advanced imaging with MRI or CT in patients with severe, persistent elbow pain, stiffness, swelling, or mechanical symptoms.

Case Report

A 12 year-old otherwise-healthy male presented to the Emergency Department with a one-day history of left elbow pain. The pain began after a fall from bicycle in which he landed onto his outstretched left arm. He endorsed severe pain with lateral elbow palpation and joint passive range of motion. There was a clinically-apparent effusion. The patient demonstrated intact radial and ulnar pulses and no neurologic deficits. There were no associated injuries to the remainder of his extremities noted by exam.

Initial radiographs and CT imaging with three-dimensional reconstruction demonstrated a large fractured osseous fragment of capitellum overlying the anterior distal humerus (Figure 2). Additionally noted was a minimally displaced

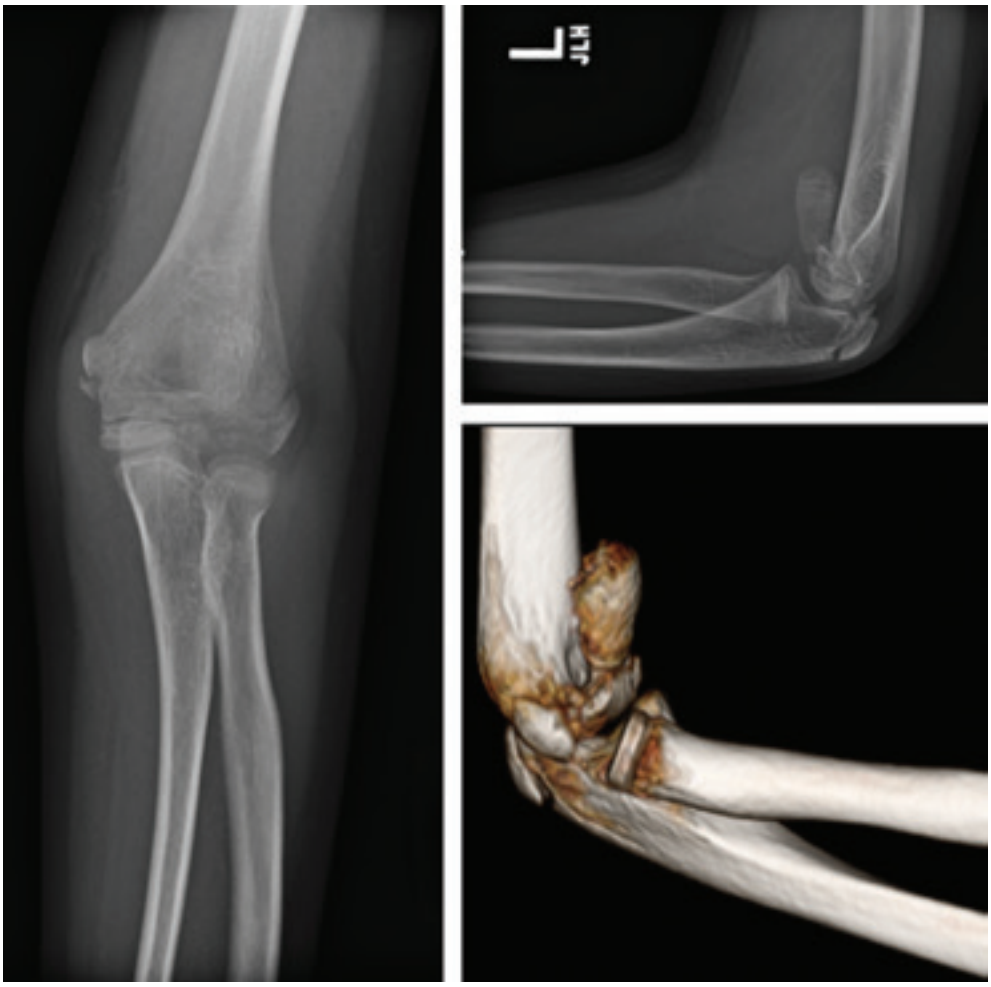


Figure 2. AP, lateral radiographs and three-dimensional computed tomography reconstruction demonstrating a large displaced capitellum fracture with associated minimally displaced medial epicondyle fracture.

avulsion fracture of the medial epicondyle. The extremity was immobilized, and the following day the patient underwent open reduction, internal fixation utilizing an anterolateral (Kocher) approach to the elbow (Figure 3). The fixation of choice was a single 3.5 mm fully-threaded cannulated screw with washer (inserted through the posterolateral aspect of the capitellum) as well as two 3.0 mm headless compression screws (inserted anteriorly to posteriorly).

At three-week follow-up, the cast was removed and converted to a hinged elbow brace; the patient was advised to begin range of motion exercises as tolerated. His post-operative course was subsequently complicated by elbow stiffness—at 6-month follow-up, he demonstrated an ulnohumeral arc of 45 degrees extension to 110 degrees of flexion. The decision was therefore made to proceed with manipulation under anesthesia with arthrography of the elbow joint demonstrating a congruent joint with no evidence of hardware penetration of the joint. During exam under anesthesia, the range of motion of the elbow was 10-135 degrees. At the time of this writing, he is awaiting clinical follow-up for this procedure.

Treatment Options

Capitellum fractures in pediatric patients are rare and challenging to diagnose, and treatment outcomes are variable depending on the timeliness of diagnosis and the treatment modality selected. Further, only a limited number of studies have been published on the treatment of capitellum fractures, of which most are limited to case reports or case series.[7-13] Despite these limitations, a general review of the available literature yields several guidelines related to the management of pediatric capitellum fractures. First, nondisplaced fractures of the capitellum, particularly types-Ia and IIa are generally amenable to non-operative treatment with cast immobilization. Although the exact frequency of missed injuries is unknown due to the paucity of published data, these fractures are likely more common than cited owing to the poor sensitivity of standard radiographs in the identification of these injuries.[5] It stands to reason that in patients for whom the diagnosis of nondisplaced capitellar fracture is missed, non-surgical treatment is generally successful with limited immobilization.

The treatment of displaced anterior and posterolateral shear injuries (type-Ib and type-IIb, respectively) centers on surgical fixation. Various modalities, including suture repair, Kirschner wire fixation, bioabsorbable pin fixation, and fixation with cortical, cannulated, or variable-pitch headless compression screws, have been described. To our knowledge, there are as yet no studies directly comparing the outcomes of different fixation strategies. The choice of fixation is therefore left to the discretion of the surgeon, guided by surgeon comfort and fracture characteristics. Additionally, surgical excision of

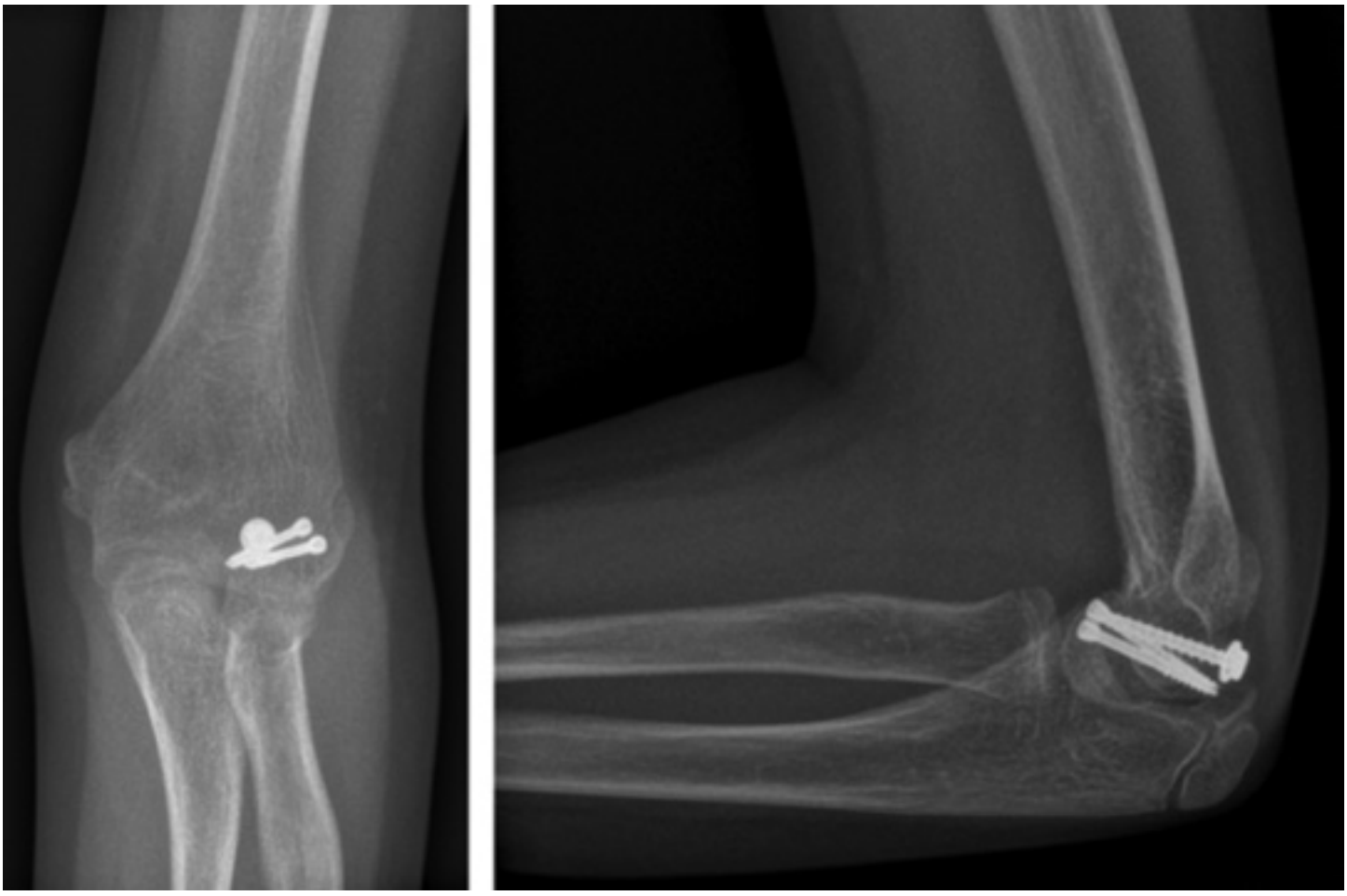


Figure 3. AP, lateral radiographs demonstrating reduction and internal fixation of capitellum fracture.

late-presenting small fracture and osteochondritis dissecans lesions has demonstrated successful outcomes in very young patients.[1,12] In particular, excision of small type-III chondral shear injuries has been shown to yield excellent restoration of motion and alleviation of pain. Fixation techniques for type-III lesions have also been wide-ranging but typically include Kirschner wire fixation and suture repair.[4,8]

Conclusions

The timely diagnosis and management of capitellar fractures are essential to ensuring restoration of articular congruity, range of motion, and joint stability in children and adolescents. Capitellum fractures in pediatric patients demonstrate unique patterns and characteristics when compared to adult fractures. Therefore, advanced imaging with MRI or CT is recommended for better characterization of the fracture pattern and to plan fixation strategies. Of the various fracture patterns, type-II posterior shear and type-III chondral injuries are most easily missed on routine screening radiographs. A high index of suspicion for these injury types is therefore imperative in patients who have a consistent history, persistent pain and swelling, and mechanical blocks to motion of the elbow. Whereas nondisplaced fractures are generally treated well without surgery, fixation and fragment excision represent the mainstays of surgical treatment for displaced fractures. Successful outcomes may be expected when the injury has been promptly diagnosed and appropriately treated.

References

1. Marion J, Faysse R. Fracture du capitellum. 1962. *Rev Chir Orthop* 48,484-490.

2. Dubberley, JH, Faber, KJ, Macdermid, JC, *et al.* Outcome after open reduction and internal fixation of capitellar and trochlear fractures. 2006. *J Bone Joint Surg Am* 88, 46–54.

3. Bryan RS, Morrey BF. Fractures of the distal humerus, in The elbow and its disorders. 1985. Morrey BF, Editor. Philadelphia, PA, *WB Saunders*, pp. 302–339.

4. McKee, MD, Jupiter, JB, Bamberger, HB Coronal shear fractures of the distal end of the

5. humerus. 1996. *J Bone Joint Surg Am* 78, 49–54.

6. Murthy, PG, Vuillermin, C, Naqvi, MN, *et al.* Capitellar Fractures in Children and Adolescents: Classification and Early Results of Treatment. 2017. *J Bone Joint Surg Am* 99, 1282–1290.

7. Palmer, I. Open treatment of transcondylar T-fracture of the humerus. 1961. *Acta Chir Scand* 121, 486–490.

8. De Boeck, H, Pouliart, N. Fractures of the capitellum humeri in adolescents. 2000. *Int Orthop* 24, 246–248.

9. Frank, JM, Saltzman, BM, Garbis, N., *et al.* Articular shear injuries of the capitellum in adolescents. 2016. *J Shoulder Elbow Surg* 25, 1485–1490.

10. Sułko, J, Oberc, A. Capitellar fractures in children. 2014. O*rtop Traumatol Rehabil* 16, 573-579.

11. Cornelius, AL, Bowen, TR, Mirenda, WM. Anterolateral approach for an unusual pediatric capitellar fracture: a case report and review of the literature. 2012. *Iowa Orthop J* 32, 215–219.

12. Sodl, JF, Ricchetti, ET, Huffman, GR. Acute osteochondral shear fracture of the capitellum in a twelve-year-old patient. A case report. 2008. *J Bone Joint Surg Am* 90, 629–633.

13. Fowles, JV, Kassab, MT. Fracture of the capitulum humeri. Treatment by excision. 1974. *J Bone Joint Surg Am* 56, 794–798.

14. Letts, M, Rumball, K, Bauermeister, S, *et al.* Fractures of the capitellum in adolescents. 1997. *J Pediatr Orthop* 17, 315–320.

U·P·O·J

Duration of Legg-Calvé-Perthes Disease Stages in Children Under Four Years of Age at Disease Onset

Jigar S. Gandhi, PharmD
Arianna Trionfo, MD
Wudbhav N. Sankar, MD

Division of Orthopaedic Surgery
Children's Hospital of Philadelphia,
Philadelphia, PA

Introduction

Although it has been more than a century since its original description by Henning Waldenström and Arthur T. Legg, the etiology and natural history of Legg-Calve-Perthes disease (LCPD) remain controversial.[1] This rare condition of idiopathic osteonecrosis of the femoral head in children has a variable incidence of 0.2 to 29 per hundred thousnad children less than fifteen years of age, depending on the geographic location and ethnicity of the children.[2,3] Additionally, the disease is most commonly diagnosed in males between the ages of four years and fourteen years.[2]

As initially recognized by Waldenström, the affected femoral head in LCPD progresses through four distinct radiographic stages over the course of the disease.[4] These four stages are the initial (I) stage, fragmentation (II) stage, reossification (III) stage, and residual (IV) stage. Joseph *et al* later modified Waldenström's classification system by further sub-categorizing the first three stages as either early (A) or late (B) in order to determine when radiographic changes occur in the femoral epiphysis during evolution of the disease.[5] In terms of classification, the lateral pillar grading system, described by Herring *et al*, stratifies the femoral head into four distinct groups (A, B, B/C, and C) based on the height of the lateral third of the epiphysis during "early" fragmentation.[6] Several publications have correlated increasing severity of Herring grade with poorer functional and radiographic outcomes.[6-8]

Several studies have evaluated long-term outcomes in LCPD patients under six years old. However, to our knowledge, there is a paucity of data on the disease progression and natural history of LCPD in patients diagnosed at a very young age. Thus, the purpose of this study was to describe the presentation and duration of modified Waldenström stages in patients with LCPD diagnosed prior to four years of age. We hypothesized that the length of modified Waldenström stages would be shorter in young patients compared to typical-aged children with LCPD, which might explain, in part, the favorable outcomes seen in younger patients with the disease.

Methods

After obtaining approval from our institutional review board, the medical records and radiographs of all patients diagnosed with LCPD between 2007 and 2017 at a single pediatric tertiary care institution were reviewed. We included only those patients who were diagnosed with LCPD prior to their fourth birthday, and who had adequate radiographs obtained at initial diagnosis and during the active stages of the disease. Patients were excluded if they were diagnosed with a skeletal dysplasia, Meyer's dysplasia, had other diagnoses known to cause osteonecrosis (e.g. septic arthritis, sickle cell disease etc.), did not have at least 3 radiographs during the disease course, or were treated surgically as this would affect the natural history of the disease. When a patient had bilateral involvement, only the hip(s) that were diagnosed with LCPD prior to the patient's fourth birthday were included.

The time intervals between radiographs showing features of subsequent stages were calculated in order to determine the length of each stage. Mean and standard deviations, medians, and ranges were used to describe continuous variables. Non-normally distributed data were analyzed using non-parametric Mann-Whitney U test. The relationships between age at diagnosis, weight, BMI, presence or absence of symptoms at the time of diagnosis, Herring grades, and stage lengths were analyzed using Pearson Chi-square test or Fisher exact probability test with IBM SPSS statistics 15.0 software (Chicago, IL). Significance was set at two-sided alpha level of $p < 0.05$. In order to relate our findings to those in typical-aged patients, we compared our results with those reported by Joseph *et al*.[5]

Results

Twenty-seven patients (32 hips) were included in the study. The age at presentation ranged from 1.8 years to 4.0 years with a mean age of 3.1 years (SD = 0.6 years). Twenty-three patients (85%) were male; mean BMI was 16.7 kg/m^2 (range 14.4 to 24.0) at the time of diagnosis. Five patients had bilateral disease with onset under four years of age in both hips. Twenty-two patients presented with a limp and 25 patients presented with pain in the affected hip joint. The overall mean and median interval between sequential radiographs were 138 days (SD = 53.9 days) and 126 days (range, 29-272 days), respectively. The average follow-up interval during early stages (IA-IIA) and late

stages (IIB-IIIA) were similar (Table 1). Patients had an average of 5.6 radiographs (range 3-13) during the disease course, and all hips were treated conservatively without surgery as per our inclusion criteria.

Overall, sixteen hips (50%) were graded as Herring B, and 16 (50%) as grade C in the fragmentation stage. All 4 females (5 hips) were graded as Herring C while 9 males (11 hips) were Herring grade C. The remaining 14 males (16 hips) were graded as Herring B (Table 2). All hips remained in the same Herring grade throughout the duration of active disease. With the exception of one hip which presented during modified Waldenström stage IA, all hips presented at stage IB or later. At most recent follow-up, fifteen hips were in Waldenström stage IV; 6 in stage IIIB; 5 in stage IIIA; 5 hips in stage IIB; and 1 in IIA. Mean age at last follow-up was 5.0 years (SD = 1.6 years).

Based on the time intervals between radiographs showing features of subsequent stages, the median duration of early stage disease (modified Waldenström IA-IIA) was 513 days, and of late stage disease (IIB-IIIB) was 833 days (Table 3). In our series, age, weight, BMI, and presenting symptoms at the time of diagnosis showed no association with duration of disease stages (all p values > 0.05).

Discussion

To our knowledge, this series is the first to specifically describe the course of LCPD in very young patients. Most literature describing LCPD in younger patients consists of smaller, retrospective studies with patients ranging from 18 months to 12 years.[5,8-10] The scarcity of data is even more pronounced in children with disease onset under the age of four years as none of the recent studies have been performed exclusively in this very young patient population with LCPD.

In their landmark series of 164 LCPD hips with disease onset under six years of age, Rosenfeld *et al* noted that the patients with disease onset prior to age four had a greater than 84% probability of a favorable disease course.[10] They also observed that the combination of age at onset and lateral pillar involvement correlated more strongly with a favorable outcome compared to age at onset alone. In spite of the authors' conclusions that younger patients with LCPD tended to have improved outcomes, the authors did not separately report the number of patients in their series younger than four years of age, nor did they comment on the duration of disease stages in any of these younger patients. Similarly, other investigators have confirmed this apparent positive influence of younger age at onset on disease outcome.[8,11,12] However, none of these studies in very young children report on the duration of Waldenström stages, which may be a factor that influences outcome. In an important study evaluating the natural history of LCPD in children up to 12 years of age, Joseph *et al* reported the length of modified Waldenström stages.[5] The mean age in their series was 9.08 ± 2.91 years for males and 8.48 ± 3.56 years for females. Although the authors did not stratify their findings according to age at onset, it is the

Table 1. Mean and median follow-up intervals during early and late stages of LCPD.

	Follow-up Intervals (days)		
	Early stages (IA-IIA)	**Late stages (IIB-IV)**	***P value***
Median (range)	119 (29-252)	133 (36-272)	0.155
Mean ± SD	126 ± 51.7	143 ± 59.3	

Table 2. Modified Waldenström stages and Herring grades of the hips.

Herring grades assigned during early fragmentation	**Modified Waldenström stages at the time of presentation**			
	IA*	**IB***	**IIA**	**IIB**
B	1 (3.1%)	7 (21.9%)	6 (18.8%)	2 (6.3%)
C	0 (0.0%)	5 (15.6%)	6 (18.8%)	5 (15.6%)
Total no. of hips	1 (3.1%)	12 (37.5%)	12 (37.5%)	7 (21.9%)

* For hips presenting in Stage IA and IB, the Herring grades were assigned when they progressed to the fragmentation stage.

Table 3. Duration of Waldenström stages in children with LCPD presenting before age 4 years.

Stage (no. of hips)	**Median duration (days)**	**Mean duration, in days (95% CI)**
IA (1)	240	240 (n/a)
IB (12)	130	141 (108-173)
IIA (14)	199	162 (140-243)
IIB (17)	283	240 (140-339)
IIIA (15)	273	257 (194-320)
IIIB (11)	384	420 (312-528)

only other study in the literature that we are aware of which quantifies the duration of Waldenström stages.

Our study found that the modified Waldenström stages were longer in our LCPD patients with disease onset prior to four years of age compared to the cohort of older patients previously reported by Joseph *et al* (Figure 1).[5] In their patient population, the combined median duration of the initial four stages of the disease (IA to IIB) was approximately 3.5 to 4 months, whereas the median durations of stage IIIA and IIIB were twice and three times as long as the initial four stages, respectively. In our patient sample, the median durations of stage IB, IIA, IIB, IIIA and IIIB were longer by 35 days, 80 days, 57 days, 58 days and 49 days, respectively, than those reported by Joseph et al.[5] We also found that the combined duration of stages IIIA and IIIB was almost twice as long as the duration of stages IB-IIB. Since only one patient in our series initially presented during stage IA, the duration of stage IA was not included in the comparison.

Our findings suggest that factors other than stage duration may be responsible for the favorable outcomes seen in very young patients. From an anatomical perspective, younger children have a relatively greater proportion of cartilage in their hips, which may serve to resist mechanical deformation of the femoral head; however, biomechanical studies are warranted to establish a definitive relationship between the disease outcome and cartilage content of the affected hips. Another potential explanation for the more favorable disease course in younger patients is the longer period for potential remodeling prior to skeletal maturity.[13]

As a retrospective investigation of a sub-population of patients with an already rare disorder, our study has several inherent limitations.The duration of each stage was determined by measuring the time interval between radiographs showing features of one stage and radiographs demonstrating features of the next stage. In reality, the stage may have progressed at any point between images. Thus, the accuracy of the stage duration depended on the time interval between subsequent radiographs. To partially address this issue, we included only patients with a minimum of 3 radiographs showing sequential progression through disease stages. In addition, the median follow-up interval during early stages was not significantly different compared to during late stages (119 days and 133 days, respectively; $p = 0.155$). However, the difference between median combined duration of early stages and that of late stages was found to be statistically significant (513 days and 833 days, respectively; $p = 0.011$). These findings suggest that our reported stage durations are not merely a function of the time intervals between successive radiographs. However, we certainly acknowledge that our calculated durations of LCPD stages are still an estimated value at best. That being said, our methodology for computing duration of stages is comparable to the one used by Joseph *et al*, and represents a good faith attempt to measure a continuous variable (i.e. stage length) using periodic data.[5] Secondly, it is important to acknowledge that Joseph *et al* conducted their study on children from the Indian subcontinent where the incidence of LCPD is much lower and the age at onset is greater compared to North American population.[3,5,14] While their study is the only previous work in the literature that reports on the duration of Waldenström stages, our direct comparison may not be generalizable to typical aged patients in North America.

Despite its limitations, this study is the first to characterize the duration of LCPD stages in very young patients. Our findings, in contrary to our original hypothesis, suggest that the duration of LCPD stages may actually be longer in these younger patients as compared to typical-aged LCPD patients. This may imply that factors other than a shorter duration of disease stages could be responsible for the improved outcomes seen in these children.

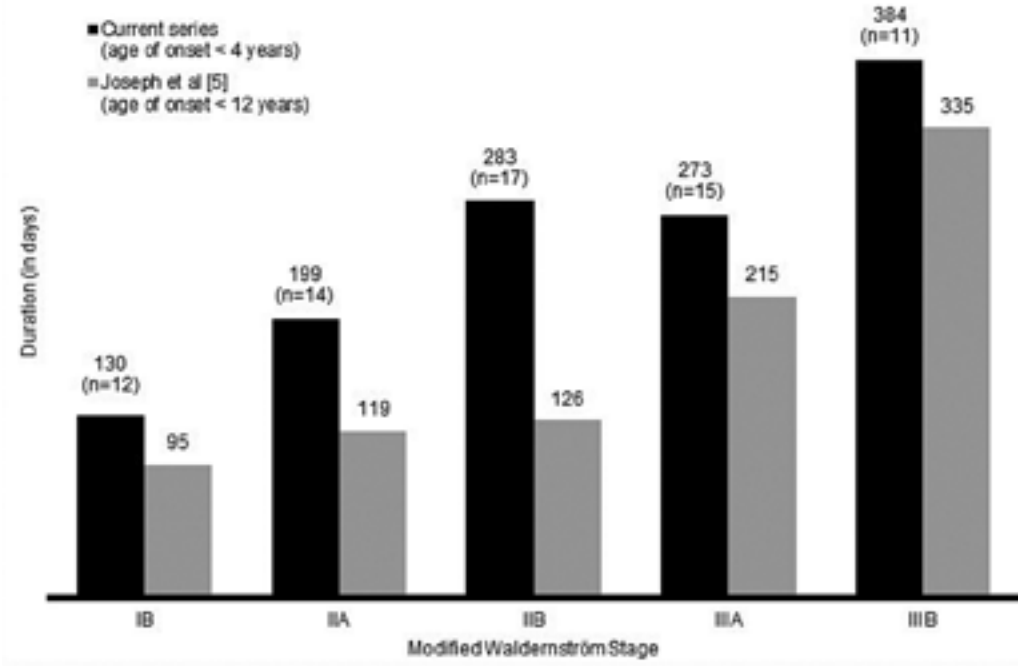


Figure 1. The median duration of modified Waldenström stages of LCPD in children younger than four years of age at the onset compared to older children.

References

1. **Waldenström H.** The classic. The first stages of coxa plana by Henning Waldenstrom. 1938. *Clinical orthopaedics and related research.* 1984(191):4-7.

2. **Perry DC, Machin DM, Pope D, *et al.*** Racial and geographic factors in the incidence of Legg-Calve-Perthes' disease: a systematic review. *Am J Epidemiol.* 2012;175(3):159-166.

3. **Loder RT, Skopelja EN.** The epidemiology and demographics of legg-calve perthes' disease. *ISRN Orthop.* 2011;2011:504393.

4. **Waldenström H.** The difinite form of the coxa planaa. *Acta Radiologica.* 1922;1:384-394.

5. **Joseph B, Varghese G, Mulpuri K, *et al.*** Natural evolution of Perthes disease: a study of 610 children under 12 years of age at disease onset. *Journal of pediatric orthopedics.* 2003;23(5):590-600.

6. **Herring JA, Kim HT, Browne R.** Legg-Calve-Perthes disease. Part I: Classification of radiographs

with use of the modified lateral pillar and Stulberg classifications. *J Bone Joint Surg Am.* 2004;86-A(10):2103-2120.

7. **Wiig O, Terjesen T, Svenningsen S.** Prognostic factors and outcome of treatment in Perthes' disease: a prospective study of 368 patients with five-year follow up. *J Bone Joint Surg Br.* 2008;90(10):1364-1371.

8. **Schoenecker PL, Stone JW, Capelli AM.** Legg-Perthes disease in children under 6 years old. *Orthop Rev.* 1993;22(2):201-208.

9. **Fabry K, Fabry G, Moens P.** Legg-Calve-Perthes disease in patients under 5 years of age does not always result in a good outcome. Personal experience and meta analysis of the literature. *J Pediatr Orthop B.* 2003;12(3):222-227.

10. **Rosenfeld SB, Herring JA, Chao JC.** Legg-calve-perthes disease: a review of cases with onset before six years of age. *J Bone Joint Surg Am.* 2007;89(12):2712-2722.

11. **Kelly FB, Jr., Canale ST, Jones RR.** Legg-Calve-Perthes disease. Long-term evaluation of non-containment treatment. *J Bone Joint Surg Am.* 1980;62(3):400-407.

12. **Grasemann H, Nicolai RD, Patsalis T, *et al.*** The treatment of Legg-Calve-Perthes disease. To contain or not to contain. *Arch Orthop Trauma Surg.* 1997;116(1-2):50-54.

13. **Lindstrom JR, Ponseti IV, Wenger DR.** Acetabular development after reduction in congenital dislocation of the hip. *J Bone Joint Surg Am.* 1979;61(1):112-118.

14. **Joseph B, Chacko V, Rao BS, *et al*.** The epidemiology of Perthes' disease in south India. *Int J Epidemiol.* 1988;17(3):603-607.

Force Variability in a Classic Distraction Technique

Vincent Ruggieri, BS
Patrick J Cahill, MD
John M Flynn, MD
Robert M Campbell, MD
Jason B Anari, MD

Department of Orthopaedic Surgery
Children's Hospital of Philadelphia,
Philadelphia, PA

Introduction

Given the advent of the magnetically controlled growing rod (MCGR) and how much force we know it delivers onto the spine, understanding what the older systems impart on anatomy is critical to further technology advancements.[1] Nordeen reported on the traditional growing rod (TGR) in vivo and Sankar taught us about the increasing force requirement/law of diminishing returns.[2,3] Knowledge of the forces imparted by the Vertical Expandable Prosthetic Titanium Rib (VEPTR) by different surgeons will help us advance remote lengthening technology.

Methods

Six surgeons performed an expansion on four different VEPTR constructs (pelvis to rib, spine to rib, pelvis to spine, and spine to spine) that had been previously inserted into cadavers. They approximated the amount of force they would apply during a standard expansion operation. A strain gauge adhered to the distraction tool wired to a strain indicator and recording device was used to collect data and was zeroed after every measurement. All data were withheld from the surgeons during the expansions as to not influence their applied force. A compression spring acted as a conversion tool to convert the strain to pounds. The data was converted to Newtons, graphed (Figure 1), and averages and relative standard deviations were calculated.

Results

The average force applied across all constructs was 321N with a relative standard deviation of approximately 11% (36N). Of the four different constructs, the spine to spine was the only construct that on average required over one standard deviation less force than the average (270N). This seems to be due to only five of the surgeons performing on the construct. When compared to the average of only surgeons who performed on it (272N), it fell well within one standard deviation. Amongst the six surgeons, each maintained a force standard deviation of 5% to 20% between constructs, though trends can be seen indicating different constructs requiring different amounts of force. Five of the surgeons used a single hand technique while one of the surgeons, the most experienced one, used a second hand.

Conclusion

The prosthetic rib construct expansion in cadaveric specimens imparts on average 320N of force per surgeon with surgeon experience playing some role in the amount force accepted during a lengthening procedure. Construct design does appear to play a role in forces imparted to the deformity.

References

1. Poon S, Spencer HT, Luong V, *et al*. Maximal force generated by magnetically controlled growing rods at different magnetic controlled growing rod length decreases with rod lengthening. *Spine* 2017;17(10): S178.
2. Noordeen HM, Shah SA, Elsebaie HB, *et al*. In vivo distraction force and length measurements of growing rods: Which factors influence on the ability to lengthen? *Spine (Phila Pa 1976)* 2011; 36(26): 2299-2303.
3. Sankar WN, Skaggs DL, Yazici M, *et al*. Lengthening of dual growing rods and the law of diminishing returns. *Spine (Phila Pa 1976)* 2011;36(10):806–809.

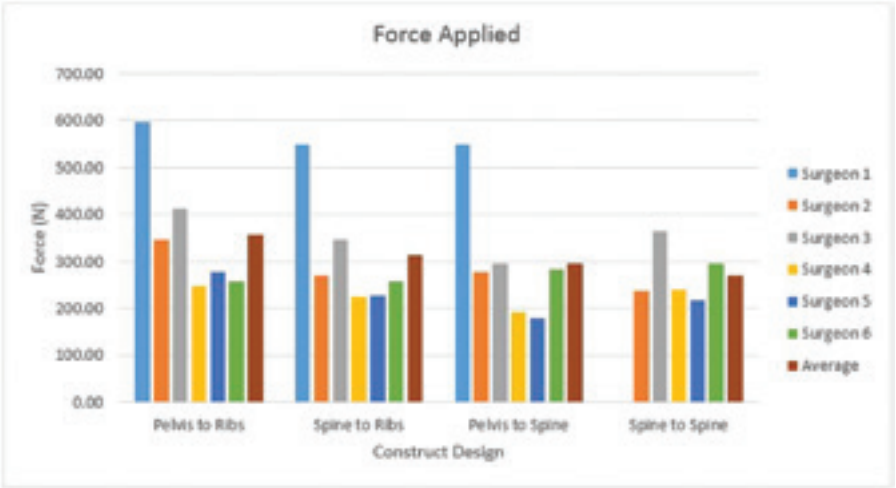


Figure 1. Various forces recorded by 6 spine surgeons on 4 different prosthetic rib constructs during an expansion operation.

Fracture Healing in Pediatric Patients with Neurofibromatosis Type 1: A Case Series and Review of the Literature

Daniel J. Miller, MD[1]
Todd J. Blumberg, MD[2]
Susan E. Nelson, MD MPH[3]
Wudbhav N. Sankar, MD[4]

1 Department of Orthopaedic Surgery, Gillette Children's Specialty Healthcare, St. Paul, MN

2 Department of Orthopaedic Surgery, Seattle Children's Hospital, Seattle, WA

3 Department of Orthopaedic Surgery, University of Rochester Medical Center, Rochester, NY

4 Division of Orthopaedic Surgery, Children's Hospital of Philadelphia, Philadelphia, PA

Introduction

Neurofibromatosis type 1 (NF-1) is an autosomal dominant genetic disorder that affects 1 in 3,000 persons worldwide.[1] Approximately 50% of patients with NF-1 will demonstrate one or more musculoskeletal conditions such as congenital pseudarthrosis of the tibia (CPT), scoliosis, or plexiform neurofibromata during childhood.[2] Patients with NF-1 frequently demonstrate a generalized abnormality of bone metabolism and management of the musculoskeletal manifestations of NF-1 is often challenging.[1,3]

The treatment of CPT is complicated by a high rate of re-fracture, malunion, and nonunion (up to 65%). Dystrophic and nondystrophic forms of scoliosis are common in patients with NF-1 and are associated with an increased risk of pseudarthrosis following instrumented spinal fusion when compared to patients with idiopathic scoliosis. Although significant attention has been paid to treatment of CPT and spinal deformity in NF-1, fracture healing in patients with NF-1 is relatively poorly understood. While it is accepted that patients with NF-1 have a higher incidence of metabolic bone disease, the significance of this with respect to fracture incidence and healing is controversial.[3]

The purpose of this study was to examine fracture healing in pediatric patients with NF-1 treated at our tertiary care center. We hypothesized that patients with NF-1 demonstrate normal healing in response to traumatic fractures in normal, non-dysplastic long bones.

Methods

Following internal review board (IRB) approval, a retrospective review was performed of all subjects 20 years or younger who presented to an orthopaedic provider between 2008 and 2016 at our tertiary referral center with a diagnosis of NF-1 (ICD 10 code Q85.01, ICD9 code 237.71). Charts, billing records, and radiographs were reviewed to identify all cases of long bone fractures within this cohort. For the purposes of this study, we defined long bones as the humerus, radius, ulna, clavicle, femur, tibia, and fibula. Cases were included if they had clinical follow-up until evidence of radiographic healing. Subject with a long bone dysplasia (defined as dysplastic tibial bowing with or without pseudarthrosis) were included as potential subjects. Fractures in these subjects were included if the fracture bone appeared radiologically normal. Management (operative and non-operative) of fractures in dysplastic bone and/or pseudarthroses was excluded.

For each fracture, we recorded patient demographics (age, sex), fracture characteristics (location, pattern, mechanism of injury, open vs. closed), fracture treatment, and outcomes (including time to radiographic union, time to return to full activities, and presence of delayed union). Radiographic union was defined as visible fracture callus on at least three of four cortices of all involved bones as assessed on biplanar imaging. Delayed union was defined as union occurring at more than 12 weeks after initial treatment. Descriptive statistics were calculated utilizing SPSS Statistics, version 24.0 (IBM Corp., Armonk, N.Y., USA),

Results

Between 2008 and 2016, 1259 unique pediatric patients with NF-1 were evaluated and treated by an orthopaedic surgeon at our institution. Sixty patients were identified as having fractures based on billing codes.Twenty-four patients were identified as having CPT and were excluded. Seventeen patients were excluded from analysis because they had fractures of non-long bone (e.g. phalangeal fracture, metacarpal fractures, or metatarsal fractures). This study included the remaining 19 fractures (Table 1) which occurred in 18 patients (11 males, 7 females). No patients were lost to follow up. Mean age at the time of fracture was 9 years (1 to 15 y). Mechanisms of injury included ground level fall (13 cases), fall from a height $>$ 3 feet (4 cases), motor vehicle accident (1 case), and non-contact rotational injury (1 case).

Ninety-five percent (18/19) of fractures were closed injuries and were treated non-operatively. In these patients, the mean time to radiographic union was 46 days (range 27-76 days) and the mean time to full activities was 67 days (range 27-97 days). Complete healing occurred in all patients. There were no instances of re-fracture at most recent follow up. One patient presented with a Gustilo and Anderson type 1 open mid-shaft both bone forearm fracture after a fall

Table 1: Fracture patterns and characteristics for patients with NF-1 treated between 2008 and 2016. GLF = ground level fall; FFH = fall from height; MVA = motor vehicle accident.

Sex	Age at Injury (years)	Fracture (bone)	Location within Bone	Mechanism of Injury	Fracture Pattern	Open vs Closed	Time to Union (days)
M	7.5	Radius + Ulna	Distal 1/3	GLF	Transverse	Closed	42
F	9.9	Radius + Ulna	Middle 1/3	GLF	Oblique	Closed	64
M	13.3	Ulna	Distal 1/3	GLF	Transverse	Closed	40
M	15.2	Tibia + Fibula	Proximal 1/3	FFH	Transverse	Closed	61
F	8.1	Radius	Distal 1/3	GLF	Transverse	Closed	30
F	1.3	Tibia	Distal 1/3	GLF	Buckle	Closed	30
M	1.8	Femur	Middle 1/3	GLF	Spiral	Closed	43
F	6.3	Tibia	Proximal Physeal	FFH	Physeal, SH-II	Closed	58
M	12.6	Clavicle	Middle 1/3	GLF	Oblique	Closed	34
M	12.2	Tibia	Distal Physeal	MVA	Physeal, SH-I	Closed	28
F	12.0	Radius + Ulna	Middle 1/3	FFH	Oblique	Closed	76
F	9.4	Radius + Ulna	Middle 1/3	GLF	Oblique	Closed	50
F	9.9	Radius	Distal 1/3	GLF	Torus	Closed	34
M	13.5	Radius + Ulna	Distal 1/3	GLF	Oblique	Closed	43
M	11.3	Tibia	Medial Mall	Rotational	Transverse	Closed	78
M	7.7	Fibula	distal physeal	GLF	Physeal SH-I	Closed	27
M	9.5	Radius + Ulna	distal 1/3	GLF	Oblique	Closed	54
M	1.9	Tibia	Distal 1/3	GLF	Spiral	Closed	39
F	11.0	Radius + Ulna	Middle 1/3	FFH	Oblique	Open (Type 1)	220

from a height. This patient was treated with irrigation and debridement and internal fixation with compression plates. The post op course was complicated by a deep surgical site infection requiring repeat irrigation and debridement and partial hardware removal. This patient had a delayed union, with eventual radiographic healing at 31 weeks.

Discussion

The purpose of this study was to examine fracture healing in pediatric patients with NF-1. In this case series, we found that routine healing of traumatic fractures in non-dysplastic bone was observed in 95% of cases in patients with NF-1. The one fracture that went on to delayed union in this series was an open both-bone forearm fracture which was complicated by deep surgical site infection.

Although a substantial amount of research has been devoted to nature and treatment of osseous manifestations of NF-1, few studies have examined fracture incidence and healing in patients with NF-1.Tucker *et al* performed laboratory analyses of various measures of bone metabolism in 72 adult patients with NF-1 and found that over half had low serum 25-hydroxy-vitamin D levels and a third of the group had elevated levels of serum parathyroid hormone.[3] They found that patients with NF-1 had a comparatively higher frequency of fractures when compared to unaffected siblings or spouses.[3] This study did not examine characteristics of fracture healing in the NF-1 population.

In contrast, George-Abraham *et al* surveyed children at two multidisciplinary NF clinics and found an equivalent prevalence rate of a fracture history compared to age matched controls.[4] They did note that patients with NF-1 tended to have lower rates of physical activity than controls which may have had a protective effect against fracture. Again, this study did not examine characteristics of fracture healing in the NF-1 population. Heerva *et al* examined a cohort of 460 Finnish patients with NF-1 and compared them to a group of 3988 appendectomy patients as age and sex matched controls.[5] They found that patients with NF-1 had a significantly higher risk for fractures (relative risk 3.8, $p < 0.001$). 98% (59/60) of fractures in patients with NF-1 went on to heal with one patient developing a pseudarthrosis of an ulnar fracture.[5] This study did not comment on fracture or injury characteristics nor did it discuss the type of management (operative vs non-operative) employed.

To date, there is only one report of a delayed union in a patient with NF-1. Kaempffe *et al* presented a case report of a pseudarthrosis of the radius after fracture through non-dysplastic bone in a child with NF-1.[6] This fracture ultimately

went on to union following open reduction and internal fixation.[6]The strengths of this paper include a large population of patients with NF-1 and follow up to union in all cases. To our knowledge, this is the first series to examine traumatic fracture healing in patients with NF-1 from an orthopaedic viewpoint.

This study has several limitations. First and foremost, we relied on billing records to identify patients with NF-1 and fractures, which is susceptible to misclassification and information bias. Although patients with NF-1 present to our tertiary multidisciplinary center from a wide geographic area, it is certainly possible that they could seek routine fracture care at outside institutions. As such, it is impossible for us to determine the true incidence of fractures in the NF-1 population based on this data. Additionally, this study is retrospective in nature and as such is subject to the limitations inherent to that study design.

In conclusion, based on this series, fractures of non-dysplastic bone in patients with NF-1 can be expected to heal in routine fashion when treated according to general pediatric orthopaedic trauma principles. We believe that it is important to recognize features of dysplastic bone that may increase the risk of fracture and/or delayed union. Practitioners should remain cognizant of the increased prevalence of metabolic bone disease in this population and should be concurrently evaluating patients for other manifestations of NF-1, such as spinal deformity.

References

1. Feldman DS, Jordan C, Fonseca L. Orthopaedic manifestations of neurofibromatosis type 1. *J Am Acad Orthop Surg*. 2010;18(6):346-57.

2. Crawford AH, Jr., Bagamery N. Osseous manifestations of neurofibromatosis in childhood. *J Pediatr Orthop*. 1986;6(1):72-88.

3. Tucker T, Schnabel C, Hartmann M, *et al*. Bone health and fracture rate in individuals with neurofibromatosis 1 (NF1). *J Med Genet*. 2009;46(4):259-65.

4. George-Abraham JK, Martin LJ, Kalkwarf HJ, *et al*. Fractures in children with neurofibromatosis type 1 from two NF clinics. *Am J Med Genet A*. 2013;161A(5):921-6.

5. Heerva E, Koffert A, Jokinen E, *et al.* A controlled register-based study of 460 neurofibromatosis 1 patients: increased fracture risk in children and adults over 41 years of age. *J Bone Miner Res*. 2012;27(11):2333-7.

6. Kaempffe FA, Gillespie R. Pseudarthrosis of the radius after fracture through normal bone in a child who had neurofibromatosis. A case report. *J Bone Joint Surg Am*. 1989;71(9):1419-21.

Mechanical and Microstructural Properties of Native Pediatric Posterior Cruciate and Collateral Ligaments

Elaine C. Schmidt[1]
Matthew Chin[1]
Julien T. Aoyama[2]
Theodore J. Ganley[2]
Kevin G. Shea[3]
Michael W. Hast[1]

1 University of Pennsylvania, Philadelphia, PA,

2 Children's Hospital of Philadelphia, Philadelphia, PA

3 Stanford University, Stanford, CA

Introduction

Increases in youth sport participation has come with a concomitant rise in the number of diagnosed knee ligament tears in pediatric patients.[1] High rates of injury to the medial collateral ligament (MCL) have been reported, and although injuries to the lateral collateral ligament (LCL) and posterior cruciate ligament (PCL) occur with less frequency, they can be severe and may require surgical intervention.[2,3] There is currently a lack of knowledge about the mechanical and microstructural properties of native pediatric ligaments, which impedes the improvement and optimization of surgical treatment for this young population. The purpose of this study was to provide a detailed characterization of mechanical and microstructural properties of pediatric MCLs, LCLs, and PCLs using a rare cadaveric cohort.

Methods

MCLs, LCLs, and PCLs were fine dissected from five fresh-frozen pediatric knee specimens (3 male, 2 female, average age 9.2 years) (AlloSource, Centennial, CO). Ligaments were prepared for uniaxial tensile testing by cutting them into dog-bone shapes at the mid-substance with a custom-built jig (Figure 1A). Cross sectional areas were measured using a laser-based measurement system (Figure 1B). Grip-to-grip uniaxial testing was performed in a universal test frame (ElectroForce 3330, TA Instruments, New Castle, DE) (Figure 1C). The tensile testing protocol consisted of preconditioning, stress-relaxation, and a ramp-to-failure at 0.03% strain/s. Ligaments from the contralateral knee of one donor (female, age 9) were available for microstructural analyses. Brightfield, polarized light, and transmission electron microscopy were conducted to measure cellularity, collagen crimp frequency, and collagen fibril diameter distribution, respectively. Statistical differences between groups were determined by performing one-way ANOVAs with $\alpha = 0.05$.

Results

MCLs and LCLs demonstrated similar values for ultimate stress, ultimate strain, and Young's Modulus that were similar to values for the LCLs (Table 1). The LCL exhibited mechanical properties that had greater variability than the LCL or PCL. PCLs exhibited diminished ultimate stress, stiffness, Young's modulus, and strain energy density when compared to the collateral ligaments, but none of these findings were statistically significant. All three tissues had similar crimp wavelengths (MCL 32.8 ± 3.6 μm; LCL 27.2 ± 3.5 μm; PCL 25.8 ± 3.5 μm) and collagen fibril diameters (MCL 88.0 ± 26.0 nm; LCL 93.3 ± 34.6 nm; PCL 90.9 ± 34.0 nm) (Figure 2). However, the distribution of their profiles had distinct modalities, with the MCL

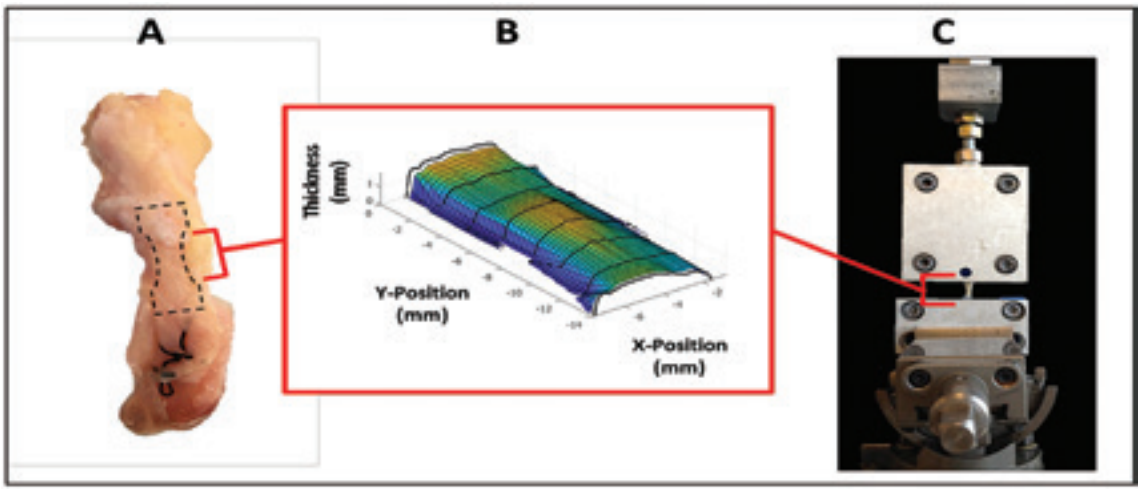


Figure 1. Overview of the mechanical testing protocol. Pediatric specimens were sectioned into dog-bone shapes **(A)**; the CSA of the gauge length was measured using a laser-based scanner **(B)**; and the ends of the specimens were clamped and attached to the testing frame **(C)**.

Table 1. Results (mean ± standard deviation and p-values) for the pediatric MCL, LCL, and PCL specimens obtained from tensile testing.

	Ultimate Stress (MPa}	Ultimate Strain(%)	Young's Modulus (MPa}	Stiffnes (N/mm)	Strain Energy Density (MPa)
MCL	11.7 ± 6.7	18.2 ± 6.8	93.7 ± 56.5	28.6 ± 6.1	1.2 ± 0.9
LCL	11.4 ± 11.5	27.7 ± 12.9	64.4 ± 76.6	30.8 ± 37.5	1.3 ± 1.0
PCL	4.2 ± 1.8	28.8 ± 11.9	19.8 ± 10.4	19.8 ± 10.8	0.7 ± 0.4
			P-values		
MCL v. LCL	0.952	0.347	0.418	0.881	0.849
MCL v. PCL	0.390	0.384	0.159	0.800	0.576
LCL v. PCL	0.307	0.876	0.401	0.843	0.602

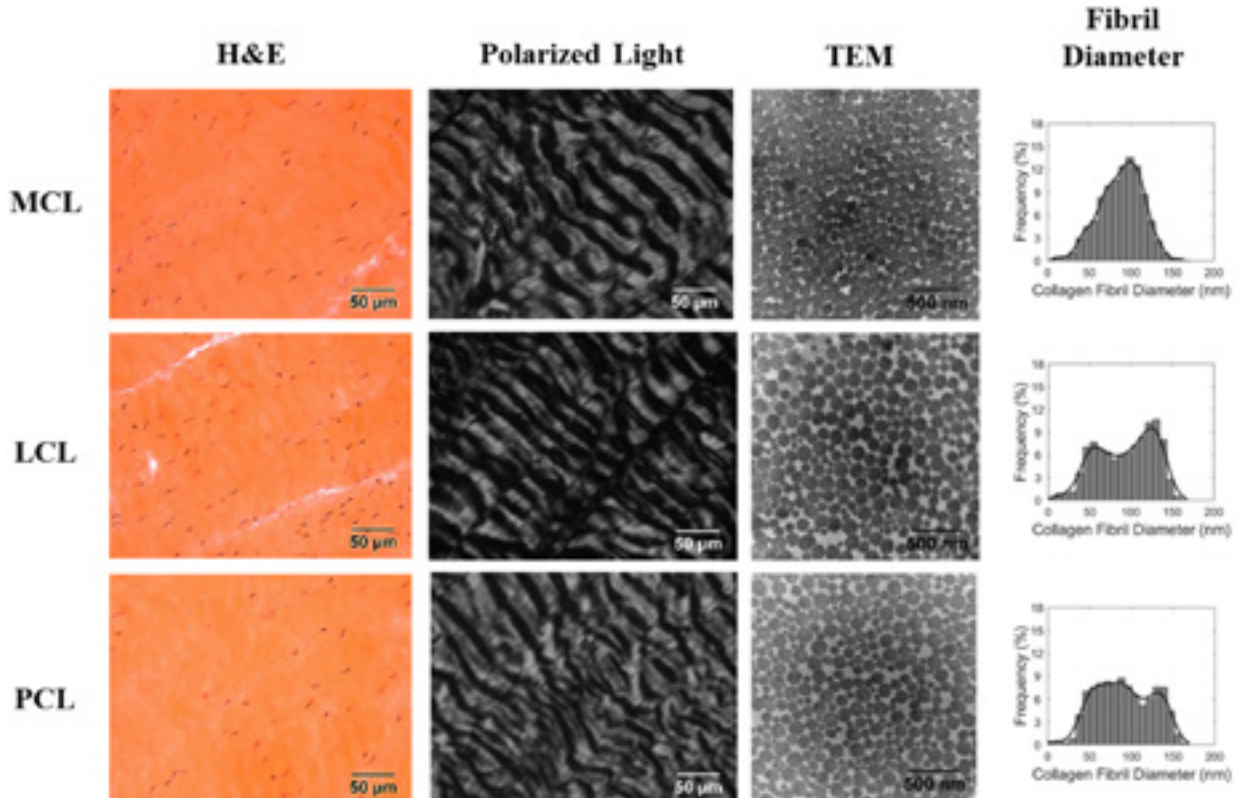


Figure 2. Microstructural results for the contralateral MCL, LCL, and PCL from one donor. First column: representative H&E images for each specimen; Second column: polarized light images demonstrating crimp morphology; Third column: TEM micrographs of collagen fibril cross sections; Fourth column: histograms of relative frequency of collagen diameters.

exhibiting a unimodal profile and the LCL and PCL trending towards bimodal profiles.

Discussion

Pediatric MCLs and LCLs within this small cohort possessed similar mechanical properties. The pediatric PCL may be weaker, but it is able to tolerate high amounts of strain before failure. All tested specimens exhibited weaker mechanical properties than what has been reported in the literature for adult cohorts. Based on a previous study with the same donor cohort, the microstructural properties of the pediatric MCL appear to be most similar to that for pediatric iliotibial band (ITB).[4] Pediatric ITBs are also stronger than the native MCL and when used as a graft source for extra-articular augmentation could prevent re-rupture in cases of multi-ligament injuries and severe instability. Results from this study are inherently limited due to the small sample size associated with this rare cohort of donors.

The results from this study represent the first attempt to establish baseline mechanical and microstructural data for pediatric collateral and posterior cruciate ligaments. In the context of graft augmentation for the pediatric knee, the ITB may be a promising source of knee tendon graft.

References

1. **Caine+** *Clin Biomech* 2008.
2. **Swenson+** *Med Sci Sports Exerc* 2013.
3. **Meislin** *Phys Sportsmed* 1996.
4. **Schmidt+** *bioRxiv*, 2018.

Simultaneous Bilateral Femur Fractures in Children: A Case Series from a Pediatric Level I Trauma Center and Review of the Literature

Ronit Shah, BS
Daniel J. Miller, MD
Mahmoud Abo-elm Mahmoud, MD
Alexandre Arkader, MD

Department of Orthopaedic Surgery
Children's Hospital of Philadelphia,
Philadelphia, PA

Introduction

Bilateral femur fractures are rare injuries with an unknown incidence. In the pediatric population, these fractures occur in a bimodal distribution with most occurring at 2-3 years of age as well as 17-18 years of age.[1] Most femur fractures in children are typically caused by high energy trauma such as car accidents or falls, while low energy fractures are rare and usually due to genetic, metabolic, or endocrine disorders.[2] Complications following femur fractures have been well described before and include wound infection, re-fracture, nonunion/malunion, avascular necrosis, growth arrest, and limb-length discrepancy.[3-6]

The current literature on pediatric bilateral femur fractures is limited to sparse case reports. The purpose of this study was to review our institutional experience with a case series of simultaneous bilateral femur fractures and highlight the presentation, treatment, and outcomes of these rare injuries as well as perform a comparison to similar unilateral femur fractures in order to identify any clinically relevant differences that may guide future management. We hypothesized that simultaneous bilateral femur fractures would have initially greater severity at time of presentation due to higher energy trauma and also have worse outcomes and/or a higher incidence of complications.

Methods

A retrospective review of a prospectively collected institutional femur fracture database was conducted for patients aged 0-18 years who presented with bilateral femur fractures sustained between 2007 and 2017. All patients had a minimum of 1 year follow up. Data was collected which included demographics, mechanism of injury, fracture location, pattern, treatment modality, length of stay, physical therapy usage, return to activity, and short/long-term complications. Further analysis was conducted to compare unilateral and bilateral femur fractures in a 2:1 fashion. Unilateral femur fractures that met case matched criteria (identical age, gender, and fracture location) were identified from the same femur fracture database.

Results

We identified eight children with simultaneous bilateral femur fractures (Figure 1). The mean age at the time of injury was 11 ± 2.7

Age	Gender	Mortality	Mechanism	Left Fracture	Left Fracture Treatment	Right Fracture	Right Fracture Treatment	Associated Injuries	Length of Stay	Complications
12	Male	N	Peds struck vs MVA	Oblique Midshaft	Rigid IMN	Physeal SH2 Distal	CRPP	TBI	27	Acute Psychosis
8	Male	N	Peds struck vs MVA	Oblique Midshaft	Flexible IMN	Physeal SH2 Distal	CRPP	TBI, Facial Fracture, Hearing Loss	11	Central bar involving 20% of R distal physis
15	Male	N	Ground level Fall	Transverse Distal 1/3	CRPP	Delbet IV Proximal	ORIF- Plate/Screw	None	6	None
9	Male	N	Jet Ski Injury	Transverse Midshaft	Flexible IMN	Transverse Midshaft	Flexible IMN	Liver Laceration	7	None
11	Female	N	MVA	Transverse Proximal	Rigid IMN	Comminuted Midshaft	Rigid IMN	Mesenteric vein laceration, Renal artery avulsion, Multiple spine fractures, Tibia and ulnar shaft fracture, Pulmonary contusion	19	None
7	Male	N	Peds struck vs MVA	Comminuted Midshaft	Flexible IMN	Transverse Proximal 1/3	Flexible IMN	None	4	R Genu Valgum
11	Male	N	Peds struck vs MVA	Transverse Midshaft	Flexible IMN	Transverse Midshaft	Flexible IMN	TBI, Splenic laceration, Renal contusion, Cervical fracture, Rib fracture, Concussion	12	None
13	Male	N	Peds struck vs MVA	Transverse Midshaft	Rigid IMN	Physeal SH2 Distal	ORIF- Screws	TBI, Tongue laceration, Concussion, Hemorrhagic shock, Pneumothorax	10	None

Figure 1. Case Series of Bilateral Femur Fractures.

years (range: 7-15 years). Seven of eight patients were male. The mechanism of injury was high energy trauma in seven of eight patients, including five instances of pedestrians struck by a motor vehicle. One patient sustained bilateral femur fractures after a ground level fall in the setting of Duchenne Muscular Dystrophy and osteoporosis. Six patients had at least one significant associated injury, including four patients with traumatic brain injury (TBI), four patients with intra-abdominal injuries, and two patients with spinal fractures.

All injuries were closed. Twelve out of sixteen fractures involved the femoral shaft, three involved the distal femur physis, and one was intertrochanteric. All patients underwent operative fixation bilaterally. Method of fracture fixation varied according to patient age as well as fracture location and pattern. Treatment options included rigid/flexible Intramedullary Nail (IMN), Plate/Screw constructs, and Closed Reduction with Percutaneous Pinning (CRPP). Average length of stay was 12 days (range 4-27 days). Four patients required admission to inpatient rehab facility.

There were no mortalities in the perioperative period or at long term follow up. All fractures went on to union. There were no instances of infection or re-fracture. One patient experienced unilateral genu valgum deformity treated successfully with medial hemi-epiphysiodesis and plating. Another patient experienced a unilateral bony bar of approximately 20% of the physis which did not result in angular deformity or limb length discrepancy. There was one case of acute psychosis. Patients returned to full activity at an average of 5.8 months respectively (range 3-9 months).

The bilateral femur fracture case involving a patient with Duchenne's muscular dystrophy was excluded from the following comparisons. Subsequent analysis was conducted comparing seven bilateral femur fracture cases to sixteen unilateral femur fracture cases that were matched based on age, gender, and fracture location. There were no statistically significant differences found between the bilateral and unilateral groups when comparing age and gender. The number of associated injuries at time of presentation was different, with the bilateral fractures cohort having a significantly greater number of associated injuries ($p < 0.05$) (Table 1). Two patients required blood transfusion in the bilateral cohort, one of whom had sustained multiple abdominal injuries. No patients required blood transfusion in the unilateral cohort. Average length of stay in the bilateral group was 12.9 days compared to 4.5 days in the unilateral group, which was found to be statistically significant ($p < 0.05$). The mean number of complications in the unilateral patient cohort was 0.5, compared to 0.7 in the bilateral cohort. The difference in complications between the two groups was not found to be significant ($p > 0.05$). Average number of months required to return to activity was also not significantly different between the bilateral and unilateral groups ($p>0.05$).

Discussion

Patients with bilateral femur fractures had a statistically significant greater number of associated injuries at time of presentation. These associated injuries included traumatic brain injuries, multiple fractures, and cardiothoracic/abdominal injuries. This is most likely attributed to the greater trauma/force sustained in order to produce bilateral fractures in comparison to the force needed to produce a unilateral fracture. High impact pedestrian-motor vehicle accidents were the cause of injury for six out of eight patients in our series.

Few cases of bilateral femur fractures have been reported in the literature. Most are related to high speed trauma. Scott *et al* reported bilateral proximal femur fractures in a four year old following an ATV injury.[7] The patient underwent bilateral open reduction and internal fixation which was complicated by left hip avascular necrosis. Smith reported a case of a four-year old who presented with bilateral femoral shaft fractures after a high speed MVA while restrained with a standard factory fitted lap belt instead of a car seat.[8] The patient was treated with flexible intramedullary nailing and had an uneventful recovery[8]. Dhar reported a case of a nine-year old girl who presented with bilateral femoral neck fractures following a motor vehicle accident. The patient was managed with early open reduction and internal fixation with a successful outcome.[9] These reports are consistent with the results of our series.

There are numerous limitations to this study. Despite being the largest series of patients with bilateral pediatric femur fractures, the sample size remains relatively small and is retrospective in nature. As a result, comparisons to the unilateral group would benefit from a larger cohort. Longer-term follow-up is also necessary to accurately assess complications.

Conclusion

This report of eight patients demonstrates that bilateral femur fractures in the pediatric population are commonly a result of high energy trauma and highlights the importance of careful preoperative evaluation. Although bilateral femur fractures may have worse initial presentation, greater length of stay, and more complicated multi-specialty management, once appropriately treated, their short-term outcomes and

Table 1. Clinical Characteristics of Unilateral vs. Bilateral Femur Fractures

	Unilateral Cohort	Bilateral Cohort
Mean Number of Associated Injuries	0.4	2.9
Mean Length of Stay	4.5 days	12.9 days
Mean Number of Complications	0.5	0.7

complications are similar to their unilateral counterparts. We believe that with coordinated pediatric trauma care, successful management is possible as with the majority of patients in this series.

References

1. Hedlund R, Lindgren U. The incidence of femoral shaft fractures in children and adolescents. *J Pediatr Ortho* 1986; 6: 47-50.

2. Ju DG, Mogayzel PJ, Jr., Sponseller PD, *et al.* Bilateral midshaft femoral fractures in an adolescent baseball player. *Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society* 2016; 15: e41-43.

3. Kruppa C, Wiechert G, Schildhauer TA, *et al.* Complications after operative treatment of femoral shaft fractures in childhood and adolescence. *Orthopedic reviews* 2017; 9: 7493.

4. Arom GA, Yeranosian MG, Petrigliano FA, *et al.* The changing demographics of knee dislocation: a retrospective database review. *Clinical orthopaedics and related research* 2014; 472: 2609-2614.

5. Yeranosian M, Horneff JG, Baldwin K, *et al.* Factors affecting the outcome of fractures of the femoral neck in children and adolescents: a systematic review. *The bone & joint journal* 2013; 95-b: 135-142.

6. Bali K, Sudesh P, Patel S, *et al.* Pediatric femoral neck fractures: our 10 years of experience. *Clinics in orthopedic surgery* 2011; 3: 302-308.

7. Scott B, Taylor B, Shung JR, *et al.* Bilateral femoral neck fractures associated with complex pelvic ring injuries in a pediatric patient: a case report. *J Pediatr Orthop B* 2016.

8. Smith A. Bilateral femur fractures in a four year old. *N Z Med J* 2001; 114: 409-410.

9. Dhar D. Bilateral traumatic fracture of neck of femur in a child: a case report. *Malays Orthop J* 2013; 7: 34-36.

Tibial Spine Fractures in Children: Is there Historical and Geographic Variability in Epidemiology?

Scott M LaValva, BA[1,2]
Julien T Aoyama, BA[1]
Sprikena Nako[1]
Alexander J Adams, BS[1]
Theodore J Ganley MD[1,2]

1 Department of Orthopaedic Surgery Children's Hospital of Philadelphia, Philadelphia, PA

2 Perelman School of Medicine University of Pennsylvania, Philadelphia, PA

Introduction

Tibial spine fractures are intra-articular avulsion fractures of the intercondylar eminence which tend to afflict younger, skeletally immature patients in the vast majority of cases.[1] In the pediatric patient, incomplete ossification of the tibial spine increases the vulnerability of this structure to injury compared to the anterior cruciate ligament (ACL) to which it attaches.[2,3] Thus, when patients between 8–14 years of age are exposed to the "classic" mechanism of deceleration, hyperextension, and/or rotation of the knee for ACL rupture, they may instead experience avulsion of the tibial spine rather than ligamentous tear.

Given the relatively rare nature of these injuries, the epidemiology is not well-understood. There have been several estimates reported from single centers, though the potential for historical and regional variability in activities and risk factors limits the generalizability of their findings. Thus, the aim of the present investigation was to characterize the epidemiology of tibial spine fractures at our single high-volume pediatric hospital.

Methods

After obtaining IRB approval, a respective chart review was conducted to identify patients who presented to our level 1 pediatric trauma center for a tibial spine fracture from 2009 to 2016. Information regarding patient demographics, injury mechanism/activity, and imaging reports were extracted from the electronic medical record. Fractures were classified according to the modified Meyers and McKeever method which groups the injuries as nondisplaced (Type I), minimally displaced with an intact hinge (Type II), completely displaced (Type III), or completely displaced and comminuted (Type IV).[2,4] Descriptive analyses were performed to evaluate the epidemiology of these fractures at a single center.

Table 1. Demographics of 64 patients with tibial spine fractures.

	Value
Age	12 ± 3 years (range 7–17)
Sex	63% Male
BMI	20.6 ± 4
Laterality (R/L)	50% Right
Meyers and McKeever Classification	Type I – 0% Type II – 33% Type III – 41% Type IV – 26%

All values are expressed as means ± standard deviations or percentages.

Results

Sixty-four patients with tibial spine fractures over an eight-year period were identified (Table I). The mean age at the time of injury was 12 ± 3 years (range 7–17) and 75% of patients were 14 years or younger. The majority of patients were male (63%). With respect to fracture severity, 33% of patients were Meyers and McKeever Type II, 41% Type III, and 26% Type IV. None of the patients with a recorded classification were Meyers and McKeever Type 1. Overall, 67% of the fractures were completely displaced (Types III and IV).

The majority (51%) of patients with recorded mechanisms of injury reported a contact injury, while 39% reported a non-contact twisting mechanism (Figure 1). Only 10% reported knee hyperextension. Of note, mechanism of injury was uncertain in 6 patients and not recorded in 19. With regard to activity at the time of injury, over half (53%) of patients were involved in sports and 21% of patients were riding a bike (Figure 2A). Less common causes included a fall from height (8%), riding a scooter (8%), motor vehicle accident (3%) and horseplay (2%). Of

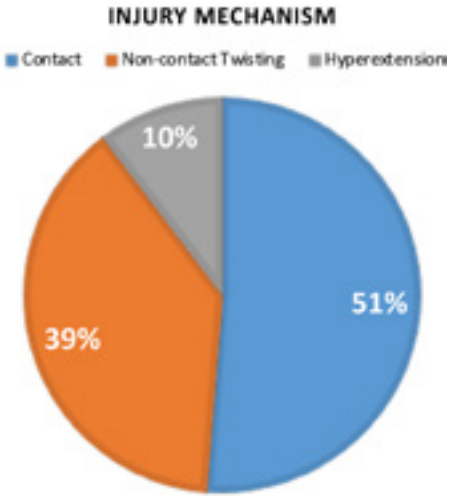


Figure 1. Reported mechanism-of-injury.

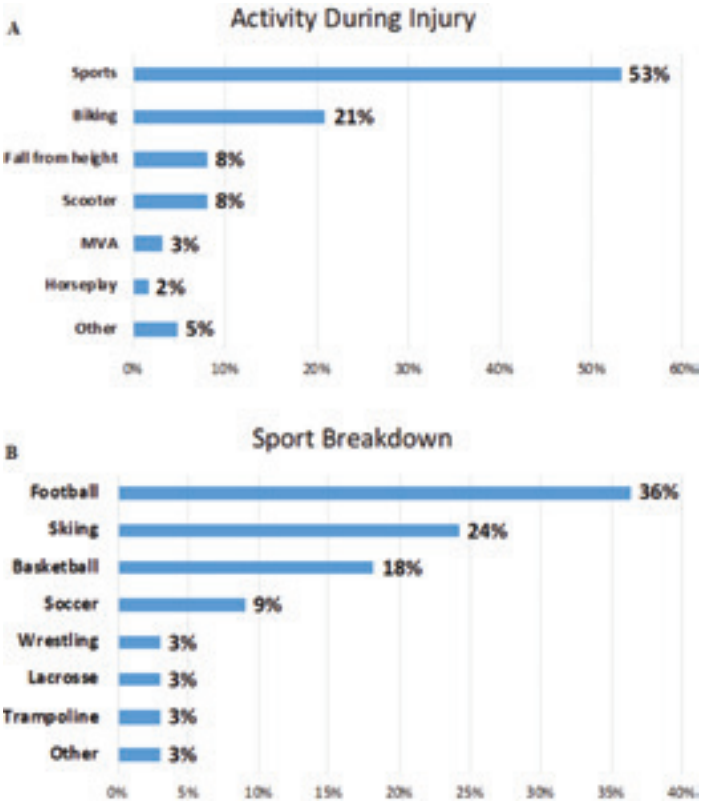


Figure 2. Activities **(A)**; and sports **(B)** at the time of injury.

those injured playing sports, football (36%), skiing (24%), basketball (18%) and soccer (9%) accounted for almost 90% of the injuries in this cohort. Wrestling (3%), lacrosse (3%), and a trampoline injury (3%) were each reported in one patient.

Of the 64 patients who presented to our center with a tibial spine fracture, 73% initially presented to a provider outside of our institution, including 23% to an orthopaedic surgeon, 6% to a pediatrician, and 44% to "other providers", which were most commonly outside emergency rooms or urgent care clinics.

Discussion

The epidemiology of tibial spine avulsion fractures has been reported in several small studies over the course of a few decades.[5] In one of the earliest descriptions of tibial spine fractures from 1970, Meyers and McKeever reported on 47 patients with these injuries and showed that 24 (51%) were injured in a bicycle accident.[2] In addition, only 21% of these fractures were completely displaced. Subsequent studies throughout the 1980s and 1990s reported similar findings[5–8] and bicycling was acknowledged as the top risk factor for this injury.

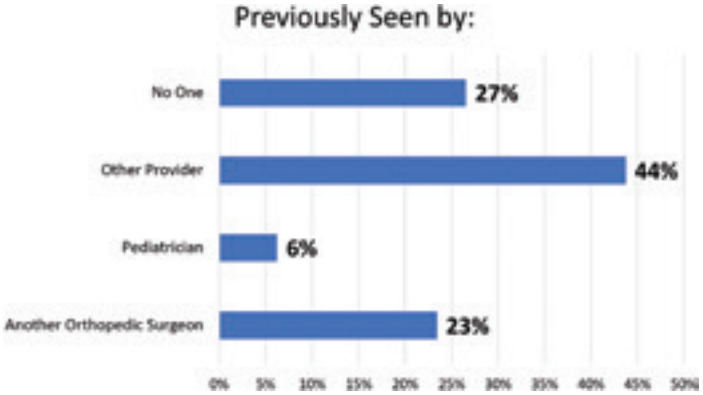


Figure 3. Initial evaluation of injury.

In the present study from our high-volume pediatric center, our findings suggest that sports-related injuries appear to have surpassed bike accidents as the top cause of tibial spine fractures, accounting for 53% in the present study.This finding is consistent with the growing popularity of competitive youth sports and year-round play, which has resulted in increased rates of several knee injuries in this patient population.[9–11] Our findings also strengthen the historical notion that these are injuries of young patients and that males are affected more frequently.

A large study in Colorado recently presented the epidemiology of this injury in 122 consecutive patients and ultimately showed similar findings, including a preponderance of sports-related injuries relative to biking accidents.[12] There were, however, a couple unique features of our cohort. First, while ACL ruptures and tibial spine fractures have most commonly been considered injuries resulting from a non-contact, twisting mechanism, contact injuries (51%) were actually the most common mechanism reported in our cohort. Second, the majority (67%) of patients at our center were diagnosed with completely displaced (Meyers and McKeever Type III or IV) fractures, in contrast to previous investigations which report mostly less severe (Type I or Type II) fractures.

There are a few possible explanations for these two findings. First, the higher proportion of contact injuries may be further evidence of the growing role of sports participation, since these are the patients at greatest risk for contact-induced knee injuries. Second, the increased fracture severity in our cohort may be explained by (1) the higher rate of contact-induced injuries, which may generate a greater degree of force through the ACL and its bony attachment to the tibia, yielding a greater degree of fracture displacement, or (2) possible selection bias in our cohort given the high rate of referral from outside institutions, including orthopaedic surgeons. Nonetheless, the link between injury mechanism and fracture severity should be investigated in future studies, as severity plays a significant role in determining treatment strategy.[1,13–15]

Conclusions

Ultimately, our study expands the existing literature which aims to understand the epidemiology of this rare injury. The patient demographics and mechanism of injury for tibial spine fractures appears relatively consistent across geographic distributions. However, the recent rise in youth sports participation, single sport specialization, and year-round play in pediatric athletes appears to have generated a new principal risk factor for this injury in sports participation.

References

1. Adams AJ, Talathi NS, Ganley TJ *et al.* Tibial Spine Fractures in Children: Evaluation, Management, and Future Directions. *J Knee Surg.* 2018.

2. Meyers MH, McKeever FM. Fracture of the intercondylar eminence of the tibia. *J Bone Joint Surg Am.* 1970.

3. Woo SL-YY, Hollis JM, Adams DJ *et al.* Tensile properties of the human femur-anterior cruciate ligament-tibia complex. *Am J Sports Med.* 1991.

4. Zaricznyj B. Avulsion fracture of the tibial eminence: treatment by open reduction and pinning. *J Bone Jt Surg - Ser A.* 1977.

5. Coyle C, Jagernauth S, Ramachandran M. Tibial eminence fractures in the paediatric population: A systematic review. *J Child Orthop.* 2014.

6. Baxter M, Wiley J. Fractures of the tibial spine in children. An evaluation of knee stability. *J Bone Joint Surg Br.* 2018.

7. Kendall N, Hsu S, Chan K. Fracture of the tibial spine in adults and children. A review of 31 cases. *J Bone Joint Surg Br.* 2018.

8. Willis RB, Blokker C, Stoll TM *et al.* Long-term follow-up of anterior tibial eminence fractures. *J Pediatr Orthop.* 1993.

9. Jayanthi N, Pinkham C, Dugas L *et al.* Sports Specialization in Young Athletes: Evidence-Based Recommendations. *Sports Health.* 2013.

10. Swenson DM, Collins CL, Best TM *et al.* Epidemiology of knee injuries among U.S. high school athletes, 2005/2006-2010/2011. *Med Sci Sports Exerc.* 2013.

11. Beck NA, Patel NM, Ganley TJ. The pediatric knee: Current concepts in sports medicine. *J Pediatr Orthop Part B.* 2014.

12. Axibal DP, Mitchell JJ, Mayo MH, *et al.* Epidemiology of Anterior Tibial Spine Fractures in Young Patients: A Retrospective Cohort Study of 122 Cases. *J Pediatr Orthop.* 2019.

13. Jackson TJ, Storey EP, Ganley TJ, Tibial Spine Interest Group. The Surgical Management of Tibial Spine Fractures in Children: A Survey of the Pediatric Orthopaedic Society of North America (POSNA). *J Pediatr Orthop.* 2017.

14. Ganley TJ, Brusalis CM. Surgical Reduction and Fixation of Tibial Spine Fractures in Children. *JBJS Essent Surg Tech.* 2016.

15. Gans I, Baldwin KD, Ganley TJ. Treatment and management outcomes of tibial eminence fractures in pediatric patients: A systematic review. *Am J Sports Med.* 2014.

Shoulder and Elbow Tips and Tricks: Loss of Elbow Flexion in Congenital Arthrogryposis Treated with a Bipolar Latissimus Transfer

Matthew Stein, MS, MD
Blair Ashley, MD
David Falk, MD
Daniel Gittings, MD
David Glaser, MD
Lawrence Scott Levin, MD, FACS

Department of Orthopaedic Surgery, University of Pennsylvania

Introduction

Arthrogryposis multiplex congenita is a rare disorder characterized by the presence of multiple congenital limb contractures. These contractures present most often as deficits in passive and active range of motion [ROM] with coexistent structural and/or functional abnormalities of surrounding soft tissue anatomy[1]. There are many etiologies for this presentation however the clinical presentation is the end product of decreased fetal movement leading to multiple joint contractures in utero with increased collagen proliferation, the fibrotic replacement of muscle and a marked thickening of joint capsules[2,3].

It has been reported in the literature previously that up to 72% of patients with arthrogryposis have upper extremity involvement with 25% of them involving the elbow. Other studies report a 59%–92% elbow involvement[3-5]. Of those with elbow involvement the most common presenting deformity is extension contracture of the elbow, absent skin creases and atrophy of the involved limb[1-5]. The elbow joint is thought to be the most critical for allowing the performance of activities of daily living which involve the upper extremity including self-feeding, self-care of the face and hair and independent toileting[6]. As such, restoration of biceps dysfunction is critical in improving the quality of life in arthrogrypotic patients with elbow involvement and decreased ability to care for themselves.

Though non-operative measures consisting of range of motion exercises and splinting are effective management for the majority of children when these measures fail there are several surgical techniques available to restore active elbow flexion in these patients[7]. Most discussed are the Steindler flexorplasty, a triceps-to-biceps transfer, pectoralis major transfer, and the latissimus dorsi transfer.

We chose to use a bipolar latissimus transfer as it has a large, mobile and robust vascular pedicle with minimal donor site morbidity. The purpose of this report is to present a case of a 20-year-old man with congenital arthrogryposis and elbow extension contracture treated with a bipolar latissimus transfer to restore active elbow flexion to the right upper extremity. 7 months out form surgery the patient achieved active ROM of the elbow up to 117 degrees and reports being pain-free a majority of the time.

Statement of Informed Consent

The patient presented in this report was informed that data concerning the case would be submitted for publication and provided consent.

Case Report

A 20-year-old male with congenital arthrogryposis presents to the office with right elbow flexion weakness 0/5. His wrists are bilaterally flexed and ulnar deviated with attendant restrictions in ROM. He had previously been able to use his left upper extremity for all self-care including washing hair, brushing teeth and shaving, but his ROM has regressed in that arm as well. His passive right elbow arc of rotation is from 0 to 110 degrees. An MRI of the right latissimus was obtained to determine its suitability for transfer. Results showed minimal intramuscular fat without significant muscular atrophy. To achieve active elbow range of motion the patient elected to perform a right upper extremity pedicle latissimus dorsi myocutaneous flap transfer.

The patient was placed in a lateral decubitus position. An oblique skin paddle was designed and then incised over the center of the right latissimus dorsi muscle. Skin and subcutaneous tissue were divided, and the anterior border of the latissimus was identified. The entire muscle was taken with dissection performed to its insertion on the humerus (Figure 1). The insertion was detached with the tendinous portion of the latissimus intact with the pedicle transfer. The circumflex scapular vessel and serratus branches were taken down to isolate the muscle on its neurovascular pedicle which included the thoracodorsal nerve, artery and vena comitans

Figure 1. Development of latissimus skin paddle and dissection.

(Figure 2). When the muscle was completely isolated a tunnel was placed between the posterior chest wall and the anterior axilla for the neurovascular pedicle. Checkpoint nerve stimulator was used to confirm intraoperative contraction.

A deltopectoral approach was then utilized proximally. Distally at the elbow a Z-incision was made to prevent contracture and allow exposure of the ulna. Proximally the conjoint tendon and proximal and distal aspects of the pectoralis major muscles were isolated. We tunneled underneath the pectoralis major staying close to its insertion point to identify the remnant long head of the biceps tendon. The tendinous portion of the latissimus was placed through this tunnel with capacious space ensuring no pressure would be put on the pedicle as it came anterior to the chest wall. Distally the best location for the transfer was identified to be laterally at the subcutaneous border of the ulna. Suture anchors were placed in the ulna for distal attachment. The proximal portion of the tendon was reattached to the tip of the coracoid with a suture anchor (Figure 3). This anchor was then double loaded, and the tendon was reefed back onto the tip of the coracoid for a second attachment. It was reinforced with additional sutures sewn along the conjoint tendon and the graft allowing for multiple points of fixation.

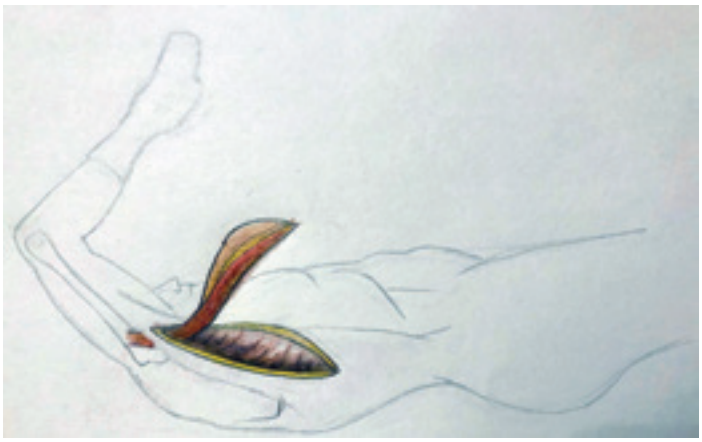


Figure 2. Latissimus isolated on its neurovascular pedicle; tunnel development.

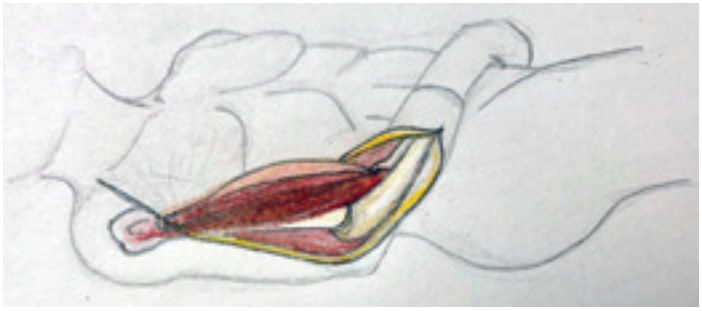


Figure 3. Distal attachments to ulna, proximal attachments to coracoid.

Figure 4. Closure of extended deltopectoral and distal z-shaped incisions.

The latissimus had been marked in-situ 5 cm apart to create proper tensioning. This was recreated when the muscle was transferred anteriorly. Extended deltopectoral approach and distal z-shaped incisions were closed (Figure 4).

The patient was taking to the intensive care unit for flap monitoring with his right upper extremity immobilized in a posterior slab at 90 degrees of flexion. At his post-operative day two visit the flap was warm, and well-perfused with grossly intact elbow flexion. For the first four weeks only passive ROM from 90-130 degrees was permitted at which point active physical therapy began. At approximately three weeks post-op the patient developed a mild cellulitis at the donor site which resolved without issue with oral antibiotics. By three months post-op the patient was able to volitionally flex the right elbow.

At most recent follow-up 7 months post-op the patient was able to achieve full elbow extension and 117 degrees of active flexion. Passive ROM was up to 130 degrees. On the Manual Muscle Testing Grading system his strength in the right upper extremity was 4-/5 in flexion.

References

1. Kowalczyk B, Feluś J. Arthrogryposis: an update on clinical aspects, etiology, and treatment strategies. *Arch Med Sci.* 2016;12(1):10-24. doi:10.5114/aoms.2016.57578.

2. Wiesel BB. *Orthopedic Surgery : Principles of Diagnosis and Treatment.* Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011.

3. Bevan WP, Hall JG, Bamshad M, *et al.* Arthrogryposis multiplex congenita (amyoplasia): an orthopaedic perspective. *J Pediatr Orthop.* 2007;27(5):594-600. doi:10.1097/BPO.0b013e318070cc76.

4. Gibson DA, Urs ND. Arthrogryposis multiplex congenita. *J Bone Joint Surg Br.* 1970;52(3):483-493. http://www.ncbi.nlm.nih.gov/pubmed/5455080. Accessed March 12, 2019.

5. Lloyd-Roberts GC, Lettin AWF. ARTHROGRYPOSIS MULTIPLEX CONGENITA. *J Bone Joint Surg Br.* 1970;52-B(3):494-508. doi:10.1302/0301-620X.52B3.494.

6. Miller, R, Sawatzky, B. Outcomes at 2-Year Minimum Follow Up of Shoulder, Elbow and Wrist Surgery in Individuals with Arthrogryposis Multiplex Congenita. *J Clin Exp Orthop.* 2017;03(01). doi:10.4172/2471-8416.100028.

7. Staheli LT. *Arthrogryposis : A Text Atlas.* Cambridge University Press; 1998. https://books.google.com/books/about/Arthrogryposis.html?id=I3KPVwhDgDgC. Accessed March 14, 2019.

Localized Delivery of Ibuprofen via a Bilayer Delivery System (BiLDS) for Supraspinatus Tendon Healing in a Rat Model

Brittany L. Taylor[1,2]
Dong Hwa Kim[1,2]
Julianne Huegel[1,2]
Sophie J. Burkholder[1]
Stephanie N. Weiss[1,2]
Courtney A. Nuss[1,2]
Harina A. Raja[1,2]
Louis J. Soslowsky[1,2]
Robert L. Mauck[1,2]
Andrew F. Kuntz[1,2]
Joseph Bernstein[1,2]

1 Philadelphia VA Medical Center, Philadelphia, PA

2 McKay Orthopaedic Research Laboratory, University of Pennsylvania, Philadelphia, PA

Introduction

The high prevalence of tendon re-tear following rotator cuff repair motivates the development of new therapeutics to promote improved tendon healing. Controlled delivery of non-steroidal anti-inflammatory drugs (NSAIDs) to the repair site via an implanted scaffold is a promising option for modulating inflammation in the healing environment. Previous work confirmed the *in vitro* sustained release of ibuprofen (IBP) from Labrafil- modified poly(lactic-co-glycolic) acid (PLGA) microspheres within sintered poly(ε-caprolactone) (PCL) electrospun scaffolds[1]. Biocompatibility of this bilayer delivery system (BiLDS) was also demonstrated with primary rat bicep and Achilles tenocytes *in vitro*[1,2]. However, the effect of these IBP- releasing BiLDS on tendon healing *in vivo* is unknown. Therefore, the objective of this study was to investigate the effects of sustained release of IBP from BiLDS implanted at the repair site in a rat supraspinatus injury and repair model. We hypothesized that the controlled release of IBP from BiLDS would improve tendon healing by decreasing the expression of pro-inflammatory cytokines, thus improving tendon remodeling and mechanics.

Methods

BiLDS Fabrication

PLGA microspheres with 300μL of Labrafil® M1944CS oil and with or without 30mg/mL of IBP were created as described[1]. 170μg of the microspheres, with or without IBP, were entrapped between two sintered 3x5mm scaffolds to generate BiLDS_IBP or BiLDS implants, respectively. Based on *in vitro* release studies, we predicted that the100μm thick BiLDS would deliver approximately 270μg of IBP to the injury site over 8 weeks. *BiLDS In Vivo Implantation*: 90 adult male Sprague-Dawley rats (400-450g) underwent bilateral supraspinatus detachment and repair (IACUC approved)[3]. Animals were randomly divided into groups receiving no scaffold (No_BiLDS), BiLDS with empty microspheres (BiLDS), and BiLDS with IBP-loaded microspheres (BiLDS_IBP) (n=30/group). BiLDS were secured proximally to the tendon via sutures and distally to the bone tunnel drilled through the greater tuberosity. Animals were sacrificed at 1, 4, and 8 weeks post-surgery. The right supraspinatus tendons and blood serum were collected at the time of sacrifice for biological assessment.

Biological Assessment

Sagittal sections were stained with H&E, imaged at 20X and graded for cell shape and cellularity (n = 6/group/timepoint). RNA was extracted from tendons harvested one week post-surgery (n = 6/group) and qRT-PCR was run in quadruplicate using TaqMan assays on a QuantStudio 12K Flex Real-Time PCR System[4]. Genes of interest included markers of inflammation (TNF-α IL-1b, IL- 6, and IL-10, Prostaglandin E2, CD68, CD163, and CD45), tendon repair (TGF-β1, TGF-β3, and VEGFb) and tendon remodeling (COL I, III, and IV, MMPs −2, −3, −8 and −10, tenascin, tenomodulin, and aggrecan). Expression was normalized to the internal control (GAPDH) and fold change was calculated by normalizing treatment groups to the untreated control, No_BiLDS. ELISA for TNF-α and IL-6 was performed on protein isolates from the excised tendons and for IBP in serum samples collected at 4 and 8 weeks (n = 6/group/timepoint).

Tensile Mechanical Testing

The cross-sectional area of the left intact supraspinatus tendons from animals sacrificed at 4 and 8 weeks (n = 12/group/timepoint) was measured using a custom laser device. Ex vivo tensile testing was performed as follows: preload, preconditioning, stress relaxation, and ramp to failure. Modulus, stiffness, maximum load, and maximum stress were computed.

Statistics

Two-way ANOVA and normality tests were performed on all datasets. To compare between groups at each timepoint, one-way ANOVA or Kruskall-Wallis tests were performed, depending on normality. To compare over time within each treatment group, Welch's t-tests or Mann-Whitney U tests were performed. Significance was set at $p < 0.05$ (*); ** denotes $p < 0.01$ and ***denotes $p < 0.001$.

RESULTS

There were no statistically significant differences in cell shape, cellularity, and

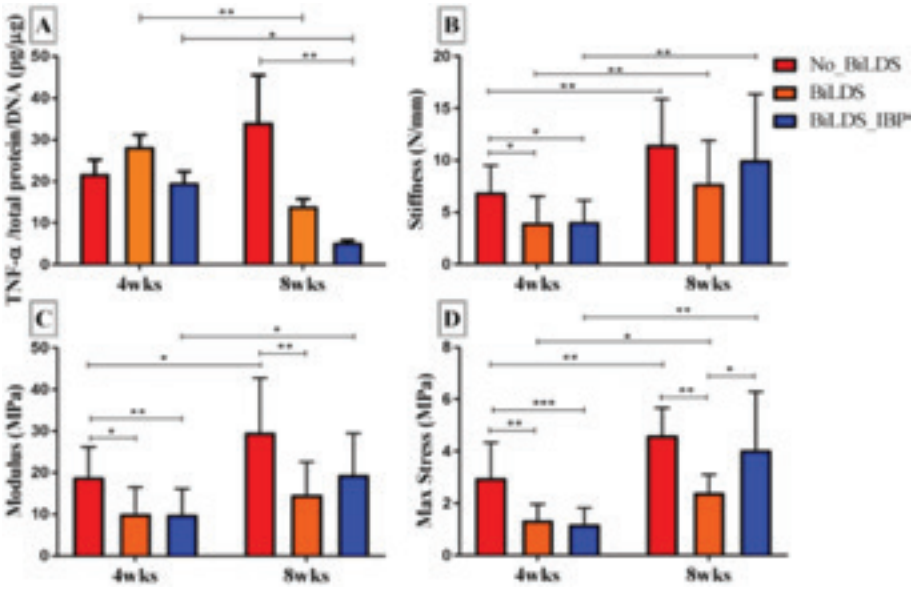


Figure 1. (A) Treated tendons BiLDS and BiLDS_IBP, significantly decreased in cytokine expression of TNF-a overtime and IBP-treated tendons expressed significantly less TNF-a than the untreated tendons, No_BiLDS, at 8 weeks. The untreated tendons No_BiLDS, exhibited significantly greater **(B)** stiffness, **(C)** modulus, and **(D)** maximum stress at 4 weeks in comparison to the treated tendons, BiLDS and BiLDS_IBP. Data presented as mean ± SD. (*$p < 0.0$, **$p < 0.01$ ***$p < 0.001$)

expression of tendon healing genes or IL-6 cytokine expression between the treatment groups at each timepoint (data not shown). IBP was undetectable in the serum of all animals at 4 and 8 weeks (data not shown). Tendons treated with BiLDS_IBP expressed significantly less TNF-α compared to untreated tendons, No_BiLDS, at 8 weeks and both BiLDS groups decreased in TNF-α at the protein level over time (Figure 1A). Stiffness, modulus, maximum stress, and maximum load of the untreated tendons (No_BiLDS) were significantly greater than in either of the treated groups, BiLDS and BiLDS_IBP, at 4 weeks (Figure 1B-D). Stiffness, maximum stress, and maximum load increased for all groups over time (Figure 1B & 2D). Modulus and maximum stress of the treated tendons in the BiLDS group were lower in comparison to the No_BiLDS group at 8 weeks, but there were no differences in these parameters between the No_BiLDS and BiLDS_IBP groups at 8 weeks (Figure 1C & 1D). There were no significant differences in stiffness (Figure 1B) and maximum load at 8 weeks or in tendon cross-sectional area at either 4 or 8 weeks (data not shown).

Discussion

Although the use of BiLDS and BiLDS_IBP was not therapeutically beneficial for rat rotator cuff healing in terms of mechanics, the release of IBP from BiLDS significantly decreased pro-inflammatory signaling in the late healing phase. There were no substantial changes in gene expression 1 week post-repair with either treatment (BiLDS or BiLDS_IBP) compared to standard surgical repair (No_BiLDS). Therefore, we are unable to conclude the biological effect of the BiLDS with and without IBP on tendon repair at this time. Further investigation is ongoing to evaluate additional tendon healing markers at the protein level up to 8 weeks post-repair. Mechanical testing results indicated both BiLDS and BiLDS_IBP were detrimental to tendon mechanics compared to surgical repair alone, especially at early timepoints. Previous work revealed no significant differences in structural properties after surgical repair with and without the implantation of a single layered PCL scaffold in a rat rotator cuff injury and repair model[5]. Therefore, the decreased mechanics seen with the use of BiLDS in this study may be due to the increased size of the BiLDS compared to a single-layer PCL scaffold. Implanting a substantially thicker scaffold into the tight subacromial space in the rat shoulder may have caused supraspinatus impingement and negatively affected early tendon healing. Despite this, the BiLDS and BiLDS_IBP constructs remained intact, led to decreased pro-inflammatory expression over time, and recovered the tendon structural properties by 8 weeks. Future studies are required to elucidate the effect of the BiLDS and BiLDS_IBP on tendon mechanics at later timepoints and in larger defects in which supplementation with a scaffold may be necessary to stabilize repair.

Significance

This study investigates a biocompatible nanofibrous bilayer delivery system (BiLDS) for localized delivery of ibuprofen to mitigate inflammation in a rat rotator cuff repair model. Further evaluation is necessary to elucidate the beneficial effects of the system in a larger animal model.

References

1. Taylor BL, Kim DH, Riggin CN, *et al.* *Prolonged Release of Ibuprofen from a Nanofibrous Delivery System Under Physiological Conditions.* Poster presented at the Orthopaedic Research Society Annual Meeting, New Orleans, LA.

2. Kim DH, Huegel J, Nuss CA, *et al.* (March 2018). *Biocompatibility and Bioactivity of an FGF-Loaded Microsphere-Based Bilayer Delivery System.* Poster presented at the Orthopaedic Research Society Annual Meeting, New Orleans, LA.

3. Huegel, J, Kim DH, Cirone JM, *et al.* Autologous tendon-derived cell-seeded nanofibrous scaffolds improve rotator cuff repair in an age-dependent fashion. *J Orthop Res.*2016;35:1250-1257.

4. Reno C, Marchuk L, Sciore P, *et al.* Rapid Isolation of Total RNA form Small Samples of Hypocellular, Dense Connective Tissues. *BioTechniques.* 1997;22:1082-1086.

5. Beason DP, Connizzo BK, Dourte LM, *et al.* Fiber-aligned polymer scaffolds for rotator cuff repair in a rat model. *J Shoulder Elbow Surg.* 2012; 21:245-250.

Reproduction and Lactation Lead to Long-Term Changes in Supraspinatus Tendon and Humeral Trabecular Bone Properties in a Rat Model

Ashley K. Fung
Yihan Li
Thomas P. Leahy
Snehal S. Shetye
X. Sherry Liu
Louis J. Soslowsky

McKay Orthopaedic Research Laboratory, University of Pennsylvania, Philadelphia, PA

Introduction

Physiological changes due to pregnancy increase the risk of developing musculoskeletal complications such as shoulder, lower back, and knee pain[1].Altered levels of estrogen and relaxin during pregnancy increase knee joint and ligament laxity, compromising joint function, and these changes persist years after pregnancy[2]. Further, tibial and lumbar vertebral trabecular bone structure in reproductive female rats has been shown to be inferior compared to virgins but not different when compared to male, suggesting that reproduction and lactation induce bone loss that is not fully recovered post-weaning[3]. However, the long-term effects of reproduction on tendons and bones of the shoulder have not yet been studied. Therefore, the objective of this study was to evaluate the supraspinatus tendon mechanical response and humeral trabecular bone properties of male, virgin female, and reproductive female rats. We hypothesized that reproduction and lactation would induce long-term changes leading to inferior supraspinatus tendon properties and humeral trabecular bone microstructure in reproductive females as compared to virgin females.

Methods

20 Sprague-Dawley rats (IACUC approved) across three groups were used in this study: male (n = 9), virgin female (n = 6) and reproductive female (n = 5). At age 6 months, reproductive female rats underwent two reproductive cycles, each consisting of a 3-week pregnancy, 3 weeks of lactation, and 6 weeks of post-weaning recovery. Rats were sacrificed at 12-14 months of age, and shoulders were harvested for supraspinatus tendon mechanical testing and trabecular bone analysis. *Mechanics:* Supraspinatus tendons were fine dissected and marked with stain lines for optical strain tracking. Cross-sectional area was measured using a custom laser device, and humeri were secured in polymethyl methacrylate. Right supraspinatus tendons underwent quasi-static tensile testing, consisting of pre-conditioning, stress relaxation at a 5% strain hold for 600s, a dynamic frequency sweep at 5% strain (0.1-10Hz), and ramp to failure at rate of 0.3%/s. Left supraspinatus tendons underwent fatigue testing, consisting of pre-conditioning and fatigue loading until failure at 2Hz between loads corresponding to 7% and 40% maximum stress, as determined from quasi-static testing. Fatigue parameters, including peak cyclic strain, secant modulus, tangent modulus, hysteresis, and laxity, were recorded at two breakpoints marking the ends of the primary (BP1) and secondary (BP2) phases of a triphasic fatigue life curve. *Trabecular bone analysis:* Left proximal humeri were scanned using μCT (10.5μm, μCT35, Scanco Medical). A 100-slice volume of interest proximal to the humeral growth plate was identified for trabecular bone microstructure analysis. *Statistics:* Comparisons across groups were made using one-way ANOVAs with Bonferroni post-hoc corrections. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

Male tendons exhibited significantly higher stiffness compared to virgin and reproductive female tendons (Figure 1A). However, reproductive females had significantly lower

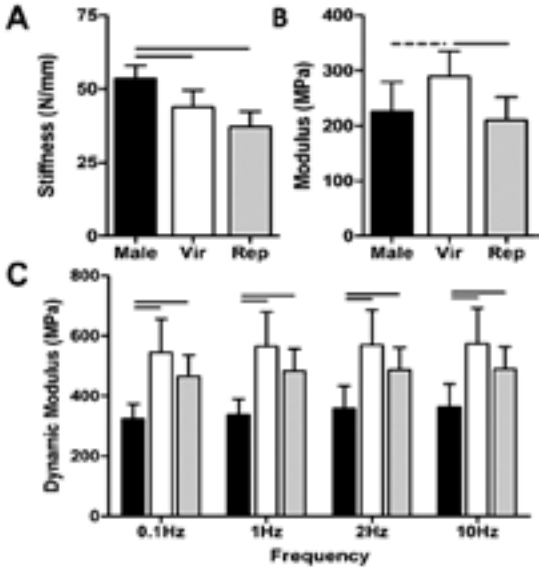


Figure 1. (A) Males had higher stiffness, while virgin females had increased (B) linear modulus and (C) dynamic modulus. Solid lines denote significance at $p \leq 0.05$ and dashed lines denote trends at $p \leq 0.1$.

modulus compared to virgin females but no difference compared to males (Figure 1B). Males had significantly lower dynamic modulus for all frequencies compared to both female groups (Figure 1C) but no difference in percent relaxation or tan(δ) (not shown). For fatigue properties at BP1, virgin females had significantly higher tangent and secant modulus compared to males and trended towards increasing compared to reproductive females (Figure 2A). However, there were no differences in secant or tangent modulus at BP2. No differences in hysteresis were observed at BP1, but reproductive females had significantly increased hysteresis compared to males at BP2 (Figure 2B). Cycles to failure and peak cyclic strain at BP1 was significantly higher in males compared to both female groups, and there were no differences in laxity at either breakpoint (not shown). Additionally, trabecular bone analysis revealed reduced bone volume fraction (BV/TV) and trabecular number (Tb.N) in reproductive females compared to virgin females but no difference compared to males (Figure 3A,B). Trabecular separation (Tb.Sp) in reproductive females was significantly increased compared to virgin females but trended towards a decrease when compared to males (Figure 3C). While trabecular thickness (Tb.Th) was significantly higher in males, there was no difference between female groups (not shown).

Discussion

This study identified substantial differences in supraspinatus tendon and proximal humerus trabecular bone properties based on sex and reproductive history. Proximal humerus bone microstructure was superior in virgin females, consistent with previous findings in the tibia and vertebra. Previous research has linked ovariectomy to decreased failure stress of rotator cuff tendons and a less pronounced tidemark at the enthesis[4,5], and a similar mechanism may govern irrecoverable reproductive bone loss. Fatigue results also indicate that virgin and reproductive females experience a greater reduction in moduli and capacity to store energy, respectively, and together, these results suggest that females, regardless of reproductive history, may be more susceptible to early tendon degeneration. During pregnancy, hormonal fluctuations induce increased pelvic ligament laxity in preparation for parturition. Though the mechanisms are still unclear, several clinical studies have found sustained biomechanical changes in these ligaments despite a return to pre-pregnancy hormone levels[6,7]. Therefore, supraspinatus tendons following reproduction may be synergistically influenced by a direct effect of hormone changes and an indirect effect of bone loss near the insertion site. Shoulder pain after pregnancy has been associated with frequent breastfeeding that places added stress on the upper extremities. However, these findings suggest that biological changes during reproduction may inherently increase the risk for rotator cuff injury. Future studies will explore transient changes during pregnancy and investigate the mechanisms underlying long-term changes in tendon and bone properties following reproduction.

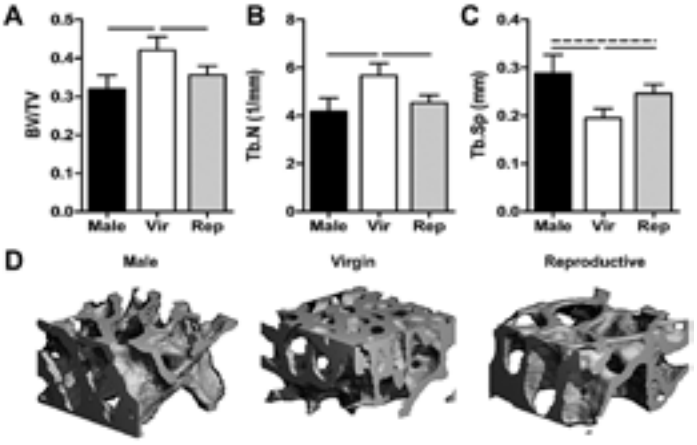


Figure 3. Virgin rats exhibited (A) higher bone volume fraction, (B) higher trabecular number, and (C) lower trabecular spacing compared to male and reproductive rats. Solid lines denote significance at $p \leq 0.05$ and dashed lines denote trends at $p \leq 0.1$. (D) Representative 3D humeral trabecular bone images.

Significance

This study identifies long-term changes in supraspinatus tendon and humeral trabecular bone properties that result following pregnancy and lactation, highlighting the importance of considering reproductive history in the diagnosis and treatment of shoulder injuries.

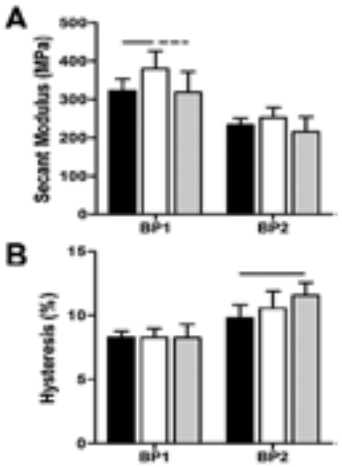


Figure 2. (A) Secant modulus was higher in the virgin group at BP1 and (B) reproductive females had increased hysteresis compared to males at BP2.

References

1. Koyasu K, Kinkawa M, Ueyama N, *et al.* The prevalence of primary neck and shoulder pain, and its related factors in Japanese postpartum women. *Clin Exp Obstet Gynecol.* 2015;42(1):5-10.

2. Chu SR, Boyer EH, Beynnon B, *et al.* Pregnancy Results in Lasting Changes in Knee Joint Laxity. *PM R.* 2019;11(2):117-124.

3. de Bakker CMJ, Zhao H, Tseng WJ, *et al.* Effects of reproduction on sexual dimorphisms in rat bone mechanics. *J Biomech.* 2018;77:40-47.

4. Cadet ER, Vorys GC, Rahman R, *et al.* Improving bone density at the rotator cuff footprint increases supraspinatus tendon failure stress in a rat model. *J Orthop Res.* 2010;28(3):308-14.

5. Chen X, Giambini H, Ben-Abraham E, *et al.* Effect of Bone Mineral Density on Rotator Cuff Tear: An Osteoporotic Rabbit Model. *PLoS One.* 2015;10(10):e0139384.

6. Segal NA, Boyer ER, Teran-Yengle P, *et al.* Pregnancy leads to lasting changes in foot structure. *Am J Phys Med Rehabil.* 2013;92(3):232-40.

7. Damen L, Buyruk HM, Güler-Uysal F, *et al.* The prognostic value of asymmetric laxity of the sacroiliac joints in pregnancy-related pelvic pain. *Spine.* 2002;27(24):2820-4.

U·P·O·J

Arthroplasty Tips and Tricks: Short-Stay Total Joint Arthroplasty—The Way Forward?

Joseph Koressel, MD
Neil P. Sheth, MD

Department of Orthopaedic Surgery, University of Pennsylvania

Introduction

Over the past several years there has been increased enthusiasm for performing short-stay (<23 hour stay) total joint arthroplasty (TJA). Inpatient length of stay (LOS) following total knee arthroplasty (TKA) has decreased from almost 8 days to 3 days over the past few decades[1,2]. The advent of dedicated TJA protocols and pathways has optimized peri-operative management and has enabled patients to be discharged home with adequate pain control and improved function. Short stay TJA, including both TKA and total hip arthroplasty (THA), has been found to be safe in observational studies when adhering to strict patient selection criteria[3–5]. As medical costs continue to rise and the concept of home rehabilitation after TJA becomes more commonplace, the future may hold a place for same day TJA in select patients.

Costs and Benefits

The cost of healthcare continues to be a major focus among both the public and private healthcare sectors. According to the Centers for Medicare and Medicaid Services, the average Medicare costs for TJA, inclusive of surgery, hospitalization, and 90-day post-operative period, is between $16,500 and $33,000. One area of successful cost containment has been in the arena of decreasing inpatient LOS. Compared to patients that were discharged within 3-4 days following TKA, patients discharged within 2 days and 1 day had lower costs of $1,967 and $8,527, respectively. However, as rapid recovery protocols for short-stay TJA continue to improve, there is cost associated with increased ancillary staff required to ensure patient safety throughout the process[6]

Another critical consideration is that short-stay TJA may result in improved patient satisfaction. After being educated on the procedure and post-operative rehabilitation, patients indicate a preference for recovery at home rather than in the hospital or rehab facility[3]. This preference has been validated post-operatively, as patient satisfaction has been recorded to be higher following same day discharge TJA[5].

Risks

Short-stay TJA programs should be approached with caution as there is a potential for increased post-operative complications[7,8]. The trend of decreased LOS has been coupled with increased all cause 30-day readmission rates following TKA[1]. However, recent studies suggest that short-stay TJA is not associated with an increase readmission rate, acute office visits, emergency department visits, and complications when compared to inpatient TJA[8–11].

One study suggests that Medicare patients (> 65 years of age) who underwent a short stay TJA (< 23 hours) had fewer complications (2%) when compared to same day discharge (8%) and inpatient stay (8%) TJA. This suggests that short stays may be ideal particularly for older patients[12], regardless, patient selection is critical in determining which patients should be considered candidates.

Risk Assessment and Patient Selection

The key to successful and safe short-stay TJA is the implementation of a systematic and structured pre-operative evaluation process which identifies appropriate patients. Several risk assessment tools have been used to reproducibly identify these patients[13]. Courtney et al. retrospectively identified complications that occurred in 1,012 consecutive patients who underwent TJA that stayed > 24 hours post-operatively. The study found that COPD (OR 4.16), CAD (OR 2.80), CHF (OR 9.71), and cirrhosis (OR 8.43) were significant risk factors for a post-operative complication, and having just one of these comorbidities led to a 10% risk of late complication, compared to 3.1% in the absence of one of these comorbidities. A point system was subsequently created to determine the risk of late complication in patients undergoing TJA (Table 1)[14].

This demonstrates that a multi-disciplinary approach and pre-operative risk assessment are needed to properly screen and risk stratify patients that may safely benefit from short-stay TJA.

Implementation

Strict pre, peri, and post-operative protocols should be in place and closely followed to ensure safety and provide patients with the ability to recover quickly in the hospital and rehabilitate at home. Multimodal pain protocols, preemptive anti-nausea treatment, physical

Table 1: Short Stay TJA Risk Score

Risk Factor	Score
CHF	2
Cirrhosis	2
COPD	1
CAD	1

therapy, education, and discharge planning have been observed to aid in reducing the LOS following TKA[15]. Prior to hospital discharge, patients must complete physical therapy and successfully transfer from bed to standing, rise from a chair to standing, walk 100 feet, and negotiate one flight of stairs. Patients must also have stable vital signs, tolerate a regular diet, receive adequate pain control with oral medications, and most importantly, feel comfortable going home[5]. Regardless, a short-stay TJA program must be based on a clearly defined and regimented process for patients to follow in order to assure the desired clinical outcome (Table 2).

The Patient Perspective

Establishing a short-stay TJA practice is logistically complicated, and the patient is the most integral key to success. Patient expectations must be set pre-operatively and reinforced in the post-operative period. Through information, clearly defined expectations, and continued encouragement, patients feel more autonomous in their decision making and are better equipped to tackle the challenges encountered in the early post-operative period. Most importantly, patients must feel safe and comfortable to rehabilitate at home and have appropriate social support to be able to do so. It is imperative that interventions be in place in the pre-hospital setting, inpatient, and home following discharge to provide patient education and reassurance.

Providing an encouraging environment for the patient can be challenging when hospital staff are not familiar with short-stay TJA. Many nurses, pharmacists, social workers, and case managers are very familiar with standard inpatient TJA, and my inadvertently inform the patient that patients typically "need" at least 2 night in the hospital. This sends mixed messages to the patient who is now more likely stay in the

Table 2. Peri-operative Protocol for Outpatient THA, Adapted from Berger et al.5

	Planning	Safety	Pain/nausea	Rehabilitation
Pre-op	Meeting with hospital discharge planner	Internist evaluation, 2 units packed red blood cells donated for future autologous transfusion		Nurse taught class (reassurance and expectations), Physical therapy session
Morning prior to Surgery			400 mg celecoxib, 10 mg OxyContin, Epidural	
Intra-op		Prophylactic antibiotics, 1 unit autologous packed red blood cell transfusion	4 mg ondansetron, 10 mg metoclopramide	Propofol for minimal sedation, Foley catheter
Recovery		1 unit autologous packed red blood cell transfusion	Epidural continued until 4 hours post-op, 4 mg ondansetron	
Pre-op	Meeting with hospital discharge planner	Internist evaluation, 2 units packed red blood cells donated for future autologous transfusion		Nurse taught class (reassurance and expectations), Physical therapy session
Morning prior to Surgery			400 mg celecoxib, 10 mg OxyContin, Epidural	
Intra-op		Prophylactic antibiotics, 1 unit autologous packed red blood cell transfusion	4 mg ondansetron, 10 mg metoclopramide	Propofol for minimal sedation, Foley catheter
Recovery		1 unit autologous packed red blood cell transfusion	Epidural continued until 4 hours post-op, 4 mg ondansetron	
2 hours post-op			20 mg OxyContin, Norco for breakthrough pain	Foley discontinued
5-6 hours post-op		Prophylactic antibiotics		Physical therapy and occupational therapy evaluation
Discharge		325 mg aspirin twice daily for 3 weeks	200 mg celecoxib, OxyContin, Hydrocodone	Home physical therapy

hospital. When the entire medical team is familiar with the process of short-stay TJA, and "speak" the same language, the patient's desire to move forward with rehabilitation at home is reinforced at every step of the episode of care. Experience with short-stay TJA and staff education are equally as important as patient education in standardizing patient expectations.

References

1. Cram P, Lu X, Kates SL, *et al.* Total Knee Arthroplasty Volume, Utilization, and outcomes Among Medicare Beneficiaries 1991-2010. *JAMA 2012; 308: 1227.*

2. Hunt GR, Crealey G, Murthy BV, *et al.* The consequences of early discharge after hip arthroplasty for patient outcomes and health care costs: comparison of three centres with differing durations of stay. *Clin Rehabil 2009; 23: 1067-77.*

3. Berger RA, Sanders S, Gerlinger T, *et al.* Outpatient Total Knee Arthroplasty With a Minimally Invasive Technique. *J Arthroplasty 2005; 20: 33-8.*

4. Dorr LD, Thomas DJ, Zhu J, *et al.* Outpatient Total Hip Arthroplasty. *J Arthroplasty 2010; 25: 501-6.* Newer Anesthesia and Rehabilitation Protocols Enable Outpatient Hip Replacement in Selected Patients. *Clin Orthop Relat Res 2009; 467: 1424-30.*

5. Berger RA, Sanders SA, Thill ES, *et al.* Newer Anesthesia and Rehabilitation Protocols Enable Outpatient Hip Replacement in Selected Patients. *Clin Orthop Relat Res 2009; 467:1424–30.*

6. Sah A. Considerations for Office and Staff Protocols for Outpatient Joint Replacement. *J Arthroplasty 2019.*

7. Otero JE, Gholson JJ, Pugely AJ, *et al.* Length of Hospitalization After Joint Arthroplasty: Does Early Discharge Affect Complications and Readmission Rates? *J Arthroplasty 2016; 31:2714–25.*

8. Lovecchio F, Alvi H, Sahota S, *et al.* Is Outpatient Arthroplasty as Safe as Fast-Track Inpatient Arthroplasty? A Propensity Score Matched Analysis. *J Arthroplasty 2016;31:197–201.*

9. Goyal N, Chen AF, Padgett SE, *et al.* Otto Aufranc Award: A Multicenter, Randomized Study of Outpatient versus Inpatient Total Hip Arthroplasty. *Clin Orthop Relat Res 2017;475:364–72.*

10. Sutton JC, Antoniou J, Epure LM, et al. Hospital Discharge within 2 Days Following Total Hip or Knee Arthroplasty Does Not Increase Major-Complication and Readmission Rates. *J Bone Jt Surg 2016;98:1419–28.*

11. Courtney PM, Boniello AJ, Berger RA. Complications Following Outpatient Total Joint Arthroplasty: An Analysis of a National Database. *J Arthroplasty 2017;32:1426–30.*

12. Courtney PM, Froimson MI, Meneghini RM, *et al.* Can Total Knee Arthroplasty Be Performed Safely as an Outpatient in the Medicare Population? *J Arthroplasty 2018;33:S28–31.*

13. Meneghini RM, Ziemba-Davis M, Ishmael MK, *et al.* Arthroplasty Be Performed Safely as an Outpatient in the Medicare Population? *J Arthroplasty 2018;33:S28–31.*

14. Courtney PM, Rozell JC, Melnic CM, *et al.* Who Should Not Undergo Short Stay Hip and Knee Arthroplasty? Risk Factors Associated With Major Medical Complications Following Primary Total Joint Arthroplasty. *J Arthroplasty 2015;30:1–4.*

15. Ayalon O, Liu S, Flics S, *et al.* A Multimodal Clinical Pathway Can Reduce Length of Stay After Total Knee Arthroplasty. *HSS J 2011;7:9–15.*

Traumatic Arthritis Increases Total Knee Arthroplasty Complication Rates

Chelsea Hendow, MD, MS
Matthew Sloan, MD, MS
Neil P. Sheth, MD

Department of Orthopaedic Surgery, University of Pennsylvania

Background

Total knee arthroplasty (TKA) is one of the most common elective surgical procedures in the United States. TKA has proven successful in treating primary osteoarthritis (OA), but less is known about complications following surgery for post-traumatic arthritis (PTA). The aim of this study is to assess postoperative complication rates after TKA performed for PTA compared with primary OA.

Methods

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database from 2008 to 2016 was queried. Patients were identified using the CPT code for TKA and the diagnosis codes for primary OA and PTA. Univariate and bivariate statistics were performed. Multivariate and propensity-matched logistic regression analyses were performed.

Table 1. Comparison of continuous variables among the primary TKA population.

	TKA for Osteoarthritis			TKA for Post-traumatic arthritis			P Value*
	OA TKA, n	Mean ± SD	95% CI	PTA TKA, n	Mean ± SD	95% CI	
Operative time, min	217,110	92.7 ± 37.21	92.55 – 92.86	1,712	113.7 ± 46.11	111.51 - 1115.88	<0.0001
Age, years	216,110	66.73 ± 9.49	66.69 – 66.77	1,711	59.3 ± 10.68	58.79 - 59.81	<0.0001
LOS, days	215,390	3 ± 3.21	2.99 – 3.01	1,698	2.83 ± 2.89	2.69 - 2.96	0.027
BMI, kg/m^2	216,449	33.05 ± 6.98	33.03 – 33.08	1,710	31.48 ± 6.6	31.16 - 31.79	<0.0001

*P value represents t-test value comparing post-traumatic arthritis with osteoarthritis control group. (LOS = Length of Stay, BMI = Body Mass Index).

Table 2. Univariate analyses of primary TKA postoperative complications and secondary outcomes.

	Overall (n [%])	OA TKA (n [%])	PTA TKA (n [%])	P Value*
Death or serious morbidity	17,750 (8.38)	17,614 (8.39)	136 (8.09)	0.659
Death	233 (0.11)	232 (0.11)	1 (0.06)	0.540
Serious morbidity	17,690 (8.35)	17,554 (8.36)	136 (8.09)	0.689
Surgical site infection	15 (0.01)	15 (0.01)	0 (0)	0.728
Respiratory	339 (0.15)	337 (0.16)	2 (0.12)	0.687
Cardiac	3,740 (1.71)	3,710 (1.71)	30 (1.75)	0.890
Bleeding (requiring transfusion)	14,066 (6.43)	13,957 (6.43)	109 (6.37)	0.918
Sepsis	441 (0.20)	437 (0.20)	4 (0.23)	0.766
Long operative time (1 SD > Mean)	26,703 (12.2)	26,225 (12.08)	478 (27.92)	<0.001
Total length of stay > 5 days	16,034 (7.33)	15,909 (7.33)	125 (7.3)	0.968
Discharged to home	152,126 (74.3)	150,760 (74.23)	1,366 (83.24)	<0.001
Readmission within 30 days	6,824 (3.37)	6,752 (3.36)	72 (4.39)	0.021
Required reoperation	2,400 (1.17)	2,356 (1.16)	44 (2.68)	<0.001

*P value represents Chi-square value comparing post-traumatic arthritis group with the osteoarthritis control group.

Table 3. Summary of propensity-matched logistic regression of postoperative complications and secondary outcomes.

	OR	95% CI	P Value*
Death or serious morbidity	1.05	0.80 – 1.36	0.738
Death	1.00	0.06 – 16.00	1.000
Serious morbidity	1.04	0.80 – 1.36	0.738
Length of stay > 5 days	1.44	1.05 – 1.98	0.022
Reoperation	2.63	1.47 – 4.71	0.001
Readmission	1.52	1.04 – 2.23	0.031
Discharge home	1.29	1.08 – 1.56	0.006

*P value represents propensity score-matched logistic regression analysis comparing post-traumatic arthritis group with osteoarthritis control group.

Results

Analyses included 218,838 patients undergoing TKA. TKA for OA comprised 217,126 (99.2%) cases, while 1,712 (0.78%) TKA cases for PTA were identified. Propensity matching identified 1,516 OA and PTA patient pairs. Mean operative time in the PTA group was 114 minutes, compared with 93 minutes in the OA group. Patients in the PTA group were significantly younger (59.3 years) than OA patients (66.7 years) and had lower body mass index (BMI) (31.5 vs. 33.1 kg/m^2). Propensity-matched analysis demonstrated 2.5-times increased risk of reoperation, 52% increased risk for readmission, and 29% increased likelihood of discharge to home postoperatively for PTA compared with OA patients. There was no significant difference in death within 30 days or medical morbidity between groups.

Conclusion

Compared with primary OA patients, PTA patients undergoing TKA are much more likely to have a prolonged operative time, and require reoperation or readmission within 30 days. They are not at increased risk of death within 30 days or major medical morbidity. Surgeons should perform adequate preoperative planning to minimize need for these complications, and counsel PTA patients on these risks.

Albumin as a Predictor of Total Joint Arthroplasty Complications: A Systematic Review

Chukwuemeka Mbagwu, BS[1]
Matthew Sloan, MD, MS[2]
Alexander L. Neuwirth MD[2]
Keith D. Baldwin MD, MSPT, MPH[2]
Atul F. Kamath MD[3]
Bonnie Simpson Mason MD[3]
Charles L. Nelson MD[2]

[1]Howard University College of Medicine

[2]Department of Orthopaedic Surgery, University of Pennsylvania

[3]Department of Orthopaedic Surgery, Cleveland Clinic

[4]Nth Dimensions

Introduction

The purpose of this paper is to identify whether poor nutrition, as defined by low albumin, will lead to more perioperative complications. If so, then should patients with hypoalbuminemia be considered eligible for elective total joint arthroplasty (TJA) procedures? It is known that there is a risk of perioperative complications after any surgery, including total joint arthroplasty, such as surgical site infection[1,2,19] acute kidney injury (AKI)[14], wound complications[9], pneumonia[2,19], readmission[2,17], unplanned intensive care unit admission[12], and mortality[25]. Albumin is known as a surrogate for nutrition, with the most common lower limit of normal nutrition for normal albumin being 3.5 g/dL[5].

Alternative nutritional markers have been reviewed in the literature with regard to TJA, including total lymphocyte count[16,9] and serum transferrin[8]. However, numerous studies indicate that albumin is associated with risk of perioperative mortality[1,24]. There is variation in selected cutoffs for the lower limit of albumin that leads to perioperative complications with some authors selecting less than 3.0 g/dL[14], less than 3.5 g/dL[2], or less than 3.9 g/dL[24]. Despite variability in albumin cut-point selection, hypoalbuminemia remains an important indicator of malnutrition and its associated perioperative risks[1,14,2]. In this review we hypothesize that hypoalbuminemia as defined by study authors will be associated with increased perioperative complications following TJA. Additionally, we will quantify the extent to which risk is elevated in these patients by combining results from multiple studies.

Methods

Literature Search and Study Selection

A systematic review of online databases was conducted in PubMed, EMBASE, and Cochrane Library from November 2017-February 2018. The studies contained keywords relevant to the question, including "albumin", "pre-albumin", "total hip arthroplasty","total knee arthroplasty", and "total joint arthroplasty". The search term used for all three databases [(((albumin) OR pre-albumin) OR prealbumin) AND ((((((total joint arthroplasty) OR total joint replacement) OR total hip arthroplasty) OR total hip replacement) OR total knee arthroplasty) OR total knee replacement) AND ((((((infection) OR complication) OR readmission) OR readmit) OR postoperative) OR perioperative)] yielded 312 total results in PubMed, 15 total results in EMBASE, and 88 total results in Cochrane Library. These titles were reviewed by independent reviewers (IR): MS and RC. Pertinent English-language articles were considered for inclusion in the final review.

1. 312 PubMed titles, 15 EMBASE titles, and 88 Cochrane Library articles were reviewed for inclusion, and subsequent abstract evaluation.
2. 35 PubMed abstracts, 5 EMBASE abstracts, and 8 Cochrane Library abstracts from the selected titles were reviewed for inclusion, and subsequent full-text evaluation. Abstract review yielded 23 articles from PubMed, 5 articles from EMBASE, and 1 article from Cochrane Library. These 29 articles were selected for full-text review.
3. Of those selected, 28 of 29 articles were able to be obtained for full-text review. Of the 29 original articles included in our search, 3 of the articles were duplicates, with the articles being listed in both PubMed and EMBASE. One additional article, which was not part of the original list of titles, was found during retrieval of full-text articles and was subsequently included in the systematic review. An additional relevant additional article which was published after the start of the systematic review was included.
4. Upon retrieval of 29 of 30 articles, we systematically reviewed the following items: Title, Author, Journal of publication, Year of publication, Primary Outcome, Albumin cutoff used for definition of hypoalbuminemia, Patient Source, Sample Size, Duration of Follow up, Study Design, Complications evaluated, Relative Risk of complication among patients with hypoalbuminemia

Data Abstraction

Two IR's reviewed all studies and recommended inclusion, based on the title and relevancy to the study question. Next, the IR's recommended inclusion based on the abstract

and relevancy to the study question. Finally, articles were recommended for inclusion based on the full-text article based on relevancy to the study question. Citations from all full-text articles under review were evaluated for additional relevant studies for inclusion. Please see appendix for figures.

Outcomes of the Papers

After final selection, included studies evaluated numerous perioperative outcomes associated with albumin status. These outcomes included, though are not limited to, postoperative infection, readmission, AKI, mortality, and any cause complication. A meta-analysis was performed using data from all studies that met criteria for inclusion.

Results

Thirty studies were included for final analysis. Among these, associations between hypoalbuminemia and outcomes of interest were identified in 24 studies. The results showed hypoalbuminemia is significantly associated with higher mortality (OR: 3.17-9.81, 95% CI: 1.46-28.49, p-value: <0.001-0.004), surgical site infection (RR: 2, 95% CI: 1.5-2.8, p-value: <0.011-0.024), pneumonia (RR: 2.5, 95% CI: 1.34-5.89, p-value: <0.001-0.005), revision for septic indication (RR: 3.6, 95% CI: 3.2-4.1, p-value: <0.001), revision for aseptic indication (RR: 2.2, 95% CI: 1.3-3.5, p-value: 0.002), any complication (RR: 1.5, 95% CI: 1.2-1.7, p-value: <0.001), any complication without transfusion (OR: 1.98-2.4, 95% CI: 1.10-3.58, p-value: <0.001-0.023), any major complication (OR: 1.32-2.91, 95% CI: 1.00-7.60, p-value: <0.001-0.05), wound complications (OR: 1.78-2.35, 95% CI: 1.20-3.59, p-value: <0.001-0.005), respiratory complications (OR: 2.35-3.75, 95% CI: 1.27-5.71, p-value: <0.001-0.007), blood transfusions (OR: 1.71-2.34, 95% CI: 1.35-2.83, p-value: <0.001), return to operating room within 30 days (OR: 1.7, 95% CI: 1.15-2.53, p-value: 0.008), extended length of stay (OR: 1.35, 95% CI: 1.14-1.59, p-value: <0.001-0.032), cardiac complications (OR: 2.23, 95% CI: 1.21-4.12, p-value: 0.01), neurovascular complication (OR: 41.95, 95% CI: 3.07-574.07, p-value: 0.005), renal complication (OR: 2.85, 95% CI: 1.2-6.77, p-value: 0.017), hematoma/seroma (OR: 8.37, 95% CI: 1.57-44.66, p-value: 0.013), superficial surgical site infection (OR: 1.27-2.61, 95% CI: 1.09-4.06, p-value: 0.02), deep incisional surgical site infection (OR: 2.3-3.64, 95% CI: 1.12-8.63, p-value: 0.003-0.019), organ space surgical site infection (OR: 2.71-3.79, 95% CI: 1.23-6.21, p-value: <0.001-0.013), unplanned intubation (OR: 2.24-4.11, 95% CI: 1.07-11.74, p-value: 0.008-0.033), acute renal failure (OR: 5.19-7.89, 95% CI: 1.90-32.71, p-value: 0.001-0.004), urinary tract infection (OR: 1.63-3.01, 95% CI: 1.11-5.45, p-value: <0.001-<0.01), sepsis (OR: 5.3, 95% CI: 3.31-8.5, p-value: <0.001), septic shock (OR: 3.73-4.4, 95% CI: 1.11-12.55, p-value: 0.002-0.034), systemic infection (OR: 2.05-3.53, 95% CI: 1.08-4.59, p-value: <0.001-0.028), wound infection (OR: 2.57, 95% CI: 1.79-3.69, p-value: <0.001), cardiac pulmonary complication (OR: 2.49-3.58, 95% CI: 1.01-12.66, p-value: 0.007-0.048), acute kidney injury (OR: 1.82, 95% CI: 1.03-3.24, p-value: 0.041), readmission within thirty days (OR: 0.668 [those with higher albumin levels had a lower chance of being readmitted], 95% CI: 0.477-0.992, p-value: 0.045), unplanned hospital readmission (RR: 1.4, 95% CI: 1.2-1.7, p-value: <0.001), remain on a ventilator for more than 48 hours (OR: 4.03, 95% CI: 1.64-9.90, p-value: 0.002), progressive renal insufficiency (OR: 2.71, 95% CI: 1.21-6.07, p-value: 0.015), cardiac arrest requiring cardiopulmonary resuscitation (OR: 3.74, 95% CI: 1.5-9.28, p-value: 0.005), any infection (OR: 2, 95% CI: 1.53-2.61, p-value: <0.001), acute postoperative infection complicating an aseptic revision arthroplasty (OR: 5.9, 95% CI: 1.317-26.057, p-value: 0.02), chronic septic failure (OR: 2.131, 95% CI: 1.294-3.512, p-value: 0.003).

Meta-analysis was performed among the 9 studies that included sufficient data on patient groups with hypoalbuminemia and normal albumin to perform a combined risk rate (Figure 1).

Conclusions

Prior studies identified surgical site infection, extended length of stay, acute kidney injury, serous drainage, readmissions, revisions/increased return to operating room, unplanned intensive care unit admission/increased intubations, postoperative complications, major complications, mortality, and a category titled "any complication" that were associated with preoperative hypoalbuminemia. Albumin is a reliable marker for risk of perioperative complications[25,6,7,12,13,2,26,15,19]. With many articles pulling from the ACS-NSQIP[2,3,7,6,19,20,25], and some being done by one surgeon on the team in order to limit variability[26]. Of these, nine studies identified large patient populations undergoing TJA from national databases[2,25,7,13,3,19,6,17,20], sixteen studies were single-surgeon or institution studies[1,18,24,14,8,9,23,4,22,26,15,12,16,21,11,10], and one was a review article and thus did not analyze any patients directly[5]. The purpose of this systematic review is to analyze and merge the results of pertinent studies to provide a summary of the risk for perioperative complications associated with hypoalbuminemia. Based on analysis of the studies, the results show that lower levels of albumin are associated with an odds ratio ranging from 1.27 to 41.95 and relative risks ranging from 2.0 to 3.6 for surgical site infection, pneumonia, revision for septic indications, revision for aseptic indications, postoperative complications, intensive care unit intervention, return to operating room, ninety day readmission, readmission within thirty days, any complication, any complication without transfusion, any major complication, wound complications, respiratory complications, blood transfusions, return to operating room within thirty days, extended length of stay, cardiac complications, mortality, neurovascular complications, renal complications, hematomas/seromas, superficial surgical site infection, deep incisional surgical site infection, organ space surgical site infection, acute postoperative infection complicating an aseptic revision arthroplasty, chronic septic failure/chronic periprosthetic joint infection, any infection, unplanned intubation, acute renal failure, acute kidney injury, progressive renal insufficiency, urinary tract infection, sepsis, septic shock, systemic infection, wound infection, cardiac pulmonary complication, higher resource consumption/

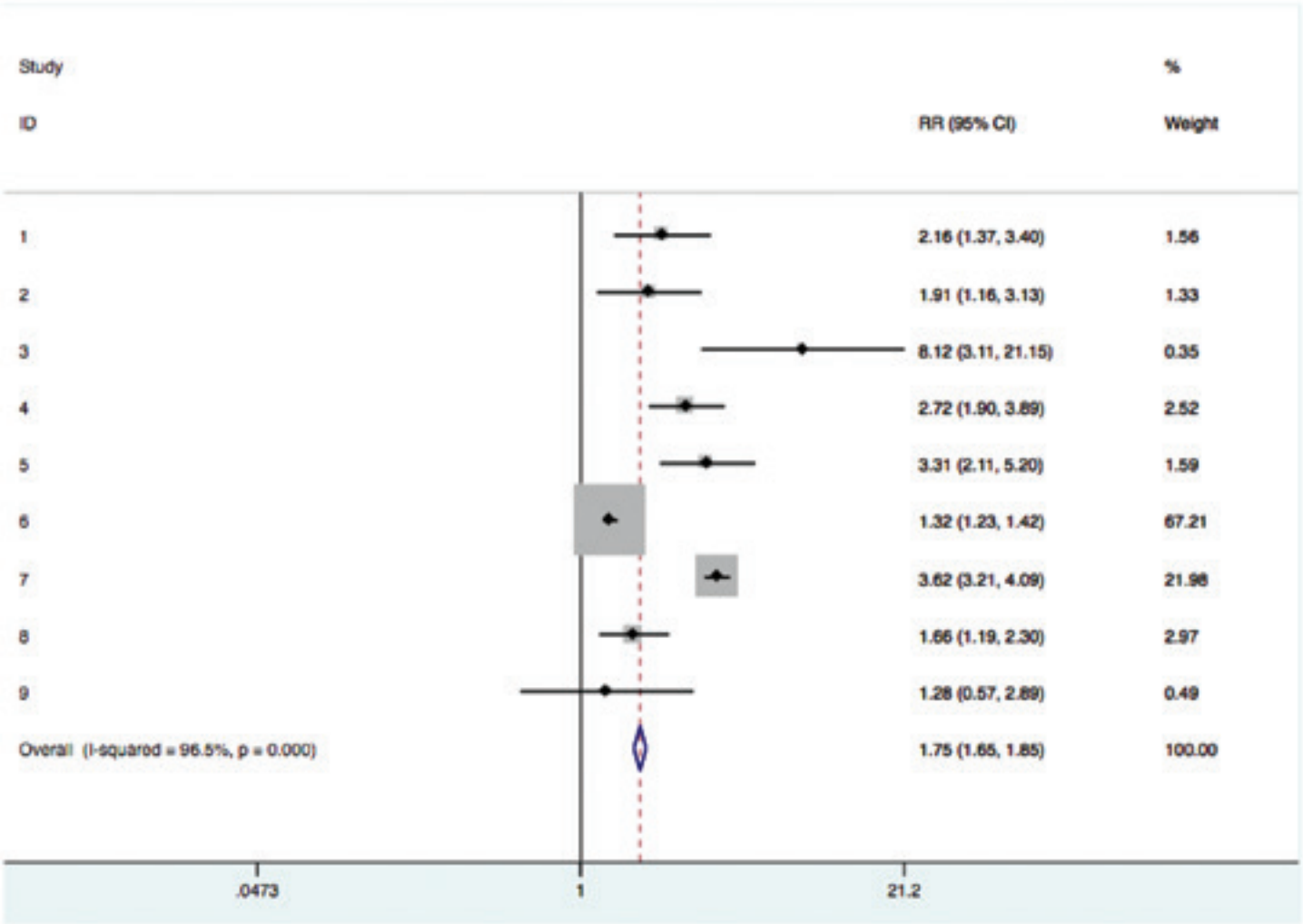


Figure 1.

higher charges, higher medical severity of illness, remain on a ventilator for more than forty-eight hours, cardiac arrest requiring cardiopulmonary resuscitation, mortality.

Discussion and Recommendations

The purpose of this systematic review is to gather all relevant literature on the use of preoperative albumin levels to determine associated risk for perioperative complications. The goals of TJA are to allow patients to improve functional status and reduce pain. Hypoalbuminemia has been previously associated with worsening outcomes after TJA[1,24,25]. Authors have identified numerous types of perioperative complications associated with hypoalbuminemia including mortality, surgical site infection, and renal injury[1,14,9,2,25,7,13,22,19,6,11,10]. However, no prior studies have performed a systematic review or meta-analysis of the data from these many studies to provide a summary risk assessment of hypoalbuminemia.

The main limitation of this project is the heterogeneous complications are incorporated into a single statistic. This limitation is addressed by individual study systematic review.

Our findings show there is an association between hypoalbuminemia and increased perioperative morbidity and mortality. The all-cause combined risk rate was 1.75 (95% CI: 1.65-1.85, p-value: 0.000). Perioperative complications associated with hypoalbuminemia can lead to increased costs, as a result of increased length of stay[6,21,24], increased readmission[17], increased incidence of AKI [Kim], surgical site infection[2], pneumonia[2], urinary tract infection[13,25], cardiopulmonary complications[19], sepsis[13], and death[7,13]. It is important for surgeons to use this information to screen patients[6,7,4] during the perioperative period in order to determine those most at risk for adverse surgical complications. Surgery may be postponed until nutrition is optimized as evaluated by improvement to albumin in the normal range[20], though one study questioned whether postponing surgeries to improve albumin would lead to better perioperative outcomes[4]. This study demonstrates that patients with hypoalbuminemia are associated with increased risk for perioperative complications compared to patients with normal albumin. Patients with normal serum albumin have demonstrated lower rates of reoperation for infection[4], ICU intervention[4], acute renal failure[13], revision total joint arthroplasty for a septic indication[3], early prosthetic joint infection after revision for an aseptic indication[3], fewer postoperative complications[4,6,7], shorter length of stay[15] compared with low serum albumin.

Prospective research into the effect of preoperative albumin optimization is lacking. Future research may focus on the impact of improving albumin and whether this leads to mitigates the risk of perioperative complications imparted by preoperative hypoalbuminemia.

References

1. **Alfargieny R, Bodalal Z, Bendardaf R, *et al.*** Nutritional status as a predictive marker for surgical site infection in total joint arthroplasty. *Avicenna Journal of Medicine 2015; 5(4), 117.*

2. Bohl, DD, Shen MR, Kayupov E, *et al.* Hypoalbuminemia Independently Predicts Surgical Site Infection, Pneumonia, Length of Stay, and Readmission After Total Joint Arthroplasty. *The Journal of Arthroplasty 2016; 31(1), 15-21.*

3. Bohl DD, Shen MR, Kayupov E, *et al.* Is Hypoalbuminemia Associated With Septic Failure and Acute Infection After Revision Total Joint Arthroplasty? A Study of 4517 Patients From the National Surgical Quality Improvement Program. *The Journal of Arthroplasty 2016,31*(5), 963-967.

4. Courtney PM, Rozell JC, Melnic CM, *et al.* Effect of Malnutrition and Morbid Obesity on Complication Rates Following Primary Total Joint Arthroplasty. *Journal of Surgical Orthopaedic Advances 2016, 25*(2), 99-104.

5. Cross MB, Yi PH, Thomas CF, *et al.* Evaluation of Malnutrition in Orthopaedic Surgery. *Journal of the American Academy of Orthopaedic Surgeons 2014, 22*(3), 193-199.

6. Fu MC, D'Ambrosia C, Mclawhorn AS, *et al.* Malnutrition Increases With Obesity and Is a Stronger Independent Risk Factor for Postoperative Complications: A Propensity-Adjusted Analysis of Total Hip Arthroplasty Patients. *The Journal of Arthroplasty 2016, 31*(11), 2415-2421.

7. Fu MC, Mclawhorn AS, Padgett DE, *et al*. Hypoalbuminemia Is a Better Predictor than Obesity of Complications After Total Knee Arthroplasty: A Propensity Score-Adjusted Observational Analysis. *HSS Journal 2016, 13*(1), 66-74.

8. Gherini S, Vaughn BK, Lombardi AV, *et al.* Delayed Wound Healing and Nutritional Deficiencies After Total Hip Arthroplasty. *Clinical Orthopaedics and Related Research 1993, &NA,*(293).

9. Greene KA, Wilde AH, Stulberg BN. Preoperative nutritional status of total joint patients. *The Journal of Arthroplasty 1991, 6*(4), 321-325.

10. Gunningberg L, Persson C, Åkerfeldt **T, *et al.*** Pre- and postoperative nutritional status and predictors for surgical-wound infections in elective orthopaedic and thoracic patients. *E-SPEN, the European E-Journal of Clinical Nutrition and Metabolism 2008, 3*(3).

11. Huang R, Greenky M, Kerr GJ, *et al.* The Effect of Malnutrition on Patients Undergoing Elective Joint Arthroplasty. *The Journal of Arthroplasty 2013, 28*(8), 21-24.

12. Kamath AF, McAuliffe CL, Kosseim LM, *et al.* Malnutrition in Joint Arthroplasty: Prospective Study Indicates Risk of Unplanned ICU Admission. *Archives of Bone and Joint Surgery 2016, 4*(2), 128–131.

13. Kamath AF, Nelson CL, Elkassabany N, *et al.* Low Albumin Is a Risk Factor for Complications after Revision Total Knee Arthroplasty. *The Journal of Knee Surgery 2016, 30*(03), 269-275.

14. Kim H, Koh W, Kim S, Park H, *et al.* Early postoperative albumin level following total knee arthroplasty is associated with acute kidney injury. *Medicine 2016, 95*(31).

15. Lavernia CJ, Sierra RJ, Baerga L, *et al.* Nutritional Parameters and Short Term Outcome in Arthroplasty. *Journal of the American College of Nutrition 1999, 18*(3), 274-278.

16. Marín LA, Salido JA, López A, *et al.* Preoperative nutritional evaluation as a prognostic tool for wound healing. *Acta Orthopaedica Scandinavica 2002, 73*(1), 2-5.

17. Mednick RE, Alvi HM, Krishnan V, *et al.* Factors Affecting Readmission Rates Following Primary Total Hip Arthroplasty. *The Journal of Bone and Joint Surgery-American Volume 2014, 96*(14), 1201-1209.

18. Morey VM, Song YD, Whang JS, *et al.* Can Serum Albumin Level and Total Lymphocyte Count be Surrogates for Malnutrition to Predict Wound Complications After Total Knee Arthroplasty? *The Journal of Arthroplasty 2016, 31*(6), 1317-1321.

19. Nelson CL, Elkassabany NM, Kamath AF, *et al.* Low Albumin Levels, More Than Morbid Obesity, Are Associated With Complications After TKA. *Clinical Orthopaedics and Related Research 2015, 473*(10), 3163-3172.

20. Nelson CL, Kamath AF, Elkassabany NM, *et al.* The serum albumin threshold for increased perioperative complications after total hip arthroplasty is 3.0 g/dL. *HIP International 2018.*

21. Nicholson JA, Dowrick AS, Liew SM, *et al.* Nutritional Status and Short-Term Outcome of Hip Arthroplasty. *Journal of Orthopaedic Surgery 2012, 20*(3), 331-335.

22. Nussenbaum FD, Rodriguez-Quintana D, Fish SM, *et al.* Implementation of Preoperative Screening Criteria Lowers Infection and Complication Rates Following Elective Total Hip Arthroplasty and Total Knee Arthroplasty in a Veteran Population. *The Journal of Arthroplasty 2018, 33*(1), 10-13.

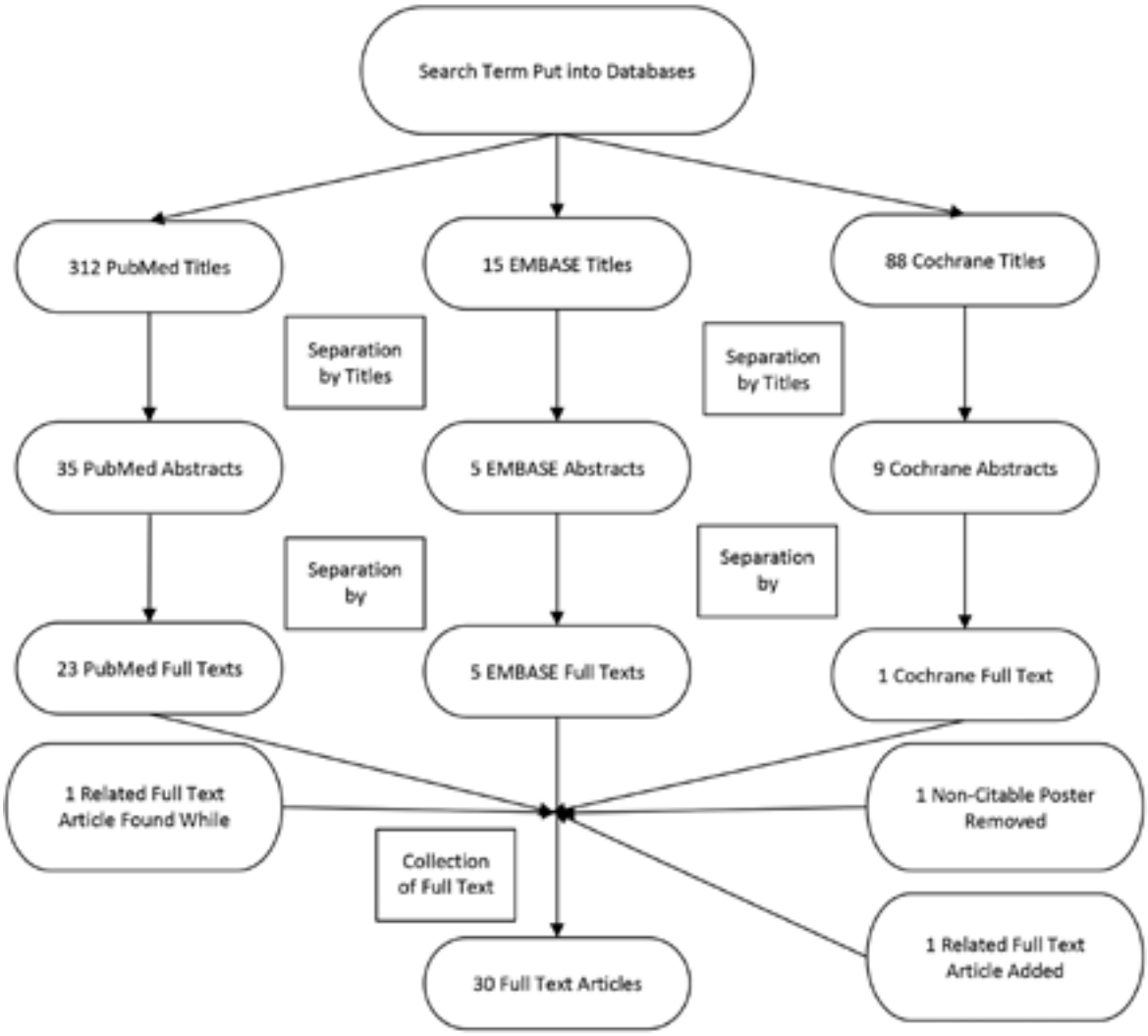
23. Rai J, Gill S, Kumar BS, *et al.* The Influence of Preoperative Nutritional Status in Wound Healing After Replacement Arthroplasty. *Orthopedics 2002, 25*(4), 417-421.

24. Savio GC, Zelicof SB, Wexler LM, *et al.* Preoperative Nutritional Status and Outcome of Elective Total Hip Replacement. *Clinical Orthopaedics and Related Research 1996, 326*, 153-161.

25. Walls JD, Abraham D, Nelson CL, *et al.* Hypoalbuminemia More Than Morbid Obesity is an Independent Predictor of Complications After Total Hip Arthroplasty. *The Journal of Arthroplasty 2015, 30*(12), 2290-2295.

26. Yi PH, Frank RM, Vann E, *et al.* Is Potential Malnutrition Associated With Septic Failure and Acute Infection After Revision Total Joint Arthroplasty? *Clinical Orthopaedics and Related Research 2014, 473*(1), 175-182.

Appendix:



THA and TKA Studies

Author Name	Study Population	Normal Albumin Cutoff
Alfagierny et al [1]	THA and TKA	Not given
Bohl et al [2]	THA and TKA	Albumin <3.5 g/dL is abnormal
Bohl et al [3]	THA and TKA	Albumin <3.5 g/dL is abnormal
Courtney et al [4]	THA and TKA	Albumin <3.5 g/dL is abnormal
Greene et al [5]	THA and TKA	Albumin <3.5 g/dL is abnormal
Gunningberg et al [10]	THA, TKA, Coronary Artery Bypass	Albumin <35 g/L is abnormal
Huang et al [11]	THA and TKA	Albumin ≤ 3.5mg/dl OR transferrin <200 mg/dl
Kamath et al [12]	THA and TKA	Albumin <3.5 g/dL is abnormal
Lavernia et al [15]	THA and TKA	Albumin 34 g/L is abnormal
Marin et al [16]	THA and TKA	Albumin <3.5 g/dL is abnormal
Nussenbaum et al [22]	THA and TKA	Not given
Rai et al [23]	THA and TKA	Albumin < 3.5 g/dL or serum transferrin <200 mg/dL or total lymphocyte count <1500 cells/mm^3

THA and TKA Studies

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Alfagierny et al [1]	Not given	Not given
Bohl et al [2]	47639	1964
Bohl et al [3]	3762	755
Courtney et al [4]	587	83
Greene et al [5]	211	6
Gunningberg et al [10]	51	4
Huang et al [11]	Not given	Not given
Kamath et al [12]	913	185
Lavernia et al [15]	97	22
Marin et al [16]	152	18
Nussenbaum et al [22]	Not given	Not given
Rai et al [23]	Not given	Not given

THA and TKA Studies

Author Name	Study Type	Control Group
Alfagierny et al [1]	Retrospective Cohort	N/A
Bohl et al [2]	Retrospective Cohort	N/A
Bohl et al [3]	Retrospective Cohort	N/A
Courtney et al [4]	Retrospective Cohort	N/A
Greene et al [5]	Retrospective Cohort	N/A
Gunningberg et al [10]	Prospective Cohort	N/A
Huang et al [11]	Prospective Cohort	N/A
Kamath et al [12]	Prospective Cohort	N/A
Lavernia et al [15]	Prospective Cohort	N/A
Marin et al [16]	Prospective Cohort	N/A
Nussenbaum et al [22]	Retrospective Cohort	520 THA and TKA
Rai et al [23]	Retrospective Cohort	N/A

THA and TKA Studies

Author Name	Experimental THA	Experimental TKA
Alfagierny et al [1]	25	110
Bohl et al [2]	29628	19975
Bohl et al [3]	2199	2318
Courtney et al [4]	236	434
Greene et al [5]	126	91
Gunningberg et al [10]	32	23
Huang et al [11]	910	1001
Kamath et al [12]	Not given	Not given
Lavernia et al [15]	Not given	Not given
Marin et al [16]	92	78
Nussenbaum et al [22]	475 THA and TKA	475 THA and TKA
Rai et al [23]	33	7

THA and TKA Studies

Author Name	Outcomes
Alfagierny et al [1]	Surgical Site Infection
Bohl et al [2]	Multiple Complications
Bohl et al [3]	Aseptic and Septic Indications for Revision Arthroplasty
Courtney et al [4]	Multiple Postoperative Complications
Greene et al [5]	Persistent Serous Drainage, Wound Dehiscence
Gunningberg et al [10]	Surgical Wound Infection
Huang et al [11]	Multiple Complications
Kamath et al [12]	Unplanned Postoperative Intensive Care Unit Admission
Lavernia et al [15]	Multiple Complications, Length of Stay
Marin et al [16]	Delayed Wound Healing
Nussenbaum et al [22]	Multiple Complications, Death
Rai et al [23]	Wound Healing

THA and TKA Studies

Author Name	Conclusions
Alfagierny et al [1]	Perioperative albumin is a significant risk factor for surgical site infection.
Bohl et al [2]	Patients with hypoalbuminemia had higher risk of surgical site infection, pneumonia, extended length of stay, and readmission.
Bohl et al [3]	Patients with hypoalbuminemia were more likely to have septic and aseptic indications for revision arthroplasty compared to patients with normal albumin levels.
Courtney et al [4]	Hypoalbuminemic patients are more likely to have postoperative complications. Morbidly obese patients are more likely to be hypoalbuminemic that nonmorbidly obese patients. When stratifying albumin with obesity, the difference lied in albumin levels.
Greene et al [5]	A low total lymphocyte count has increased risk of a major wound complication, and a low albumin level of an even higher risk.
Gunningberg et al [10]	Low preoperative S-albumin was identified as the only significant predictor for surgical wound infection.
Huang et al [11]	Malnutritioned patients have higher risk of complications than in non-malnutritioned patients, regardless of obesity. Renal complications were the most common complication experienced by malnourished patients.
Kamath et al [12]	Patients with low albumin have a higher risk of unplanned postoperative intensive care unit admission.
Lavernia et al [15]	Patients with low albumin levels have higher charges, higher severity of illness, and longer length of stay.
Marin et al [16]	Low preoperative lymphocyte count is associated with increased risk of healing complications, whereas preoperative serum albumin and transferrin levels had no significant predictive value.
Nussenbaum et al [22]	Implementation preoperative screening criteria for THA and TKA decreased complications. No single criterion was found to individually predict the complication and infection reductions.
Rai et al [23]	Controlling surgeon-dependent factors allows decreases in wound healing complications related to malnourishment.

THA and TKA Studies

Author Name	Year	Mean Follow-Up Time
Alfagierny et al [1]	2015	6 months
Bohl et al [2]	2016	30 days
Bohl et al [3]	2016	30 days
Courtney et al [4]	2016	6 months
Greene et al [5]	1991	1 year
Gunningberg et al [10]	2008	30 days
Huang et al [11]	2013	12 months
Kamath et al [12]	2016	Not given
Lavernia et al [15]	1999	Not given
Marin et al [16]	2002	Not given
Nussenbaum et al [22]	2018	2 years
Rai et al [23]	2002	Not given

THA Studies

Author Name	Study Population	Normal Albumin Cutoff
Fu et al [6]	THA	Albumin < 3.5g/dL is abnormal
Gherini et al [8]	THA	Not given
Mednick et al [17]	THA	Not given
Nelson et al [20]	THA	Albumin < 3.5 g/dL is abnormal
Nicholson et al [21]	THA	Albumin < 3.5 g/dL is abnormal and TLC < 1.50 cells/m
Savio et al [24]	THA	Albumin < 3.5 g/dL is abnormal, then they changed it to albumin < 3.9 g/dL is normal after analyzing their data
Walls et al [25]	THA	Albumin < 3.5 g/dL is abnormal

THA Studies

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Fu et al [6]	19465	745
Gherini et al [8]	Not given	Not given
Mednick et al [17]	Not given	Not given
Nelson et al [20]	23409	1177
Nicholson et al [21]	64	26
Savio et al [24]	51	35
Walls et al [25]	23116	1122

THA Studies

Author Name	Study Type	Control Group
Fu et al [6]	Retrospective Cohort	N/A
Gherini et al [8]	Prospective Cohort	N/A
Mednick et al [17]	Retrospective Cohort	N/A
Nelson et al [20]	Retrospective Cohort	23409 THA
Nicholson et al [21]	Retrospective Cohort	N/A
Savio et al [24]	Retrospective Cohort	N/A
Walls et al [25]	Retrospective Cohort	N/A

THA Studies

Author Name	Experimental THA	Experimental TKA
Fu et al [6]	20210	0
Gherini et al [8]	103	0
Mednick et al [17]	9441	0
Nelson et al [20]	1177	0
Nicholson et al [21]	90	0
Savio et al [24]	86	0
Walls et al [25]	49475	0

THA Studies

Author Name	Outcomes
Fu et al [6]	Postoperative Complications: Cardiac (Myocardial Infarction or Cardiac Arrest), Septic (Sepsis or Septic Shock), Respiratory (Intubation, Ventilator Requirement, Superficial Infection, or Organ Space Infection), Urinary (Urinary Tract Infection), Blood Transfusions, Deep Vein Thrombosis or Pulmonary Embolism, Return to the Operating Room within 30 Postoperative Days, Extended Length of Stay (defined as 4 or more days), and Death. A Major Postoperative Complication was defines as any cardiac, respiratory, or septic complication, in addition to deep vein thrombosis and/or pulmonary embolism, return to operating room, or death.
Gherini et al [8]	Delayed Wound Healing
Mednick et al [17]	Readmission
Nelson et al [20]	Any Complication, Any Complication without Transfusion, Cardiac Pulmonary Complications, Major Complications, Systemic Infection, Wound Infection
Nicholson et al [21]	Length of Stay, Intraoperative Complications: Femoral Fractures, Blood Loss Treated by Transfusion, Death, Postoperative Complications: Early Revisions of the Prosthesis Within the First Month, Deep Prosthetic or Superficial Wound Infection, Dislocation, Myocardial Infarctions, Pulmonary Embolism, Acute Renal Failure, Deep Vein Thrombosis, Urinary Tract Infection, Pressure Sore, Paralytic Ileus, Peri-prosthetic Fracture following a Fall, Recurrent Dislocation, Early Subsidence of the Graft, Haematoma, Wound Infections, Death
Savio et al [24]	Length of Stay
Walls et al [25]	Complications: Mortality, Superficial Incisional Surgical Site Infection, Deep Incisional Surgical Site Infection, Organ Space Surgical Site Infection, Surgical Wound Disruption, Pneumonia, Unplanned Intubation, Pulmonary Embolism, on Ventilator > 48 Hours, Progressive Renal Insufficiency, Acute Renal Failure, Urinary Tract Infection, Stroke/CVA, Coma > 24 Hours, Peripheral Nerve Injury, Cardiac Arrest Requiring CPR, Sepsis, and Septic Shock

THA Studies

Author Name	Conclusions
Fu et al [6]	Malnutrition incidence increased significantly from obese I to obese III patients and was a stronger and more consistent predictor than obesity of complications after THA.
Gherini et al [8]	Only preoperative serum transferrin levels showed significant value in predicting which patients would have delayed wound healing. None of the other serologic variables, including serum albumin and total lymphocyte count, proved to be a predictor of delayed wound healing.
Mednick et al [17]	The risk of readmission following total hip arthroplasty increases with growing preoperative comorbidity burden, and it is specifically increased in patients with a body mass index of greater than or equal to 40 kilograms per meter squared, a history of corticosteroid use, and low preoperative serum albumin and in patients with postoperative surgical site infection, a thromboembolic event, and sepsis.
Nelson et al [20]	Three out of six of the measurable complications for patients with albumin < 3.0 g/dL showed statistical significance for increased odds ratio for complications, and when stratified for patients with albumin < 2..75 g/dL, five out of six of the measurable complications showed statistical significance for an increase in odds ratio.
Nicholson et al [21]	The rate of malnourishment was significantly higher in patients having trauma-related surgery than in those having elective surgery. Malnourished patients are at greater risk of prolonged hospital stay.
Savio et al [24]	Preoperative serum albumin was the only preoperative serum test associated with length of stay. Albumin is inversely related with length of stay. There should be a new normal range for albumin, because prolonged recovery time may be identified preoperatively be using a serum albumin level of less than 3.9 g/dL. Because specific complications occurred in so few patients, a larger sample is required to show any association with preoperative malnutrition.
Walls et al [25]	Hypoalbuminemia is a significant risk factor for mortality and major morbidity among total hip arthroplasty patients, while morbid obesity was only associated with an increased risk of superficial surgical site infection.

THA Studies

Author Name	Year	Mean Follow-Up Time
Fu et al [6]	2016	30 days
Gherini et al [8]	Not given	Not given
Mednick et al [17]	2014	30 days
Nelson et al [20]	2018	30 days
Nicholson et al [21]	2012	Not given
Savio et al [24]	1996	1.8 years
Walls et al [25]	2015	30 days

TKA Studies

Author Name	Study Population	Normal Albumin Cutoff
Fu et al [7]	TKA	Albumin 3.5 g/dL is abnormal
Kim et al [14]	TKA	Albumin ≥ 3.0 g/dL is normal
Morey et al [18]	TKA	Albumin < 3.5 g/dL is abnormal
Nelson et al [19]	TKA	Albumin < 3.5 g/dL is abnormal

TKA Studies

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Fu et al [7]	33400	1400
Kim et al [14]	839	470
Morey et al [18]	2956	213
Nelson et al [19]	35573	1570

TKA Studies

Author Name	Study Type	Control Group
Fu et al [7]	Retrospective Cohort	N/A
Kim et al [14]	Retrospective Cohort	N/A
Morey et al [18]	Retrospective Cohort	N/A
Nelson et al [19]	Retrospective Cohort	N/A

TKA Studies

Author Name	Experimental THA	Experimental TKA
Fu et al [7]	0	34800
Kim et al [14]	0	1309
Morey et al [18]	0	3169
Nelson et al [19]	0	77785

TKA Studies

Author Name	Outcomes
Fu et al [7]	Postoperative Complications: Wound (Superficial Infection, Deep Surgical Site Infection, Organ Space Surgical Site Infection, or Wound Dehiscence), Septic (Sepsis or Septic Shock), Cardiac (Cardiac Arrest or Myocardial Infarction), Respiratory (Pneumonia, Intubation, or Ventilator Requirement), Blood Transfusions (Intra- or Postoperative), Urinary Tract Infection, Return to the Operating Room within 30 days, Deep Vein Thrombosis or Pulmonary Embolism, Extended Length of Stay (defined as 4 days or longer), and Death. Major complications were defined as any septic, cardiac, or respiratory complications, as well as DVT, PE, or return to OR, and death.
Kim et al [14]	Incidence of Acute Kidney Injury, Hospital Stay, and Overall Mortality
Morey et al [18]	Wound Complications (Drainage, Hemarthrosis, Skin Necrosis, Dehiscence), or Periprosthetic Joint Infection
Nelson et al [19]	Mortality, Superficial Wound Infection, Deep Incisional Wound Infection, Organ Space Surgical Site Infection, Surgical Wound Disruption, Pneumonia, Unplanned Intubation, Pulmonary Embolism, on Ventilator More than 48 Hours, Progressive Renal Insufficiency, Acute Renal Failure, Urinary Tract Infection, Stroke/Cerebrovascular Accident, Coma More than 24 Hours, Peripheral Nerve Injury, Cardiac Arrest Requiring Cardiopulmonary Resuscitation, Myocardial Infarction, Blood Transfusion, Prosthesis Failure, Deep Vein Thrombosis, Sepsis, and Septic Shock

TKA Studies

Author Name	Conclusions
Fu et al [7]	Hypoalbuminemia is a more consistent independent predictor of complications after TKA than obesity.
Kim et al [14]	Low albumin within 2 postoperative days is an independent risk factor for acute kidney injury and increased length of hospital stay in patients undergoing TKA.
Morey et al [18]	Our findings call into question the values of serum albumin level and TLC as a surrogate of malnutrition for predicting wound complications after TKA.
Nelson et al [19]	Morbid obesity is not independently associated with the majority of perioperative complications measured by the NSQIP and was associated only with increases in progressive renal insufficiency, superficial surgical site infection, and sepsis among the 21 perioperative variables measured. Low serum albumin was associated with increased mortality and multiple additional major perioperative complications after TKA. Low serum albumin, more so than morbid obesity, is associated with major perioperative complications.

TKA Studies

Author Name	Year	Mean Follow-Up Time
Fu et al [7]	2017	30 days
Kim et al [14]	2016	4.2 years
Morey et al [18]	2016	1 year
Nelson et al [19]	2015	30 days

Revision THA Studies

Author Name	Study Population	Normal Albumin Cutoff
Yi et al (26)	Revision THA	Albumin < 3.5 g/dL is abnormal

Revision THA Studies

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Yi et al (26)	Not given	Not given

Revision THA Studies

Author Name	Study Type	Control Group
Yi et al (26)	Retrospective Cohort	N/A

Revision THA Studies

Author Name	Experimental THA	Experimental TKA
Yi et al (26)	501	0

Revision THA Studies

Author Name	Outcomes
Yi et al (26)	Septic Revision, Aseptic Revision

Revision THA Studies

Author Name	Conclusions
Yi et al (26)	The presence of one or more laboratory parameters suggestive of malnutrition (low albumin, low transferrin, low lymphocyte count), though common in both normal weight and overweight patients, is independently associated with both chronic PJI and the development of an acute postoperative infection after an aseptic revision arthroplasty.

Revision THA Studies

Author Name	Year	Mean Follow-Up Time
Yi et al (26)	2014	90 days

Revision TKA Studies

Author Name	Study Population	Normal Albumin Cutoff
Kamath et al [13]	Revision TKA	Albumin < 3.5 g/dL is abnormal

Revision TKA Studies

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Kamath et al [13]	3838	713

Revision TKA Studies

Author Name	Study Type	Control Group
Kamath et al [13]	Retrospective Cohort	N/A

Revision TKA Studies

Author Name	Experimental THA	Experimental TKA
Kamath et al [13]	0	4551

Revision TKA Studies

Author Name	Outcomes
Kamath et al [13]	Mortality, Superficial Wound Infection, Deep Incisional Wound Infection, Organ Space Surgical Site Infection, Surgical Wound Disruption, Pneumonia, Unplanned Intubation, Pulmonary Embolism, on Ventilator More than 48 Hours, Progressive Renal Insufficiency, Acute Renal Failure, Urinary Tract Infection, Stroke/Cerebrovascular Accident, Coma More than 24 Hours, Peripheral Nerve Injury, Cardiac Arrest Requiring Cardiopulmonary Resuscitation, Myocardial Infarction, Bleeding Transfusion, Prosthesis Failure, Deep Vein Thrombosis, Sepsis, and Septic Shock

Revision TKA Studies

Author Name	Conclusions
Kamath et al [13]	Patients in the low serum albumin group were statistically more likely to develop deep surgical site infection, organ space surgical site infection, pneumonia, urinary tract infection, sepsis, unplanned intubation, blood transfusion intraoperatively or postoperatively, remain on a ventilator for more than 48 hours, develop acute renal failure, coma, and mortality.

Revision TKA Studies

Author Name	Year	Mean Follow-Up Time
Kamath et al [13]	2017	30 days

Review Paper

Author Name	Study Population	Normal Albumin Cutoff
Cross et al [5]	N/A	N/A

Review Paper

Author Name	Normal Albumin Patient (total)	Low Albumin Patient (total)
Cross et al [5]	N/A	N/A

Review Paper

Author Name	Study Type	Control Group
Cross et al [5]	N/A	N/A

Review Paper		
Author Name	**Experimental THA**	**Experimental TKA**
Cross et al [5]	N/A	N/A

Review Paper		
Author Name	**Outcomes**	**Conclusions**
Cross et al [5]	N/A	N/A

Review Paper		
Author Name	**Year**	**Mean Follow-Up**
Cross et al [5]	2014	N/A

Foot and Ankle Tips and Tricks: The Operative Management of Os Trigonum Syndrome in Dancers Through a Posteromedial Approach

Karim Mahmoud, MD
Sreenivasulu Metikala, MD
Viviana M. Serra López, MD MS
Wen Chao, MD

University of Pennsylvania,
Department of Orthopaedic Surgery
Foot and Ankle Division

Introduction

Os trigonum syndrome (OTS) is a common cause of posterior ankle impingement, and is especially prominent in dancers. This problem occurs when the os trigonum of the talus and surrounding soft tissues impinge between the posterior aspect of the distal tibia and the calcaneus.[1,2] Os trigonum of the talus arises as a result of failure of fusion of a secondary ossification center, which happens between ages 11–13 in males and 8-10 years in females. It was first described by Rosenmuller in 1804 and it is the second most common accessory bone of the foot. It has an incidence of 10–25% in the general population and is bilateral 50% of the time. While it is usually asymptomatic, posterior ankle pain can develop in those individuals performing activities necessitating repetitive forced plantarflexion of the ankle such as in soccer players and ballet dancers.[2] Os trigonum syndrome can also develop in individuals who have a os trigonum which is fused to the talus, when the posterior process of the talus (also known as Stieda process or trigonal process of the talus) is prominent (Figure 1).

OTS most often presents in the classical ballet dancers because the position of the foot and ankle involves full weight bearing on a forced plantarflexed ankle during *relevé* in *demi pointe*.[1] The repetitive dorsiflexion of the first metatarsophalangeal joint and hyper plantarflexion of the ankle can also predispose dancers to flexor hallucis longus FHL tenosynovitis, which occurs in 63% to 85% of cases of OTS.[2]

Conservative treatment for OTS includes rest, ice, immobilization, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound guided cortisone injections, and physical therapy. Surgical intervention to excise symptomatic os trigonum can be considered when the non-operative treatment fails. Both arthroscopic and open surgical approaches have been described in the literature. In general, an open approach is preferred to arthroscopic technique, as the latter method requires the patient to be prone and makes it challenging to address the concomitant FHL pathology.[1,3] The open posterolateral approach was described in order to avoid exploration of the tarsal tunnel, but is associated with high incidence of sural nerve injury.[1] Furthermore, evaluation of the FHL tendon is more difficult because it lies medial to the os trigonum. A common cause of persistent posterior or posteromedial pain in a dancer who underwent complete excision of an os trigonum via a posterolateral approach is often due to unaddressed FHL tendon or tendon sheath pathology.[1] Therefore, the posteromedial approach for surgical excision of symptomatic os trigonum is recommended, especially in dancers.

Pre-operative Evaluation

Preoperative evaluation includes a thorough history and physical exam. The appropriate candidate should have pain with tenderness to palpation of the posteromedial and/or posterolateral aspect of the ankle joint in the region of the os trigonum. Passive plantarflexion should reproduce the posterior ankle pain (positive plantarflexion test). If pain is present at posterior ankle with full dorsiflexion of the ankle and passive dorsiflexion of the first metatarsophalangeal joint, then FHL tendonitis is also present. Weight bearing lateral radiographs of the ankle will show the presence of the os trigonum, or a prominent trigonal process of the talus (Figure 1). CT scan can be helpful

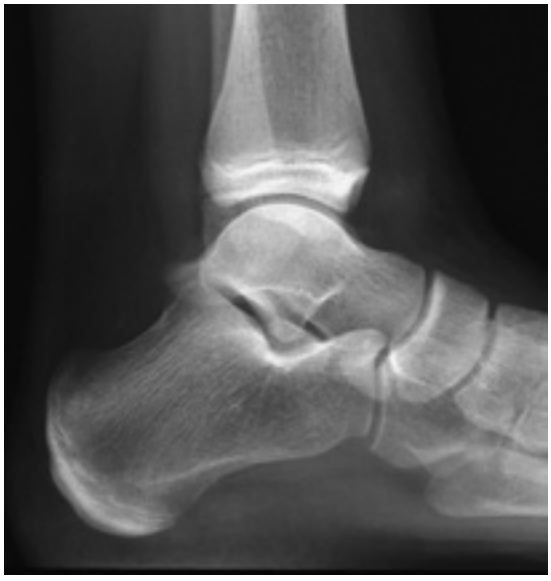


Figure 1. Lateral radiograph of left ankle in a 12 year-old female ballet dancer with os trigonum.

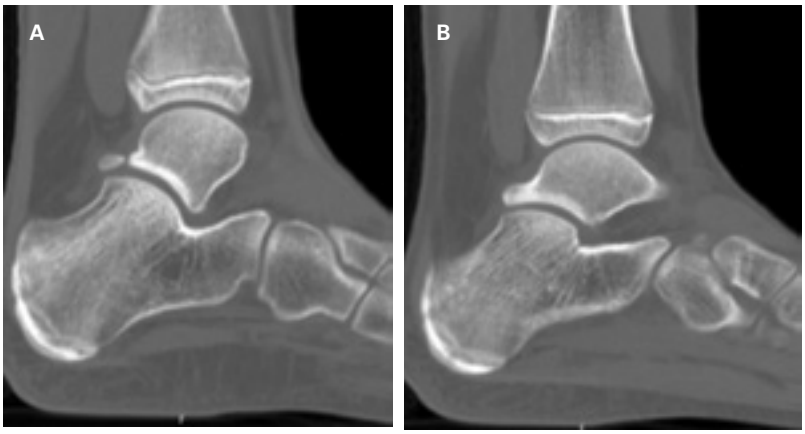


Figure 2. Weight-bearing CT scan of the same patient demonstrating **(A)** os trigonum and **(B)** enlarged posterolateral tubercle of the talus.

to determine the size of the os trigonum and will also help demonstrate enlargement of the posterolateral tubercle of talus (Figure 2). An MRI of the ankle can also show co-existent FHL pathology. Surgical excision of the os trigonum is indicated after failed non-operative treatment.

Surgical Technique

Exposure

The surgery is typically performed as an outpatient procedure. General anesthesia is preferred. A thigh tourniquet is applied, and a bump is placed under contralateral hip to place the surgical extremity into external rotation. A 5-7 cm curvilinear longitudinal incision is made along the posteromedial ankle centered on the posterior talus and tarsal tunnel. Subcutaneous tissue is dissected to identify the laciniate ligament. This is carefully incised using Stevens scissors in order to gain access to the tarsal tunnel. The neurovascular bundle is identified and gently retracted posteriorly. The small perforating branches found anteriorly are cauterized as anteriorly as possible using bipolar electrocautery. The FHL tendon sheath is then incised to the fibro-osseous tunnel using Stevens Scissors and inspected. Tenosynovectomy is performed as needed. If there is a tear in the FHL tendon, it is repaired using a 3-0 non-absorbable suture.

Surgical steps

The FHL tendon and the neurovascular bundle are then retracted posteriorly using a blunt retractor. The os trigonum is then identified. Limited capsulotomy is performed around the os trigonum using a Freer Elevator and Stevens Scissors. The elongated posterolateral tubercle of talus, if present, is then resected using a small osteotome (Figure 3). The ankle is then placed into full plantarflexion with direct visualization of the posterior talus to make sure that there is no impingement. This can also be performed under fluoroscopy on the lateral view of the ankle. The wound is irrigated and skin is closed with a 4-0 nylon suture. Sterile dressings are applied, and a well-padded posterior splint is placed with a "U" shaped stirrup, with the ankle in slight plantarflexion. The tourniquet is deflated at this time and care is taken to make sure that all toes are well perfused.

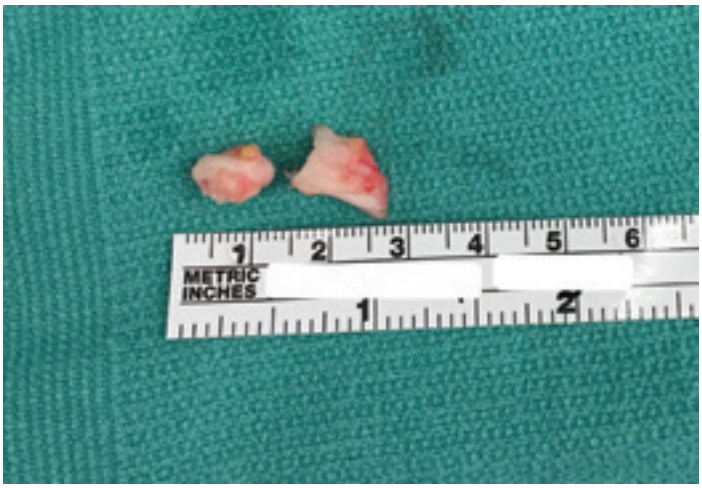


Figure 3. Intraoperative picture of an excised os trigonum (left) and enlarged posterolateral tubercle of talus (right).

Post-op care and follow-up

The first post-operative visit typically occurs 10 to 14 days post-operatively. The splint and skin sutures are removed. The ankle is placed in a removable CAM walker and patients are allowed to bear partial weight as tolerated. Formal physical therapy is initiated to help with range of motion, proprioception and strengthening. Gradual return to dancing is resumed at around 8–12 weeks.

Conclusion

The posteromedial open approach to excise symptomatic os trigonum is a safe and reliable technique, especially in dancers. It gives direct access to the neurovascular bundle, which can be protected throughout the procedure. Furthermore, the FHL tendon is easily visualized with this approach and any concurrent pathology can be effectively addressed.

References

1.Heyer, J. H. & Rose, D. J. Os Trigonum Excision in Dancers via an Open Posteromedial Approach. *Foot Ankle Int.* 2017; 38: 27–35.

2.Chao, W. Os trigonum. *Foot Ankle Clin. 2004*; 9: 787–796.

3.Morelli, F. *et al*. Endoscopic Excision of Symptomatic Os Trigonum in Professional Dancers. *J. Foot Ankle Surg.* 2017; 56: 22–25.

A Novel Technique of Triplane Tarsometatarsal (TMT) Joint Corrective Arthrodesis in Hallux Valgus

Karim Mahmoud, MD[1]
Sreenivasulu Metikala, MD[1]
Daniel C. Farber, MD[1]

Pennsylvania Orthopaedic Foot and Ankle Surgery
Department of Orthopaedic Surgery
University of Pennsylvania
Philadelphia, PA 19106

Introduction

Hallux valgus is a slowly progressing complex three-dimensional biomechanical process. The horizontal and vertical components of this deformity have been widely explored in conventional weight-bearing radiographs and also are routinely taken into account in the various procedures of surgical correction. The frontal rotation component, in contrast, has been generally overlooked.[1-3] Advanced imaging with weight bearing computed tomography (WBCT) scans allow better understanding of its true three-dimensional anatomy, especially first metatarsal pronation and sesamoid position.[2]

Among the available surgical techniques, the 1st tarsometatarsal (TMT) joint fusion (Lapidus) is a procedure that can correct the deformity close to the center of rotation of angulation (CORA)[3]. The traditional surgical technique involves deformity correction by biplanar wedge resection of the 1st TMT joint followed by fixation with a dorsal plate or two cross screws or a combination of plate and screw. Correction of pronation, however, is not routinely included and weight-bearing may be delayed for up to 3 months to avoid the risk of nonunion. In addition, 1st TMT joint fusion can result in shortening of the 1st metatarsal due to bone resection with a further risk of transfer metatarsalgia.[3]

Recently we have begun utilizing a modified technique of 1st TMT joint fusion performed with special instrumentation (Lapiplasty - Treace Medical Concepts, Ponte Vedra Beach, FL, USA).[1] It allows precise correction of the pronation of 1st metatarsal. In addition, the available cutting guides simplify the performance of a biplanar wedge resection with minimal bone sacrifice. Finally, stabilization of osteotomy with two locking plates oriented in 90-90 conFigureuration permits early weight-bearing ambulation with assistive devices. Thus, this modified technique can effectively circumvent the problems encountered with traditional Lapidus procedure.

Pre-operative Evaluation

Preoperative evaluation requires a thorough history and physical exam. The appropriate candidate should have pain at the first metatarsophalangeal joint or other problems associated with the hallux valgus deformity. Standard weight-bearing radiographs should be obtained. These include anterior-posterior (AP), oblique and lateral views. Radiographic evaluation includes measurement of hallux valgus angle (HVA), intermetatarsal angle (IMA), distal metatarsal articular angle (DMAA), hallux valgus interphalangeus angle (HVI) and tibial sesamoid position (TSP). This procedure is chosen for those patients with larger 1-2 intermetatarsal angle (usually >15 degrees) (Figure 1), 1st TMT joint instability, or 1st metatarsal rotational instability.

Surgical Technique

Exposure

The surgery is performed as a day care procedure under nerve block anesthesia. A

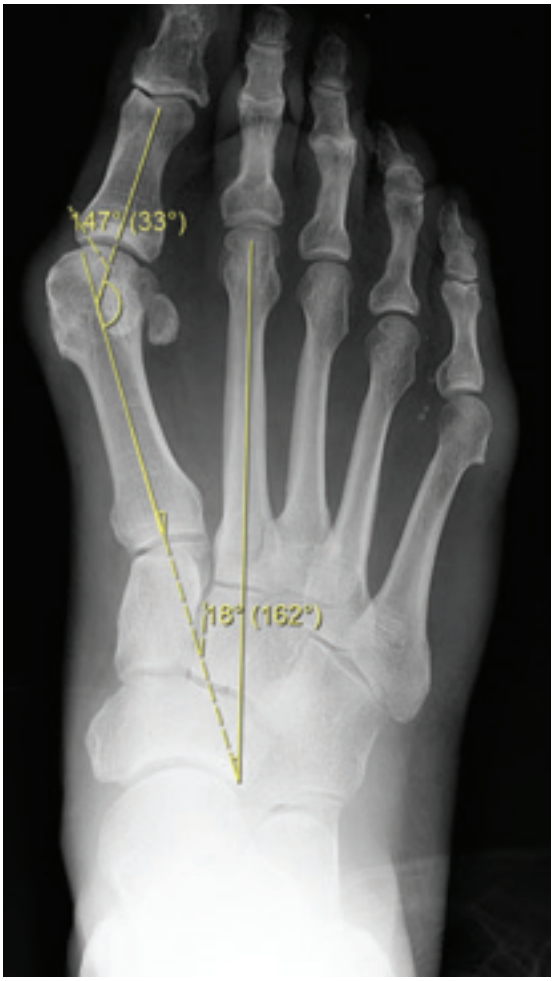


Figure 1. Preoperative weight-bearing AP radiograph of a 68-year man with significant right hallux valgus deformity (HVA 33^0 and IMA 18^0) and displacement of sesamoids.

tourniquet is applied to the calf and a mini C-arm is used throughout. A standard lateral release of the 1st MTP joint is performed through a small incision in the 1st webspace. The 1st TMT joint is then exposed subperiosteally by a direct longitudinal incision placed just medial to the EHL and the joint is freed from its periosteal attachments.

Surgical steps

A derotation pin is placed on the medial side of 1st MT to gain rotation control. At this point, the 1st metatarsal can be manipulated under fluoroscopy to obtain adequate correction in all planes If not, then additional release at the 1st metatarsophalangeal or tarsometatarsal joint may be necessary. A fulcrum is inserted between the bases of 1st and 2nd metatarsals followed by the application of a bone positioner clamp that aids in bringing the 1st metatarsal to the 2nd metatarsal and closing the IM angle. At the same time the derotation pin helps to achieve proper metatarsal rotation. Once the deformity correction is obtained in all 3 planes, it is secured with a temporary holding pin through the bone positioner clamp. A joint "seeker" is placed in the 1st TMT joint and then a special cutting guide is placed over this "seeker" and employed to remove thin bone wedges around the 1st TMT. There are several cutting guides available that allow varying amounts of bone resection and angulation of the bone cuts. A compression/distraction device is then utilized to distract the joint and remove the bone wedges. The fusion surfaces are further prepared by drilling with a 2.0 mm drill and leaving the drillings as autograft. The joint is subsequently compressed with the same device taking care to maintain appropriate correction of the metarsal position in all planes. Temporary fixation may be achieved by two crossed olive wires if one desires to remove the compression/distraction device to make plating easier. Final fixation is completed by the placement of two 4-hole locking plate construct in 90-90 conFigureuration (Figure 2). Medial eminence resection and capsulorrhaphy can be performed as per the need. However, our experience has been that up to 50% of patients do not need such ancillary procedures once the rotational deformity has thoroughly been addressed. All wounds are copiously irrigated and closed meticulously followed by a standard bunion dressing.

Post op care and follow up

The operated extremity is placed in a controlled ankle motion boot. The patient is discharged with crutches and followed up in the office at regular intervals. Sutures are removed in 2 weeks and gradual weight bearing ambulation is commenced as soon as tolerated. Weight-bearing radiographs are performed at 6 weeks (Figure 2) and all the assistive devices are then weaned as indicated. Regular supportive footwear is encouraged and permitted to increase activity as tolerated. Radiographs are again checked at three months postoperative to ensure successful arthrodesis.

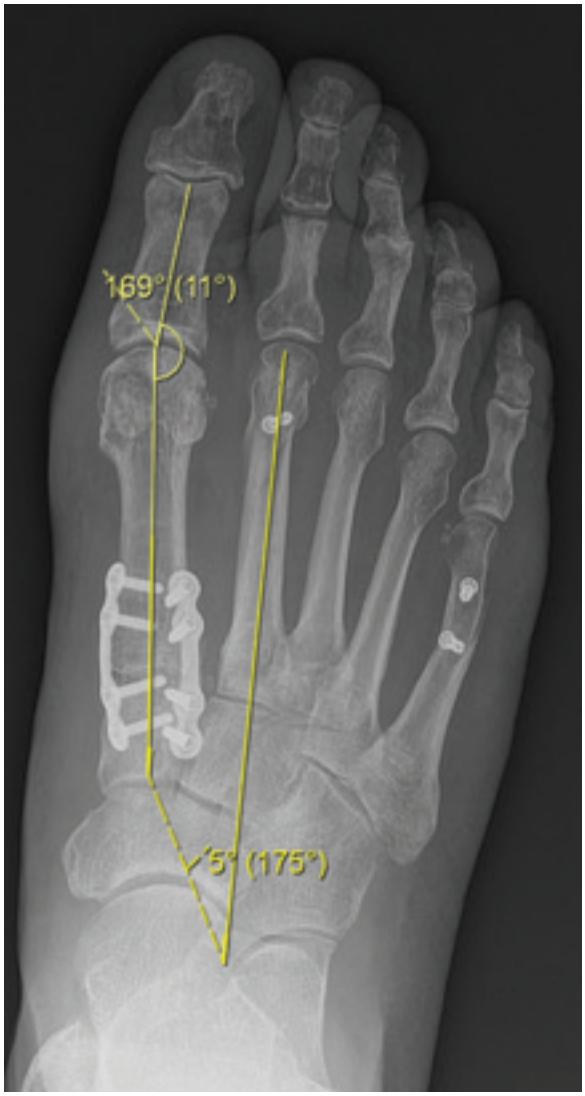


Figure 2. Postoperative weight-bearing AP radiograph of the same patient at 8 weeks showing dual plates at 1st TMT joint. Healing of fusion can be noted along with anatomical restoration of angles (HVA 11^0 and IMA 5^0) and position of sesamoids. He also had 2nd metatarsal shortening osteotomy and bunionette correction done at the same time.

Conclusion

This modified technique of 1st TMT joint fusion using modern reproducible instrumentation is a reliable procedure to achieve tri-plane correction of hallux valgus close to the CORA. This technique has allowed early weight-bearing and consistent results with a classically challenging technique that previously required prolonged non weight-bearing.

References

1. Santrock RD, Smith B. Hallux valgus deformity and treatment: A three-dimensional approach: Modified technique for Lapidus procedure. *Foot Ankle Clin.* 2018 Jun; 23(2): 281-295

2. Kim YJ, Kim JS, Young KW, et al. A new measure of tibial sesamoid position in hallux valgus in relation to the coronal rotation of the first metatarsal in CT scans. *Foot Ankle Int.* 2015 Aug; 36(8): 944-52

3. Yi Y, Lee WC. Comparison of three-dimensional displacement among different metatarsal osteotomies. *Foot Ankle Clin N Am* 2018; 23(2): 193-203

Automated Fascicle Tracking to Characterize Changes in Muscle Architecture During Isokinetic Contractions

John F. Drazan
Todd J. Hullfish
Josh R. Baxter

Department of Orthopedic Surgery, University of Pennsylvania, Philadelphia, PA

Introduction

Characterizing muscle architecture during functional movements provides important insight into the muscle mechanics underpinning musculoskeletal pathologies. Ultrasound imaging is a valuable tool to non-invasively observe changes in muscular structure for pennate muscles throughout a contraction. However, quantifying architectural parameters such as muscle fascicle length and pennation angle from ultrasound frames remains a challenge. Manually measuring these parameters are time and labor intensive. Conversely, automated tracking using computer vision offers efficient techniques improved research workflow and reliability. To address this research need, we have developed an automatic fascicle tracking algorithm that can be used by researchers to track fascicles and automatically extract pennation angle and fascicle length throughout a contraction. The purpose of this study was to quantify the reliability of this algorithm for quantifying medial gastrocnemius architecture during maximal effort plantarflexion contractions performed on a dynamometer.

Methods

Five healthy-young adults performed maximal effort plantarflexion contractions and provided written informed consent in this IRB approved study. Images of the medial gastrocnemius of the right leg were acquired using an ultrasound transducer at 60 Hz at 8 MHz (LV7.5/60/128Z-2, SmartUs, TELEMED), which was secured in place using a custom-made molded cast secured by straps. Subjects were supine on a treatment table, which was secured to an isokinetic dynamometer (System 4, Biodex), with their right foot secured to the dynamometer footplate. Subjects performed maximal-effort isometric contractions at neutral ankle position and isokinetic contractions at 30, 120, 210, 300, and 500 degrees per second. We provided subjects with real-time feedback of plantarflexion torque using a computer monitor to encourage maximal effort. Subjects performed 3-4 contractions per condition until torque output plateaued over three trials. During each contraction, we synchronized ultrasound images with dynamometer angular position, velocity, and torque. We analyzed these videos using a three observation-three observer design to determine intra-rater and inter-rater reliability, respectively. To analyze each trial, users identified the deep and superficial aponeuroses and a muscle fascicle in the first frame of the video. Each of these structures were seeded with 100 tracking points, which were used to fit a line and define the aponeuroses and fascicle (Figure 1:A). Next, we tracked each one of these points frame by frame using affine optical flow in the MATLAB computer vision toolbox (Nanick MA, Mathworks) and automatically redrew the lines in each frame based on the movement of the seeded points to calculate fascicle length and pennation angle. Following the completion of automatic tracking for a given contraction, users identified the fascicle by drawing a line from the fascicle insertion in the deep aponeurosis in six evenly spaced frames across each contraction to serve as a comparison to the automatic tracking measurement (Figure 1). We used linear regression to evaluate the correlation between the manual and automatic measurements of fascicle length and pennation angle across all contractions for all subjects. We also calculated the reliability of both the manual and automatic

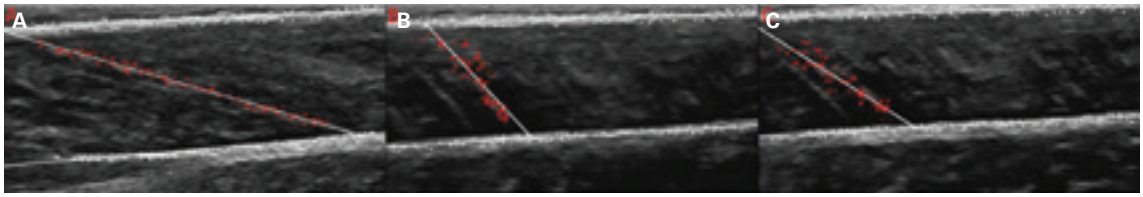


Figure 1. Dynamic ultrasound images of the medial gastrocnemius muscle while a patient performs a maximal plantarflexion contraction demonstrates the shortening dynamics of the muscle. To increase analysis speed and repeatability, users identify the deep and superficial aponeurosis as well as a single-continuous fascicle with the foot in dorsiflexion **(A).** Next, an affine optical flow paradigm tracks these structures through neutral position **(B)** and into peak plantarflexion **(C).** Our automated tracking algorithm has the strongest agreement with manual tracking when the muscle is actively shortening **(AB)** but tends to under-approximate fascicle pennation and over-approximate fascicle length when the muscle is fully shortened **(C).**

tracking paradigms between days and examiners was using intraclass correlation coefficient (ICC). This test produced values ranging between 0 and 1 where values above 0.7 indicated "good" reliability between measurement methods.

Results

Over 5,000 individual muscle fascicles were manually identified by the three examiners. The mean difference between manual and automatic fascicle length measurement was -4.49 ± 7.1 mm. The mean difference between manual and automatic pennation angle was 5.56 ± 7.6 degrees. These differences represent errors of 5.13% and 10.2 % of the dynamic range of fascicle lengths and pennation angle respectively. Manual and automatic fascicle length and pennation angle measurements were highly correlated across all contractions, subjects, examiners, and days (0.89 and 0.85, respectively). Both the manual and automatic fascicle length measurements had 'good' reliability between days for each examiner (0.75 and 0.92, respectively). Manual and automatic measurements of fascicle length also had 'good' reliability between all examiners (0.88 and 0.79, respectively).

Discussion

We observed good measurement reliability across examiners between days and between examiners across all days for both manual and automatic tracking. Our findings indicate that this tool can be used by different users to reliably quantify fascicle architecture from ultrasound images acquired during maximal effort contractions. While the automatic measurements of fascicle geometry were on average longer and less pennate than manual measurements, especially at end-stages of contraction, there were many well-tracked fascicles as shown in (Figure 1:AB). We have observed that this under approximation (Figure 1:C) occurs when seeded points are initially selected over non-fascicle tissue such as veins which upon contraction do not move in concert with the rest of the muscle. These structures are often not evident in the first fame of the video and could be avoided by selecting a different fascicle if given another chance to initialize the program. This study used only the first attempt at tracking regardless of observed tracking quality. As such, these results represent a "worst-case-scenario" for tracking performance which we believe will drastically improve if users can reinitialize the program after observing a poorly tracked fascicle. Current work is focused on optimizing this automatic tracking paradigm to improve measurement fidelity.

Clinical Relevance

Muscle function is dictated by the ability of muscles to change shape during contractions. However, the technical challenges of analyzing large data sets of ultrasound images limits the feasibility of implementing these measurements in a large scale. This work provides a reliable automated framework for extracting these architectural data from images of patient muscle.

Acknowledgements

This work was supported by the Thomas B. McCabe and Jeannette E. Laws McCabe Fund. We would like to thank Rena Mathew and Shilpa Donde for assistance in data collection and analysis.

Functional Deficits Following Acute Achilles Tendon Rupture are Correlated with Changes in Muscle Structure

Todd J. Hullfish
Kathryn M. O'Connor, MD
Josh R. Baxter, PhD

Department of Orthopaedic Surgery, University of Pennsylvania

Summary

Plantarflexor functional deficits are associated with poor outcomes in patients following Achilles tendon rupture. In this study, we established the link between changes in gastrocnemius structure with plantarflexor function 3 months after injury. We found that deficits in peak isokinetic torque were positively correlated with decreases in resting fascicle length following tendon rupture. These findings suggest that patient function is explained by plantarflexor muscle remodelling, which is a rapid and permanent response to Achilles tendon ruptures.

Introduction

Two-thirds of patients who suffer Achilles tendon ruptures have limited plantarflexor function 1-year following the injury. While tendon elongation has been reported as a possible mechanism of functional deficits [1], our recent findings suggest that changes in muscle structure [2] are detrimental to patient function [3]. However, the link between muscle remodelling and isokinetic plantarflexor function has not been well described. Therefore, the purpose of this study was to establish the link between detrimental changes in medial gastrocnemius structure and plantarflexor function. We hypothesized that the magnitude of fascicle length shortening at 3-months following Achilles tendon rupture would be positively correlated with isokinetic plantarflexor deficits.

Methods

Eight adults (7 males; Age: 43.9 ± 12.9; BMI: 28.7 ± 6.5) who suffered acute Achilles Tendon ruptures and were treated non-operatively were enrolled in this IRB approved study. Subjects were prospectively tracked from the first clinical visit through 3 months after injury. Measurements of the medial gastrocnemius structure and function of the uninjured (contralateral) limb were made at the first visit and repeated for the injured limb at 3 months. Images of the mid-muscle belly were acquired with an 8 MHz ultrasound transducer (LV7.5/60/128Z-2, SmartUs, TELEMED) attached to the leg with a custom made cast. Measurements of muscle structure, characterized by fascicle length and pennation, were made while the ankle was passively positioned at 16° plantarflexion. Isometric and isokinetic dynamometry was performed to quantify plantarflexor function. Subjects lay prone with their knee fully extended and their foot affixed to a dynamometer foot plate. Each subject performed sets of 3-4 MVCs under 4 different contraction conditions. Isometric contractions were performed with the ankle at neutral, and isokinetic contractions were performed at 30, 120, and 210°/s.

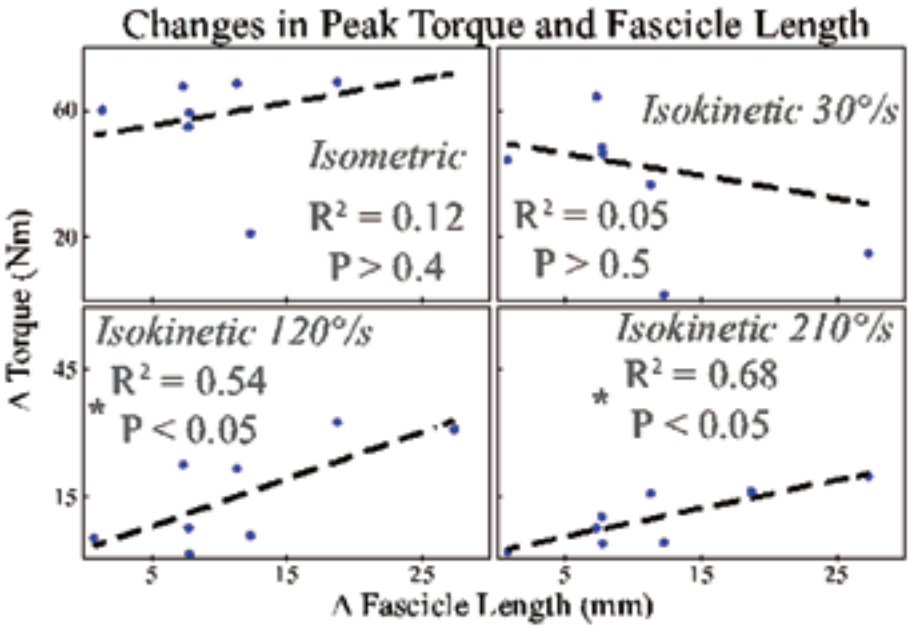


Figure 1: Decreases in fascicle length were positively correlated with decreases in isokinetic torque at 120 and 210°/s.

Results and Discussion

Medial gastrocnemius structure and plantarflexor function following an acute Achilles tendon rupture differed from the healthy contralateral limb 3 months after injury. Fascicle length was 27% shorter ($P = 0.005$) and explained functional deficits in the injured limb. These deficits in isokinetic torque were strongly correlated with changes in fascicle length at 210˚/s ($R^2 = 0.68$, $P < 0.05$) and moderately correlated at 120˚/s ($R^2 = 0.54$, $P < 0.05$). While peak isometric torque decreased by 51% ($P < 0.001$) and peak isokinetic torque measured at 30˚/s decreased by 28% ($P < 0.005$), these functional deficits were not explained by changes in fascicle length. Although and pennation angle was 33% greater ($P < 0.001$) 3 months after injury, plantarflexor kinetic deficits were not explained by these changes in pennation.

Conclusions

Plantarflexor kinetic deficits following Achilles tendon injury are explained by the magnitude of gastrocnemius muscle remodelling at 3 months after injury. These findings challenge the clinical paradigm that functional deficits are explained by tendon elongation [1]. Our ongoing work is focused on understanding the link between tendon elongation and muscle fascicle remodelling.

Acknowledgments

This study was supported by the Thomas B. McCabe and Jeannette E. Laws McCabe Fund. We thank Lauren McGarrity, Shilpa Donde, and Rena Mathew for their assistance with patient recruitment and data collection.

References

1. Silbernagel+ (2012) *Am J Sports Med*, 40(7): 1564-71.
2. Hullfish+ (2019) *bioRxiv [preprint]*, doi: 10.1101/445569
3. Baxter+ (2019) *J Biomech* [Online, Jan. 29, 2019]

Plantarflexor Torque and Work is Positively Correlated with Medial Gastrocnemius Fascicle Length in Healthy Adults

John F Drazan[1]
Todd J Hullfish[1]
Josh R Baxter[1]

1 Department of Orthopaedic Surgery, University of Pennsylvania

Summary

In this study, we determined the relationship between muscle architecture and peak torque and total work produced by the plantarflexors during maximal effort isokinetic contractions. We measured resting fascicle length and pennation angle and calculated muscle thickness in the medial gastrocnemius using ultrasound in healthy adult subjects (n = 12). Subjects performed maximal effort isokinetic contractions on an isokinetic dynamometer at 0, 30, 120 and 210 °/s. We calculated peak torque and total work at each velocity and used linear regression to examine the relationship relating fascicle length, pennation angle, and muscle thickness to peak torque and total work. We found that fascicle length was more strongly correlated with both peak torque and total work than pennation angle or muscle thickness. This provides experimental evidence linking resting muscle architecture to dynamic muscle performance in healthy adults which has been hitherto not experimentally demonstrated in existing literature.

Introduction

Plantarflexor kinetics is critical for ambulatory function in elite athletes, the elderly, and many patient populations. Despite the robust findings linking plantarflexor muscle structure with these populations[1], the link between plantarflexor fascicle length and ankle kinetics has not been established in the literature. Therefore, the purpose of this study was to determine the relationship between medial gastrocnemius architecture and plantarflexor function.

Methods

Twelve healthy adults performed maximal effort plantarflexor contractions at 0, 30, 120, and 210 °/s on an isokinetic dynamometer after providing written informed consent in this IRB approved study. We measured muscle architecture (fascicle length, pennation angle, and thickness) of the medial gastrocnemius muscle with the ankle in resting position of 16°[2] using ultrasound. We calculated peak torque and total work at each velocity. To determine the relationship between muscle architecture and plantarflexor function, we performed linear regression between the three architectural parameters and the two kinetic parameters. We hypothesized that (1) longer resting fascicles would generate higher peak torques and do more work (2) that fascicle length would have the strongest correlation to plantarflexor function.

Results and Discussion

Longer fascicles generated higher peak torque and did more total work (Figure 1, $R^2 > 0.41$, $p < 0.013$) across all velocity conditions. We found that resting fascicle length was more strongly correlated with both peak torque and total work than pennation angle and muscle thickness (Table 1). These experimental findings support our recent computational simulations[3]

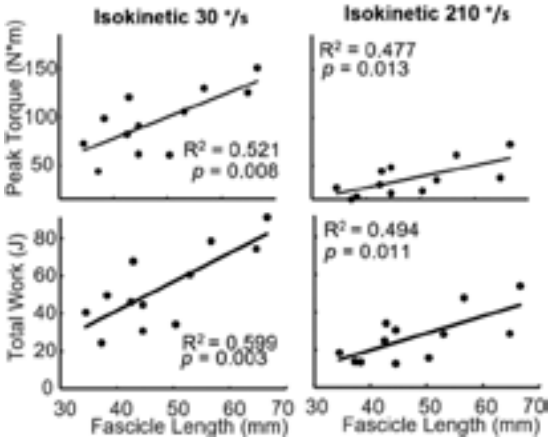


Figure 1: Peak plantarflexor torque (*top row*) and work (*bottom row*) are positively correlated with resting fascicle length at slow (30°/s) and fast (210°/s) rates of plantarflexion rotation.

Table 1: Regression Values comparing three resting architecture parameters to the two functional dynamic parameters. Bold shows p < 0.05.

	R^2 - Resting Fascicle Length				R^2 - Resting Pennation Angle				R^2 - Resting Muscle Thickness			
Angular Velocity (°/s)	0	30	120	210	0	30	120	210	0	30	120	210
Peak Torque	**0.325**	**0.521**	**0.415**	**0.477**	0.09	**0.339**	0.296	**0.417**	0.153	0.124	0.104	0.076
Total Work	–	**0.599**	**0.413**	**0.494**	–	0.326	0.255	**0.39**	–	0.172	0.117	0.089

that highlight the importance of plantarflexor fascicle length during single-leg heel raises—a clinical test of function in patients with Achilles tendon pathology.

Conclusions

These results link muscle architecture with dynamic muscle function in healthy young adults. Ongoing work is focused on understanding the implications of injury on muscle remodelling and long-term plantarflexor function.

Acknowledgments

This work was supported by the Thomas B. and Jeannette E. Laws McCabe Fund and NIH grant K12GM081259.

References

1. Abe *et al* (2000). *J Appl Physiol, 88,* 811-6
2. Zellers *et al* (2018). *F and Ank Int 39,* 343-348
3. Baxter *et al* (2019). *J Biomech,* Online 29 January 2019

Simulated Single-Leg Heel Raise Function is Governed Primarily by Optimal Fiber Length

Josh R. Baxter[1]
Daniel C. Farber[1]
Michael W. Hast[1]

1 University of Pennsylvania, Philadelphia, PA

Introduction

Long-term functional deficits are associated with poor outcomes in many patients following Achilles tendon ruptures[1]. Structural changes to both the plantarflexor muscles[2] and Achilles tendon[3] may be predictors of patient function. Single-leg heel raise performance is a key clinical benchmark for quantifying patient function following Achilles tendon ruptures and return to activity. Simple computational models can simulate the effects of small deviations in plantarflexor muscle-tendon unit (MTU) parameters and objectively quantify how these changes affect ankle and locomotor function. Therefore, the purpose of this study was to characterize how changes to various MTU parameters (optimal fiber length, resting ankle angle, pennation angle, maximum isometric force, and tendon stiffness) influence the model's ability to perform a single-leg heel raise. We hypothesized that muscle fiber length and resting ankle angle—a clinical surrogate for tendon length—would have the greatest effect on single-leg heel raise performance.

Methods

Resting ankle angle and MTU parameters were iteratively tested to estimate the effects of these parameters of single-leg heel raise function. The MTU parameters that were tested in this simulation study were optimal muscle fiber lengths, pennation angles, maximum isometric forces, and Achilles tendon stiffness values (Figure 1A); as well as resting ankle angle (Figure 1B), a surrogate measure of tendon slack length. First, the soleus and gastrocnemius MTU parameters were iteratively adjusted between 50% and 150% of model default values[5]. Next, the resting ankle angle was set to physiologic ranges between 0 and 20 degrees plantarflexion in order to provide clinical relevance. We performed the computational analog of instructing the patient to lay prone on a treatment table while the foot and ankle freely hangs at a 'resting angle'. Tendon slack lengths were changed in order to minimize the resultant ankle torque while keeping the muscle fibers near their optimal lengths.

Single-leg heel-raises were then simulated using a simplified musculoskeletal model that was constrained to move in along a vertical line travelled during a single-leg heel raise[4] (Figure 1C). The ankle was modeled as a pin-joint that was flexed by a single dorsiflexor muscle, the tibialis anterior, and extended by two plantarflexor muscles, the soleus and gastrocnemius. Single-leg heel raises were simulated for 3,125 combinations of these five MTU parameters. The effect of a 1% change in each of the MTU parameters (normalized by the physiologic ranges tested in this study) on heel-raise function (peak ankle angle) was calculated using a multi-variate linear regression model.

Results

Simulated single-leg heel raises were most affected by the optimal fiber lengths and the resting ankle angle (Figure 2). Reducing optimal fiber lengths, muscle strength, and decreasing resting ankle plantarflexion all decreased the likelihood of a successful heel raise. Changes in muscle pennation and tendon stiffness had much smaller effects on heel raise function.

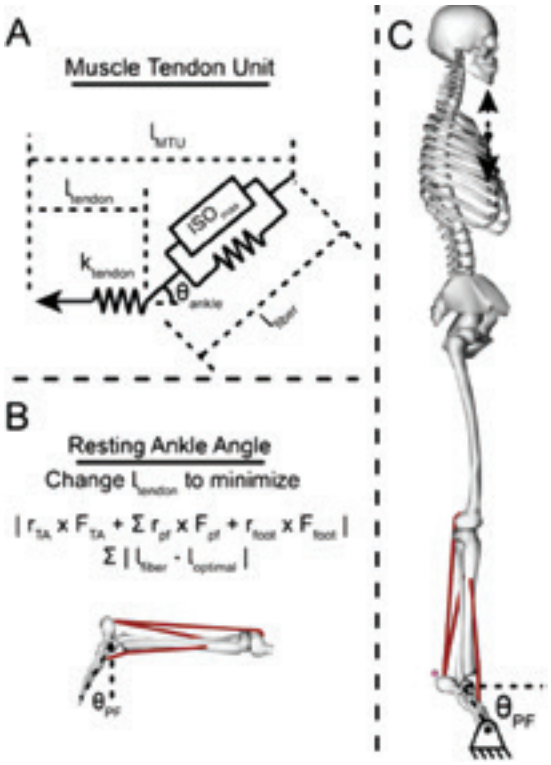


Figure 1. Muscle-tendon unit (MTU) parameters were perturbed to test their effect on heel raise function **(A).** Tendon slack lengths were calculated for each MTU combination to recreate a resting ankle angle **(B).** These MTU parameters were then simulated using simplified musculoskeletal model of a single-leg heel raise **(C).**

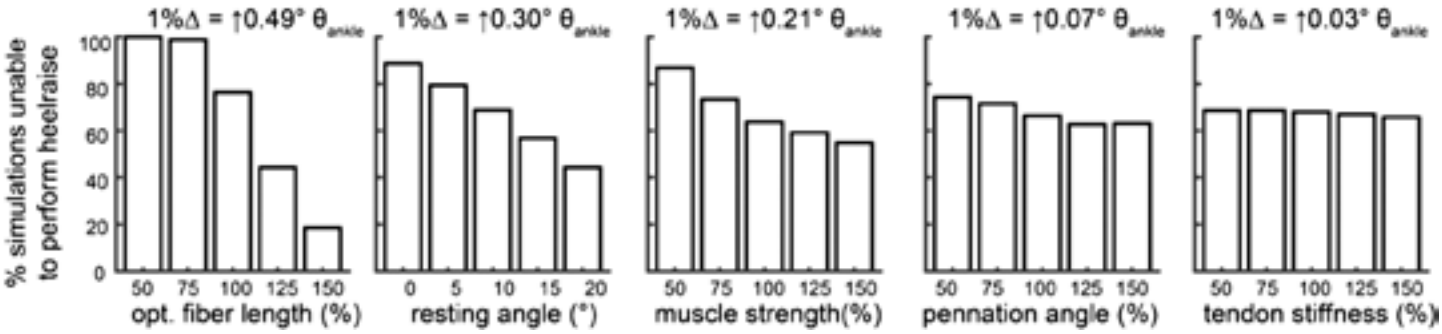


Figure 2. The ability to perform a single-leg heel raise (45 degrees of plantarflexion) was partially governed by each of the tested MTU, which each had an effect on the amount of ankle plantarflexion (1% change in MTU had some documented effect, top values). Shorter optimal fiber lengths were unable to complete the heel raise regardless of other MTU parameters. Resting ankle angle—a surrogate measure of tendon slack length—and muscle strength were also stronger predictors of heel raise function. Muscle pennation and tendon stiffness had a smaller effect on the heel raise simulations.

Discussion

In this study we tested the simulated effects of physiologically feasible changes to MTU parameters on single-leg heel raise function[2,3,6]. In support of our hypothesis, we found that heel-raise function was most sensitive to changes in optimal fiber length and resting ankle angle (achieved through changing the resting ankle angle). Additionally, these findings support prior work, which found excessive muscle fascicle length and tendon length to be associated with functional deficits[2,3]. Although the single-leg heel raise is a submaximal activity, it is an effective clinical tool for gauging plantarflexor function. Minimizing tendon elongation following surgical repair should be investigated further in order to improve long-term patient outcomes. This simplified model had motion constraints and used generic MTU parameter data from the literature[4]. Therefore, these findings should be considered in the context of ranking the effects of each MTU parameter rather than a predicted effect on patient function.

Clinical Relevance

Preserving muscle fiber and tendon slack length should be considered the most important objectives when treating acute Achilles tendon ruptures.

References

1. Brorsson+, *Am J Sports Med*, 2017
2. Baxter+, *J Biomech*, 2018
3. Silbernagel+, *Am J Sports Med*, 2012
4. Delp+, *IEEE Trans Biomed Eng*, 2007
5. Arnold+, *Annals Biomed Eng*, 2010
6. Agres+, *Scan J Med Sci Sports*, 2015

Tips and Tricks: Vascularized Free Fibula Intercalated Graft for Humeral Shaft Reconstruction after Ewing's Sarcoma Resection

Kelsey Bonilla, MD[1]
Alexandre Arkader, MD[2]

1 Department of Orthopaedic Surgery University of Pennsylvania

2 Department of Orthopaedic Surgery Children's Hospital of Philadephia

Introduction

Ewing's sarcoma (EWS) is a small round cell sarcoma which most commonly presents in the metaphysis and diaphysis of long bones, usually with a large associated soft tissue component[1]. It is the second most common primary malignant bone tumor in children after osteosarcoma. EWS is classically defined by a translocation of chromosomes 11 and 22 resulting in the EWSR1-FLI1 fusion protein that acts as an oncogenic transcription factor[2].

The most important prognostic indicator is the presence of metastases at the time of presentation. Twenty five percent of patients present with metastatic disease. Bone or bone marrow metastases portend a worse prognosis than pulmonary metastases. Ten year survival is approximately 60% for localized disease and 30% for metastatic disease[1]. Other negative features include response to chemotherapy, size greater than 8 cm, location and expression of specific genetic markers including p53, Ki-67, or HER-2/neu. The cornerstone of treatment is chemotherapy for systemic control and local control via surgical resection and/or radiotherapy.

The surgical treatment can be done with limb salvage or amputation.Among the alternatives for limb salvage are resection followed by biological reconstruction or endoprosthetic device. Here we report on the use of a vascularized free fibular autograft for humeral reconstruction following resection of a diaphyseal Ewing's sarcoma.

Case Report

History

The patient is a healthy 19 year old male who sustained a left humerus fracture while catching a lightweight object. He reported two months of antecedent humeral pain without constitutional symptoms or prior injury. Imaging obtained at the time of injury demonstrated a pathologic fracture through an aggressive appearing bone lesion at the left midshaft humerus.

Examination

On exam, he had tenderness and swelling around the fracture site. Motor and sensory function was normal in all nerve distributions in the left upper extremity. There was no palpable mass or skin lesions.

Imaging

X-rays of the left humerus were obtained at the time of injury and were notable for a nondisplaced pathologic fracture through a poorly defined, permeative, lytic lesion in the mid-humeral diaphysis (Figure 1). Subsequent contrast enhanced MRI of the humerus was obtained and demonstrated a 5.6 cm x 2.0 cm heterogenous enhancing lesion in the mid-diaphysis with periosteal reaction and a small soft tissue component (Figure 2.).

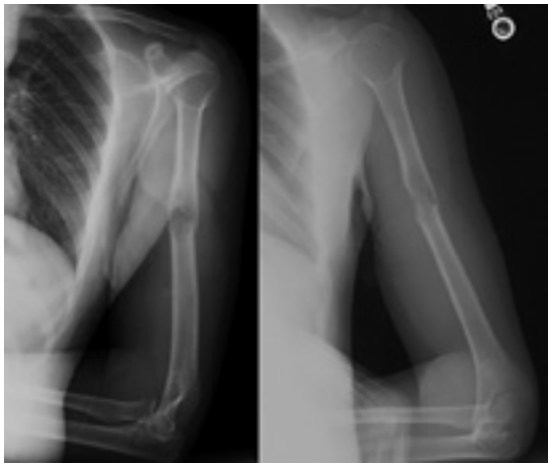


Figure 1. Injury films demonstrating pathologic fracture through lytic lesion in left humeral diaphysis.

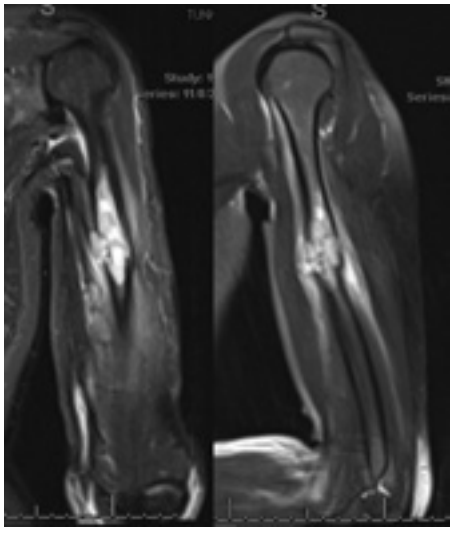


Figure 2. Coronal and sagittal T2 MRI sequences with expansile intramedullary lesion and small soft tissue component.

Management

Given the concern for a malignant process, the decision was made to proceed with a core needle biopsy with Interventional Radiology. Pathology was consistent with a small round cell tumor and RNA sequencing demonstrated EWSR1-NFATC2 fusion protein. The patient underwent the standard work-up including PET scan, CT chest, and bone marrow biopsy, which were negative for metastatic disease. Six cycles of chemotherapy alternating vincristine, Cytoxan, and doxorubicin with ifosfamide and etoposide were administered preoperatively.

Surgical Resection

After completing neo adjuvant chemotherapy, the patient was deemed to be a good candidate for limb salvage with resection of the left humeral Ewing's sarcoma with primary reconstruction with vascularized fibular autograft. This was the ideal approach because imaging suggested that wide resection was possible despite the previous pathologic fracture and that all major neurovascular structures could be spared. The tumor's size was also suitable for reconstruction with fibular autograft.

An extensile approach to the anterior left humerus was used following the deltopectoral interval. The pectoralis major, conjoined tendon, and latissimus dorsi were released and the brachial plexus was identified. The anterior humeral circumflex vessels were ligated (Figure 3A). Distally, the biceps was mobilized and brachialis transected at the predicted resection level. The radial nerve was dissected away from the tumor, the deltoid and triceps were released, and the proximal bone cut was made. After distal dissection of tumor was completed, the distal bone cut was made and the tumor was sent to pathology (Figure 3B). Frozen sections of marrow contents from proximal and distal margins were negative for tumor.

The contralateral fibula was simultaneously harvested by a microsurgeon for an intercalary vascularized bone graft. The graft was cut to the appropriate size and the proximal and distal ends of the graft were burred down and impacted into the medullary canal on either end of the remaining humeral shaft. Fixation was achieved with quadricortical small fragment screws and a long proximal humerus plate (Figure 3C). Microvascular anastomoses were performed between the peroneal artery and vein and large branches of the brachial artery and vein. Muscle flaps were then reattached to the plate or periosteum and the wound was closed with a drain in place.

Final pathology confirmed Ewing Sarcoma variant characterized by EWSR1-NFATC2 fusion protein with negative margins and 50% tumor necrosis.

Postoperative Course

The patient remained non-weight bearing on the left upper extremity in a shoulder immobilizer for 3 weeks and weight bearing as tolerated on the right lower extremity in a CAM boot. The patient was neurovascularly intact and was discharged home on postoperative day 5. His staples were removed and range of motion was initiated three weeks postoperatively.

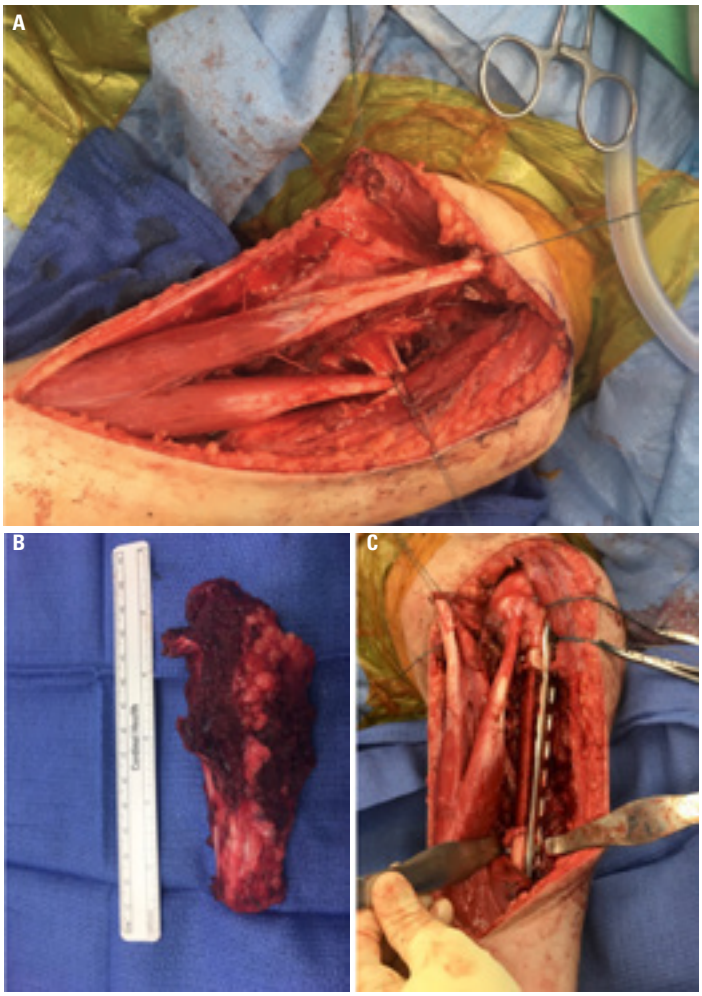


Figure 3. Intraoperative photos depicting **(A)** surgical approach, **(B)** explanted tumor, and **(C)** intercalary fibular graft.

At this time he restarted chemotherapy and completed an additional 7 cycles. The final cycle of ifosfamide and etoposide was deferred due to neutropenia and bacteremia leading to admission for septic shock.

The patient followed up at regular intervals postoperatively without wound complications or evidence of tumor recurrence at one year. Imaging demonstrates complete incorporation of the graft without hardware complications (Figure 3). Exam is notable for full forward flexion, extension, and external rotation of the shoulder and a 20 degree loss of abduction. He has normal sensation in all distributions and appropriate resisted strength. The patient has returned to full activities without pain or functional limitations.

Discussion

Ewing sarcoma is a small round cell sarcoma that is associated with significant morbidity and mortality in the pediatric population. It is most often caused by a translocation of the Ewing sarcoma breakpoint region 1 (EWSR1) gene on chromosome 22 and a member of the E26 transformation-specific (ETS) family of transcription factors on chromosome 11 leading to the formation of a fusion protein, most often EWSR1-FLI1. However, rare histological variants have been

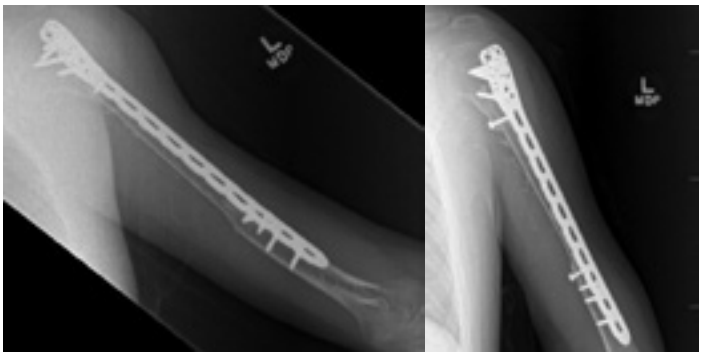


Figure 4. X-rays obtained 10 months after surgery demonstrating graft incorporation.

reported involving fusion to NFATc2 gene, as is seen in this case[2]. These variants exhibit strong cytoplasmic staining with CD99 and dot-like positivity with AE1/AE3. Cells are arranged in nests embedded in myxoid stroma and, unlike classic Ewing sarcoma, the tumor cells are pleomorphic with enlarged nuclei and prominent nucleoli.

The clinical significance of this genetic variant is not well understood. Multimodal treatment approaches with aggressive chemotherapy and radical surgical resection are the cornerstone of treatment. Advances in these techniques have led to limb salvage surgery replacing amputation for the treatment of upper extremity sarcomas without negatively impacting survival. Ultimately, the fundamental goals of limb salvage surgery in the upper extremity are to adequately resect the tumor, preserve hand function, and maintain a survival rate at least equal to that of amputation[3].

There are a variety of reconstructive options available, including prosthetics, allografts, and autografts. While prosthetics permit early use of the extremity, they are at risk of infection or mechanical complications that may require revision surgery, especially in young patients.

Reconstruction with vascularized biological grafts is an attractive alternative given their ability to remodel in response to biomechanical cues and permit longitudinal growth in pediatric patients if the physis is preserved. Free vascularized fibular grafts are the most popular choice for filling segmental defects due to their versatility and low donor site morbidity, however vascularized rib and iliac crest grafts are also reconstructive options[4]. Vascularized autografts are also at lower risk of fracture and infection than allografts and have a higher rate of union[5,6].

The most common complications seen following free vascularized fibula autograft for upper extremity reconstruction are fracture (11.7%), nerve injury/palsy (7.5%), and infection (5.7%)[7]. Although the fibula hypertrophies when used for reconstruction of intercalary defects of the femur and tibia, the rate of fracture is significantly greater than in the upper extremity. Capanna et al. describe the use of an allograft shell with an intramedullary vascularized fibula to create a graft with greater structural integrity and thus mitigate this risk in lower extremity reconstruction[8,9].

Conclusion

Ewing sarcomas are the second most common malignant primary bone sarcomas in the pediatric population. Treatment depends on wide surgical resection (and/or radiation therapy) for local control and chemotherapy for systemic control. Vascularized free fibula grafts are well suited for reconstruction of large segmental defects and offer a limb sparing approach without increasing the risk of tumor recurrence. This case highlights the typical treatment course for a patient who underwent limb salvage with free vascularized fibular autograft. His ability to return to normal activities without significant deformity or functional limitation exemplifies the current shift in focus to a patient centered approach for the management of complex diseases.

References

1. Bosma SE, Ayu O, Fiocco M, *et al.* Prognostic factors for survival in Ewing sarcoma: A systematic review. *Surg Onc* 2018; 27: 603-610.

2. Sadri V, Barroeta J, Pack SD, *et al.* Malignant Round Cell Tumor of Bone with *EWSR1-NFATC2* Gene Fusion. *Virchows Arch* 2014; 465(2): 233-239.

3. Leit ME and Tomaino MM. Principles of limb salvage surgery of the upper extremity. *Hand Clin* 2004; 20: 167-179.

4. Eward WC, Kontogeorgakos V, Levin LS, *et al.* Free Vascularized Fibular Graft Reconstruction of Large Skeletal Defects after Tumor Resection. *Clin Orthop Relat Res* 2010; 468: 590-598.

5. Gebert C, Hillmann A, Schwappach A, et al. Free Vascularized Fibular Grafting for Reconstruction after Tumor Resection in the Upper Extremity. *J Surg Oncology* 2006; 94: 114-127.

6. Estrella EP and Wang EH. A Comparison of Vascularized Free Fibular Flaps and Nonvascularized Fibular Grafts for Reconstruction of Long bone Defects after Tumor Resection. *J Reconstr Microsurg* 2017; 33: 194-205.

7. Landau MJ, Badash I, Yin C, *et al.* Free vascularized fibula grafting in the operative treatment of malignant bone tumors of the upper extremity: A systematic review of outcomes and complications. *J Surg Onc* 2018; 117: 1432-1439.

8. Campanna R, Campanacci DA, Belot N, et al. A New Reconstructive Technique for Intercalary Defects of Long Bones: The Association of Massive Allograft with Vascularized Fibular Autograft. Long-Term Results and Comparison with Alternative Techniques. *Orthop Clin North Am* 2007; 38: 51-60.

9. Bakri K, Stans AA, Mardini S, et al. Combined Massive Allograft and Intramedullary Vascularized Fibula Transfer: The Capanna Technique for Lower-Limb Reconstruction. *Semin Plast Surg* 2008; 22(3): 234-241.

Orthoplastics Tips and Tricks: Bilateral Navicular Osteonecrosis Treated with Medial Femoral Condyle Vascularized Autograft

Ivan J. Zapolsky, MD[1]
Christopher R. Gajewski, BA[2]
Matthew Webb, MD[1]
Keith L. Wapner, MD[1]
L. Scott Levin MD[1]

1 Department of Orthopaedic Surgery, University of Pennsylvania

2 Perelman School of Medicine, University of Pennsylvania

Abstract

A 17-year-old male with a history of chronic bilateral navicular osteonecrosis with fragmentation was treated with staged bilateral open reduction and internal fixation of tarsal navicular with debridement of necrotic bone and insertion of ipsilateral medial femoral condyle vascularized bone grafting. The patient progressed to full painless weight bearing on each extremity by four months post operatively. This patient's atypical presentation of a rare disease was well-treated with the application of orthoplastic tools and principles to promote return of function and avoidance of early arthrodesis procedure.

Case

A 17-year-old male with a history of bilateral Kohler's disease with 4 years of mild bilateral foot pain (Figure 1) presented to outpatient clinic with a 5-day history of severe right foot pain that began after an attempted acrobatic maneuver. Radiographs demonstrated a chronic appearing fracture of the right tarsal navicular with evidence of osteonecrosis of his navicular. (Figure 2) The prognosis, treatment, and challenge of Kohler's disease will be discussed later.

In order to address the patient's acute issue while minimizing the potential for failure of intervention it was recommended that patient undergo open reduction and internal fixation of his right tarsal navicular with debridement of necrotic bone with insertion of a medial femoral condyle vascularized bone graft.

Intraoperatively, the patient was induced under general anesthesia with epidural block. The right lower extremity was prepped and a tourniquet was applied. Incision was made over the dorsomedial aspect of the talonavicular joint with creation of a talonavicular dorsal capsulotomy. Exposure of the non-union revealed a transverse fracture in the axial plane with a smaller dorsal fragment and larger plantar fragment. On visualization, the dorsal fragment appeared well-vascularized in contrast to the avascular-appearing plantar fragment. A trough was created in the inferomedial pole of the navicular extending 3/4 of the way to the lateral pole, leaving 4 mm of bone distally and proximally at the joint surfaces. A free-floating devascularized navicular bone fragment was removed from the joint through a dorsal lateral incision and capsulotomy.

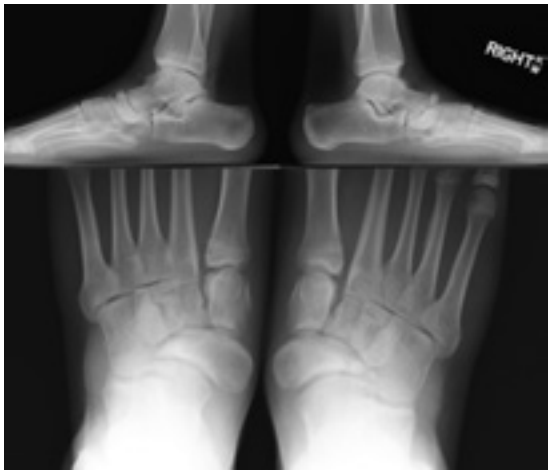


Figure 1. Early diagnostic bilateral foot weight-bearing x-rays, 18 months pre-op.

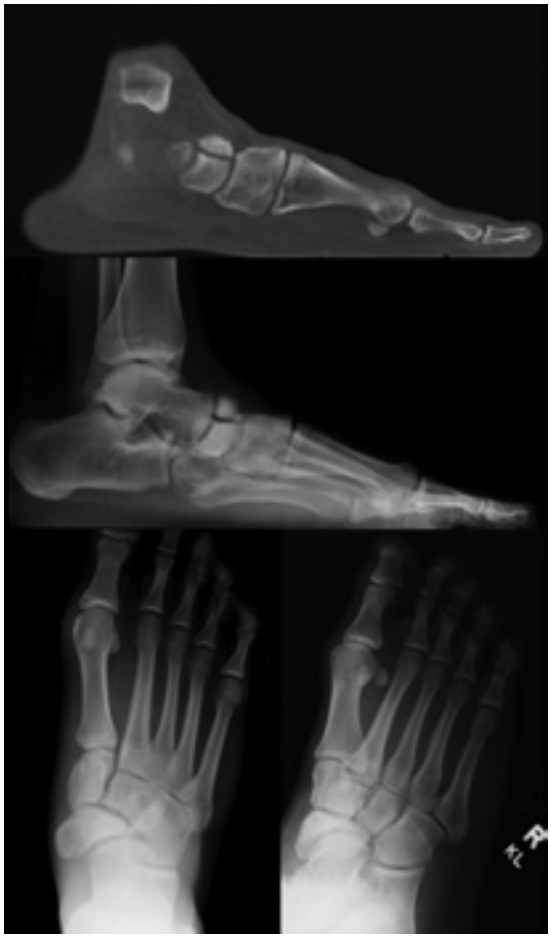


Figure 2. Preoperative x-rays and sagittal CT of patient's right foot.

Vascularized medial femoral condyle bone graft with bone block measuring 1.2 cm on a side with periosteal sleeve was harvested from ipsilateral knee. Graft was isolated on a 10 cm pedicle from the superficial femoral artery and vein (Figure 3). Anterior tibial artery and vena comitans were identified and prepped as recipient vessels for the vascularized bone graft (Figure 4). Tourniquet was released and graft perfusion was verified prior to pedicle division.

The graft was then tailored to be inserted into the trough prepared in the navicular. The bone block was secured to the navicular with 2 screws and supplemental k-wire. The cortical surface and pedicle were positioned medially (Figure 5). End-to-end anastomosis to the anterior tibial artery was performed. There was immediate venous return upon arterial connection. Couplers were utilized for venous anastomosis to vena comitantes. The wounds were copiously irrigated, closed, and a posterior splint was applied. Post operatively, doppler confirmed there was excellent arterial signal going across the dorsum of the foot to the level of the cortical cancellous bone block.

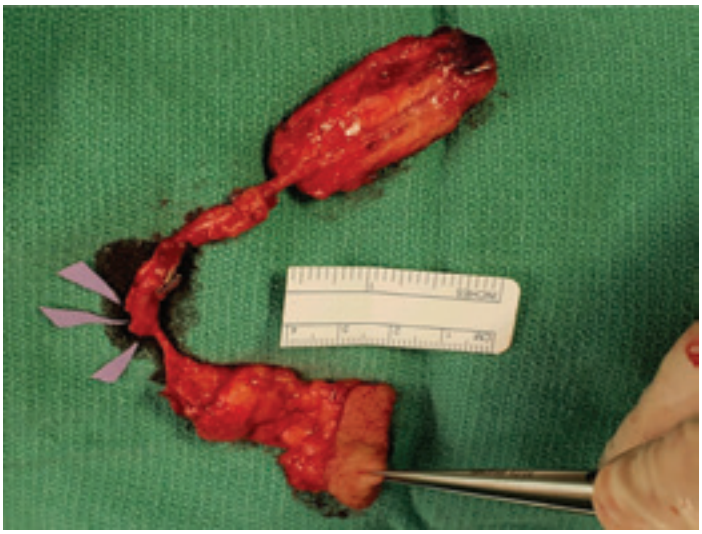


Figure 3. Prepared medial femoral condyle vascularized bone graft.

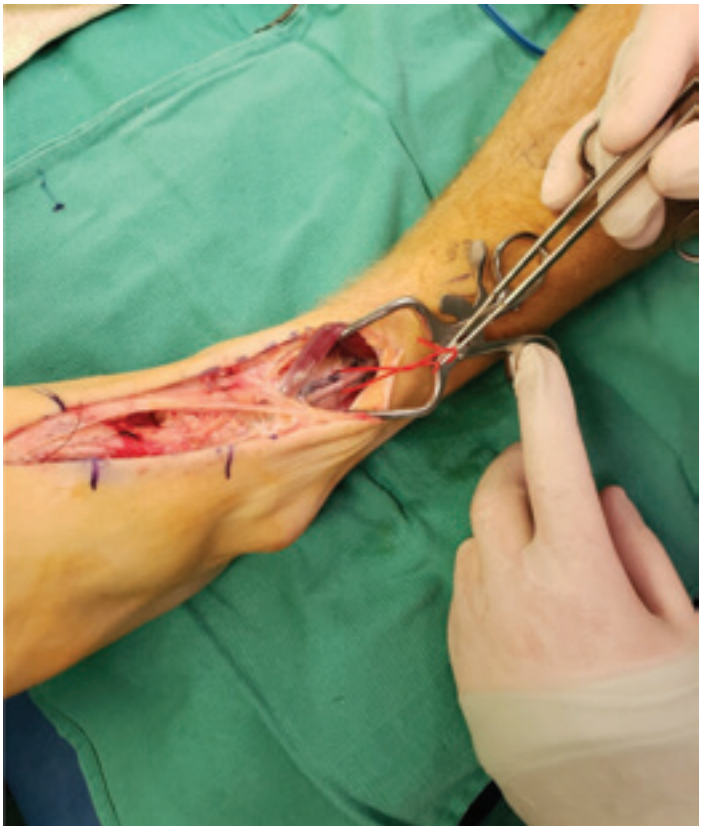


Figure 4. Intraoperative image demonstrating surgical incision and prepared recipient vessels.

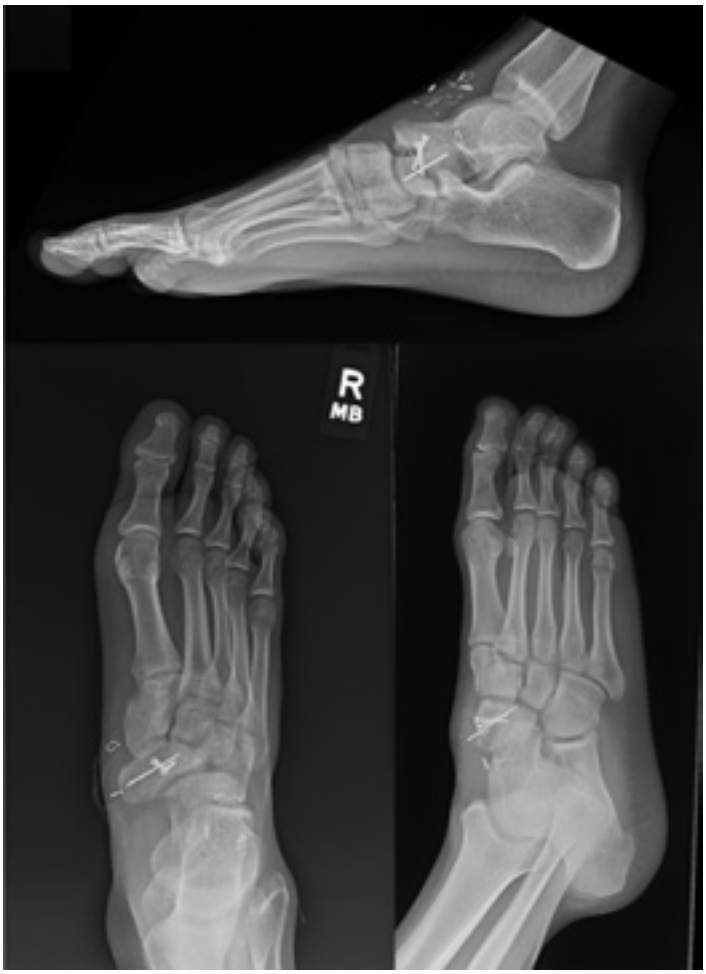


Figure 5. Postoperative right foot x-rays.

Following the procedure, patient was admitted to the ICU for monitoring. vascular checks were performed every hour by nursing and every 2 hours by orthopedic house staff for the first 24 hours after surgery. Monitoring was weaned and patient was transferred to the floor. Patient was discharged without acute events on post op day three. Upon discharge, instructions were given to remain non-weight bearing on the right lower extremity and to avoid dangling the affected limb for the first 3 weeks after surgery. Sutures were removed 3 weeks post op and a short leg cast was placed. At this point the patient was allowed to dangle 56 minutes out of an hour, but was still maintained non weight bearing. Weight bearing on the right foot was sequentially advanced to partial weight bearing in a CAM boot and crutches (25% at 6 weeks post op

and 50% at 9 weeks post op). At 12 weeks post op, CAM boot and crutches were weaned 1 hour per day every 3 days with physical therapy for foot and ankle strengthening. The patient ultimately progressed to full weight bearing without pain or complication by 4 months post op.

Following recovery from right foot intervention, the patient elected to undergo operative management to address chronic pain of his left foot. As described previously, patient also had a history of AVN with fragmentation and non-union of his left navicular (Figure 6). Patient underwent open reduction and internal fixation of his left navicular with debridement of necrotic bone and insertion of ipsilateral medial femoral condyle vascularized bone graft. Procedure was conducted in the same fashion as the contralateral side without significant complication (Figure 7). Postoperative management as planned to progress on the same protocol as right side. At the time of publication, the patient is 4 months post op from left-sided procedure and 10 months post op from the right-sided procedure.

Discussion

Regardless of the etiology or location, osteonecrosis has numerous therapeutic challenges.[5,13] Osteonecrosis has a large variability in presentation ranging from pain and deformity leading to permanent disability, as in avascular necrosis of the femoral head, to spontaneous resolution without lasting complication, as is common in Kohler's disease of the tarsal navicular.[3] This wide range of presentations and outcomes independent of management makes clinical decision making challenging when dealing with a case of osteonecrosis. Clinicians aim to provide the best possible outcome while avoiding unnecessary procedures. Since osteonecrosis may resolve spontaneously or progress to cause permanent disability it poses a situation where a physician may initially be reluctant to intervene. However, in hesitating to intervene early, one may miss an opportunity to prevent progression. Successful management of these patients involves identifying high risk fractures and patients and intervening on these early and aggressively.[2]

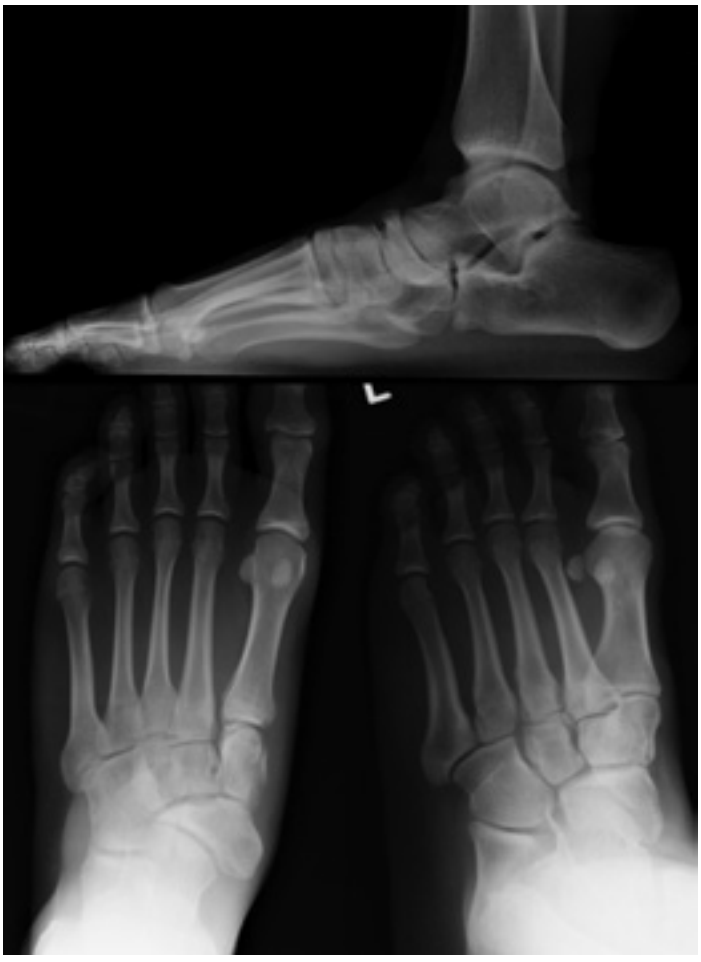


Figure 6. Preoperative left foot x-rays.

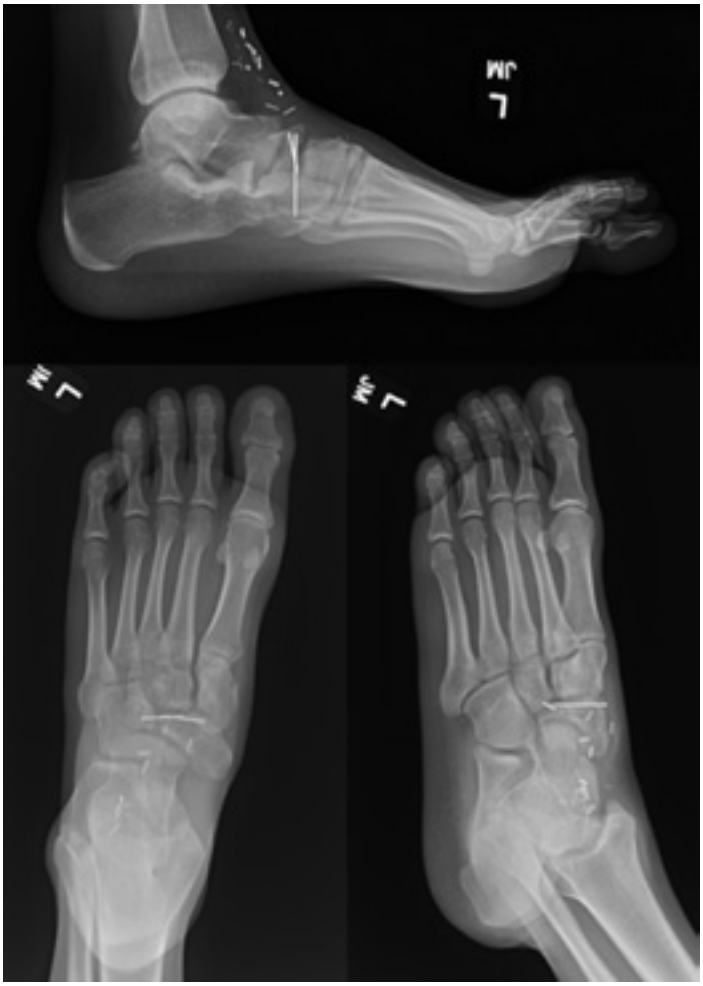


Figure 7. Postoperative left foot x-rays.

Osteonecrosis of the Navicular has multiple described causes. Kohler's disease is an idiopathic condition which occurs spontaneously in young children and has an excellent prognosis. The condition is self-limited without long-term sequelae, although recent evidence has shown that immobilization and non-weight bearing can significantly shorten the duration of symptoms.[3]

Müeller-Weiss syndrome is also an idiopathic osteonecrosis of the navicular, which presents similarly to Kohler's disease,

but occurs predominantly in middle-aged adults. Müeller-Weiss syndrome has a much more ominous prognosis and can cause progressive degeneration and fragmentation of the navicular leading to foot pain and deformity.[4,10,11,12] There have been reports of early intervention in Müeller-Weiss syndrome halting or reversing disease progression. Early interventions include drilling, decompression and bone grafting, or vascularized osseous tissue grafting of the navicular.[6,7,9] Ultimately, the goal of these interventions is to re-establish blood flow to the avascular portion of the navicular and promote reconstitution of healthy osseous architecture within the tarsal navicular.

The patient presented does not fit neatly into any of the described or well understood causes of navicular osteonecrosis. His age is consistent with a diagnosis of bilateral tarsal navicular Kohler's disease; however, this disease is almost always self-limited and does not result in permanent fragmentation, deformity, or necrosis of the navicular.[5] The patient's morbidity supports a diagnosis of Mueller-Weiss syndrome, however this is not known to affect pediatric populations.[4,10]

The patient's acute on chronic navicular injury challenged conventional treatment as simple immobilization of extremity or fixation of his fracture would likely result in non-union due to the altered metabolism of his avascular navicular.[1,2] To further complicate the situation, the patient also suffered an acute unilateral injury that lead to his presentation. Current practice standard for acute management of tarsal injuries is generally conservative, however the unique situation made traditional therapy likely to fail as it would not address his underlying condition.[8,1] In our patient, the dual therapeutic goals of healing a fracture non-union in conjunction with intervention on navicular osteonecrosis necessitated more aggressive intervention.Vascularized bone grafting was utilized to optimize the biological atmosphere for fracture healing as well as replace necrotic bone with healthy biologically active bone to promote appropriate remodeling.

A case such as this presents situations where the literature fails to provide evidence-based management guidelines. Instead, a surgeon must combine and appropriately apply basic orthopedic principals, medical knowledge of biology, and advanced surgical techniques to create solutions that provide patients with a chance of an excellent outcome.

References

1. Bishop JA, Palanca AA, Bellino MJ, Lowenberg DW. Assessment of compromised fracture healing. *J Am Acad Orthop Surg.* 2012 May;20(5):273-82.

2. Boden BP, Osbahr DC. High-risk stress fractures: evaluation and treatment. *J Am Acad Orthop Surg.* 2000 Nov-Dec;8(6):344-53.

3. Borges JL, Guille JT, Bowen JR. Köhler's bone disease of the tarsal navicular. *J Pediatr Orthop.* 15 (5) (1995), pp. 596-598

4. Brailsford, JF. Osteochondritis of the Adult Tarsal Navicular. *JBJS*: 1939 Jan 21(1):111-120.

5. DiGiovanni CW, Patel A, Calfee R, Nickisch F. Osteonecrosis in the foot. *J Am Acad Orthop Surg.* 2007 Apr;15(4):208-17.

6. Chang SM, Chen PY, Tsai MS, Shee BW. Light Bulb Procedure for the Treatment of Tarsal Navicular Osteonecrosis After Failed Percutaneous Decompression: A Case Report. *J Foot Ankle Surg.* 2019 Jan;58(1):187-191.

7. Janositz G, Sisák K, Tóth K. Percutaneous decompression for the treatment of Mueller-Weiss syndrome. *Knee Surg Sports Traumatol Arthrosc.* 2011 Apr;19(4):688-90.

8. Khan KM, Fuller PJ, Brukner PD, Kearney C, Burry HC. Outcome of conservative and surgical management of navicular stress fracture in athletes. Eighty-six cases proven with computerized tomography. *Am J Sports Med.* 1992 Nov-Dec;20(6):657-66.

9. Levinson H, Miller KJ, Adams SB Jr, Parekh SG. Treatment of Spontaneous Osteonecrosis of the Tarsal Navicular With a Free Medial Femoral Condyle Vascularized Bone Graft: A New Approach to Managing a Difficult Problem. *Foot Ankle Spec.* 2014 Aug 1;7(4):332-337.

10. Mohiuddin T, Jennison T, Damany D. Müller-Weiss disease - review of current knowledge. *Foot Ankle Surg.* 2014 Jun;20(2):79-84.

11. Mueller, W. Uebe r eine eigenartige doppelseitige veraenderung des os naviculare pedis beim erwachsenen. *Dtsch. Z. Chir.* 1- 2:84 - 89, 1927.

12. Weiss K. Uber die "malazie" des os naviculare pedis. Fortschritte auf dem Gebiete der Rontgenstrahlen 1927;45:63–7.

13. Resnick, D. Osteochondroses, ch. 81. *Diagnosis of Bone and Joint Disorders*, 3rd ed., vol. 5, pp. 358 1-3582.

Medial Femoral Condyle Free Flap Reconstruction of Complex Foot and Ankle Pathology

John T. Stranix MD[1]
Merisa Piper MD[1]
Said Azoury MD[1]
Oded Ben-Amotz MD[2]
Keith L. Wapner MD[2]
L. Scott Levin MD[2]

1 University of Pennsylvania, Department of Surgery, Division of Plastic Surgery, Philadelphia, PA

2 University of Pennsylvania, Department of Orthopedic Surgery, Philadelphia, PA

Introduction

Standard bone grafting techniques require a well vascularized recipient bed to maintain osteocyte viability and allow for successful osseous union. Due to the large articular surfaces of the navicular and talus, their blood supply is relatively tenuous and they are subjected to significant stress during ambulation. This combination predisposes them to arthrosis, AVN, and nonunion which can present a challenging problem for foot and ankle surgeons and often leaves arthrodesis as the only possible option.[1] If revision arthrodesis is required, this further exacerbates the problem by resulting in greater bone loss, soft tissue compromise, and less consistent fusion rates.[2] The medial femoral condyle (MFC) free flap enables transfer of vascularized periosteum with viable corticocancellous bone to promote osseous union in bone defects that are unlikely to achieve successful union with standard bone grafting techniques.[3,4]

Methods

A retrospective review of medial femoral condyle free flaps performed for foot and ankle reconstruction at a single institution between 2013 and 2019 was completed following institutional review board approval. MFC reconstruction was indicated for patients who presented with complex hindfoot pathology that required recruitment of additional vascularized bone in order to optimize the potential for osseous healing and successful orthopedic treatment. Patient demographics, operative details, and postoperative outcomes were obtained for analysis. Preoperative and postoperative American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scores were calculated for functional outcomes comparison.[5] Osseous union was assessed with serial radiographic or computed tomography, with complete union defined as date of imaging study when complete union noted within the official radiology report.

The MFC flap was harvested under tourniquet control as described previously.[4] Following completion of the procedure, all patients were placed in a posterior splint with leg elevation and strict non-weightbearing. Flap monitoring was most commonly performed using an external Doppler probe over the pedicle in 28 cases, however, an implantable Cook Doppler probe was used in two cases (one arterial, one venous).

Results

Over the six-year study period, 30 MFC free flap reconstructions were performed in 28 patients for complex hindfoot pathology. A history of trauma was the most common etiology (73%) followed by idiopathic avascular necrosis (17%). The majority of patients had undergone previous hindfoot surgery (67%) with an average of 3.1 prior operations (range 1-10). Most of these patients (17 out of 20) ultimately failed at least one arthrodesis procedure prior to referral. Avascular necrosis of one or more hindfoot bones was present in 83% of patients with the navicular (n = 13) and talus (n = 12) most commonly affected. Arthritis (76%) and osseous nonunion (73%) were also common upon presentation.

Orthopedic interventions performed concomitantly with MFC flap reconstruction are listed in Table 1 along with the respective bone flap insertion sites. The majority of hindfoot procedures involved arthrodesis of at least one joint (n = 24, 80%), with tibiotalocalcaneal (n = 11) and talonavicular (n = 7) fusions the most common. K-wire fixation of the MFC flap was utilized most frequently (n = 17), followed by press-fit (n = 5), K-wire and screw (n = 4), screw (n = 2), plate and screw (n= =), and plate only (n = 1).

The ipsilateral knee was the MFC donor site in all but two cases. The mean osseous volume was 10.3 cm^3 (range 1.7-18.4cm^3). Bone-only free flaps were utilized in 14 cases. A chimeric skin paddle was carried with 15 of the flaps (50%) and a segment of vastus medialis muscle was incorporated in one case for soft tissue coverage in the setting of inadequate perforators. The descending geniculate artery supplied the flap in the majority of cases (n = 26), however, in 4 cases the MFC pedicle arose from the superior condylar branch of the medial geniculate artery. The anterior tibial vessels were the most common recipient vessels (n = 25) followed by the posterior tibial vessels in 5 cases. End-to-end arterial anastomoses were performed in 23 cases and one or two venae comitantes were utilized for venous outflow.

Table 1. Operative Details of MFC Hindfoot Procedures

Orthopedic Procedure	n	MFC Insertion Site	n	Bone Flap Fixation	Bone Flap Volume, cm^3 mean (range)
Tibiotalaocalcaneal Arthrodesis	11	Tibiotalar joint	9	K-wire (n = 8); Screw (n = 1)	12.2 (6.5-18.4)
		Sinus Tarsi	2	K-wire (n = 2)	
Talonavicular Arthrodesis	7	Talonavicular Joint	7	K-wire (n = 4); K-wire and screw (n = 1); Plate and screw (n = 1); Press-fit (n = 1)	7.8 (2-16)
ORIF Navicular Nonunion	4	Navicular Waist	4	K-wire and screw (n = 3); K-wire (n = 1)	3.8 (1.7-6)
Triple Arthrodesis	4	Talonavicular Joint	2	Press-fit (n = 2)	14.4 (10.5-17.5)
		Navicular (excised)	2	K-wire (n = 1); Plate (n = 1)	
Subtalar Arthrodesis	2	Sinus Tarsi	2	K-wire (n = 1); Screw (n = 1)	10.5 (9-12)
Tibial Saucerization	2	Tibial metaphysis	2	Press-fit (n = 2)	9.8 (9-10.5)

Average postoperative length of hospital stay was 4.9 days (range 3-11 days). Flap complications occurred in 6 patients. There were 3 partial skin paddle losses and 2 total skin paddle failures, however, the underlying bone flap was noted to be viable in all cases during operative debridement. One patient required a takeback for venous thrombosis related to pedicle kinking on postoperative day 1 with successful flap salvage. One patient developed a donor site seroma that required operative drainage.

Out of 30 patients, 27 had adequate clinical and imaging follow up to be included for outcomes analysis with a mean follow up duration of 15.5 months (range 4-33 months). Average time to partial weight bearing was 49 ± 22 days (range 26-100 days) and to full weight bearing was 99 ± 39 days (range 57-208 days).

Primary osseous union was initially achieved in 20 patients (74%) by an average of 217 ± 114 days (range 110-475 days). Of the six patients who developed an interface nonunion, 5 of them underwent revision arthrodesis with bone grafting and achieved subsequent union. Ultimately, complete osseous union was achieved in 25 patients (93%) with an average time to union of 271 ± 165 days (range 110-628 days). One patient developed a chronic nonunion and refused additional surgery, while the second patient is ambulating with an asymptomatic partial union.

Risk factors for the development of nonunion following MFC reconstruction were evaluated. MFC nonunion was associated with a BMI greater than 35 ($p = 0.011$) and a history of prior failed arthrodesis ($p = 0.042$). Orthopedic procedure, bone flap insertion site, fixation method, and flap volume were not associated with subsequent nonunion.

Fifteen patients required additional procedures subsequent to their MFC flap reconstruction (6 soft tissue, 9 orthopedic). Flap soft tissue debulking was performed in 4 patients, and 2 required operative debridement for delayed wound healing at the recipient site. Revision arthrodesis for nonunion was required in 5 patients. Two patients underwent pin removal, one patient had tibial screw removal for rod dynamization, and one required excision of heterotopic bone.

In order to measure functional outcomes, AOFAS Hindfoot Scores were calculated for patients. Mean preoperative scores were 60 ± 13 (range 37-83) out of 100. When evaluated at least 6 months postoperatively, average AOFAS scores had increased significantly to 73 ± 17 (range 36-95) ($p = 0.001$).

Discussion

In the setting of compromised vascular supply to the bones of the foot and ankle related to trauma, surgery, or other mechanisms the risk of avascular necrosis (AVN) and nonunion may be as high as 30-40%.[2] Within this challenging cohort of patients, our series of vascularized bone transfer with the medial femoral condyle free flap ultimately achieved osseous union in 93% of patients. Initial interface nonunion after MFC flap reconstruction was associated with BMI over 35 and a history of failed arthrodesis. Functional status was also significantly improved after MFC reconstruction with AOFAS Hindfoot Scores increasing from 60 preoperatively to 73 in the postoperative period ($p = 0.001$).

This study is limited by the retrospective nature, lack of a control group, and heterogeneity of orthopedic procedures performed. The vascularized bone flap insertion site varied according to the area of avascular bone and required tailoring to each specific defect in terms of flap size and fixation method. Despite limitations, however, we were able to demonstrate significant improvement in functional outcomes and achieve relatively high fusion rates in a challenging patient population.

References

1. Horst F, Gilbert BJ, Nunley JA. Avascular necrosis of the talus: current treatment options. *Foot Ankle Clin.* 2004;9(4):757-773.

2. Frey C, Halikus N, Vu-Rose T, Ebramzadeh E. A review of ankle arthrodesis: predisposing factors to nonunion. *Foot Ankle Int.* 1994;15(11):581-584.

3. Doi K, Sakai K. Vascularized bone graft from the supracondylar region of the femur. *Microsurgery.* 1994;15(5):305-315.

4. Haddock NT, Alosh H, Easley ME, Levin LS, Wapner KL. Applications of the medial femoral condyle free flap for foot and ankle reconstruction. *Foot Ankle Int.* 2013;34(10):1395-1402.

5. Kitaoka HB, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. *Foot Ankle Int.* 1994;15(9):349-353.

Cervical Spine Fusion After Osteomyelitis Using Vascularized Free Fibula Autograft

Brittany Behar, MD[1]
Chelsea Hendow, MD[1]
Merisa Piper, MD[2]
L. Scott Levin, MD[1, 2]

1 Department of Orthpaedic Surgery, University of Pennsylvania

2 Division of Plastic Surgery, University of Pennsylvania

Case Report

Our patient is a 61-year-old woman with a past medical history of Raynaud's, osteoporosis and Barrett's esophagus who presented initially with cervical stenosis with myelopathy. Six months prior at an outside facility, she underwent a C4 corpectomy and anterior C3-C5 discectomy and fusion followed by C2-T2 posterior fusion three months later for failure of initial instrumentation. Unfortunately, she developed worsening upper extremity weakness and dexterity and was transferred to Penn Presbyterian Medical Center for further management.

On initial evaluation she had MRC grade 2 strength in her bilateral proximal upper extremities, and grade 4 strength in the distal upper extremities with a positive Hoffman's sign bilaterally.[1] MRI of the cervical and thoracic spine showed kyphosis at C5-6, pullout of bilateral C3 pedicle screws, an epidural phlegmon, and fluid collections both prevertebral and about the instrumentation concerning for infection (Figure 1). Intraoperative cultures from an initial washout grew methicillin-sensitive *Staphylococcus aureus*.A PEG was placed during this hospitalization to augment her nutrition. She went to a rehabilitation facility on a course of vancomycin and rifampin recommended by infectious disease and returned six weeks later for definitive staged fixation. During the first preparatory procedure, the posterior cervicothoracic hardware was removed and she underwent an occipital-T5 fusion with tricortical allograft and BMP, and halo vest placement.

In the second definitive procedure, a C3-C6 corpectomy with free fibula autograft fusion was performed using a two team (orthoplastics and neurosurgery) approach.The cervical spine was accessed using a traditional anterior approach to C2-C7 (Figure 2a).The previous corpectomy cage was noted to be loose, cut in half with a metal-cutting burr, and removed. Corpectomies of C3-C6 were then completed with removal of the C2-C3 and C6-C7 disc spaces.

Concomitantly, a vascularized free fibula graft with skin paddle was harvested from the patient's right leg using the technique outlined by Heitmann and Levin.[2] After the fibula was harvested, it was cut to the appropriate length and fitted into the corpectomy defect. The superior and inferior portions were impacted against the inferior C2 and superior C7 endplates, respectively (Figure 2b).A spring plate spanning the C6 and C7 levels anteriorly and two screws in the C7 verterbal body was used to prevent anterior subluxation of the fibula graft.

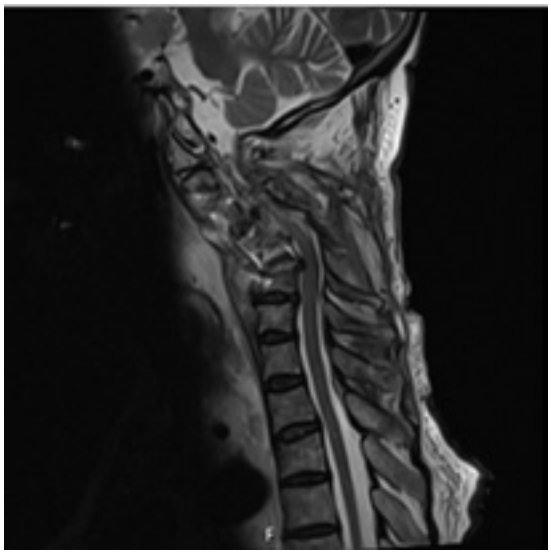


Figure 1. Cervical spine MRI showing prevertebral collection and collapse of C5 vertebral body.

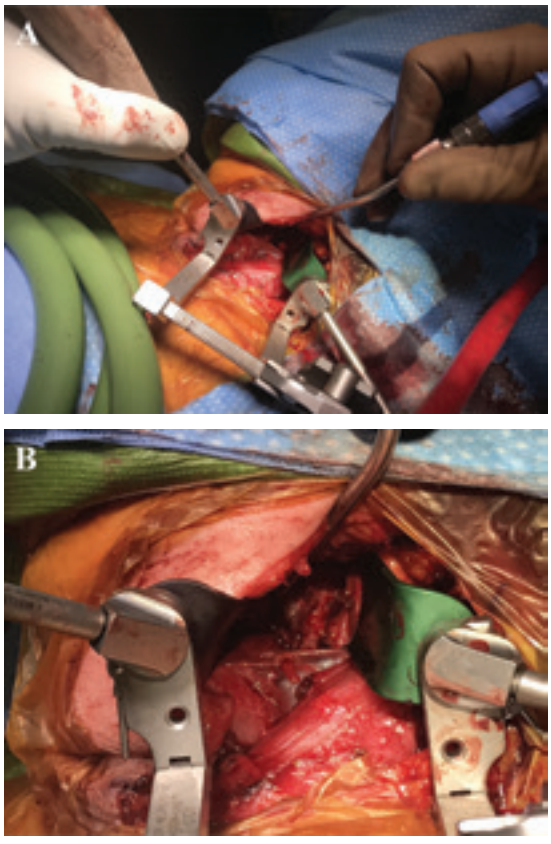


Figure 2. (A) Anterior approach to cervical spine; **(B)** Free fibula (highlighted by dotted blue line) inset at C2-C7.

The peroneal artery supplying the fibula was anastomosed in an end-to-side technique to the external carotid artery. One of the venae comitans was hand sewn to the external jugular vein and the second vena comitans to a large transverse external jugular vein branch. The flap was monitored using an implantable Cook doppler probe around the artery. The halo vest was replaced at the end of the case.

She remained NPO in the perioperative period to monitor for esophageal tears and received nutritional support through her PEG tube. She was transitioned from a halo to a Minerva (cervico-thoracic) brace at six weeks. X-rays at six weeks and a CT Scan at nine weeks after surgery demonstrated stable graft alignment (Figure 3). She was allowed to eat by mouth at that time and her PEG tube was removed. Five months post-operatively she was transitioned to a soft cervical collar due to skin erosions. X-rays continue to demonstrate stable graft position and no evidence of infection recurrence (Figure 4).

Conclusion

This case report shows that free fibula vascularized bone graft can effectively replace allograft in complex cervical spine fusion in the setting of osteomyelitis. Vascularized tissue is more resistant to reinfection after adequate debridement than non-vascularized auto or allograft. [3-5] This procedure can be done efficiently by using a two-team approach both intraoperatively and preoperatively for surgical planning.

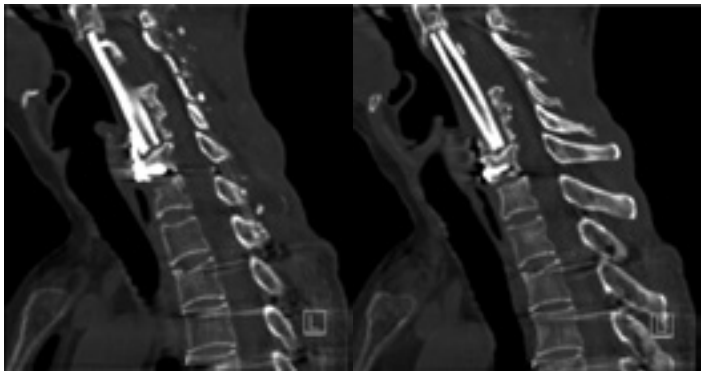


Figure 3. CT scan of cervical spine three months postoperatively demonstrating stable positioning of free fibula graft.

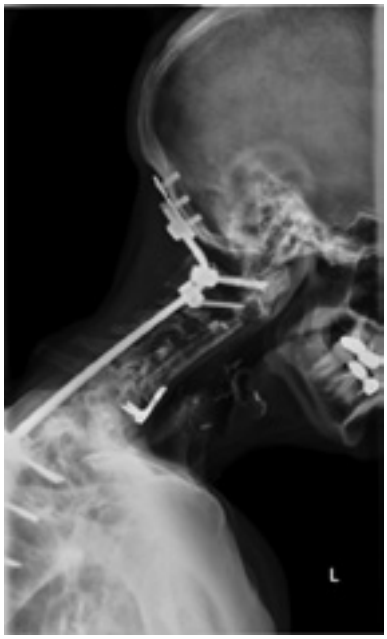


Figure 4. Xrays of cervical spine five months postoperatively with unchanged position of free fibula graft.

References

1. Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationery Office: 1942; pp. 48 (iii) and 74 Figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. *Brain* 2010; 133:2838–2844.

2. Heitmann C, Levin LS. Applications of the Vascularized Fibula for Upper Extremity Reconstruction. *Tech Hand Upper Ext Surg.* 2003; 7(1): 12-17.

3. May JW Jr, Gallico GG 3rd, Lukash FN. Microvascular transfer of free tissue for closure of bone wounds of the distal lower extremity. *N Engl J Med* 1982; 306(5):253–7.

4. Levin LS. Early versus delayed closure of open fractures. *Injury, Int J Care Injured* 2007; 38: 896-899.

5. Tu YK, Yen CY. Role of Vascularized Bone Grafts in Lower Extremity Osteomyelitis. *Orthop Clin N Am* 2007; 38:37-49.

U·P·O·J

Influence of Interviewer Number on Applicant Rank Position

Joshua T. Bram BS[1]
James Bernstein[2]
Derek J. Donegan MD[3]
Kevin Pirruccio BA[1]
Jaimo Ahn MD, PhD[3]

[1]Perelman School of Medicine at the University of Pennsylvania

[2]Columbia University in the City of New York

[3]Department of Orthopaedic Surgery, University of Pennsylvania

Introduction

Interview performance for both residency and fellowship applicants is consistently cited by program directors across multiple specialties to be one of the most important factors affecting an applicant's chances of matching at a particular institution (1-6). Often, a large number of interviewers are involved because a larger group may more effectively reduce the impact of outlier scores and perception bias when discussing applicants. On the other hand, having too few interviewers can lead to a situation where one interview proves detrimental for an applicant due to the strong influence of outliers in a small sample size (7, 8). Additionally, interviews themselves typically require significant time and resource investment on behalf of the institution (9, 10). Thus, the primary purpose of this study was to retrospectively examine how having fewer interviewers involved in the residency application process might have changed applicant interview scores and the eventual rank list position at our institution.

Another common concern among residency applicants relates to the timing of their interview session and whether or not this will impact how they are ranked by an institution. Therefore, we secondarily sought to determine if the timing of the interview sessions and potential interviewer decision fatigue impacted interview scores.

Methods

This was a retrospective exploratory study of interview scores for 77 orthopedic residency program candidates (pre-existing in a completely redacted form) for the 2016-2017 application cycle. Each applicant was individually scored by the same 16 interviewers using a previously described semi-structured interview methodology (11). Completion of all interviews required four sessions over the course of two days.

Each individual interviewer assigns applicants an overall score ranging from one to six (1 = exceptional candidate, 6 = interviewer had strong concerns). After all interviews are completed, the 16 interview scores are averaged to produce a final, overall interview score for a given applicant; this score can be ordered in a rank list of interview scores from highest to lowest for all candidates.

In order to determine how having fewer interviewers might have changed interview scores, we modelled the ranges of scores that a candidate could have received if a random sample of the 16 original interview scores was instead used to determine an applicant's final interview score. Random sample sizes of interview scores ranged from 15 interviewers down to just 2 interviewers. For each applicant, each unique combination of scores was then compared to the average score from the original set of 16 interviewers. The highest/lowest possible average interview score for each applicant based on these combinations of scores was also calculated. Those averages were then used to determine the highest/lowest possible rank that the applicant could have achieved based on the original interview score rank list. This was a ranked list of applicants based solely on their interview scores. From there, the absolute distance that the applicant could have risen or fallen in this rank list was determined. A significance threshold of $p < 0.05$ was used for all tests.

Results

Sequential reduction in the number of interviews included for comparison to an applicant's original interview scores revealed few differences across all possible combinations (Table 1). It was, however, found that applicants could move considerable distances with large reductions in the number of interviews conducted (Figure 1) when the average scores were used as a basis for generating an initial post-interview rank list. For combinations composed of 15 scores, top applicants rarely moved more than a few spots in the rank list, but with two and three-score combinations, the top applicants could fall as much as 50 or 60 places in the interview score rank list.

There was no difference for any individual interviewer and the scores he or she assigned across the four interview sessions (Table 2), nor was there a difference collectively for the interview scores assigned across the sessions ($p=0.345$). Additionally, the session during which an applicant was interviewed did not affect where he or she placed in the interview score rank list ($p=0.931$; model could not be rejected, $p=0.523$).

Table 1. Number of significantly different interview score combinations across all applicants

Number of Interviews	Combination	Number of combinations per applicant	Number of total possible combinations	Number of significant combinations	Percent significant (%)	Average Increase in Rank	Average Decrease in Rank
15	16 choose 15	16	1,216	0	0	4.3	3.3
14	16 choose 14	120	9,135	0	0	7.3	7.1
13	16 choose 13	560	42,665	0	0	10.2	10.7
12	16 choose 12	1,820	138,775	0	0	12.8	14.1
11	16 choose 11	4,368	333,333	0	0	16.0	16.6
10	16 choose 10	8,008	611,611	0	0	18.6	19.3
9	16 choose 9	11,440	874,445	0	0	21.6	21.6
8	16 choose 8	12,870	984,555	0	0	23.1	24.7
7	16 choose 7	11,440	875,875	63	0.007	25.8	26.1
6	16 choose 6	8,008	613,613	376	0.061	27.0	27.7
5	16 choose 5	4,368	334,971	261	0.078	29.6	29.0
4	16 choose 4	1,820	139,685	392	0.281	31.3	30.9
3	16 choose 3	560	43,015	164	0.381	33.5	31.5
2	16 choose 2	120	9,225	0	0	35.1	32.8
Total	---	65,518	5,012,119	1,256	0.025	---	---

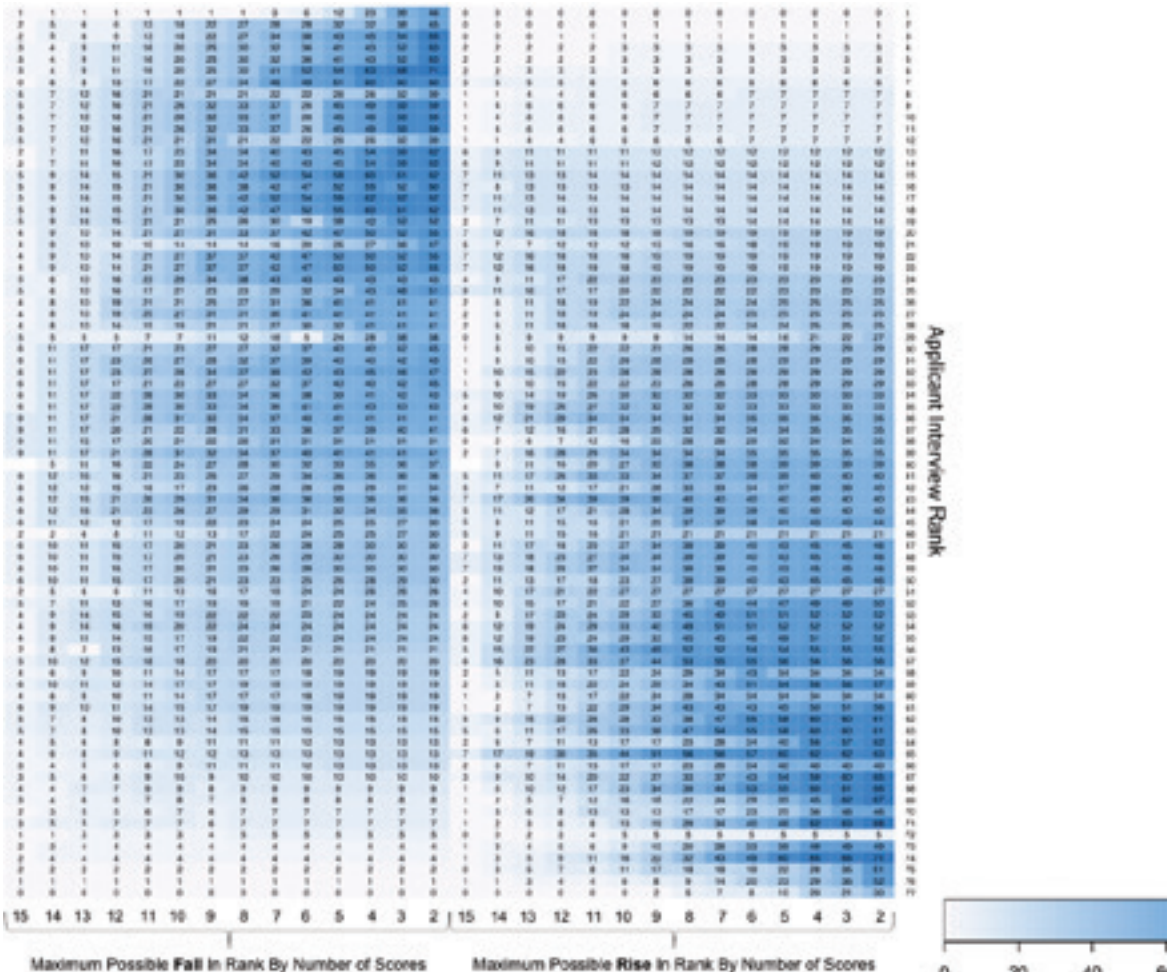


Figure 1. Maximum possible changes in an interview score-based rank list. This plot shows the maximum possible rise or fall in the interview-score rank list based on the different number of interview scores included per combination for each applicant. The distances traveled in the interview rank list are illustrated using both a color scale and the actual value, which can be found within each individual box.

Table 2. The effect of interview session on scores assigned by the interviewers

Interviewer	P value
1	0.147
2	0.142
3	0.653
4	0.729
5	0.284
6	0.240
7	0.288
8	0.262
9	0.310
10	0.645
11	0.295
12	0.689
13	0.095
14	0.871
15	0.134
16	0.108
Overall	0.345

Discussion

The results of this study demonstrate that changes in the number of interviewers would not lead to many different interview score averages for applicants. However, an applicant's post-interview rank was observed to undergo progressively larger magnitude changes with fewer interviewers due to the effects of outlier scores. While decreasing the number of interviewers would allow for a reduction in the total time and resource investment by an institution, residency selection committees must keep in the mind the increased variability that a small number of interviews may infuse into the rank order as fewer interviews are conducted.

Our data also show that none of our interviewers experienced decision fatigue, with consistent interview scores assigned across the different sessions. This suggests that our semi-structured interview format is working as intended to ensure consistent evaluation of residency candidates across a large number of applicants (11).

Residency applicants may also take solace in the fact that our study demonstrates that the timing of an interview will not impact the interview scores they receive (12). The residency application process is already stressful, and our work shows that applicants need not worry too greatly about how the interview date impacts their chances of matching to a dream residency program.

The main limitation of this study was the study design as we are generating large theoretical combinations from a small sample size in each calculation. However, we feel that the broad differences in program application formats actually warrants these types of studies to better understand the implications and consequences of our methods over time.

Conclusions

Our study demonstrated that reductions in the number of interviewers for residency programs is unlikely to statistically change the average interview scores, but that greater reductions in the number of interviewers can cause increasingly large changes in such scores and, therefore, strongly influence a score-based rank list. We also show that the timing of an applicant's interview likely does not affect perception or scoring by a residency program.

References

1. Swanson WS, Harris MC, Master C, *et al.* The impact of the interview in pediatric residency selection. *Ambul Pediatr.* 2005;5(4):216-20.

2. Gong H, Jr., Parker NH, Apgar FA *et al.* Influence of the interview on ranking in the residency selection process. *Med Educ.* 1984;18(5):366-9.

3. Bajaj G, Carmichael KD. What attributes are necessary to be selected for an orthopaedic surgery residency position: perceptions of faculty and residents. *South Med J.* 2004;97(12):1179-85.

4. Bernstein AD, Jazrawi LM, Elbeshbeshy B *et al*. An analysis of orthopaedic residency selection criteria. *Bull Hosp Jt Dis.* 2002;61(1-2):49-57.

5. Wagoner NE, Suriano JR, Stoner JA. Factors used by program directors to select residents. *J Med Educ.* 1986;61(1):10-21.

6. Baweja R, Kraeutler MJ, Mulcahey MK *et al*. Determining the Most Important Factors Involved in Ranking Orthopaedic Sports Medicine Fellowship Applicants. *Orthop J Sports Med.* 2017;5(11):2325967117736726.

7. Downard CD, Goldin A, Garrison MM, et al. Utility of onsite interviews in the pediatric surgery match. J Pediatr Surg. 2015;50(6):1042-5.

8. Camp CL, Sousa PL, Hanssen AD et al. Orthopedic Surgery Applicants: What They Want in an Interview and How They Are Influenced by Post-Interview Contact. J Surg Educ. 2016;73(4):709-14.

9. Black CC. Examination of the Residency Interview Process for Academic Pathology Departments: How to Make the Most of a Resource-Heavy Process. Acad Pathol. 2016;3:2374289515623551.

10. Milne CK, Bellini LM, Shea JA. Applicants' perceptions of the formal faculty interview during residency recruitment. Acad Med. 2001;76(5):501.

11. Schenker ML, Baldwin KD, Israelite CL et al. Selecting the Best and Brightest: A Structured Approach to Orthopedic Resident Selection. J Surg Educ. 2016;73(5):879-85.

12. Martin-Lee L, Park H, Overton DT. Does interview date affect match list position in the emergency medicine national residency matching program match? Acad Emerg Med. 2000;7(9):1022-6.

Levels of Influence in Orthopaedic Surgery Journals Vary by Specialty

Meghan L. Morley, MD
Sara Weintraub, BA
Jaimo Ahn, MD, PhD
Joseph Bernstein, MD

Department of Orthopaedic Surgery
University of Pennsylvania Philadelphia, PA

Introduction

In recognition that conflicts of interest cannot be fully eliminated, but at best managed, the International Committee of Medical Journal Editors (ICMJE) developed a system of disclosure under which authors are required to disclose "all financial and personal relationships that might bias or be seen to bias their work."[1]. With the ICMJE data available for all authors, it now becomes possible to categorize manuscripts based on Bernstein and colleagues'[2] "Level of Influence" classification system. According to this system, manuscripts can be assigned to one of four categories: Level A, where there is neither external funding for the study nor any industry relationships; Level B, where there is external funding from governmental or not-for-profit entities, but no relationships with industry; Level C, where one or more authors has a relationship with industry, but the study was not funded by industry; and Level D, studies funded directly by industry. The Level A and B studies can be collectively denoted as having no industry relationships, contrasted with Level C and D studies which do.

In their report, Bernstein et al[2] found that 68% of Journal of Bone and Joint Surgery (JBJS) manuscripts reported industry relationships (Level of Influence C or D). It is unknown whether the high Level of Influence as seen in JBJS papers is representative of the field of orthopedic surgery. To that end, a sample of papers from the journals Clinical Orthopedics and Related Research (CORR), The Journal of Arthroplasty (JOR), The American Journal of Sports Medicine (AJSM), and The Spine Journal (Spine J) were evaluated according to the Level of Influence system.

A second question posed is whether there is a loss of information when the Level of Influence status is aggregated for all authors. In particular, journals may employ a phrase such as "one or more of the authors received payments or services…one or more of the authors has had a financial relationship…that could be perceived to influence or have the potential to influence what is written in this work."This phrase would apply even if the first or last (and presumably most important) authors did not have a financial relationship, though a middle (and presumably less important) author did. Accordingly, the sample of 400 papers was scrutinized to determine how often papers use the term "one or more authors… [has an industry relationship]" when both the first and the last author did not report conflicts.

Methods

A sample of 100 scientific manuscripts was selected from CORR, JOR, AJSM, and Spine J. The first 10 papers appearing in 10 consecutive issues beginning with January 2014 were identified and categorized according to Bernstein's Levels of Influence classification system as described in Figure 1. The manuscripts were also categorized according to a simplified classification: "type I", which had no industry involvement, namely the combination of studies categorized above as A and B; and "type II" which had some industry involvement, the category C and D studies combined. The set of scientific manuscripts were classified by two independent readers; there were 4 discrepancies in classification that were resolved by the senior author. Studies that reported to have received only incidental contributions from industry (testing materials or medications, for example) were not considered to be "industry supported." For those studies which did report an industry relationship for "one or more authors," the conflict of interest documents were scrutinized to determine which of the authors triggered that clause, noting specifically whether it was a first, last, or middle author.

Statistical significance for differences between journals and the JBJS historical control was assessed using the Chi-square test at the $p < 0.05$ level.

Results

Of the 100 scientific papers from CORR, 45 were designated as Level A, 26 were Level B, 20 were Level C, and 9 were Level D. AJSM had 47 Level A, 27 Level B, 16 Level C, and 10 Level D manuscripts. In JOA, there were 29 manuscripts designated as Level A, 4 as Level B, 67 as Level C, and 0 as Level D. Spine J had 28 Level A, 22 Level B, 45 Level C, and 5 Level D papers.

Applying the simplified classification, 29 manuscripts from CORR and 26 from AJSM reported industry relationships. JOA and Spine

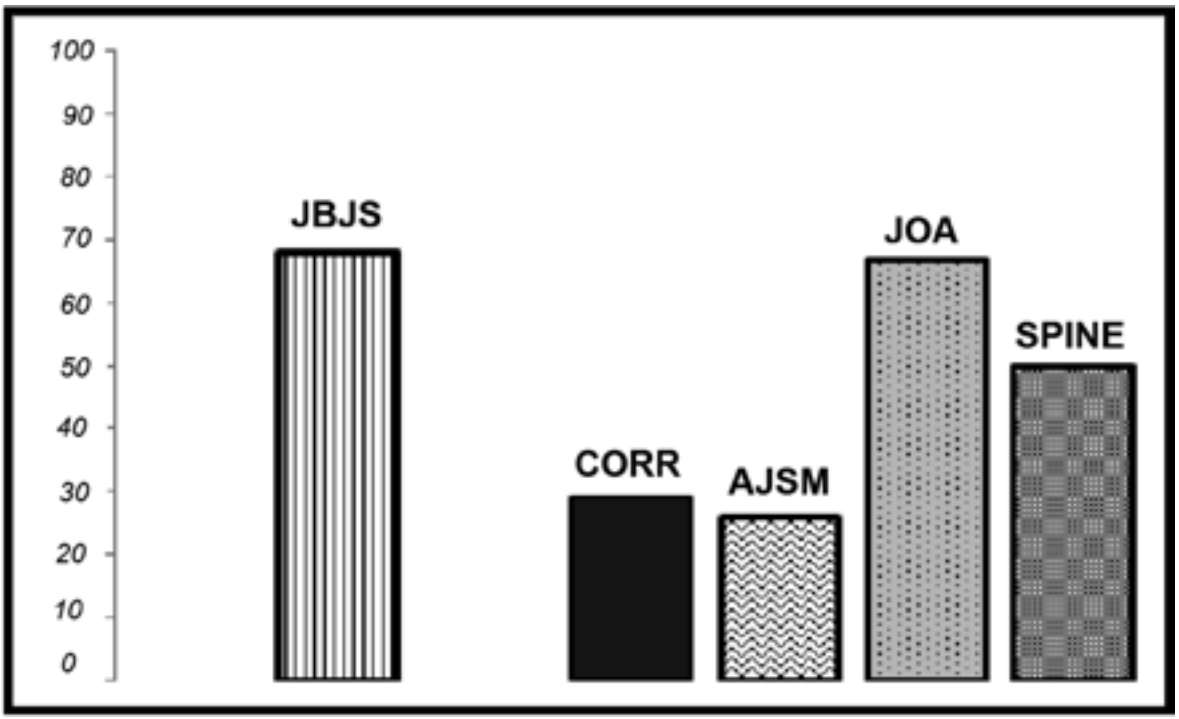


Figure 1. Flow chart diagramming the classification of papers according to their Level of Influence (NFP: Not for profit.).

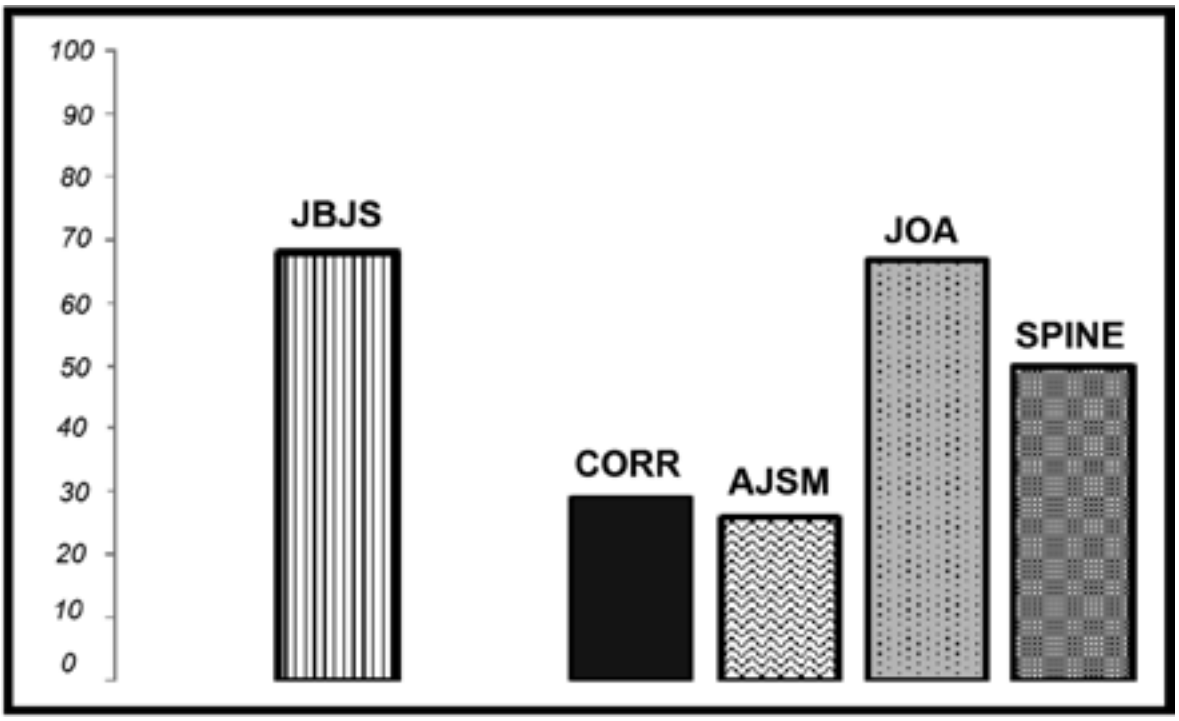


Figure 2. Comparison of the four journals to the JBJS, which was seen to have 68 of 100 papers reporting an industry relationship. As shown, the JBJS rate was nearly matched by JOA, though CORR and AJSM reported far fewer such studies.

J had 67 and 50 such studies, respectively. Using the rate of industry relationships previously reported in JBJS (68 out of 100) [2], the differences in rates between JBJS and CORR, ASJM, and Spine J were statistically significant ($p < 0.01$); the difference between JBJS and JOA was not (Figure 2).

In all four journals combined, there were 154 Level C papers with a total of 802 authors. Of these 802 authors, 299 (37%) declared a potential conflict of interest. In 23 (15%) of the 154 Level C papers, neither the first nor the last author declared a potential conflict (Table 1).

Discussion

In our study, we have shown that the high rate of industry-related authors in JBJS as reported in a prior review is indeed not pervasive in orthopedics. As noted, CORR and AJSM had rates of 29% and 26%, respectively. As such, it would be incorrect to infer from the original study that the field of orthopaedic surgery is characterized by papers written by industry-related authors. Rather, certain journals have a high prevalence, whereas other leading journals do not. Further, the relatively high Levels of Influence typically seen

Table 1: Fraction of Level C studies in which neither the first nor the last author declared a conflict.

	CORR	AJSM	JOA	Spine	Total
Level C manuscripts	26	16	67	45	154
Level C manuscripts in which neither the first nor the last author declared a conflict	2	4	9	8	23

in JOA and Spine J may suggest that the degree of influence is a feature of subspecialty: arthroplasty and spine typically use expensive implants and thus there is mutual appeal for industry-surgeon collaboration. It would be interesting in future work to examine the rates of industry relationships in other sub-specialties in orthopaedic surgery.

The study also confirmed that using a single phrase such as "one or more authors…" may not adequately represent the status of the paper. It was shown that in 15% of Level C papers, the "one or more authors..." clause was triggered by a middle (neither first nor last) author whose contribution, it may be inferred, was relatively minor.

Conclusion

The field of orthopedic surgery cannot be broadly characterized as having a high rate of industry-related authors. The use of a single phrase to encapsulate the potential conflicts of all authors may be imprecise (and overstate the degree of industry influence). Reporting Levels of Influence in the abstract and designating authors' individual Levels of Influence with a superscript next to their names would present this information more clearly to readers and maximize their ability to correctly infer what the study shows.

References:

1. ICMJE. Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals. Available at: http://www.icmje.org/recommendations/. Accessed September 11, 2018.

2. Bernstein JR, Maliha G, Ahn J, et al. Levels of Influence: Habituation and the Prevalence of Declared Conflicts of Interest. *JBJS.* 2016 Nov 16;98(22):e99.

Deciphering the in vivo Heterogeneity of Mouse Bone Marrow Mesenchymal Progenitors at Single Cell Resolution

Leilei Zhong[1]
Robert J Tower[1]
Jihwan Park[2]
Luqiang Wang[1]
Rojesh Shrestha[2]
Patrick Seale[3]
Kaitlin Susztak[2]
Ling Qin[1]

1 Department of Orthopaedic Surgery, University of Pennsylvania

2 Department of Medicine and Genetics, University of Pennsylvania

3 Cell and Developmental Biology, University of Pennsylvania

Introduction

In bone, it is commonly believed that mesenchymal progenitors (MPs), including their most primitive form mesenchymal stem cells (MSCs), constantly generate bone surface osteoblasts and marrow adipocytes via sequential, unidirectional, and branched differentiation steps. Almost all types of osteoporosis are associated with diminished bone formation and increased marrow adiposity. Stem cell heterogeneity has been well-recognized in mammalian tissue stem cells. However, owing to a lack of proper *in vivo* investigative tools, in the past we deliberately ignored this feature of mesenchymal progenitors by simply referring to them as MSCs or MPs, and searched for a single marker to label them. Recently, we discovered that in *Col2-Cre Rosa-tdTomato* (*Col2/Td*) mice, Td signal labels all endosteal (metaphyseal) mesenchymal lineage cells but no other cell types[1], thus providing a perfect system to comprehensively analyze the subpopulations of mesenchymal lineage cells from MSCs to mature cells. In this project, we applied the most advanced large scale single-cell sequencing (scRNA-seq) technique to this animal model and solved the in vivo heterogeneity of bone marrow MPs.

Methods

Animals

All animal work performed was approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pennsylvania. *Col2/Td* and *Adiponectin-Cre Rosa-tdTomato* (*Adipoq/Td*) mice were obtained by crossing *Col2-Cre* or *Adipoq-Cre* mice with *Rosa-tdTomato* mice.

Endosteal bone marrow Td+ cell isolation

The outer surfaces of long bones were scraped and digested to remove the periosteum. After cutting off the epiphyses and flushing out the central bone marrow, metaphyseal bone fragments were longitudinally cut into two halves and digested by proteases to collect endosteal bone marrow cells [2]. Those cells were then sorted for the top 1% Td^+ cells.

Large scale scRNA-seq

20,000 sorted cells were loaded in the chromium controller (10X Genomics) to generate barcoded, single-cell libraries of 10,000 cells for sequencing via Ilumina HiSeq 2500. After stringent quality controls, 8,456 cells were analyzed. Unsupervised clustering was conducted by Seurat to generate a t-SNE plot of the overall cell populations. Trajectory analysis was conducted using Monocle.

Whole mount immunofluorescence

Freshly dissected bones were fixed in 4% PFA, decalcified in 10% EDTA, and immersed into 20% sucrose and 2% polyvinylpyrrolidone. After frozen embedding, bones were cryosectioned at 50 μm in thickness and stained with Lepr1, Endomucin, Perilipin, and CD45 antibodies for immunofluorescent imaging analysis.

Statistics

All analyses were conducted using t-tests or two-way ANOVA with a bonferroni's post-test for multiple comparisons using Prism (GraphPad).

Results

We harvested endosteal bone marrow from 1-month-old *Col2/Td* mice and sorted for the top 1% Td^+ cells (Figure 1A). Those cells contained all CFU-F forming cells found in unsorted parental cells (Figure 1B) and all their CFU-Fs were Td^+ (Figure 1C). Our harvest method also collects Td^+ osteoblasts [3]. Therefore, the top 1% Td^+ cells contain enriched and all-inclusive mesenchymal lineage cells ranging from MSCs to mature cells in bone. We subjected those cells to large scale scRNA-seq. After excluding hematopoietic and endothelial cells, we identified 2,489 mesenchymal lineage cells expressing ~2500 sequenced genes per cell. Clustering analysis divided those cells into 8 clusters with known markers in some of them: early MSCs (Sca1), late MSCs, chondrocytes (Col2a1), mesenchymal bi-potent progenitors (MBPs), osteoblasts (Osteocalcin), osteocytes (SOST), adipoprogenitor (AP)1, and AP2 (adiponectin) (Figure 2A). Interestingly, plots suggest that these cells exist in a continuum, rather than in discrete

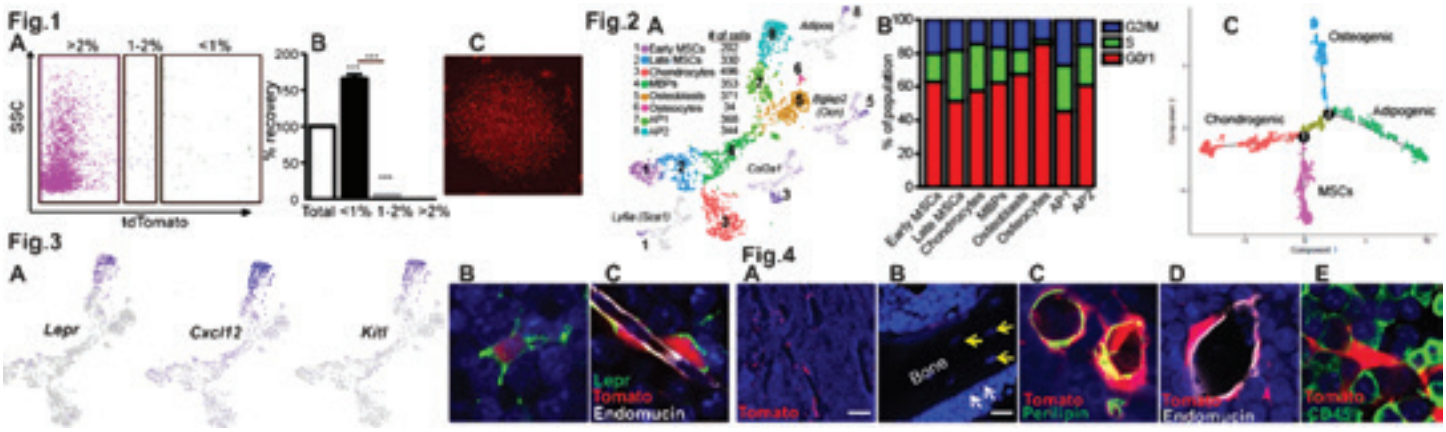


Figure 1. (A) FACS sorting of bone marrow cells from Col2/Td mice into 3 groups: top 1% (< 1%), 1-2%, and > 2% Td+ expressing cells; **(B)** CFU-F assay of unsorted and sorted groups. N = 3-4/group; **(C)** All CFU-F colonies from top 1% group are Td+. **Figure 2. (A)** Clustering of bone marrow mesenchymal lineage cells reveals the identity of MSCs and their multi-differentiation routes. The gene expression tSNE plots of some cluster markers are shown on the side. Cells with a high expression of indicated gene are labeled in blue; **(B)** Cell cycle state of each cluster; **(C)** Clustered cells were subjected to dimensional reduction by Monocle to generate a trajectory plot with 4 directions. **Figure 3. (A)** tSNE plots of CAR cell markers and LepR show their high expression (blue) in AP clusters, especially AP2; **(B)**, **(C)** Fluorescence images of Col2/Td tibia revealed that LepR+ cells are mostly Td+ cells in **(B)** bone marrow; **(C)** and at perivascular niche. **Figure 4**. Fluorescence images of Adipoq/Td tibia revealed abundant adipogenitors in bone marrow. **(A)** Metaphyseal bone marrow; **(B)** Trabecular bone. Yellow arrows point to osteocytes and white arrows point to bone surface. Scale bar: 100 μm; **(C)** Td+ marrow adipocytes; **(D)** Td+ pericytes; (E) Td+ bone marrow cells are CD45- stromal cells.

states. Cell cycle analysis based on the expression levels of > 90 cell cycle-related genes revealed that early MSCs are quiescent, osteocytes are the least proliferative cells and that AP1 and late MSCs are the most proliferative cells (Figure 2B). Monocle trajectory analysis generated three differentiation directions with the first branch separating chondrocytes from MBPs and the second branch bi-pronged into osteoblasts and APs (Figure 2C). Positioning individual cells along a linear pseudotimeline with MSC as the root revealed known and novel genes differentially expressed during MSC tri-differentiation processes (data not shown). Cells in AP clusters, particularly those in AP2, highly and specifically express LepR, Cxcl12 and Kitl (Figure 3A), resembling the previously identified CAR/LepR$^+$ MSC population [4]. Fluorescence imaging revealed that 40.2% of Td$^+$ cells in bone marrow are LepR$^+$ cells and almost all LepR$^+$ stromal (Figure 3B) and pericytes cells (Figure 3C) were Td$^+$. To validate AP clusters, we generated *Adipoq/Td* mice (Figure 4). At 1 month of age, these mice had abundant Td$^+$ cells in metaphyseal bone marrow (Figure 4A) but not on bone surfaces as osteoblasts or inside bone as osteocytes (Figure 4B). Td$^+$ cells included all adipocytes (Figure 4C), many pericytes (Figure 4D) and stromal cells (Figure 4E) and contributed to a large portion of CFU-Fs, demonstrating that AP clusters are fate-determined progenitors.

Discussion

Our work demonstrated the power of large scale scRNA-seq at identifying and characterizing subpopulations of mesenchymal lineage cells. To our knowledge, this is the first study that computationally delineates the entire in vivo differentiation process of MSCs and put true MSCs and their descendants in an ordered fashion. One unexpected finding is that we identified and validated abundant APs in 1-month-old mouse bone marrow when mature adipocytes are rarely detected in the metaphyseal area. Based on our sequencing data, APs are a major source of cytokines and chemokines. Together with their abundance and high proliferation ability, our data indicate that they play an essential role in regulating bone metabolism.

Significance

Our study established the *in vivo* heterogeneity of bone marrow MPs by identifying their novel subpopulations and delineating their relative positions along the MSC tri-differentiation axes.

References

1. **Chandra A, *et al***. *J Bone Miner Res*, 2017. 32:360-372.
2. **Zhu J, *et al.*** *Methods Mol Biol*, 2015:19-29.
3. **Siclari, VA, *et al.*** *Bone*, 2013. 53:575-86.
4. **Zhou, BO, *et al.*** *Cell Stem Cell*, 2014. 15:154-68.

U·P·O·J

Lithium Treatment Improves Vertebral Trabecular Bone Architecture in Mucopolysaccharidosis I Dogs during Postnatal Growth

Sun H. Peck
Yian Khai A. Lau
Justin R. Bendigo
Megan Lin, Toren Arginteanu
Jessica H. Bagel
Patricia O'Donnell
Neil R. Malhotra
Peter S. Klein
Eileen M. Shore
Margret L. Casal
Lachlan J. Smith

Introduction

Mucopolysaccharidosis (MPS) I is a lysosomal storage disease characterized by deficient alpha-L-iduronidase activity, which leads to abnormal accumulation of incompletely degraded dermatan and heparan sulfate glycosaminoglycans (GAGs)[1]. MPS I patients present with severe spinal deformity, due in part to impaired vertebral bone formation during postnatal growth, which decreases quality of life and increases mortality[2]. Enzyme replacement therapy (ERT), the current clinical standard of treatment for MPS I, has been shown to attenuate progression of spine disease in MPS I dogs[3,4]. However, ERT is expensive, requires frequent and regular administration throughout the duration of the patients' lifetimes, and does not fully normalize bone formation even when commenced at birth[5]. Thus, it is important to identify alternative therapies that specifically target and enhance bone formation. Our previous work in other MPS subtypes with similar bone manifestations showed that impaired bone formation is due to failed hypertrophic differentiation of vertebral epiphyseal chondrocytes during postnatal development[6], which is associated with decreased Wnt signaling[7], an important regulator of endochondral ossification during postnatal growth. Therefore, we hypothesized that stimulating the Wnt signaling pathway would result in improved bone formation in MPS I. Lithium activates the Wnt pathway by inhibiting GSK-3β and is FDA-approved for human use for the treatment of bipolar disorder[8]. Thus, the objectives of this study were to 1) establish a lithium dosing and monitoring regimen and 2) investigate whether treatment with lithium can enhance bone formation during postnatal growth in MPS I in the naturally-occurring canine model.

Methods

We used the naturally-occurring MPS I canine model, which mimics both the progression and pathological phenotype of the skeletal abnormalities found in human patients[9]. With Institutional Animal Care and Use Committee (IACUC) approval, MPS I dogs (n = 3) were treated orally with lithium carbonate daily from 14 days to 6 months-of-age. Following an initial 1 week period of low dose acclimation, the dose was gradually increased to 30-50 mg/kg in order to maintain serum lithium levels in the putative therapeutic range (0.5-1.5 mmol/L)[10]. Throughout the study, lithium doses were adjusted twice a week based on animal weight and serum analyses. At 6 months-of-age, serum was collected from the three lithium-treated MPS I dogs as well as age-matched unaffected control dogs (n = 4) and untreated MPS I dogs (n = 5) in order to measure bone-specific alkaline phosphatase (BAP) activity using a commercially available ELISA kit. All animals were euthanized following serum collection, and thoracic vertebrae were excised postmortem and analyzed using micro-computed tomography (μCT). Significant differences in BAP levels between all groups were determined using 1-way ANOVA with post-hoc Bonferroni test ($p < 0.05$). Significant differences in μCT measurements between lithium-treated and untreated MPS I animals were determined using unpaired t-tests ($p < 0.05$).

Results

After the acclimation period, lithium treated MPS I dogs generally maintained serum lithium levels within the desired therapeutic range (Figure 1). While control dogs had significantly higher serum BAP than either the untreated or treated MPS I dogs, BAP levels were significantly higher in lithium-treated than untreated MPS I dogs (Figure 2). While bone volume fraction, bone mineral density, and trabecular thickness were not significantly different in lithium-treated MPS I dogs compared to untreated MPS I dogs, connectivity density and trabecular number were significantly higher, and trabecular spacing was significantly lower (Figure 3A, B). Preliminary cortical bone analysis showed no differences between groups. Upon clinical examination, forelimb and hindlimb joints of the MPS I lithium-treated animals presented with less swelling, less fluid retention, and better mobility than untreated MPS I animals.

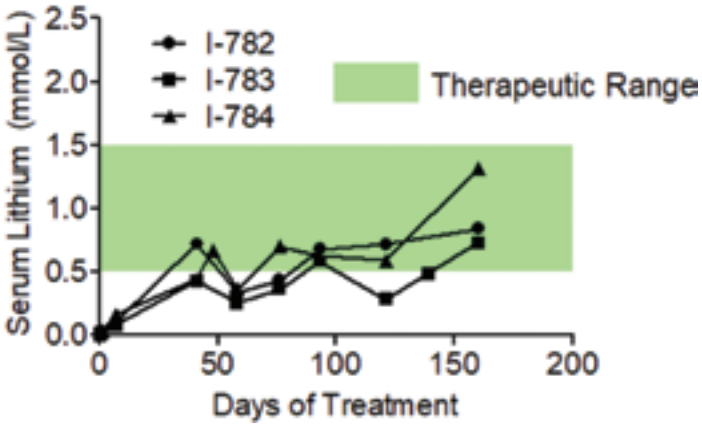


Figure 1. Lithium-treated MPS I animals generally maintained serum lithium levels in the therapeutic range throughout the duration of the study under our dosing regimen. N = 3, each line represents a lithium-treated MPS I animal.

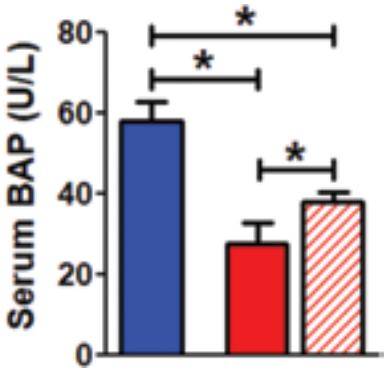


Figure 2. Lithium-treated MPS I animals exhibited higher levels of BAP activity compared to untreated animals. Control (n = 4), MPS I (n = 5), MPS I lithium treated (n = 3). $p < 0.05$.

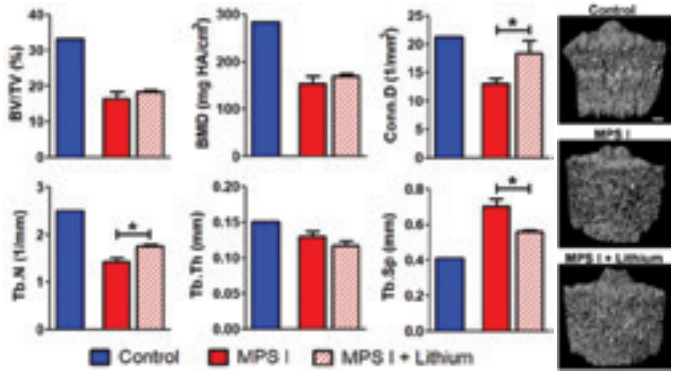


Figure 3. Micro-computed tomography (μCT) measurements of T12 vertebrae showed improvements in trabecular bone microarchitecture. (**A).** Bone volume fraction (BV/TV), bone mineral density (BMD), connectivity density (Conn.D), trabecular number (Tb.N), thickness (Tb.Th), and spacing (Tb.Sp) from control (representative baseline), MPS I (n = 3), and lithium-treated animals (= =3). *$p < 0.05$;)**B).** Representative 3D reconstructions of vertebral trabecular bone. Scale bar = 2 mm.

Discussion

Overall, these findings suggest that activating the Wnt pathway with lithium can alter bone turnover in MPS I animals. Our dosing regimen maintained serum lithium levels in the therapeutic range. Higher serum BAP levels in lithium-treated animals suggest increased bone formation, potentially due to increased osteoblast numbers or activity with treatment. Higher connectivity density and trabecular number and lower trabecular spacing in the lithium-treated animals also suggest improvements in bone microarchitecture. Importantly, these findings demonstrate that bone cells in MPS I are still able to respond to activating stimuli despite significant GAG storage and that Wnt pathway agonists may represent a potential therapeutic strategy for stimulating bone formation in MPS I. Furthermore, measuring BAP levels is a non-invasive method to detect increases in bone formation in patients as a result of therapeutic intervention. Decreased swelling and improved mobility of joints suggest that lithium treatment may be able to alleviate other related musculoskeletal symptoms of MPS I. Ongoing work will establish the underlying cellular basis of improved bone formation with lithium treatment in MPS I dogs and whether these alterations in trabecular bone architecture are associated with improved mechanical properties.

Clinical Relevance

MPS I is associated with debilitating skeletal disease stemming from impaired bone formation for which there is no effective treatment. Our results suggest that Wnt activation is a potential therapeutic strategy for stimulating bone formation in MPS I patients.

References:

1. **Scott, *et al.*** *Hum Mutat* 1995;
2. **White,** *Rheum* 2011
3. **Chiaro, *et al.*** *J Bone Min Res* 2014
4. **Dickson, *et al.*** *Mol Gen Met* 2010
5. **Yasin, *et al.*** *Spine* 2014
6. **Peck, *et al.*** *Mol Gen Met* 2015
7. **Peck, *et al.*** *ORS Trans* 2016
8. **Hedgepeth, *et al.*** *Dev Biol* 1997
9. **Haskins, *et al.*** *Pediat Res* 1984
10. **Rosenthal, *et al.*** *J Vet Pharmacol Therap* 1983

An Engineered Biomaterial Microenvironment to Direct the Formation of a Living Barrier to Seal Cartilage Defects

Jay M Patel, PhD[1,2]
Claudia Loebel, MD, PhD[2,3]
Brian C Wise, BS[1,3]
Kamiel S Saleh, BS[1,2]
James L Carey, MD, MPH[1]
Jason A Burdick, PhD[3]
Robert L Mauck, PhD[1,2,3]

1 McKay Orthopaedic Research Laboratory
University of Pennsylvania

2 Translational Musculoskeletal Research Laboratory
Corporal Michael J Crescenz VA Medical Center

3 Department of Bioengineering
University of Pennsylvania

Introduction

Articular cartilage consists of a dense extracellular matrix that allows the tissue to undergo fluid pressurization during compressive loading. Cartilage defects compromise this function, introducing free boundaries that result in the flow of proteoglycans and other matrix elements out of the tissue.[1] Decreases in matrix density at defect boundaries make them vulnerable to progressive erosion, instigating a vicious cycle that gradually increases defect size and concludes with joint-wide osteoarthritis (OA). A barrier at this interface may functionally restore the mechanical properties of the defect boundary[2], however synthetic materials may wear or delaminate with time. In this study, we aimed to direct the formation a living fibrous barrier at the damaged cartilage interface (via targeted progenitor cell recruitment and differentiation —Figure 1A), to restore normal cartilage biomechanical function. Specifically, we sought to establish a biomaterial microenvironment (modified hyaluronic acid) that 1) enhances the attachment and mechano-biological response of MSCs at the damaged cartilage interface, 2) induces the cells to undergo fibrogenesis via mechanical cues, and 3) promotes the deposition of fibrous matrix.

Methods

Biomaterial Microenvironment

Methacrylated hyaluronic acid (MeHA; 75kDa, 35-42% modification) was conjugated with fluorescent peptides (FITC) for visualization and fibronectin-mimicking peptides (RGD) for cellular adhesion (Figure 1B). The material was oxidized to introduce aldehydes (~30% substitution), which form covalent linkages with exposed amines in damaged tissue.[3]

Cellular Response

Bovine cartilage plugs were retrieved and sectioned (6mm diameter × 100μm thick). These discs were maintained as naïve samples (ND; mimicking a focal defect) or were digested in collagenase (0.01% for 30 minutes) to mimic degenerated cartilage (D). Biomaterial was applied with 0, 5 or 15 minutes of UV cross-linking, followed by PBS washes to remove non-adhered biomaterial. Cartilage discs (both ND and D) without biomaterial served as controls. Disc-biomaterial composites were seeded with juvenile bovine MSCs (P1-P3, 500 cells per disc) for 24 hours. Samples were fixed in 10% buffered formalin, followed by staining for F-actin with phalloidin to quantify cellular spread area and

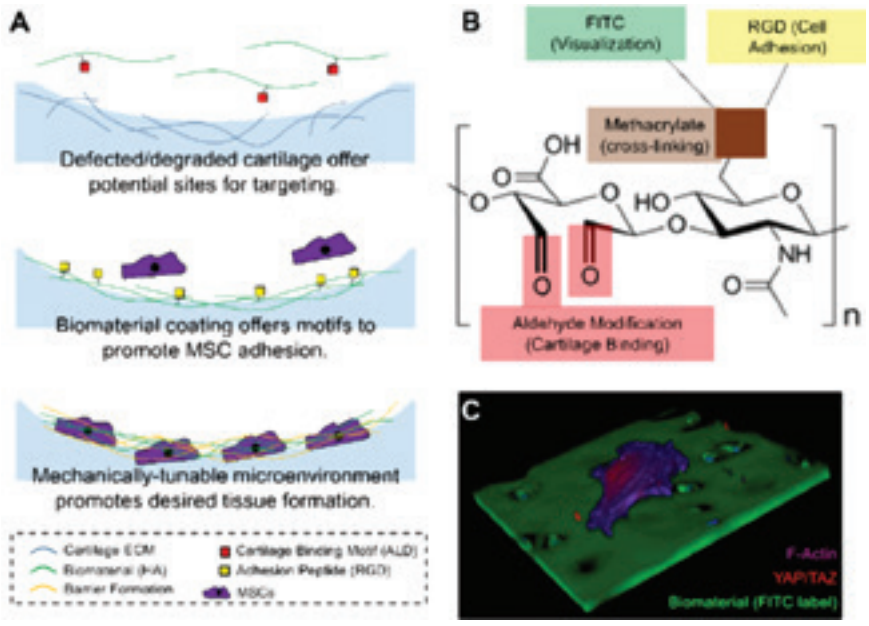


Figure 1. Approach Schematic. **(A)** Schematic of biomaterial binding to damaged cartilage, promoting MSC adhesion, and ultimately guiding cells towards formation of a barrier; **(B)** Biomaterial design with modifications to hyaluronic acid (HA); **(C)** Example of material applied to cartilage disc, with an adhered MSC.

for the nuclear co-factors YAP/TAZ to quantify cell mechano-response (Figure 1C).[4] YAP/TAZ signal intensity in the nucleus and cytoplasm were quantified to obtain a measure of nuclear localization (> 100 cells per group).

Fibrogenesis and Matrix Deposition

Additional cartilage discs (both ND and D) were subjected to biomaterial application/cross-linking. Discs were seeded with 500 cells and cultured for seven days in basal media. Cells on the discs were fixed and stained for α-smooth muscle actin (α-SMA), a marker of fibrogenesis.[5] The percentage of cells positive for α-SMA fibers was calculated for six replicates. Finally, an additional set of samples (ND vs D, no biomaterial vs biomaterial + 15 min UV) were cultured in medium containing L-azidohomoalanine (AHA), an alternative to L-methionine that incorporates into newly-deposited matrix. Subsequently the AHA can be stained with fluorescently-labeled dibenzocyclooctyne (DBCO) in order to visualize matrix deposition.

Statistical Analysis

Cell area and YAP/TAZ nuclear ratio were analyzed with a one-way analysis of variance (ANOVA) with post-hoc Tukey's test. α-SMA data was compared using a replicate-matched Kruskall-Wallis test. ND and D samples were analyzed separately.

Results

Confocal microscopy showed that the MeHA biomaterial infiltrated throughout the 100μm section prior to cross-linking, forming an integrated biomaterial microenvironment, around and in between chondrocytes in the cartilage matrix (Figure 1C). The biomaterial also promoted MSC adhesion (Figure 1C, Figure 2A) to the tissue-biomaterial interface, increasing cell spread area (Figure 2B). Biomaterial application and cross-linking increased YAP/TAZ nuclear localization (Figure 2C) of MSCs on both non-degraded and degraded cartilage, consistent with the increased MSC spread area (Figure 2B) and higher substrate mechanical properties (Figure 2A—insets) with biomaterial augmentation.

MSCs cultured for 7d on both nondigested and digested cartilage discs (without biomaterial; Figure 3A top) yielded a low percentage of cells positive for α-SMA fibers (13.96 and 6.95%, respectively). Biomaterial application/cross-linking (Figure 3A, bottom) significantly increased (Figure 3B) the percent of α-SMA positive MSCs on both nondigested and digested discs, indicating enhanced fibrogenesis.

Finally, samples without biomaterial (ND, D) showed little to no matrix deposition, as visualized by AHA staining (Figure 4, top). Conversely, application of biomaterial prior to cell seeding promoted new matrix formation (Figure 4, bottom).

Discussion

The results of this study detail the use of a modified biomaterial to 1) promote attachment and mechano-sensation of MSCs; 2) guide attached cells towards a fibrogenic

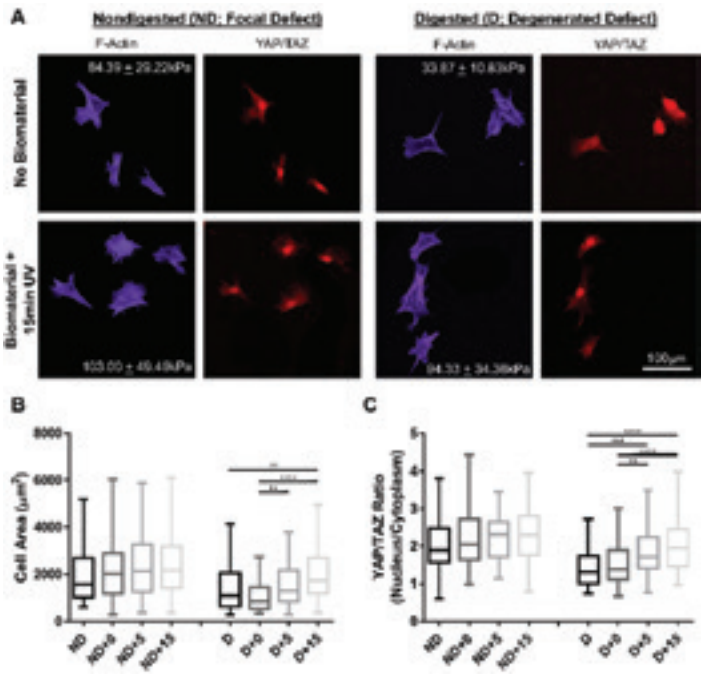


Figure 2. Cell Spreading and YAP/TAZ. **(A)** Representative images of F-actin and YAP/TAZ in cells on nondegraded and degraded samples, both without biomaterial (top row) and with biomaterial and cross-linking (bottom row); Quantification of **(B)** cell spread area and **(C)** YAP/TAZ ratio (nuclear:cytoplasmic) of cells on ND and D samples without biomaterial, with biomaterial (+0), and with biomaterial and crosslinking (+5, +15). n > 100 cells per group. *, **, ***, **** indicate p < 0.05, 0.01, 0.001, 0.0001, respectively.

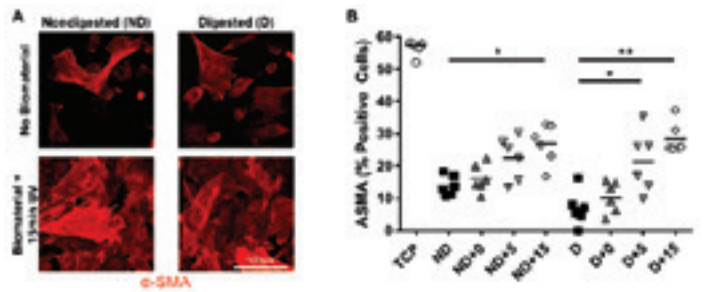


Figure 3. α-Smooth Muscle Actin. **(A)** Representative images of cells stained for α-SMA; **(B)** Percentage of cells positive for α-SMA stress fibers. n > 50 cells per data point (n = 6 replicates). *, ** indicate p < 0.05, 0.01, respectively.

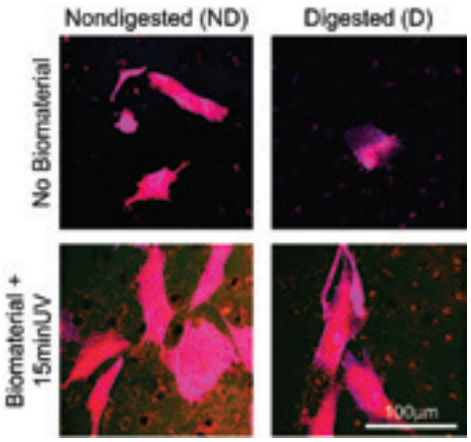


Figure 4. Matrix Deposition. Red stain depicts incorporation of AHA into new matrix. Biomaterial application and crosslinking results in increased deposition (bottom row). Scale bar depicts 100 microns.

phenotype; and 3) promote matrix deposition to cover cartilage defects. These findings support the promise of creating tunable microenvironments to home and retain stem cells at the defect interface, and ultimately control their biologic response. The behavior of cells in this study is consistent with prior cell-hydrogel studies, in that cell attachment and fibrogenesis increase with substrate stiffness. The biomaterial microenvironment in this study does just that, as it utilizes both cell-adhesive and mechanical cues at the damaged interface to induce a fibrotic response. Future studies will investigate the ability of the tissue barrier to functionally seal defects and preserve cartilage integrity in both *in vitro* cartilage explant and *in vivo* trochlear defect models.

Acknowledgements

This work was supported by the NIH, VA, AOSSM, and CEMB. The authors thank the Mauck and Burdick Labs at Penn for their help.

References

1. Basalo IM, Mauck RL, Kelly TN, *et al.* Cartilage interstitial fluid load support in unconfined compression following enzymatic digestion. *J Biomech Eng* 2004; 126(6): 779-786.

2. Grenier S, Donnelly PE, Gitten J, *et al.* Resurfacing damaged articular cartilage to restore compressive properties. *J Biomech* 2015; *48*(1): 122–129.

3. Wang DA, Varghese S, Sharma B, *et al.* Multifunctional chondroitin sulphate for cartilage tissue-biomaterial integration. *Nat Mater* 2007; 6(5): 385-392.

4. Dupont S, Morsut L, Aragona M, *et al.* Role of YAP/TAZ in mechanotransduction. *Nature* 2011; 474(7350): 179-183.

5. Talele NP, Fradette J, Davies JE, *et al.* Expression of alpha-smooth muscle actin determines the fate of mesenchymal stromal cell. *Stem Cell Rep* 2015; 4(6): 1016-1030.

Developing a Biologic Replacement for the Porcine Accessory Carpal as a Model for the Treatment of Thumb OA

Brendan Stoeckl[1,2]
Hannah Zlotnick[1,2,4]
Michael Hast[1]
Mackenzie Sennett[1,2]
Thomas Schaer[3]
Robert Mauck[1,2,4]
David Steinberg[1,2]

1 Department of Orthopaedic Surgery
University of Pennsylvania

2 Translational Musculoskeletal Research Center
CMC VAMC, Philadelphia, PA

3 Comparative Orthopaedic Research Laboratory
School of Veterinary Medicine, Kennett Square, PA

4 Department of Bioengineering
University of Pennsylvania

Introduction

Trapeziometacarpal (TMC) osteoarthritis (OA) is one of the most common conditions affecting middle and older aged adults[1]. Given that the thumb is central to all activities of daily living, loss of function has a significant impact on quality of life. Patients with TMC OA are initially managed with activity modification, NSAIDs, splinting, and corticosteroid injections[2]. These treatments fail in the long term, however, and many patients eventually require destructive surgical intervention, involving removal of all or part of the trapezium, and replacement with tendon, fascia, or an artificial implant[2]. While effective at reducing pain, these procedures compromise grip strength and, in some cases, result in subsidence and disFigurement of the hand[2]. Efforts to replace articular cartilage (and bone) with living, functional tissue have matured substantially over the last two decades[3], as has technology for generating constructs that can match the anatomical complexity and geometry of native articulating surfaces[3,4]. For these technologies to progress towards translation, appropriate large animal models are required. In our previous work, we identified the porcine accessory carpal (AC) as a potential model for TMC OA, given its similar shape, size, and loading[5]. Here, we develop strategies for the fabrication of tissue engineered biologic replacements for the porcine AC bone and cartilage, and demonstrate feasibility.

Methods

Eight AC bones were isolated from the right forelimbs of adult Yucatan minipigs and four human trapezia were isolated from cadaveric donors. Samples were fixed in formalin and imaged via μCT (VivaCT 75, Scanco), before and after immersion in Lugol's solution (5% I_2, 10% KI in water) to enhance cartilage contrast. DICOMs from the initial scan were imported into ITK-SNAP[6] and bone segmented. A surface mesh was exported to Meshlab (ISTI) for simplification and Solidworks (Dassault Systèmes) to render 3D objects and compute bone volume and surface features. Post-Lugol's scans were manually registered with the bone and processed similarly, with the cartilage layer segmented in a semi-automated manner. After imaging, samples were decalcified, processed into paraffin, sectioned, and stained with Safranin-O/fast green to visualize cartilage, bone, and fibrous tissue and Picrosirius red, to visualize collagen. Immunohistochemistry was used to assess distribution of collagen II. In Solidworks, an implant of the articulating cartilage surface and first third of the AC bone was designed. A cylindrical peg was included for fixation into the parent bone. Negative molds were designed for both the bone portion and the composite implant. The bone mold was 3D printed out of aluminum alloy using direct metal laser sintering (DMLS), and the composite mold was 3D printed in an ABS-like photopolymer. To form the bone integrating portion of the construct, poly(ε-caprolactone) (PCL) was dissolved in chloroform at 20% wt/vol and mixed with NaCl crystals sieved to ~106 μm with inclusion of Zirconium nanoparticles for radioopacity. The slurry was poured into the bone mold and the solvent was evaporated for 5 days. The units were demolded and washed in distilled water to remove salt. The resultant construct was imaged via μCT (μCT50, Scanco medical). As a proof of concept, a 5 wt% agarose solution doped with red food coloring for visualization was poured into the composite mold, and the PCL bone integrating component was added to shape the cartilage portion. Finally, a 1% wt/vol methacrylated hyaluronic acid (MeHA) solution with 20 million juvenile bovine mesenchymal stem cells (MSCs) per mL was dispensed into the composite mold and the porous bone component placed into the mold to form the final shape of the cartilage. Gelation occurred via inclusion of APS/TEMED, with entire mold placed at 37°C for 10 minutes. After 24 hours in culture, construct viability was assessed.

Results

The porcine AC bone shows marked anatomical similarity to the human trapezium in both its size and saddle shape of its major articulating surface. (Figure 1A, 1B) Both species show strong staining for proteoglycans on their cartilage surfaces (Figure 1C), and collagen throughout the tissue depth (Figure 1D). Type II collagen is high in the cartilage surface of both the human trapezium and porcine AC (Figure 1E). Using surface meshes generated from μCT, an implant was designed to replace the full

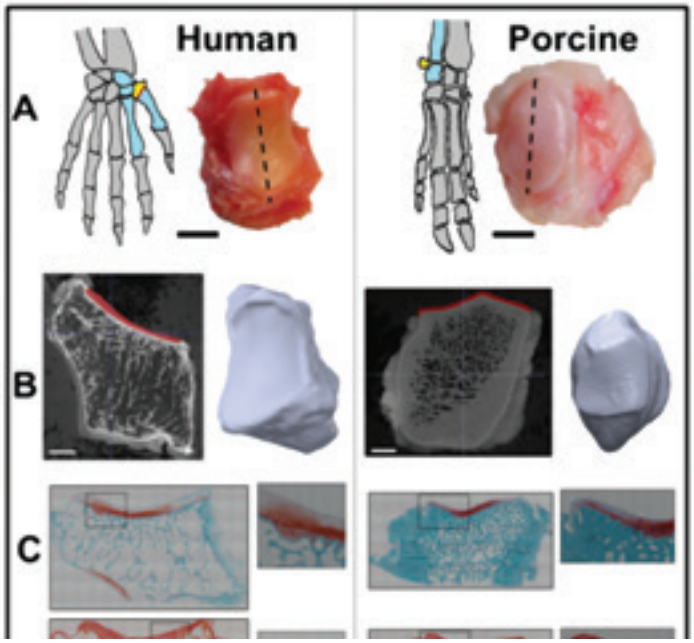


Figure 1. **(A)** Diagram and gross view of the human trapezium and porcine AC. Dotted line represents sectioning plane. Scale = 3mm. **(B)** μCT slices in ITK-SNAP showing cartilage segmentation in red and 3D renderings in Solidworks. Scale = 3mm. **(C)** Safranin-O/fast green. **(D)** Picrosirius Red. **(E)**. Immunohistochemistry for collagen II. Scale = 3mm (1mm for insets).

articulating surface of the porcine AC. (Figure 2A) The boney portion of this implant was generated using PCL foam (Figure 2B-D). MicroCT showed that this recapitulated the geometry of the original design yielding a volume that was 76% similar to the template (Figure 2E). A second mold with both the bone-mimicking and cartilage portion of the implant formed a combined implant (Figure 2F). When cast into this composite, MSCs remained viable (Figure 2G).

Discussion

In this study, we evaluated the histological and geometric properties of the porcine AC compared to the human trapezium. The two showed remarkable anatomic and compositional similarities. Furthermore we developed a method to fabricate a composite implant, mimicking the boney (using PCL foam) and cartilage (using a hydrogel) regions of the AC. Future work will improve integration between the hydrogel and foam and

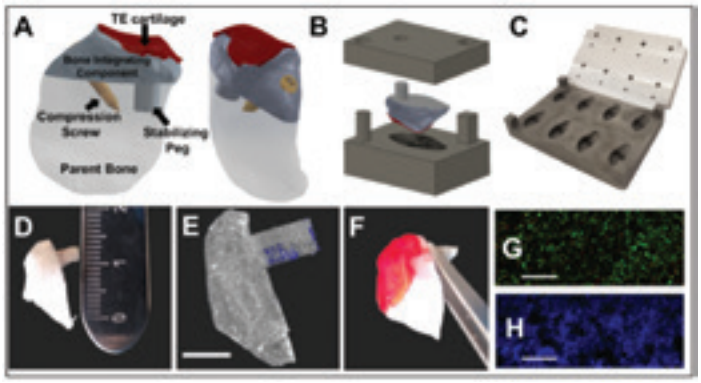


Figure 2. (A) Design of composite implant for biologic resurfacing of the porcine AC**. (B, C)** Mold for fabrication of implant. **(D)** PCL foam AC **(E)** μCT scan of construct. Scale = 5mm **(F)** Composite construct with PCL foam and hydrogel (red) **(G)** Live (green)/Dead (red) image of MSCs in MeHA in the cartilage layer. Scale = 200μm. **(H)** Confocal image of PCL foam (blue is auto-fluorescence of PCL). Scale = 200μm.

refine methods for maturing the construct, to establish means for functional biologic joint resurfacing in a large animal model.

Significance

This study compared the porcine accessory carpal and human trapezium and refined strategies for the fabrication of tissue engineered osteochondral implants for biologic joint resurfacing, providing a route for effective biologic joint replacement for patients with TMC OA.

Acknowledgments

This work was supported by the National Institutes of Health and the Department of Veterans Affairs.

References

1. Becker+, *CORR*, 2013.
2. Wajon+, *Cochrane Database*, 2015.
3. O'Connell+ *J Knee Surg*, 2012.
4. Saxena+ *Tissue Eng*, 2016.
5. Stoeckl+, *ORS* 2018.
6. Yushkevich+, *Neuroimage*, 2006.

Dual Biofactor Release from Acellular Hyaluronic Acid Scaffolds for Cartilage Repair in a Pig Model

Anthony Martín, BSE[1,2]
Jay Patel, PhD[1,4]
Michael Eby, MD[1,2]
Mackenzie Sennett, BS[1,4]
Hannah Zlotnick, BSE[1,3]
Kamiel Saleh, BSE[1]
Andrew Chang, BS[2]
Matthew Davidson, PhD[3]
James Carey, MD[1,2]
Jason Burdick, PhD[3]
Robert Mauck, PhD[1,3,4]

1 McKay Orthopedic Research Laboratory
University of Pennsylvania

2 Perelman School of Medicine
University of Pennsylvania

3. Department of Bioengineering
University of Pennsylvania

4 Translational Musculoskeletal Research Center
Philadelphia VA Medical Center

Introduction

Large focal cartilage injuries often progress to osteoarthritis, a costly epidemic affecting over 30% of adults in the United States[1]. To treat these patients, we developed a cell-free hyaluronic acid (HA) scaffold with two embedded signaling proteins designed to enhance cartilage repair: Stromal Cell-Derived Factor-1α (SDF-1α; SDF) chemokine to increase the recruitment of mesenchymal stem cells (MSC)[5] and Transforming Growth Factor-β3 (TGF-β3; TGF) to enhance cartilage regeneration[6]. The objective of this study was to evaluate the effect of SDF and TGF incorporation into electrospun nanofibrous HA scaffolds on cartilage regeneration in a large-animal full-thickness chondral defect model. We hypothesized that SDF and TGF would synergistically improve cartilage defect repair

Materials and Methods

Scaffold Fabrication

Four scaffold groups were tested: 1) Scaffold (w/o biofactor), 2) SDF, 3) TGF, and 4) SDF + TGF. A solution of Methacrylated HA (76kDa, 45% mod, 4% w/v), polyethylene oxide (PEO, 900kDa, 2% w/v), and photoinitiator (Irgacure 2959, 0.05% w/v) in ddH20 was electrospun into nanofibrous scaffolds[6], +/− growth factor. Samples (4.5mm diameter) containing protein had a theoretical maximum of 21.25ng SDF and/or 106.29ng TGF, embedded within the electrospun nanofibers

Scaffold Characterization

Scaffold degradation (uronic acid assay; n = 8), and biofactor release (ELISA assays; n = 5) were measured. To determine *in vitro* bioactivity, scaffolds were co-cultured with bovine MSC pellets (250,000 cells) for 5 weeks. Pellets were analyzed with DMMB (sGAG) and Pico Green (DNA) assays (n = 4), and sectioned for histology (n = 4). Scaffolds were seeded with bovine MSCs (100,000 cells), cultured for 1 week, and imaged on a confocal microscope to measure infiltration (n = 5).

Animal Model

6 male juvenile Yucatan Minipigs underwent bilateral stifle joint surgery[6]. In each knee, 4 full-thickness 4mm trochlear cartilage defects were created, followed by microfracture (MFx). 3 defects per joint were loaded with identical scaffolds to prevent protein cross-contamination, and 1 defect per joint was left as a MFx control (Figure 1A) (n = 3 animals, 3 replicates per knee). Animals were euthanized 12 weeks post-op and underwent second-look arthroscopy (Figure 1B) for ICRS Cartilage Repair Assessment. Defect sites and healthy control regions (Figure 1C) were harvested as osteochondral blocks and mechanically tested using a 2 mm spherical indenter for equilibrium modulus at 30% strain. Samples were then sectioned for evaluation using the ICRS II Histology Scoring system.

Results

Scaffolds degraded uniformly over time with roughly 50% degradation at 5 weeks. ~40%max SDF was released after 7 days incubation and ~45%max TGF was released after 3 days. MSC pellets cultured with scaffolds releasing TGF showed increased proteoglycan and DNA content. MSCs seeded onto scaffolds releasing SDF and/or TGF showed greater infiltration into scaffolds. Second look arthroscopy did not reveal any significant difference between groups. Indentation testing showed the TGF scaffold group had a higher equilibrium modulus than the MFx group (Figure 2). ICRS II Histology

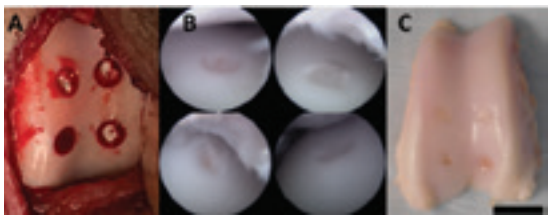


Figure 1. Cartilage defects in a minipig trochlea. **(A)** Scaffolds implanted in 4mm defects at the time of implantation. **(B)** Second-look arthroscopy 12 weeks post-op. **(C)** Gross trochlea harvested 12 weeks post-op, same samples as in B, S+T group (scale bar = 10mm).

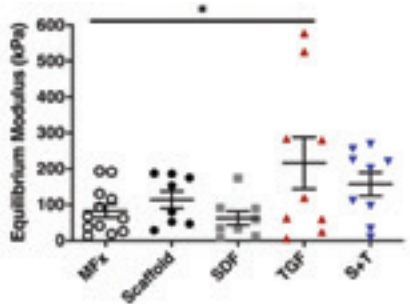


Figure 2. Equilibrium modulus of repair tissue measured via indentation testing at 30% strain.

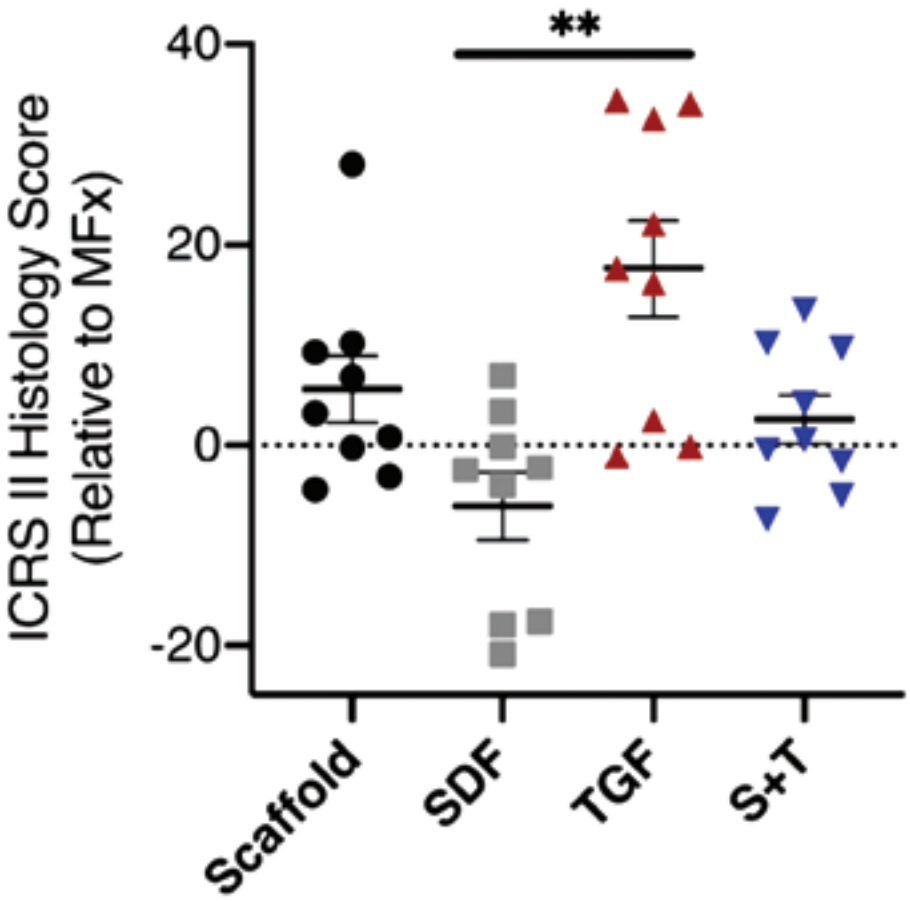


Figure 3. ICRS II Histology scoring by 3 blinded reviewers. * = $p < 0.05$, *** = $p < 0.0005$

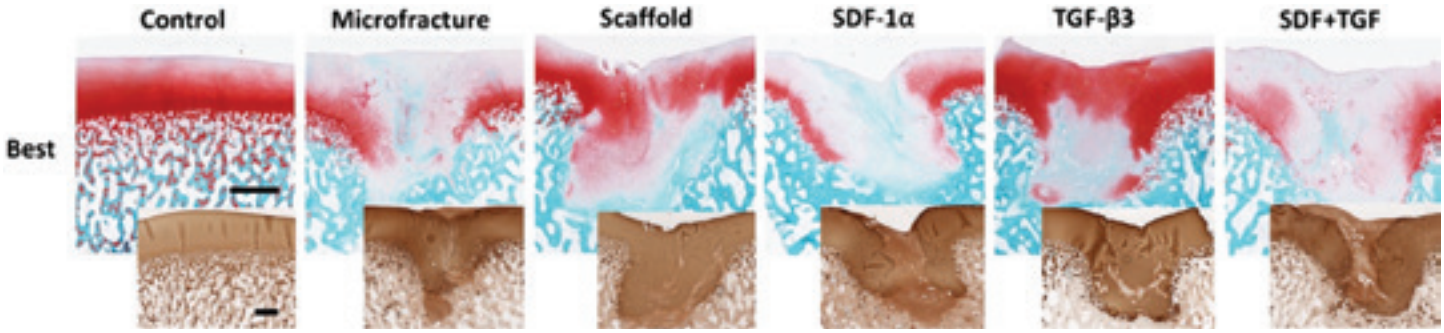


Figure 4. SAfO/FastGreen staining and Type 2 Collagen immunohistochemistry of the best-scoring sections from each group. Scale bar = 2mm

scoring revealed the TGF group outperformed the SDF and S+T groups, but not the drug-free scaffold group (Figure 3). While SDF seemed beneficial *in vitro*, it was detrimental in the large animal model, possibly via the recruitment of inflammatory cells.

Conclusions

This study demonstrates the ability to incorporate more than one biofactor into electrospun HA scaffolds, which could serve as a platform for a variety of regenerative medicine applications. We failed to prove our hypothesis that SDF-1α would act synergistically with TGF-β3 to improve *in vivo* cartilage regeneration.

Acknowledgments

This work was supported by the AOSSM and the NIH NCATS.

References

1. Jafarzadeh+ 2018 *Arth Rheum*
2. Purcell+ 2012 *Biomaterials*
3. Kim+ 2015 *Tissue Eng*

The Impact of Matrix Stiffness and O-GlcNAcylation on YAP Nuclear Localization and Matrix Deposition in Mesenchymal Stem Cells

Ryan Daniels[1]
Claudia Loebel[2]
Thea Ornstein[1]
Jason Burdick[2]
Robert Mauck[1,2]

1 McKay Orthopaedic Laboratory
University of Pennsylvania

2 Department of Bioengineering
University of Pennsylvania

Introduction

Mechanotransduction, the process in which mechanical stimuli are converted into biochemical signals, can influence cellular behavior. In mesenchymal stem cell (MSCs), yes-associated protein, YAP, becomes increasingly localized to the nucleus in stiff microenvironments, impacting lineage specification and cellular activities, including matrix gene expression[1]. While the mechanical mechanisms by which YAP nuclear translocation occurs is increasingly well defined, biochemical modifiers of YAP in the cytosol also impact YAP baseline levels, bioavailability, and activity. Recent findings suggest that the transfer of an O-linked β-*N*-acetylglucosamine (O-GlcNAc) group to a specific serine or threonine on YAP can control its nuclear localization[1]. Based on this, we hypothesized that modification of YAP by O-GlcNAc transferase (OGT) would influence nuclear translocation in a mechanobiologic setting. In addition, we queried the impact of substrate stiffness on nascent extracellular matrix (ECM) deposition, using functional non-canonical amino acid labeling (FUNCAT)[2]. The timing and amount ECM deposition defines tissue maturation and structure-function relationships, and is uniquely tuned to enable musculoskeletal tissue function. While matrix stiffness increases mechanobiologic signaling (e.g., YAP nuclear localization) in MSCs, the link between mechanosensing and nascent matrix production has not yet been explored. To that end, we utilized norbornene-modified hyaluronic acid (NorHA) hydrogels to evaluate substrate stiffness and ECM formation.

Methods

Hydrogel Fabrication

Fibronectin-coated polyacrylamide (PA) gels were produced as in[3] at stiffnesses of 5, 15, or 55kPa. RGD-modified NorHA hydrogels were produced as in[4] to a stiffness of 5kPa or 15kPa.

Cell culture

For YAP O-GlcNAcylation studies, juvenile bovine bone marrow MSCs (bMSCs) and NIH3T3 (3T3) cells were cultured in DMEM with 10% FBS. For nascent ECM studies, hMSCS were cultured in DMEM (without methionine) supplemented with the methionine analog azidohomoalanine (AHA) to mark nascent proteins. For this, cells were seeded on NorHA gels for 24 hours before fixing.

Pharmacological inhibition

OGT was inhibited with OSMI-1 (at 50mM). Cells were resuspended in media with or without OSMI-1, and seeded on PA hydrogels overnight before fixing. Cellular contractility was inhibited by Y-27632 (at 10uM) and increased with LPA (at 50uM).

Immunocytochemistry and AHA labeling

To visualize YAP, cells were fixed in 4% PFA, permeabilized, incubated in primary antibody overnight, and nuclei were stained with DAPI. To identify nascent matrix, DBCO-488 was used to label all proteins containing AHA. A membrane stain was used to create a mask for subsequent analysis. In order to identify only exogenous proteins, labeling was performed on live cells prior to fixation.

Image and statistical analysis

The ratio of nuclear to cytoplasmic (N:C) YAP was determined by tracing cell and nuclear boundaries and calculating fluorescence intensity with Image J. Nascent matrix was quantified using the cell membrane stain as a mask to eliminate cell surface receptors; this was subtracted from the ECM stain in ImageJ. Resulting images were quantified using the 3D objects plugin in ImageJ to obtain ECM volume, and was normalized to cell volume. Statistical analysis was performed by one-way ANOVA with Tukey's post-hoc tests.

Results

In 3T3 cells and bMSCs, YAP N:C ratios increased with increasing substrate stiffness (Figure 1A,B). In bMSCs and 3T3 cells on 15kPa and 55kPa PA gels, YAP N:C ratios decreased in the presence of OSMI-1, to levels matching that of a 5kPa gel (Figure 1A,B). Cells on glass showed a partial (but significant) reduction in YAP N:C ratio in bMSCs with OSMI-1 treatment. Qualitatively,

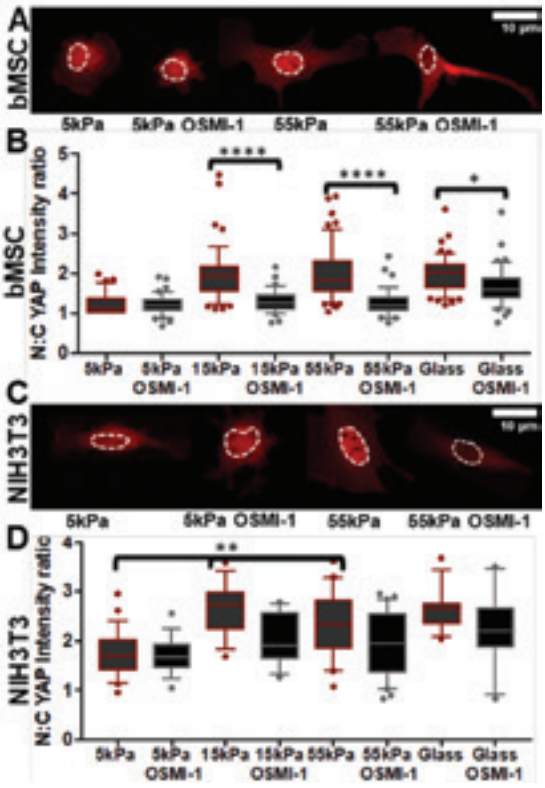


Figure 1. OSMI-1 decreases N:C YAP in bMSCs and 3T3 cells. Images of YAP (red) in **[A]** bMSCs and **[C]** 3T3s at varying stiffnesses. Nuclei depicted with dotted line. Box and whisker plots for **[B]** bMSCs (N = 3 replicates, n = 39-53 cells) and **[D]** 3T3 cells (N = 2 replicates, n = 14-30 cells).

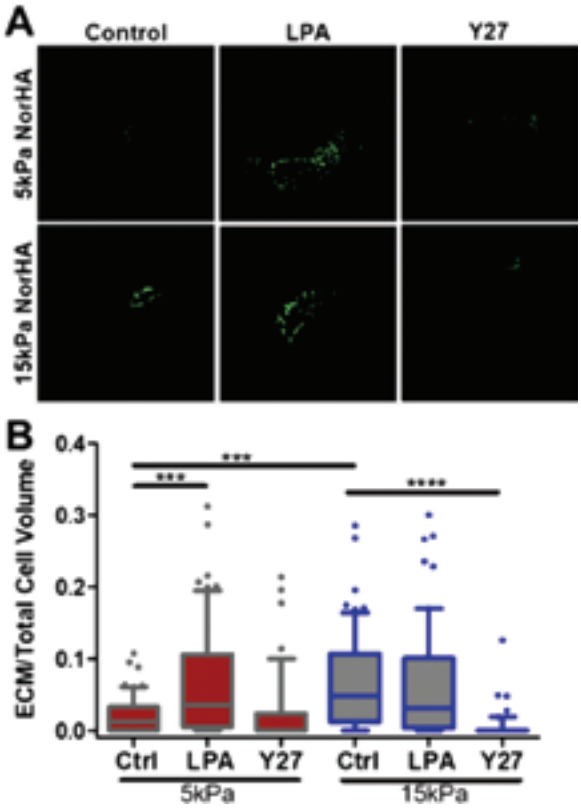


Figure 2. Substrate stiffness and contractility increase nascent ECM production. AHA staining (green) in hMSCs on gels of 5kPa or 15kPa, with or without contractility agonist (LPA) or antagonist (Y27) **[A].** Quantification of AHA staining (ECM/total cell volume) **[B].** Box and whisker plots for **[B]** (N = 3 replicates, n = 45-63 cells).

total YAP levels and cell spreading were not changed with OGT inhibition. However, preliminary findings suggested that inhibition of OGT in hMSCs on NorHA gels decreased the number of focal adhesions, compared to untreated cells. This would suggest a decrease in traction force exerted by cells with OGT inhibition. With regards to nascent ECM, hMSCs on 5kPa NorHA gels produced little matrix, while hMSCs on 15kPa NorHA gels produced *significantly* more matrix after 1 day (Figure 2A,B). Matrix production was abrogated on both stiffnesses with inhibition of cellular contractility with Y27 (Figure 2A, right panels). Conversely, increasing contractility with LPA on 5kPa NorHA gels increased ECM production to levels matching that of cells on 15kPa NorHA gels (Figure 2A,B). After 3 days of culture, however, no differences in nascent matrix accumulation were seen, with cells on both stiffnesses accumulating similar amounts (data not shown).

Discussion

Taken together, our results demonstrate that OGT is a powerful biochemical regulator of YAP, which can impact its nuclear localization under mechanically inductive conditions. Because glucose availability regulates O-GlcNAc[1], and native tissues have different levels of glucose availability, it could be that certain tissues mechanotransduce in a different manner based on metabolic mechanisms. Our results also show that cellular contractility directly regulates nascent matrix deposition and assembly. Biomaterials for tissue engineering have intrinsic mechanical and adhesive properties, and this may impact nascent matrix produced by cells. Future work will be investigate the downstream consequences of cell autonomous ECM production on MSC differentiation. Further, given that O-GlcNAcylation processes mediate modification of both YAP and extracellular proteins (which is necessary for their function) future work will identify possible crosstalk between the metabolic state of the cell and its mechanobiological state.

Significance

O-GlcNAcylation of YAP is an important metabolic modifier of cell mechano-transduction. The role of cellular contractility and baseline mechano-signaling on nascent matrix production is important for the design of biomaterials that may direct tissue formation by MSCs.

Acknowledgements

This work was supported by the National Institutes of Health.

References

1. Totaro *et al.* YAP/TAZ upstream signals and downstream responses, 2018
2. Mcleod *et al.* High fidelity visualization of cell-to-cell variation and temporal dynamics in nascent extracellular matrix formation, 2016
3. Tse *et al.* Preparation of hydrogel substrates with tunable mechanical properties, 2010.
4. Caliari *et al.* Dimensionality and spreading influence MSC YAP/TAZ signaling in hydrogel environments, 2016

The Regulatory Role of EGFR Signaling in Adult Cartilage Homeostasis and Osteoarthritis

Yulong Wei[1]
Xiaoyuan Ma[1]
Hao Sun[1]
Biao Han[2]
Lin Han[2]
Motomi Enomoto-Iwamoto[3]
Ling Qin[1]

1 Department of Orthopaedic Surgery University of Pennsylvania

2 School of Biomedical Engineering Drexel University, Philadelphia, PA

3. Department of Orthopaedics University of Maryland, Baltimore, MD

Introduction

Osteoarthritis (OA) is the most common chronic condition of the joints with debilitating clinical symptoms including continuous pain, stiffness and limited motion. The uppermost superficial zone of articular cartilage is the first line of defense against OA initiation. It plays multifaceted roles in maintaining cartilage structure, function, and mechanical properties. We previously demonstrated that epidermal growth factor receptor (EGFR), a tyrosine kinase receptor, plays an essential role in maintaining this superficial zone during articular cartilage development using a cartilage-specific *Egfr*-deficient mouse model (*Col2-Cre Egfr*$^{Wa5/flox}$, *Egfr CKO*^{Col2Cre})[1]. However, this system did not distinguish whether the severe OA phenotypes observed in the *Egfr CKO*^{Col2Cre} mice after DMM is due to the inferior nature of cartilage before the surgery or the requirement of EGFR signaling in response to acute insults. We hypothesized that EGFR signaling is necessary for protection of adult articular cartilage from OA, and examined EGFR activity in human OA samples at different stages and studied surgery-induced OA phenotypes in mice with EGFR inactivation at adult stage.

Methods

Human OA articular cartilage samples

They were prepared from de-identified specimens obtained at the total arthroplasty of the knee joints. Their paraffin sections were stained by Safranin O/Fast green to evaluate OA stage[2] and neighboring sections were used for p-EGFR staining. *Animals- Aggrecan-CreER* mice were first crossed with *Egfr*$^{Wa5/+}$ (*Wa5* is a dominant negative allele of *Egfr*) to obtain *aggrecan-CreER Egfr*$^{Wa5/+}$, which was then crossed with *Egfr*$^{flox/flox}$ to generate *Egfr CKO*^{AgcER} mice and their *WT* (*aggrecan-CreER Egfr*$^{flox/+}$ and *Egfr*$^{flox/+}$) and *Wa5* (*Egfr*$^{Wa5/flox}$) siblings. Male mice at 3 months of age received tamoxifen (tam) injections (75 mg/kg/day × 5) followed by surgical destabilization of the medial meniscus (DMM) in right knees and sham operation in left knees a week later. In DMM surgery, the joint capsule was opened and the medial meniscotibial ligament was cut to destabilize the meniscu. In sham surgery, the joint capsule was opened but no further damage. All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pennsylvania.

Histology and immunohistochemistry (IHC)

Knee joints were fixed in 4% PFA, decalcified in 10% EDTA, and processed for paraffin sections followed by Safranin-O/fast green staining or p-EGFR, Ki67, TUNEL staining.

AFM Nanoindentation

Freshly dissected femoral condyle cartilage at 1 month post surgery was indented at more than 10 locations by a borosilicate colloidal spherical tip (R = 5 μm, nominal spring constant k = 7.4 N/m) with maximum indentation depth of ~1 μm at a 10 μm/s indentation rate using a Dimension Icon AFM (BrukerNano). The effective indentation modulus, E_{ind} (MPa), was calculated by fitting the whole loading portion of each indentation force–depth curve using the Hertz model as previously described[3].

Statistics

Data are expressed as means±SEM and analyzed by paired, two-tailed Student's t-test.

Results

Healthy human articular cartilage exhibited strong staining of p-EGFR, the activated EGFR, in chondrocytes at the superficial layer and gradually decreased staining in chondrocytes deep into the middle zone (Figure 1A, B). This staining was remarkably reduced at early OA when superficial zone is still intact (Figure 1C, D). At middle OA stage when superficial layer is depleted, p-EGFR was detected in some chondrocytes in middle and deep zones (Figure 1E, F). At late stage OA, most cell clusters beneath damaged cartilage surface had strong p-EGFR staining (Figure 1G, H). To explore the role of EGFR signaling in adult cartilage and in OA progression, we injected tam into 3-month-old *Egfr CKO*^{AgcER} mice and their *WT* and *Wa5* controls and then performed sham/DMM surgeries. The sham legs in the tam-treated *CKO*^{AgcER} mice showed great decreases in p-EGFR and Ki-67 (proliferation marker) staining and an increase in TUNEL (apoptosis marker) staining in the superficial chondrocytes at 4 months of age (Figure 2). At 6 months of

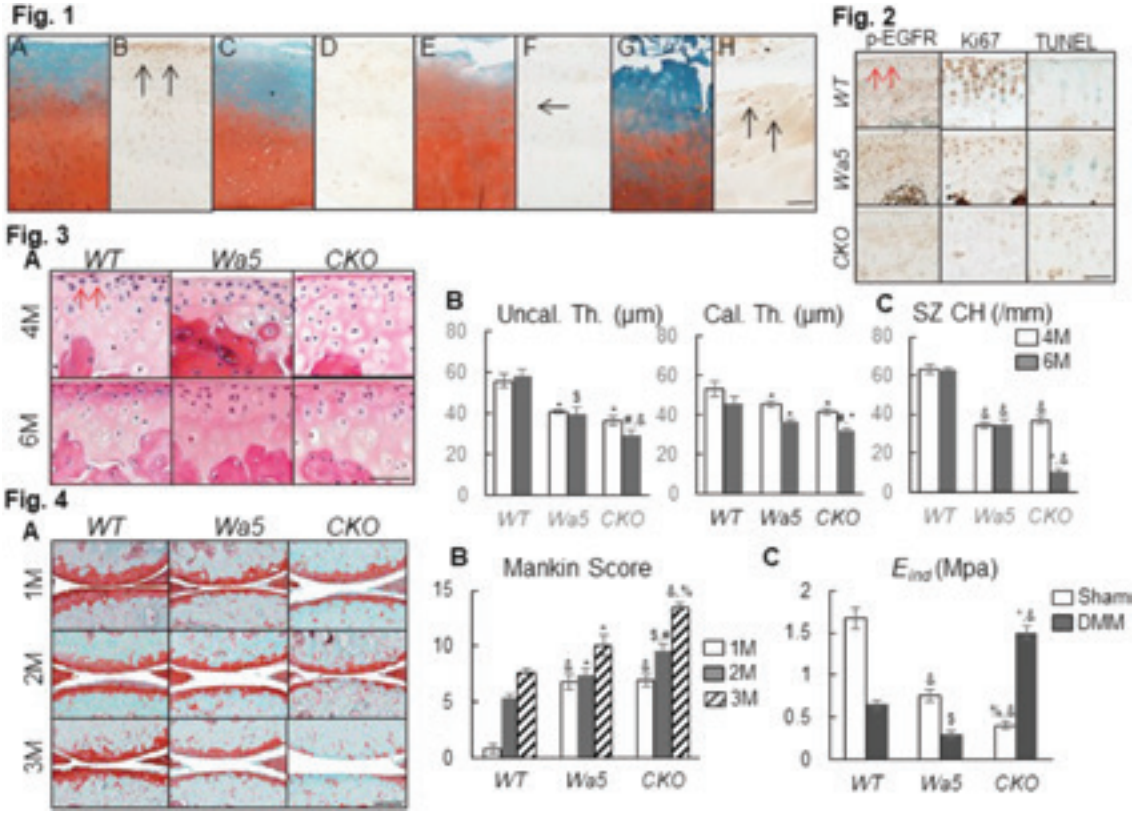


Figure 1. EGFR signaling in human healthy and diseased articular cartilage samples. **(A, B)** Healthy cartilage. **(C, D**) OA cartilage at early stage (OARSI Score 1-2). **(E, F)** OA cartilage at middle stage (OARSI Score 3-4). **(G, H)** OA cartilage at late stage (OARSI Score 5-6). **(A, C, E, G):** Safranin O/fast green staining; **(B,D,F,H):** IHC of p-EGFR. Arrows point to positive cells. n= 3/stage. Bar: 200 μm. **Figure 2.** IHC of p-EGFR, Ki67, and TUNEL in 4-mo-old sham tibia of *WT*, *Wa5*, and *Egfr CKO*^{AgcER} (Tam: 3-mo-old). Arrows point to superficial layer. Bar, 100 μm. **Figure 3.** EGFR signaling maintains adult cartilage structure. **(A)** H&E staining of femoral articular cartilage in 4 and 6-mo-old mice (Tam: 3-mo-old). Bar, 50 μm. **(B)** The thicknesses of uncalcified and calcified cartilage were quantified. **(C)** The number of superficial chondrocytes was quantified. n = 5/group. **Figure 4.** Chondrogenic EGFR deficiency in adult mice causes severe OA after DMM. **(A)** Safranin O staining of *WT*, *Wa5*, and *Egfr CKO*^{AgcER} joints at 1, 2, and 3 mo post DMM (Tam: 3-mo-old). Bar, 200 μm. **(B)** OA severity was measured by Mankin score. n = 6/age/genotype. **(C)** Femoral cartilage surface E_{ind} was measured at 1 mo post DMM. n = 6/genotype. *: $P < 0.05$, $: $p < 0.01$, &: $p < 0.001$ vs. *WT*; #: $p < 0.05$, %: $p < 0.01$, ^: $P < 0.001$ vs. *Wa5*.

age, these mice displayed reduced cartilage thickness at both uncalcified and calcified zones and diminished superficial chondrocytes (Figure 3), demonstrating that EGFR signaling is critical for adult cartilage homeostasis. One month after DMM, while WT joints remained intact, both *CKO*^{AgcER} and *Wa5* joints showed moderate cartilage damage (Figure 4A, B). Nanoindentation of femoral cartilage surface revealed that DMM causes a similar decrease of E_{ind} in *WT* and *Wa5* cartilage but an increase of E_{ind} in *CKO*^{AgcER} surface (Figure 4C), suggesting that *CKO*^{AgcER} has more advanced OA progression than *WT* and *Wa5*. At 2 months postsurgery, *CKO*^{AgcER} joints developed severer phenotype than controls with erosion of a large part of articular cartilage (Figure 4A, B). At 3 months postsurgery, *CKO*^{AgcER} joints developed late OA phenotypes characterized by loss of most articular cartilage (Figure 4A, B) and subchondral bone plate thickening at the medial site (data not shown). The OA phenotypes were also seen at the lateral sites in the *CKO*^{AgcER} (data not shown), which were not observed in control mice.

Discussion

Analyzing EGFR activity profile in human articular cartilage samples with different OA stages strongly implicates a potential role for EGFR signaling in the superficial layer of healthy and diseased articular cartilage. By using an inducible system, we were able to demonstrate that EGFR is an essential growth factor pathway in adult mouse cartilage that regulates the superficial layer by preserving their proliferation ability and promoting their survival. Reduction in EGFR activity in adult articular cartilage leads to accelerated cartilage degeneration under surgically induced OA conditions, indicating protective function of EGFR signaling on articular cartilage against OA degeneration.

Significance

Our studies uncover critical EGFR actions in adult knee articular cartilage and provide proof-of-principle evidence for targeting this novel pathway as OA therapies.

References

1. Jia H, et al. Proc Natl Acad Sci U S A 2016;113:14360–5
2. Pritzker KP, et al. OsteoArthritis and Cartilage, 2006;14:13-29.
3. Doyran B, et al. Osteoarthritis Cartilage 2017; 25:108-117.

Collagen VI Plays an Important Role in FDL Tendon Mechanics that is Distinct from the Role of Biglycan

Ryan J Leiphart[1]
Snehal S Shetye[1]
Hai Pham[2]
Stephanie N Weiss[2]
Marian F Young[2]
Louis J Soslowsky[1]

1 McKay Orthopedic Research Laboratory
University of Pennsylvania

2 National Institute of Dental and
Craniofacial Research
National Institutes of Health

Introduction

While tendons are largely composed of tension-bearing collagen I fibers, other lower abundance matrix proteins with lesser known functions are also present. For example, collagen VI is a nonfibrillar collagen that enriches the pericellular matrix (PCM), and biglycan is a small, leucine-rich proteoglycan that regulates fibrillogenesis[1,2]. Deficiency in either collagen VI or biglycan is known to impact tendon mechanics[3,4]. While collagen VI and biglycan are known to interact, their interactions in native tendon, and the impact on tendon mechanics, remain unknown[5]. Therefore, the objective of this study was to determine how the roles of collagen VI, biglycan, or interactions involving both molecules affect FDL tendon mechanics. We hypothesized that knockout of collagen VI would reduce FDL tendon mechanical properties more than knockout of biglycan, while blocking interactions by knocking out both molecules would lead to a larger reduction in these properties than the reduction seen in either knockout alone.

Methods

Animals and Dissection

2 month old male wild-type (WT) (n = 16), *Col6a2*$^{-/-}$ (n = 11), *Bgn*$^{-/0}$ (n = 12), and *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ (n = 13) mice were used in this study (IACUC approved). FDL tendons were dissected from the left hind limb. The tendon sheath was fine dissected off the tendon. Tendon cross- sectional area (CSA) was measured with a custom laser device, and stain lines were applied for optical tracking[6].

Mechanical Testing

The FDL tendon was gripped with sandpaper, leaving a 5mm gauge length. The testing protocol consisted of 10 cycles of preconditioning between 0.01-0.02N at 1Hz, a 5 minute hold, a 5% stress relaxation for 10 minutes, a 1 minute hold, and a ramp to failure at 0.5% strain/s. Stress relaxation, stiffness, max load, modulus, and max stress were computed. Dynamic collagen fiber realignment was measured throughout the ramp-to-failure test using a crossed polarizer setup[7].

Statistics

For mechanical properties, a one-way ANOVA with Bonferroni post-hoc tests was used to compare across genotypes. For fiber alignment data, a two-way ANOVA with Tukey correction for multiple comparisons was used to compare across genotype and strain. Significance was set at $p < 0.05$, and trends were set at $p < 0.10$

Results

WT tendons had larger CSA than tendons from all knockout genotypes (Figure 1A). *Bgn*$^{-/0}$ tendons had larger CSA than *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ tendons. WT tendons were stiffer and had higher max loads than tendons from all knockout genotypes (Figure 1B,C). *Bgn*$^{-/0}$ tendons were stiffer than *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ tendons. *Bgn*$^{-/0}$ and *Col6a2*$^{-/-}$ tendons had higher max loads than *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ tendons. WT and *Bgn*$^{-/0}$ tendons exhibited a larger percent relaxation than *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ tendons (Figure 2A). No differences in moduli were observed between groups (Figure 2B). *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$/*Bgn*$^{-/0}$ tendons had higher max stresses than WT and *Bgn*$^{-/0}$ tendons (Figure 2C). During the

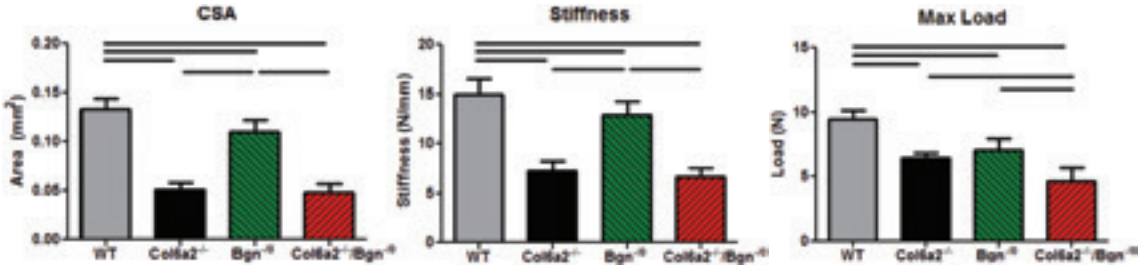


Figure 1. Cross-sectional area and structural-mechanical properties. (A) WT tendons had a larger CSA than all knockout genotypes. **(B)** WT tendons were stiffer than all knockout genotypes. **(C)** WT tendons had a higher max load than all knockout genotypes. Bars indicate $p < 0.05$.

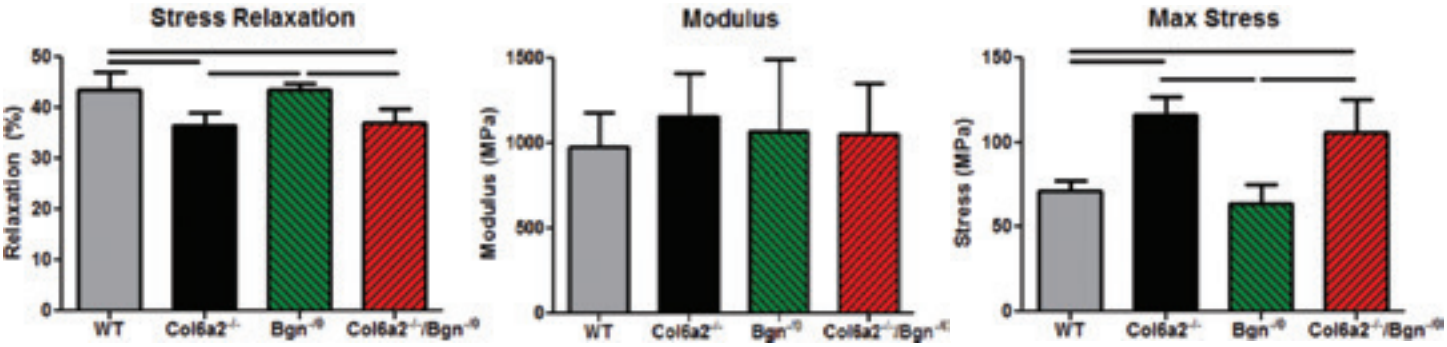


Figure 2. Viscoelastic and material properties. (A) WT and *Bgn*$^{-/0}$ tendons exhibited more stress relaxation than either collagen VI knockout models. **(B)** No differences in moduli were observed between genotypes. **(C)** Both collagen VI knockout tendons had higher max stresses than WT and *Bgn*$^{-/0}$ tendons. Bars indicate $p < 0.05$.

ramp to failure, WT tendons realigned between 3% and 5% strain (Figure 3). Bgn$^{-/0}$ tendons realigned between 5% and 7% strain. *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$*/Bgn*$^{-/0}$ tendons realigned between 1% and 3% strain. At 3% and 5% strain, *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$*/Bgn*$^{-/0}$ tendons were more aligned, and WT tendons trended towards more alignment, compared to *Bgn*$^{-/0}$ tendons.

Discussion

While biglycan deficiency led to some decreases in FDL structural-mechanical properties (stiffness, max load), collagen VI deficiency led to larger reductions in structural-mechanical and viscoelastic properties. Knockout of biglycan or collagen VI led to smaller, less stiff, and weaker tendons than WT, but *Bgn*$^{-/0}$ tendons were larger and stiffer than *Col6a2*$^{-/-}$ tendons.

Biglycan deficiency led to delayed fiber realignment compared to WT tendons, while collagen VI deficiency led to earlier realignment. *Col6a2*$^{-/-}$ tendons were less viscoelastic than *Bgn*$^{-/0}$ and WT tendons. These results agree with our hypothesis that collagen VI deficiency would reduce tendon mechanical properties more than biglycan deficiency. These mechanical and viscoelastic changes did not correspond to similar differences in material properties (modulus, max stress). There were no differences in moduli between WT, *Bgn*$^{-/0}$, and *Col6a2*$^{-/-}$ tendons, and *Col6a2*$^{-/-}$ tendons had higher max stresses than WT and *Bgn*$^{-/0}$ tendons. Our hypothesis that either knockout would reduce material properties was rejected. The different responses between the structural-mechanical and material properties could be due to smaller CSA in knockout tendons. Contrary to our hypothesis, knocking out both molecules did not amplify the differences seen in the *Col6a2*$^{-/-}$ mice. *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$*/Bgn*$^{-/0}$ tendons had similar CSA, stiffness, moduli, max stress, stress relaxation, and fiber realignment. Due to its proximity to tendon cells within the tendon PCM, collagen VI is likely an important regulator of tendon cell behavior. The results of this study suggest that collagen VI regulation is so robust that it dominates any biglycan regulatory effects. This study is limited in that the knockouts are global. Changes in neighboring tissues, such as muscle and bone, may confound the effects of these knockout models on tendon properties specifically. Future studies will aim to elucidate the mechanisms by which collagen VI and biglycan regulate tendon properties.

Another surprising finding in this study is that the biglycan knockout results differ from those of a previous study, which may be due to differences in CSA measurement[4]. The laser device used in the present study is more precise than the previous approach[6]. Overall, this study demonstrates that collagen VI and biglycan play distinct roles in regulating tendon mechanics and that collagen VI has a larger impact on mechanical properties.

This study reveals unique roles of collagen VI and biglycan in tendon mechanics and demonstrates that collagen VI has a larger impact on mechanical properties. These results provide further understanding of the role of lower abundance matrix proteins in tendon function.

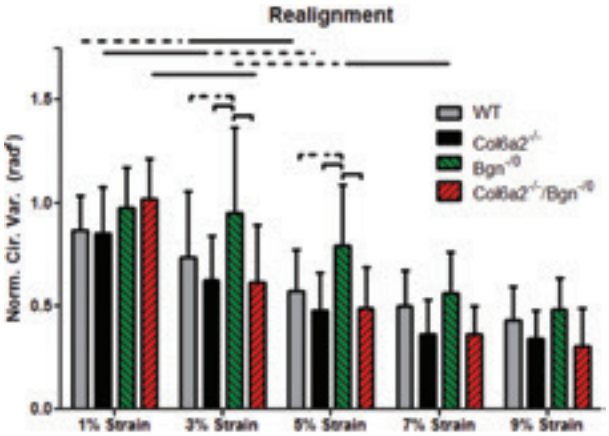


Figure 3. Fiber realignment during ramp to failure. Compared to WT tendons, *Bgn*$^{-/0}$ tendons realigned later. *Col6a2*$^{-/-}$ and *Col6a2*$^{-/-}$*/ Bgn*$^{-/0}$ tendons realigned earlier. A lower circular variance value indicates more alignment. Smooth bars compare adjacent strain values. Notched bars compare between genotypes. Solid bars indicate $p < 0.05$, and dashed bars indicate $p < 0.10$.

References

1. Ritty TM *et al.* *Structure.* 2003.
2. Ameye L *et al.* *FASEB J.* 2002.
3. Izu Y *et al.* *Matrix Biol.* 2011.
4. Robinson PS *et al.* *J Biomech Eng.* 2005
5. Wiberg C *et al.* *J Biol Chem.* 2002.
6. Favata, M. *University of Pennsylvania.* 2006.
7. Lake SP *et al.* *J Orthop Res.* 2009.

Differential Roles for Decorin and Biglycan in Tendon Aging

Beach ZM[1]
Dekhne M[1]
Rodriguez AR[1]
Weiss SN[1]
Shetye SS[1]
Adams TH[2]
Adams SM[2]
Sun M[2]
Birk DE[2]
Soslowsky LJ[1]

1 McKay Orthopaedic Laboratory
University of Pennsylvania

2 Department of Molecular Pharmacology and Physiology
University of South Florida

Introduction

Tendon injuries occur more commonly with increasing age[1], yet the mechanisms underlying the process of tendon aging are unclear. Decorin (Dcn) and biglycan (Bgn) are two small leucine-rich proteoglycans (SLRPs) that are regulators of collagen fibrillogenesis and are highly expressed during tendon development[2]. The absence of Dcn has been shown to prevent the normal decline in mechanics with decreasing age[3], while the inducible deletion of Bgn[4] and compound Dcn/Bgn[5] resulted in reduced mechanical and structural properties in mature tendon. However, the roles of Dcn and Bgn on tendon aging, independent of their influence on development, are unknown. Therefore, the objective of this study was to determine the differential roles of Dcn and Bgn during tendon aging. Due to the detrimental effects of Dcn on tendon aging, we hypothesized that the Dcn- and Dcn/Bgn-null mice will show a reduced impact of aging on mechanical and structural properties compared to WT and Bgn-null mice.

Methods

Female $Dcn^{+/+}/Bgn^{+/+}$ control (WT, n = 32), $Dcn^{flox/flox}$ (I-$Dcn^{-/-}$, n = 32), $Bgn^{flox/flox}$ (I-$Bgn^{-/-}$, n=32), and compound $Dcn^{flow/flox}/Bgn^{flox/flox}$ (I-$Dcn^{-/-}/Bgn^{-/-}$, n = 32), mice with a tamoxifen (TM) inducible Cre, (B6.129-Gt(ROSA)26Sortm1(cre/ERT2)Tyj/J, Jackson Labs) were utilized[5] (IACUC approved). Cre excision of the conditional alleles was induced in mature (120 day)[5] mice via three consecutive daily IP injections of tamoxifen (4.5mg/40g body weight). WT mice received TM injections to control for potential side effects. Mice were euthanized at 300 and 570 days of age (n = 16/group/age). The patellar tendon-bone complex from one limb of each animal was dissected and prepared for mechanical testing[6]. Tendons (n = 16) were subjected to a viscoelastic testing protocol of three stress relaxations, each followed by frequency sweeps, with the test culminating in a ramp-to-failure. Percent relaxation was quantified for each stress-relaxation. Samples for transmission electron microscopy (TEM) analysis of fibril structure (n = 4) were fixed *in situ*[5]. Cross sections through the midsubstance of the patellar tendon were examined at 80 kV. Fibril diameter was measured using images from the center of the tendon.

Histological sections of the patellar tendon-bone complex (n = 4) were prepared using standard techniques. Cell shape and cellularity were calculated using commercial software (Bioquant). A two-way ANOVA was performed followed by Bonferroni post-hoc analysis to evaluate the effect of genotype and age on tendon mechanics. Kolmogorov-Smirnov tests were used for the analysis of TEM and histology data. Significance was set at $p < 0.05$.

Results

Genotype significantly affected midsubstance modulus, while age and the interaction between age and genotype did not. Induced deletion of *Dcn* resulted in increased midsubstance elastic modulus at 300d (Figure 1A) versus WT and I-$Dcn^{-/-}/Bgn^{-/-}$. These differences were not present at 570d or in the insertion region (Figure 1B). Stress relaxation at 3% strain (Figure 2A) revealed genotype, age, and the interaction between genotype and age as significant. I-$Dcn^{-/-}/Bgn^{-/-}$ showed increased percent relaxation versus WT, while I-$Dcn^{-/-}$ exhibited decreased percent relaxation. Genotype and age significantly affected stress relaxation at 4% strain (Figure 2B), while the interaction did not. I-$Dcn^{-/-}/Bgn^{-/-}$ displayed increased relaxation versus I-$Dcn^{-/-}$ at 300d, and increased relaxation versus WT and I-$Dcn^{-/-}$ at 570d. Stress relaxation at 5% strain (Figure 2C) showed no significant differences between groups. Dynamic modulus (E*) and phase angle delta (δ) revealed no changes between genotypes, but age and the interaction was significant for I-$Dcn^{-/-}$ for E* and tan(δ) and for I-$Dcn^{-/-}/Bgn^{-/-}$ tan(δ) (Figure 3). I-$Dcn^{-/-}$ E* was decreased at 570d vs 300d, while tan(δ) was increased (Figure 3A-B). I-$Dcn^{-/-}/Bgn^{-/-}$ showed increased tan(δ) at 3% strain for 0.1-5 Hz, and 4% strain at 5 Hz (Figure 3C).

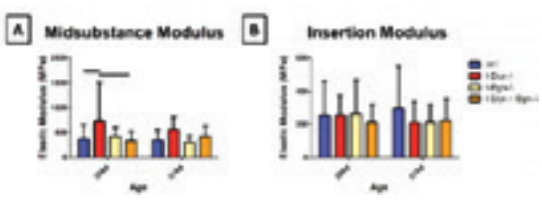


Figure 1. Quasi-static mechanical properties. Deletion of decorin resulted in increased midsubstance elastic modulus at 300d compared to WT and I-$Dcn^{-/-}/Bgn^{-/-}$ **(A)**. No differences were found at 570d or in the insertion **(B)**.

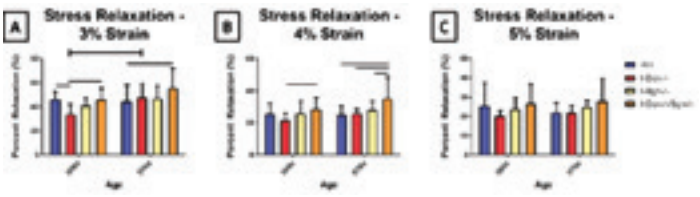


Figure 2. Stress Relaxation. I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ showe d increased stress relaxation at 3% and 4% strain at 300d & 570d **(A, B)**. At 3% strain, 570d I-*Dcn*$^{-/-}$ stress relaxation was increased vs 300dI-*Dcn*$^{-/-}$ **(A)**. No changes were seen at 5% strain **(C)**.

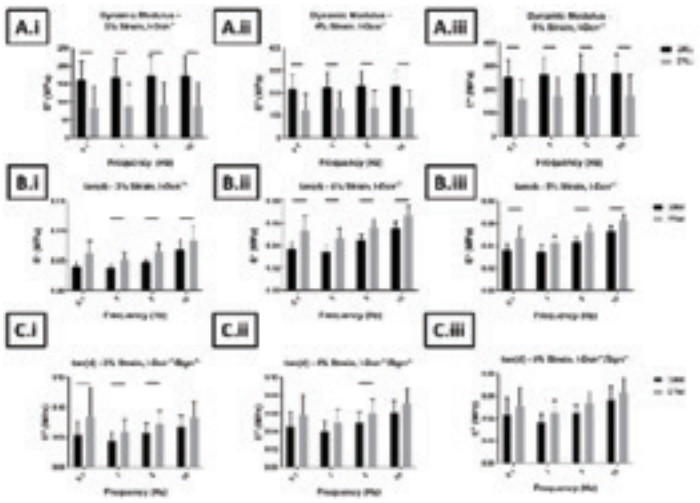


Figure 3. Age-related changes in viscoelast c mechanics. 570d I-*Dcn*$^{-/-}$ resulted in increased dynamic modulus and increased tan(δ) vs 300d I-*Dcn*$^{-/-}$ **(A, B)**. 570d I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ resulted in increased tan(δ) at 3%strain and lower frequencies vs 300d **(C.i)**. These differences were remained present at 4% strain and 5 Hz **(C.ii)**. No changes were seen between 300d and 570d I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ in dynamic modulus at any strain or frequency, or tan(δ) at 5% strain.

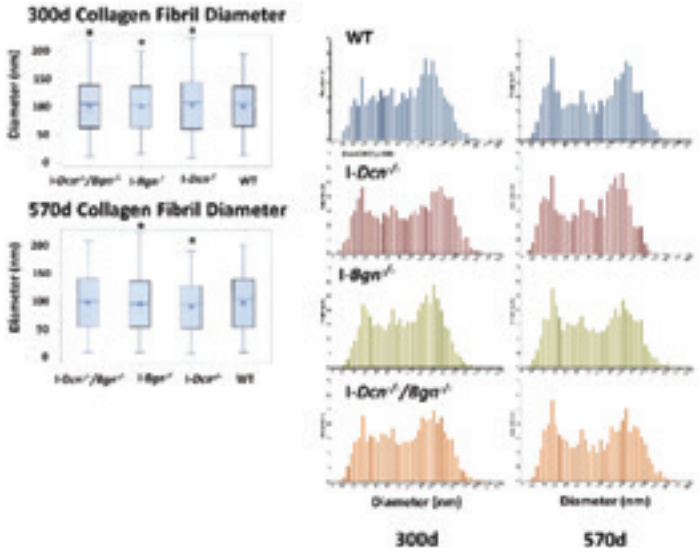


Figure 4. TEM analysis of patellar tendon collagen fibril diameter. I-*Dcn*$^{-/-}$ and I-*Bgn*$^{-/-}$ showed altered collagen fibril diameter at 300d & 570d versus WT. I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ resulted in an altered fibril diameter at 300d, but not 570d. * denotes significance vs WT

TEM analysis revealed that I-*Dcn*$^{-/-}$ and I-*Bgn*$^{-/-}$ had altered fibril diameters vs WT at 300d and 570d (Figure 4). I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ showed altered fibril diameter versus WT at 300d, but not 570d. Notably, I-*Dcn*$^{-/-}$ revealed increased fibril diameter heterogeneity, an increased maximum fibril diameter, and decreased minimum fibril diameter at 300d. At 570d, I-*Dcn*$^{-/-}$ fibril diameter was reduced versus WT in quartiles 2-4. Histology revealed no significant differences for cell shape or cellularity between any genotypes at 300d or 570d.

Discussion

Supporting our hypothesis, the absence of Dcn resulted in a reduced impact from aging on tendon mechanics, including an increased midsubstance elastic modulus and decreased stress relaxation at 300 day vs WT. Additionally, at 300d, I-*Dcn*$^{-/-}$ had an improved dynamic modulus and phase angle vs I-*Dcn*$^{-/-}$ at 570d, indicating limitations to the extent that the absence of Dcn can improve tendon mechanics during aging. I-*Dcn*$^{-/-}$ also resulted in significant alterations in collagen fibril diameter compared to WT at both 300 and 570 day. At 300 day, the fibril diameter heterogeneity was increased, while at 570 day, there was a reduction in fibril diameter in the upper 75% of the distribution. Contrary to our hypothesis, the absence of both Dcn and Bgn did not result in an improved aging phenotype, with no changes in midsubstance or insertion modulus, and increased stress relaxation versus WT and I-*Dcn*$^{-/}$. The absence of Bgn resulted in an altered fibril diameter distribution with no changes in mechanics. A role for both Dcn and Bgn was revealed in the maintenance of tendon structure at 300 and 570 days. These results support previous work examining the effects of Dcn during tendon aging, which showed no changes in mechanics between mature and aged Dcn knockout mice, while WT and Bgn knockout mice showed declining mechanics with age[3]. Further, reduced viscoelastic and elastic mechanics in I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ versus WT at 150 day[5], provides evidence that I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ has a distinct phenotype from both I-*Dcn*$^{-/-}$ and I-*Bgn*$^{-/-}$, when it was previously hypothesized that I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ would result in a true Dcn knockout phenotype, without compensatory effects of Bgn. Overall, this study provides evidence for the detrimental effects of Dcn on tendon aging and the vital role of both Dcn and Bgn in regulating tendon structure.

This study demonstrates that Dcn and Bgn play important differential roles in regulation of tendon structure during aging, with the absence of Dcn resulting in an improved tendon aging phenotype.

References

1. Buckwalter JA *et al.*, 2003. *JBJS*, 85:748-758.
2. Schonherr E *et al.*, 1995. *JBC*, 270:8877-83.
3. Dunkman AA *et al.*, 2013. *Matrix Biol.*, 32:3-13.
4. Beach ZM *et al.*, 2018. ORS Paper No. 0237.
5. Robinson KA *et al.*, 2017. *Matrix Biol*, 64:81-93.
6. Brodt MD *et al.*, 1999. *JBMR*.

Effects of Aging on the Molecular Profile of Cultured Tendon Cells

Carrie E. Barnum
Julianne Huegel
Louis J. Soslowsky
Andrew F. Kuntz

McKay Orthopaedic Research Laboratory
University of Pennsylvania

Introduction

Rotator cuff tears affect millions of individuals each year, with a higher incidence in the elderly. Although surgical repair can improve function and reduce pain, rotator cuff repair failure is common[1]. To improve surgical outcomes, biologic augmentation via delivery of cells or growth factors has been investigated[2-4]. Recently, autologous biceps cells delivered via nanofibrous scaffold to the repair site during supraspinatus repair were shown to improve healing in juvenile and aged rats, but did not affect healing in adult rats[5]. However, the molecular mechanisms behind these differential effects are not well understood. Therefore, the objective of this study was to determine the differences in the RNA signature of primary tendon-derived cells cultured from the long head of the biceps of juvenile, adult, and aged animals. Our hypotheses were: 1) tendon-derived cells from juvenile animals would exhibit a molecular profile more characteristic of stem cells than tendon-derived cells from adult or aged animals, and 2) tendon-derived cells from aged rats would have increased expression of genes associated with tendon homeostasis and differentiation compared to cells derived from juvenile or adult rats.

Methods

27 Fisher (F344) rats were used (IACUC approved) across three age groups: juvenile (4 weeks), adult (8 months), and aged (16 months) (n = 9/age group). Animals were sacrificed and the intra-articular biceps tendons were collected.

Cell Culture

Biceps tendon cells were harvested from the tissue via morselization and cell migration. Cells were expanded in culture using basal media and split at confluence. Subcultured (P1) cells were allowed to reach 75-85% confluence (average 12 days in culture) at which time they were lysed and homogenized in TRIzol.

RNA Isolation

RNA was isolated using the TRIspin method and processed via RNA Clean & Concentrator 5 columns (Zymo Research).

Rat Transcriptome Array and Bioinformatics Analysis

cDNA made with 250ng of RNA using the Affymetrix WT PLUS Kit and was run on a Clariom™ D Rat Transcriptome Array 1.0 (Applied Biosystems, n = 5/age group). Bioinformatics processing was performed using Transcriptome Analysis Console Software and DAVID analysis (cut-offs set at $|FC| > 2$ and $p < 0.05$ for all pair-wise age comparisons). *qRT-PCR*: Reverse transcription was performed using a High Capacity cDNA Reverse Transcription Kit (Applied Biosystems). To validate microarray results, qPCR was run in quadruplicate using TaqMan Assays on a QuantStudio 12K Flex Real-Time PCR system (ThermoFisher, n = 8/age group). Data was analyzed using the $\Delta\Delta Ct$ method, and expression levels were compared between age groups with one-way ANOVAs and post-hoc Tukey tests. *Cell Staining*: At 50% confluence, P1 cells were fixed, permeabilized, and stained with Alexa Fluor 488 Phalloidin and DAPI. Slides were imaged with a Leica TCS SP8 Multiphoton Confocal.

Results

Principle component analysis demonstrated that cell expression profiles grouped into distinct regions by age (Figure 1). The majority of gene expression clustered into six distinct patterns when comparing between ages (data not shown). The majority of differential gene expression exists between juvenile and aged cells (640 genes significantly decreased, 531 increased), while the

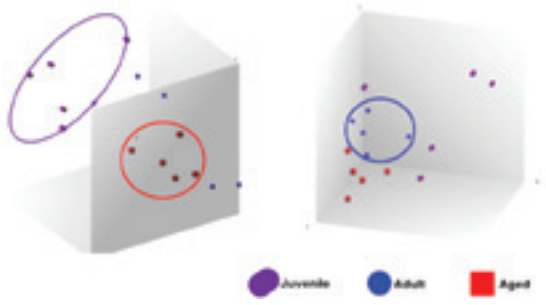


Figure 1. Two Principle Component Analysis plots from Rat Transcriptome Analysis. Juvenile cells shown as purple cylinders, adult cells are shown as blue spheres, and aged cells are represented as red cubes. Age groups are circled to demonstrate distinct clusters.

fewest differences exist between adult and aged cells (54 genes significantly decreased, 101 genes increased). Comparison of juvenile cells to adult cells identified 216 significantly increased genes and 203 significantly decreased genes. No qualitative differences were observed in cell morphology between age groups (data not shown). Gene ontology identified differences in genes related to: 1) cell adhesion, wound healing, and chondrocyte differentiation between juvenile and adult cells, 2) cell division and cell adhesion between juvenile and aged cells, and 3) wound healing and vasculogenesis between adult and aged cells. qPCR confirmed that genes associated with stemness are downregulated with age, including *Postn*, *Fgf10*, *Osr1*, and *Gpmnb* (Figure 2). Additionally, genes related to inflammation are differentially expressed with age, including increased *Cd28* and *Cd200* expression and decreased *Il6* and *Il6st* expression (Figure 3).

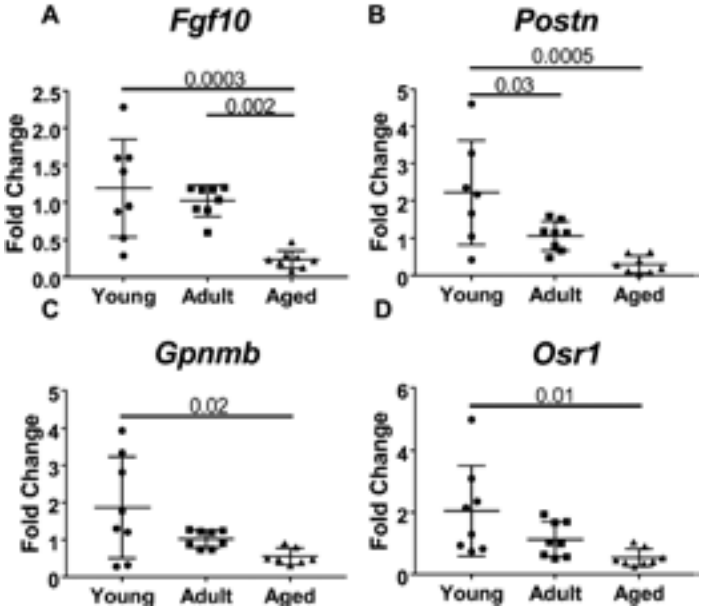


Figure 2. Decreased expression of stem related mRNAs measured via qPCR. **(A)** *Fgf10* **(B)** *Postn* **(C)** *Gpnmb* and **(D)** *Osr1* expression decreased with aging. Significance is denoted with solid lines (n = 8/group).

Discussion

Results demonstrate distinct molecular profiles for juvenile, adult, and aged biceps tendon-derived cells. Juvenile cells showed increased expression of genes associated with mesenchymal stem cells, such as *Postn and Fgf10*, supporting our first hypothesis. Furthermore, although stem cell associated markers are present in both juvenile and adult cells, they are significantly decreased in aged cells, suggesting that a greater population of aged tendon cells may have terminally differentiated. However, contrary to our second hypothesis, there were no consistent increases in the expression of tendon markers in aged cells, suggesting that there may be significant population heterogeneity. Interestingly, aged cells demonstrate a decreased pro-inflammatory signature, including decreased expression of pro-inflammatory cytokine *Il6* and its signaling receptor *Il6st,* as well as an increased anti-inflammatory milieu, including increases in both *Cd28* and *Cd200* expression

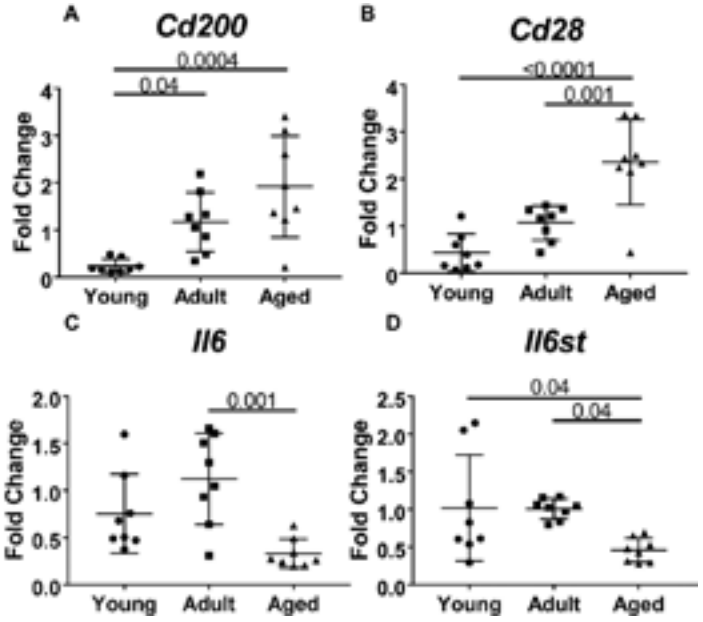


Figure 3. qPCR confirms changes in inflammatory response with age. **(A)** *Cd200* and **(B)** *Cd28* increased with age, while **(C)** *Il6* decreased in aged cells only and **(D)** *Il6st* decreased with aging. Significance is denoted with solid lines (n = 8/group).

compared to juvenile cells. Previous work demonstrated that Il6-null mice (simulating an aged phenotype) have increased native tendon mechanical properties[6], but show a similar healing response as WT mice[7], suggesting a role for this cytokine in how delivered cells integrate into and contribute to new tendon formation. This study specifically explored RNA level changes in biceps tendons in culture, and we have not yet shown that these findings relate to changes at the protein level. However, these age-specific expression signatures can begin to uncover the mechanisms behind functional differences previously shown between age groups after cell delivery[5]. Future research will investigate protein level changes as well as how these changes relate to functional differences in tendon healing with age. It will be important to discern how both population heterogeneity and inflammation affect the contribution of scaffold-delivered biceps cells for rotator cuff repair.

We previously demonstrated age-specific differences in supraspinatus healing after autologous biceps cell delivery[5]; the current study demonstrates that these cell populations display distinct molecular differences.These differences should be considered when addressing musculoskeletal regenerative medicine, particularly in the context of augmented tendon repair. Furthermore, modulating the molecular profile of adult or aged cells may further improve tendon repair.

References

1. Galatz LM *et al.* *J Bone Joint Surg Am*, 2004.
2. Hernigou P *et al.* *Int Orthop*, 2014.
3. Chen JM *et al.* *Tissue Eng*, 2007.
4. Longo UG *et al.* *Br Med Bull*, 2010.
5. Huegel J *et al.* *J Orthop Res.* 2017.
6. Lin TW *et al.* *J Biomech.* 2005.
7. Lin TW *et al.* *J Biomech.* 2006.

Effects of Pulsed Electromagnetic Field Therapy on Healing in a Rat Achilles Tendon Partial Width Injury Model Without Immobilization

Boorman-Padgett JF[1]
Huegel J[1]
Nuss CA[1]
Minnig MCC[1]
Raja HA[1]
Kuntz AF[1]
Waldorff EI[2]
Zhang N[2]
Ryaby JT[2]
Soslowsky LJ[1]

1 McKay Orthopaedic Research Laboratory, University of Pennsylvania, Philadelphia, PA, USA

2 Orthofix Inc., Lewisville, TX, USA

Introduction

Partial tears of the Achilles tendon are typically treated conservatively[1], often with various noninvasive therapies such as ultrasound. An FDA-approved Pulsed Electromagnetic Field (PEMF) therapy (Physio-Stim®, Orthofix Inc., Lewisville,TX, USA) has been shown to improve outcomes in tendon-to-bone rotator cuff healing in a rat model[2,3]. However, for partial Achilles tendon tears, the effects of PEMF therapy on in vivo joint function and ex vivo tendon fatigue properties remain inconclusive[4], as the use of postoperative plantarflexion immobilization confounded results in an earlier study.Therefore, the objective of this study was to quantify the effects of this FDA-approved PEMF therapy on joint and tendon level properties after a partial width, full thickness injury (partial tear) in the absence of limb immobilization.We hypothesized that PEMF treatment would improve Achilles tendon healing compared to a non-PEMF group.

Methods

144 adult male Sprague-Dawley rats (400-450g) were anesthetized with isoflurane, and underwent a unilateral, full thickness, partial width (1.5mm biopsy punch) Achilles tendon injury through the center of the tendon (IACUC approved). All animals were allowed cage activity throughout the study. Animals were placed into 3 groups (n = 48/group): a control group receiving no PEMF treatment (non-PEMF), or a treatment group receiving either 1 or 3 hours of daily systemic PEMF (Physio-Stim®, 1HP and 3HP, respectively) therapy.Animals were sacrificed at 1, 3, or 6 weeks (n = 16 per group per time point). All animals in the 6 week groups underwent longitudinal in vivo ambulatory assessment and passive ankle joint mechanics testing at 2, 4, and 6 weeks post-injury[5,6]. At sacrifice, the Achilles-calcaneus complex was dissected out (n = 6 per group per time point) and processed for μCT scanning (21μm resolution) followed by decalcification and histological analysis. All other animals (n = 10 per group per time point) were frozen at -20°C and thawed for dissection prior to tendon cross-sectional area measurement using a custom laser device and mechanical testing using a load controlled fatigue testing protocol[7]. For all measures, the two treatment groups (1HP and 3HP) were compared to the control (non-PEMF) group at each time point using two-tailed, t-tests after checking for normality. Bonferroni post-hoc corrections were applied for multiple comparisons and significance was set at $p < 0.025$.

Results

Joint Range of Motion

No differences were observed between the PEMF treatment groups and the non-PEMF group at any time point (data not shown).

Ambulatory Assessment

Rats receiving 3 hours of PEMF treatment walked faster than non-PEMF animals 2 and 4 weeks post-injury. Rats receiving either 1 or 3 hours of PEMF treatment loaded their injured limbs faster than non-PEMF rats 2 weeks post-injury (Figure 1).

Histology

Tendons receiving 3 hours of PEMF were less cellular than control non-PEMF tendons at

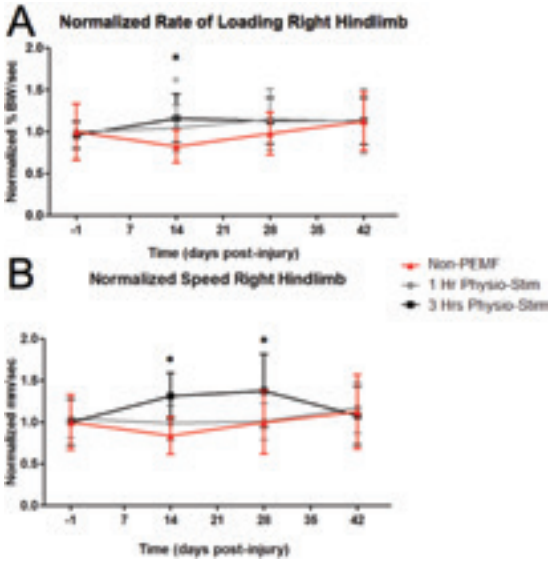


FIGURE 1. (A) Normalized rate of loading was increased in both PEMF treatment groups compared to non-PEMF animals 2 weeks after injury. **(B)** Normalized speed of the injured limb was increased in 3HP animals at 2 and 4 weeks after injury. Data are mean ± SD. Black asterisks indicate $p = 0.025$ comparing 3HP to NP. Gray asterisks indicate $p < 0.025$ comparing 1HP to NP.

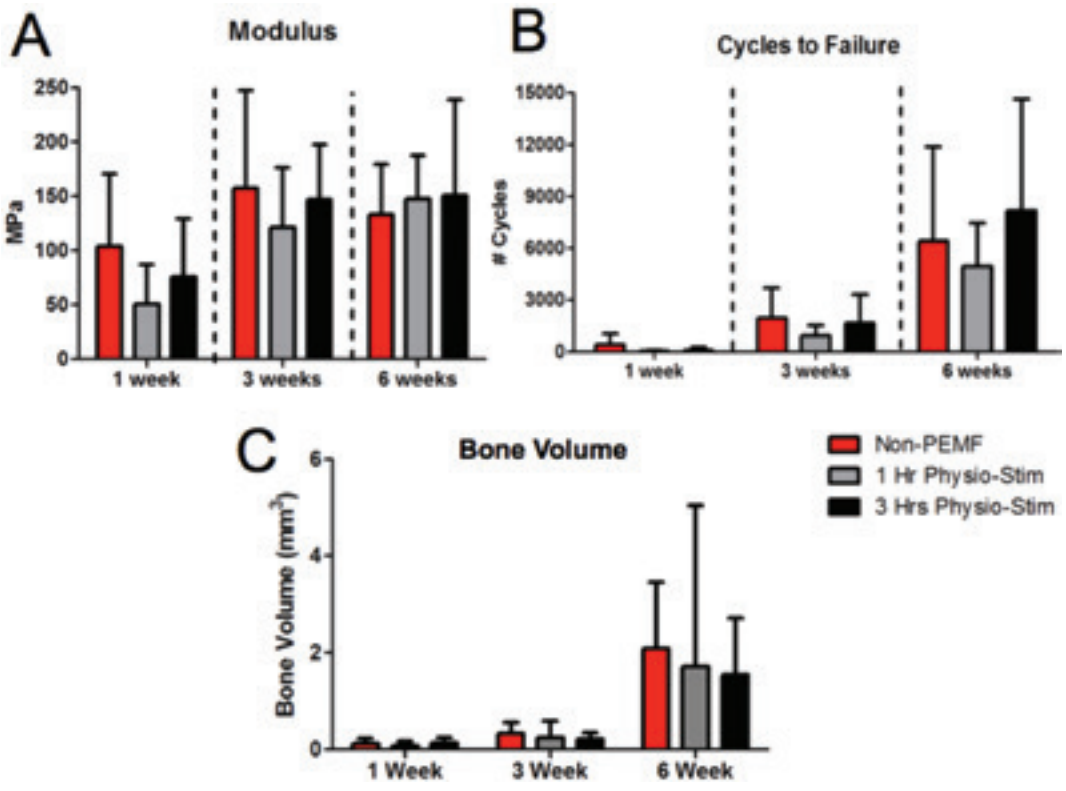


FIGURE 2. (A) Modulus values during mechanical testing were no different between PEMF treatment groups and control tendons. **(B)** Cycles to failure were no different between PEMF treatment groups and control tendons. **(C)** Bone volume was no different between treatment groups and NP control tendons but did appear to increase over time. Data are mean ± SD.

3 weeks, and exhibited greater collagen organization than control non-PEMF tendons at 6 weeks (data not shown).

Mechanical Testing

No differences were observed between PEMF treated tendons and non-PEMF control tendons at any time point (Figures 2A & 2B).

µCT

Heterotopic bone formation in the injured Achilles tendons was observed in all groups including the non-PEMF control, and at 6 weeks post-injury all scanned tendons contained bone. No differences were observed in bone volume or bone mineral density between the PEMF treated tendons and the non-PEMF control tendons at any time point (Figure 2C).

Discussion

The aim of this study was to determine the effects of an FDA-approved, non-invasive PEMF treatment on rat Achilles tendons following injury without immobilization. We hypothesized that, in the absence of immobilization, PEMF treatment would result in improved healing compared to control tendons. However, no differences were observed in mechanical testing outcome measures generally associated with tendon function and healing. While some scattered differences were observed in ambulatory measures, the lack of corresponding changes in mechanical properties suggests that these are more likely the result of animal variations than they are the result of improved tendon function. While not different between treatment groups, the observed bone formation in this Achilles tendon injury model remains interesting and appeared to increase over time. It should be noted that heterotopic bone formation has been observed clinically as well. Ultimately, it appears that PEMF treatment does not improve tendon healing in this partial width, full thickness injury model without immobilization. Surprisingly, ambulatory and joint range of motion assessments detected very little loss of function following this injury model without immobilization. These results indicate that immobilization may be detrimental in this model. Additional comparisons are being performed to quantify this effect. Conversely, a previous study demonstrated that the same PEMF treatment had a positive effect on rat rotator cuff healing suggesting site-specific efficacy[3]. Overall, it is possible that this specific injury model is too conservative to measure potential therapeutic effects in the context of rapid baseline healing in these otherwise healthy Sprague-Dawley rats.

This study shows that healing of a rat partial Achilles tendon injury is not improved by the use of PEMF therapy. Our previous study led to inconclusive results when immobilization was applied after injury[4]. This study provides clarity in the context of the earlier study and provides novel insight into the severity and complexity of this particular injury model.

References

1. **Soroceanu A *et al.*** *J Bone Joint Surg Am.* 2012
2. **Tucker JJ *et al.*** *J Orthop Res.* 2016
3. **Huegel J *et al.*** *J Shoulder Elbow Surg.* 2018
4. **Boorman-Padgett J *et al.*** *Trans ORS*, 2018; 1454.
5. **Sarver JJ *et al.*** *J Shoulder Elbow Surg.* 2008
6. **Sarver JJ *et al.*** *J Biomech.* 2010
7. **Pardes AM *et al.*** *Ann Biomed Eng.* 2016.

Estrogen Deficiency and Intermittent Parathyroid Hormone Treatment Affect Regional Achilles Tendon Vessel Microarchitecture

Thomas P. Leahy[1]
Benjamin R. Freedman[1,2,3]
Wei-Ju Tseng[1]
Snehal S. Shetye[1]
X. Sherry Liu[1]
Louis J. Soslowsky[1]

1 McKay Orthopaedic Research Laboratory University of Pennsylvania

2 John A. Paulson School of Engineering and Applied Sciences Harvard University

3 Wyss Institute for Biologically Inspired Engineering

Introduction

The Achilles tendon is frequently injured and vascularity has been implicated as a predictor of Achilles tendon injury and healing potential[1]. Estrogen deficiency and intermittent parathyroid hormone (iPTH) treatment have been shown to differentially affect tendon healing response[2-7]. In rat models of tendon injury, estrogen-deficiency results in decreased Achilles tendon mechanical properties[3], while iPTH treatment increases fibrocartilage formation near the tendon insertion during the healing response[2,6]. Despite the significant effects that estrogen deficiency and iPTH treatment have shown on the tendon healing response in animal models, there has been little research investigating their effect on vascularity of the Achilles tendon. Therefore, the objective of this study was to evaluate how estrogen deficiency and iPTH treatment modulate vessel microarchitecture in a rat Achilles tendon. We hypothesized that estrogen deficiency, simulated by bilateral ovariectomy surgery (OVX), would cause a decrease in Achilles tendon vessel microarchitecture throughout the length of the tendon, while iPTH treatment would result in increased tendon vessel microarchitecture, particularly near the insertion.

Methods

Study Design

At 3 months of age, female Sprague-Dawley rats (n =14) were divided into three groups (IACUC approved): VEH (n = 4), iPTH (n = 3), and OVX (n = 7). The OVX rats received OVX surgeries at 3 months of age to simulate estrogen deficiency for 4 weeks. At 3.5 months of age, VEH and iPTH rats received subcutaneous injections of saline solution and iPTH (PTH 1-34, 60μg/kg/day, Bachem, Bubendorf, Switzerland), respectively for 5 days a week for 2 weeks.

Vascular casting

At 4 months of age, a vascular casting procedure was performed by infusion of Microfil mixture (MV122, Flow Tech Inc., Carver, MA) in the rat vascular network as described[8-10]. Briefly, 50 mL heparin sodium solution, followed by 100 mL 0.9% normal saline and 50 mL 4% PFA into the abdominal aorta at 4.4 mL/min via a perfusion pump (Bio-Rad, Hercules, CA) while the animals were under anesthesia. A syringe was used to inject 5 mL Microfil® mixture with 3% catalyst at 0.3 mL/min and the animals were stored at 4°C for 24 hours to allow complete polymerization. Afterwards, both the left and right Achilles tendons were harvested and μCT-scanned at 3.5μm voxel size (μCT 35, Scanco Medical AG, Brüttisellen, Switzerland) at a 1.6 mm region of the tendon insertion proximal to the calcaneus and another 1.6 mm long region near the midsubstance of the tendon, 3.6 mm proximal from the end of the insertion region (Figure 1). A custom MATLAB (Mathworks, Natick, MA) script was used to apply a local thresholding technique to segment casted blood vessels from surrounding soft tissue[11]. Finally, the vascular microarchitecture parameters vessel volume (VV), vessel number (Ves.N), vessel thickness (Ves.Th), vessel separation (Ves.Sp), and connectivity density (Conn.D) were evaluated.

Analysis

Separate two-way ANOVAs for tendon region and treatment were performed comparing VEH and iPTH, and VEH and OVX. If the ANOVAs determined a significant effect ($p < 0.05$),

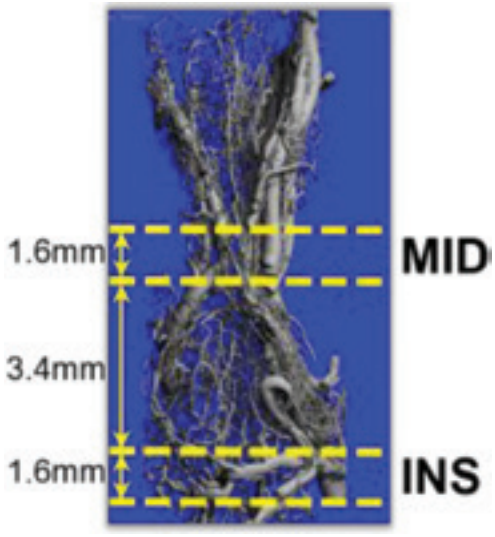


Figure 1: Achilles tendon vascularity, denoting insertion and midsubstance region.

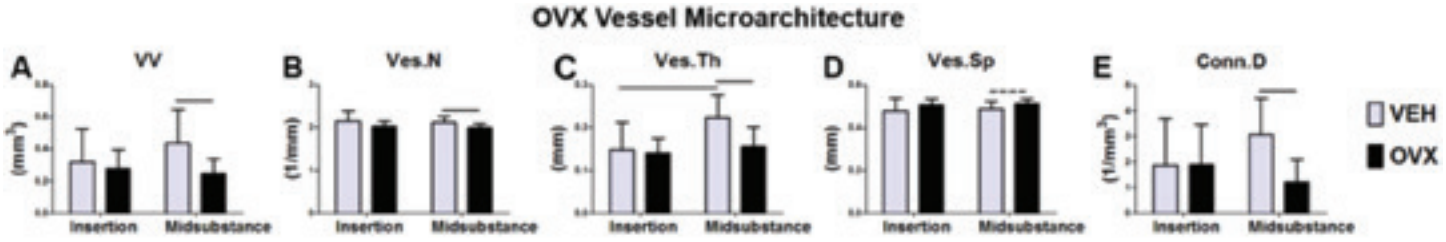


Figure 2. OVX vessel microarchitecture comparisons to the VEH group for VV **(A)**, Ves.N **(B)**, Ves.Th **(C)**, Ves.Sp **(D)**, and Conn.D **(E).** OVX shows detrimental effects on Achilles tendon vascular microarchitecture, particularly in the midsubstance region.

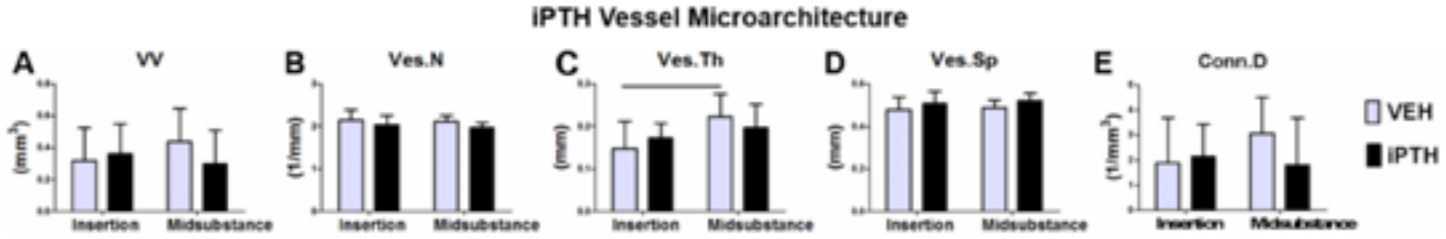


Figure 3. iPTH vessel microarchitecture comparisons to the VEH group for VV **(A)**, Ves.N **(B)**, Ves.Th **(C)**, Ves.Sp **(D)**, and Conn.D **(E)**. iPTH treatment shows no differences compared to the VEH group except for eliminating the difference in Ves.Th between the insertion and midsubstance.

Student's t-tests were performed to compare region and/or treatment between specific groups. Significant interaction terms were also evaluated.

Results

When comparing VEH-OVX, treatment was a significant factor in VV, Conn.D, Ves.N, and Ves.Th, while region was a significant factor in Ves.Th. There was a significant interaction term for Conn.D. Further, the midsubstance region of the OVX tendons had significantly lower VV, Ves.N, Ves.Th, and Conn.D, with a trend toward greater Ves.Sp relative to the VEH group (Figure 2). In addition, Ves.Th was significantly greater in the midsubstance relative to the insertion in the VEH tendons. When comparing parameters for VEH-iPTH, there were significant effects of region on Ves.Th. However, there were no significant differences between the VEH and iPTH groups (Figure 3).

Discussion

We investigated the effects of estrogen deficiency and iPTH treatment on vascular microarchitecture in the rat Achilles tendon. As hypothesized, OVX resulted in reduced vascular microarchitecture of the Achilles tendon, with the most profound effects in the tendon midsubstance. While OVX has limited effects on rat Achilles tendon homeostatic function[4], it has significant detrimental effects on Achilles tendon healing response, resulting in decreased mechanical properties, including reduced max stress and secant modulus during fatigue loading, as well as decreased joint range of motion, cell proliferation, and GAG content[3,5]. As vascularity has been implicated as a predictor of healing potential[1], the reduced Achilles tendon vessel microarchitecture observed in this study provides a potential explanation for the reduced healing potential seen in estrogen-deficient Achilles tendons. Contrary to our hypothesis, iPTH treatment did not have a drastic effect on vessel microarchitecture. In previous studies in bone, iPTH treatment did not result in osteoangiogenesis but rather relocated the vascular structure closer to the sites of new bone formation, thereby providing a favorable microenvironment for growth[12]. It may be possible that a similar effect happens in tendon, though it is also possible that the increased fibrocartilage formation in the tendon insertion observed previously is specific to the healing response[2,6]. Further studies should evaluate the effects of estrogen deficiency and iPTH treatment on vascular microarchitecture in an Achilles rupture model.

This study highlights estrogen deficiency and iPTH treatment effects on vascular microarchitecture in the rat Achilles tendon. The decrease in tendon vascular microarchitecture in the estrogen-deficient rats could be a possible explanation for the reduced healing potential with estrogen deficiency.

References

1. Theobald P *et al.*, *Injury*, 2005.
2. Hettrich CM *et al.*, *J Orthop Res*, 2012.
3. Fryhofer GW *et al.*, *J Appl Phsiol*, 2016.
4. Pardes AM *et al.*, *Ann Biomed Eng*, 2016.
5. Circi E *et al.*, *Int Orthop*, 2009.
6. Duchman KR *et al.*, *J Shoulder Elbow Surg*, 2016.
7. Lee DJ *et al.*, *J Orthop Res*, 2015.
8. Wang Y *et al.*, *J Clin Invest*, 2007.
9. Razavi H *et al.*, *Microvasc Res*, 2012.
10. Duvall CL *et al.*, *Am J Physiol Heart Circ Physiol*, 2004.
11. Waarsing JH *et al.*, *J Bone Miner Res*, 2004.
12. Prisby R *et al.*, *J Bone Miner Res*, 2011.

Female Rat Supraspinatus Tendon Mechanical Properties Exhibit a Differential Response to Estrogen-Deficiency Depending on Reproductive History

Ashley K. Fung
Snehal S. Shetye
Chantal M. de Bakker
Yihan Li
X. Sherry Liu
Louis J. Soslowsky

McKay Orthopaedic Research Laboratory
University of Pennsylvania

Introduction

The prevalence of rotator cuff tears increases with age and postmenopausal women are at an even greater risk of developing full-thickness supraspinatus tendon tears[1]. Previous animal studies have supported these findings, demonstrating that an ovariectomy model of menopause led to reduced bone mineral density of the humeral head and decreased rotator cuff tendon strength[2,3]. Interestingly, recent preliminary data showed that prior to ovariectomy, reproductive female rats have inferior supraspinatus tendon and proximal humerus trabecular bone properties compared to virgin females; however, when subjected to ovariectomy, they experience a reduced rate of bone loss in the tibia compared to virgin females[4]. While these findings suggest a differential response in bone to estrogen-deficiency depending on reproductive history, how supraspinatus tendons are affected is unknown. Therefore, the objective of this study was to investigate the effect of reproductive history on female rat supraspinatus tendon mechanical properties following ovariectomy. We hypothesized that due to a dramatic decrease in estrogen levels and a high rate of early bone loss, ovariectomy will lead to a reduction in supraspinatus tendon mechanical properties.

Methods

58 female Sprague-Dawley rats (IACUC approved) were divided into virgin and reproductive groups. At age 4 months, reproductive rats underwent three cycles of reproduction, each consisting of a 3-week pregnancy, 3 weeks of lactation, and 3-6 weeks of post-weaning recovery. Virgin and reproductive rats underwent ovariectomy (OVX) surgery at 12 months of age and were sacrificed at 1 month (n = 8/group), 3 months (n = 8/group) or 6 months (n = 5-7/group) post-OVX. Non-OVX, intact 13.5-month old virgin and reproductive female rats (n = 7/group) were used as controls.

Mechanics

Supraspinatus tendons were fine dissected and marked with stain lines for optical strain tracking. Cross-sectional area was measured using a custom laser device and humeri were secured in polymethyl methacrylate. Right supraspinatus tendons underwent quasi-static tensile testing, consisting of pre-conditioning (10 cycles from 0.5-1% strain), stress relaxation at 5% strain for 600s, dynamic frequency sweep at 5% strain (0.1-10Hz), and ramp to failure at rate of 0.3%/s.

Statistics

Two-way ANOVAs were used to compare the effects of reproductive history and time after OVX with post-hoc Bonferroni corrections. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

Cross-sectional area increased significantly in the reproductive group and trended towards increasing in the virgin group 1 month post-OVX (Figure 1A). By 6 months post-OVX, however, cross-sectional area was not different from control in either group. While stiffness trended towards increasing in the 3 month OVX reproductive group (Figure 1B), there were no changes in modulus in the reproductive groups. In contrast, modulus was significantly higher in the virgin non-OVX, control group compared to reproductive and significantly decreased in the virgin group at 1 and 3 months post-OVX (Figure 3C). At 6 months post-OVX, modulus in the virgin group increased compared to 1 month post-OVX and was significantly higher than the reproductive group. A similar trend was observed in the virgin group for dynamic modulus across all frequencies, where dynamic modulus was significantly lower at 1 month post-OVX and trended towards decreasing in the 3 month and 6 month groups, compared to control (Figure 1E). In the reproductive group, however, significant viscoelastic differences were observed at 1 month post-OVX. There was a significant increase in percent relaxation at 1 month post-OVX compared to control (Figure 1D), while dynamic modulus across all frequencies was decreased at 1 month compared to control, 3 month, and 6 month post-OVX groups (Figure 1E). Tan(δ)

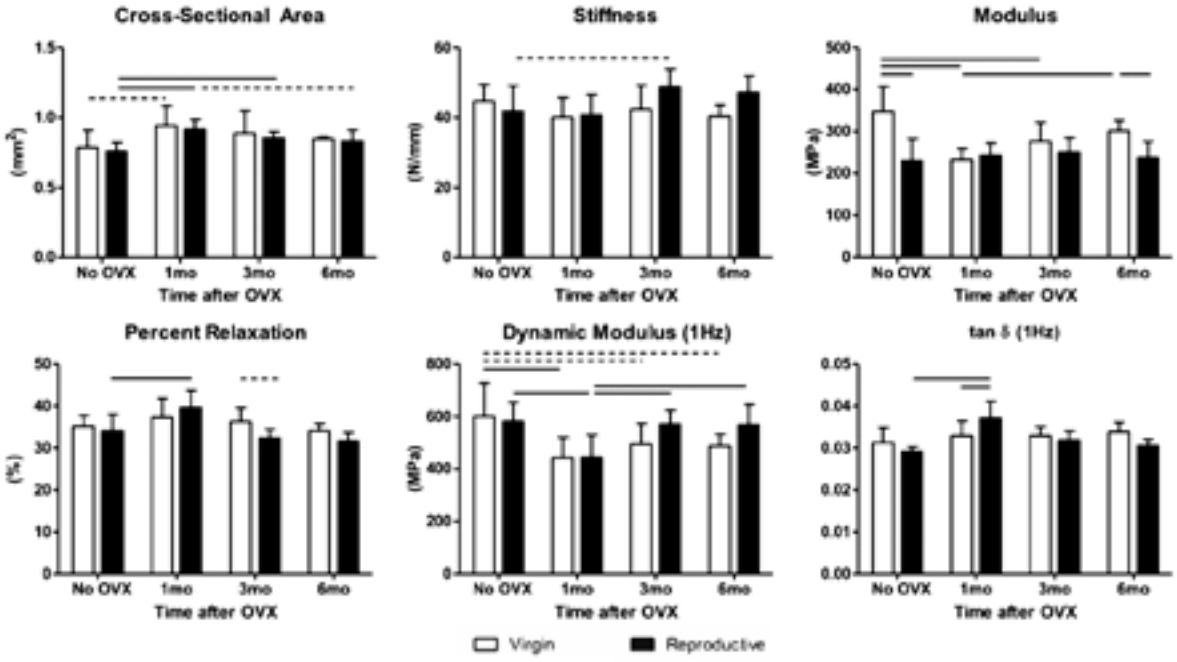


Figure 1: (A) Cross sectional area increased in the reproductive group at 1 month post-OVX but was not different from control by 6 months post-OVX. **(B)** Stiffness in the reproductive group trended towards increasing 3 months post-OVX, **(C)** but there were no differences in modulus in the reproductive rats. However, modulus significantly decreased in the virgin group at 1 and 3 months post-OVX. At 1 month post-OVX, the reproductive group exhibited **(D)** increased stress relaxation **(E)** decreased dynamic modulus and **(F)** increased tan(δ). Solid lines denote significance for $p \leq 0.05$ and dashed lines for trends $p \leq 0.1$.

increased at 1 month post-OVX and was significantly higher than the virgin group at this time point (Figure 1F) with no differences at 3 months and 6 months.

Discussion

This study investigated the effect of reproductive history on tendon properties following ovariectomy. Higher modulus in the virgin control group compared to the reproductive group was consistent with recent preliminary data for rats that had undergone 2 cycles of reproduction. Modulus had a significant interaction effect, where the virgin group experienced a reduction but the reproductive group exhibited no differences in response to OVX. Previous studies showed that rotator cuff tendon strength decreases with ovariectomy[2,3] and attributed these results to reduced structural integrity of the mineralized fibrocartilaginous insertion site. Other *in vitro* studies also found that estrogen plays a role in collagen synthesis and maintaining tissue elasticity[5,6]. Our findings suggest that, similar to bone, supraspinatus tendons of virgin and reproductive rats respond differently to estrogen deficiency. Interestingly, recent studies in bone uncovered several adaptation mechanisms, including redistribution of bone mass toward load-bearing compartments and increased bone mechano-sensitivity in reproductive rats, which may account for the protective effect of reproductive history on bone when subjected to estrogen deficiency[7]. Decreased viscoelastic parameters at 1 month post-OVX but recovery by 6 months in reproductive tendons suggest that additional tendon adaptation mechanisms developed during the course of reproduction may have altered the tendon response to estrogen deficiency later in life. Further studies are necessary to explore the mechanisms behind tendon adaptations in these models.

This study highlights the importance of considering reproductive history during the diagnosis and treatment of rotator cuff injuries in post-menopausal women, particularly in the early stages of menopause where tendon properties were observed to change substantially.

References

1.Abate et al, 2014, *Menopause*.
2. Cadet et al, 2010, *J Orthop Res.*
3. Chen et al, 2015, *PLoS One*.
4. de Bakker et al, 2018, *J Bone Miner Res.*
5. Torricelli et al, 2013, *Age*.
6. Maman et al, 2016, *Connect Tissue Res*.
7. Li et al, 2018, *ORS Meeting*, 0695.

Gender Dependent Alterations in the Mechanical Response of Injured Collagen V Haploinsufficient Murine Tendons

Carlson JA[1]
Johnston JM[1]
Bonilla KA[1]
Shetye SS[1]
Nuss CA[1]
Weiss SN[1]
Rodriguez AB[1]
Birk DE[2]
Soslowsky LJ[1]

1 McKay Orthopaedic Research Laboratory University of Pennsylvania

2 University of South Florida

Introduction

Classic Ehlers-Danlos syndrome (*c*EDS) is most commonly characterized by haploinsufficiency in *COL5α1* with patients suffering from hyperextensible skin, joint instability and laxity. Collagen V is significantly upregulated following injury[1,2] and abnormal wound healing is associated with a diminished expression of collagen V[1,3]. Furthermore, estrogen in females is suggested to be associated with decreased collagen synthesis[4,5] and altered gene expression during repair[6]. However, the way gender-specific differences influence the healing response after injury and in the presence of collagen V deficiency has not yet been investigated. Therefore, the objectives of this study were to evaluate the mechanical response of injured patellar tendons over time in normal and *c*EDS mice, as well as differences between genders. We hypothesized that gender related differences in collagen V expression would result in an abnormal wound matrix in the injury response, contributing to the abnormal wound phenotype resulting in reduced mechanical properties of injured EDS tendons compared to normal tendons. In addition, the injury response in the female *c*EDS tendons will be inferior to that of male tendons due to these gender influences, resulting in greater mechanical properties of male tendons when compared to females.

Methods

Adult male and female wild-type (WT) C57/BL6 and heterozygous (HET) ***Col5a1***$^{+/-}$ *c*EDS mice (n = 120) at 120 days of age were used (IACUC approved). All mice underwent bilateral patellar tendon injury surgery as described[7] and were sacrificed 3 weeks or 6 weeks post-injury.

Mechanics

The patella-patellar tendon-tibia complexes of all mice were dissected and prepared for mechanical testing[8]. Cross-sectional area was measured using a custom laser device[9]. Tendons were subjected to a viscoelastic testing protocol[8,10] consisting of: 1) preconditioning, 2) stress relaxation at strain levels of 2%, 3% and 4%, 3) a sinusoidal frequency sweep (10 cycles at 0.1, 1, 5, and 10 Hz) at each strain level, 4) return to gauge length, and 5) ramp to failure. Tendon length was measured at nominal load prior to test initiation.

Statistics

Two-way ANOVAs with post-hoc Tukey tests were used to assess the effects of genotype (collagen V expression), gender, and their interaction on elastic and viscoelastic mechanical properties. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

Quasi-static

WT male tendons had higher failure stress at 3w and 6w post-injury (PI), tissue modulus at 6w, and a trending increase in tissue modulus at 3w when compared to WT female tendons (Figure 1A,B). WT male tendons also had higher failure loads and failure stiffness at 3w and 6w PI (Figure 1C,D). HET males had higher failure stress and failure loads at 3w and 6w PI, and higher stiffness at 3w PI when compared to HET females (Figure 1B,C,D).

Viscoelastic

WT male tendons, when compared to WT female tendons 3w PI, had reduced dynamic moduli at 2% strain (.1 Hz and 1 Hz), with a trend towards a decrease at 2% strain, 10 Hz and 3% strain, 0.1 Hz, however no differences in HET mice between genders were seen at 3w PI (Figure 2A,B). No WT differences in dynamic modulus were seen between genders at 6w PI (Figure 2C,D). Additionally, WT males had a higher tan(δ) at 2% strain, .1 Hz at 3w and 6w PI when compared to WT females (data not shown). HET male and female tendons showed trending differences in dynamic modulus at 6w PI at lower frequencies at 3% and 4% strain (Figure 2D, only 3% shown). The viscoelastic response of HET male tendons showed an increase in tan(δ) across all strains and frequencies (excluding 4%, 1 Hz and 4%, 10 Hz) 6w PI when compared to HET females (Figure 3B, only 3% shown). Additionally, no differences were seen between genders or genotypes in cross sectional area (data not shown).

Discussion

WT and HET male injured patellar tendons demonstrated higher material and structural

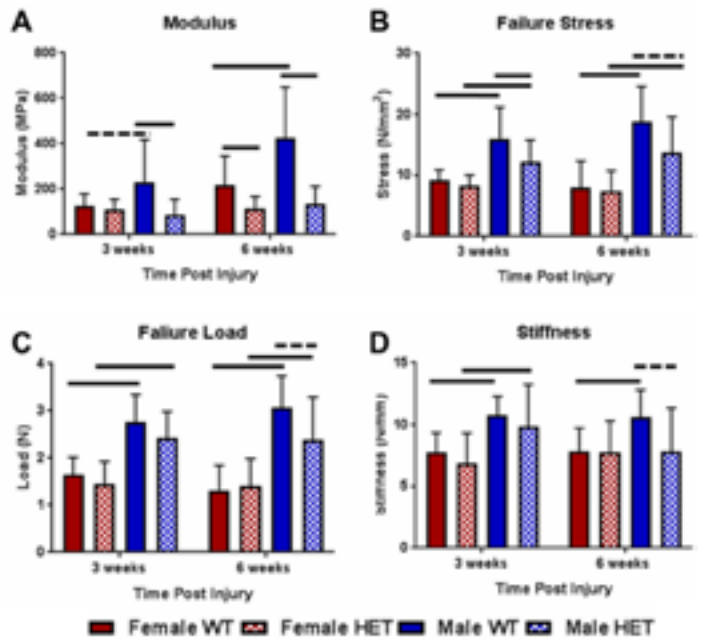


Figure 1. Material and structural and properties of female and male WT and HET patellar tendons. WT and HET male patellar tendons had increased moduli **(A)**, failure stress **(B)**, failure loads **(C)** and had increased stiffness **(D)** compared to female tendons.

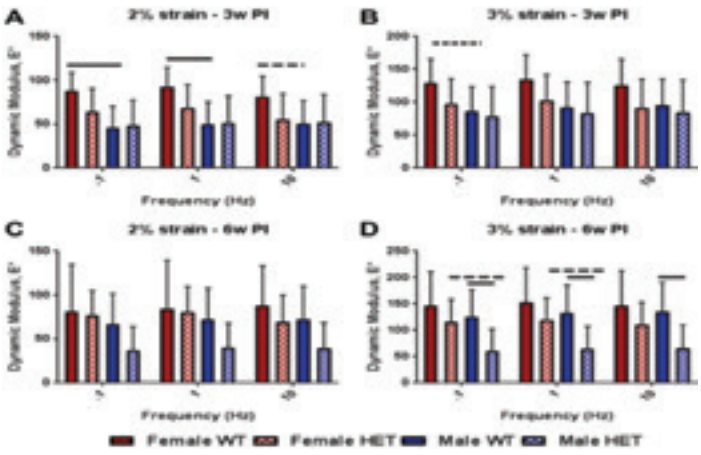


Figure 2. Dynamic moduli of female and male WT and HET patellar tendons. WT female patellar tendon dynamic moduli are increased across all frequencies at 2% strain, 3w PI **(A)**, with no differences seen at 6w PI **(C)**. Trending differences between genders were seen at lower frequencies at 3% strain, 6w PI **(D)**.

properties compared to WT and HET female injured tendons, respectively, at both time points following injury. Reduction in collagen V had a greater effect on male tendon material response than female tendon response, which is consistent with previous findings in uninjured tendons[11]. When examining the viscoelastic response, although dynamic modulus was decreased in WT male tendons compared to WT female tendons 3w PI, these differences did not persist to 6w PI. Additionally, there were no gender differences in viscoelastic properties of HET tendons 3w PI, however, gender differences in these properties were seen in HET tendons 6w PI. This could be explained by a diminished late healing response in HET females compared to males, obscuring the increased effect of reduced collagen V on male tendons versus female tendons at

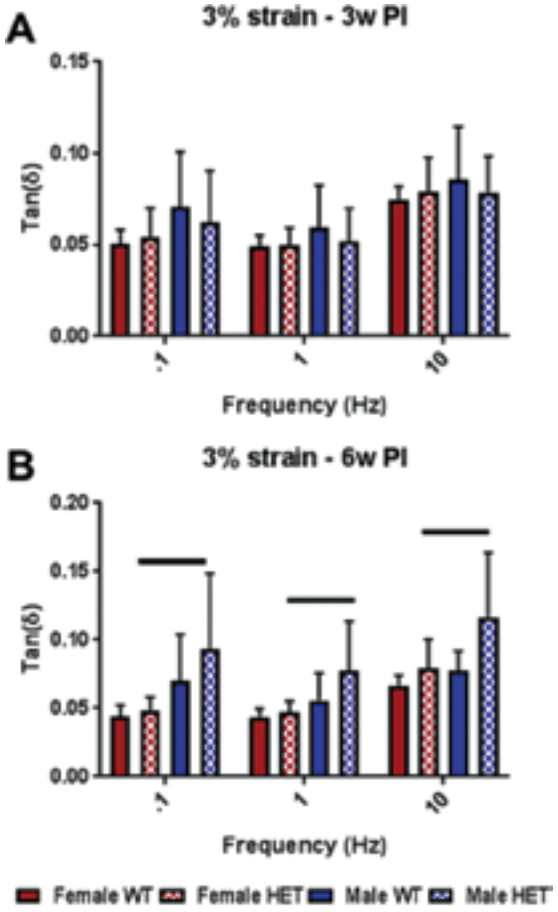


Figure 3. Tan(δ) of female and male WT and HET patellar tendons. HET male mice showed no differences in tanδ) from HET female mice at 3w PI **(A)** but had increased tan(δ) measurements across all frequencies at 3% strain, 6w PI **(B)**.

the 6w time point. Male patellar tendon properties are more dependent on collagen V than female tendon properties and the reduction of collagen V affects the healing response of male and female tendons in differing capacities. Future work may include further characterizing the healing response through histological analysis to understand cellular differences that could explain these mechanical differences.

This study demonstrates that gender-specific effects play an explicit role in tendon injury and healing and can influence the degree to which tendon properties of *c*EDS mice are affected.

References

1. **Wenstrup RJ, *et al.*** *J Biol Chem.* 2006.
2. **Ainsworth SR, *et al.*** *Clin Orthop Relat Res.* 1993.
3. **Steinmann B, *et al.*** *Connective Tissue and Its Heritable Disorders.* New York: Wiley-Liss; 2002.
4. **Yu WD, *et al.*** *Clin Orthop Relat Res.* 2001.
5. **Kjaer M, *et al.*** *J Anat.* 2006.
6. **Hart DA, *et al.*** *Clin Orthop Relat Res.* 1998.
7. **Beason DP, *et al.*** *J Biomech*, 2012.
8. **Dunkman AA, *et al.*** *Matrix Biol.* 2013.
9. **Favata M**, Bioengineering PhD Thesis Philadelphia: University of Pennsylvania. 2006
10. **Miller KS, *et al.*** *J Biomech Eng.* 2012.
11. **Carlson JA, *et al.*** Abstract, *ORS* 2018.

Quantitative Comparison of Three Rat Models of Achilles Tendon Injury: A Multidisciplinary Approach

Huegel J[1]
Boorman-Padgett JF[1]
Nuss CA[1]
Minnig MCC[1]
Kuntz AF[1]
Waldorff EI[2]
Zhang N[2]
Ryaby JT[2]
Soslowsky LJ[1]

1 McKay Orthopaedic Research Laboratory University of Pennsylvania

2 Orthofix Inc., Lewisville, TX

Introduction

The Achilles tendon, while the strongest and largest tendon in the body, is frequently injured. Even after surgical repair, patients risk re-rupture and can have long-term deficits in function, with the rate of return to pre-injury level of activity reported to be as low as 16%[1]. Animal models of tendon injury are essential for understanding physiological processes of tendon repair and for testing the effects of potential therapeutics[2]. We have adapted and utilized three rat models of Achilles tendon injury (complete, full-thickness tear with post-operative immobilization, partial tear with post-operative immobilization, and a partial tear without post-operative immobilization). However, comparisons of the effects of these injuries on tendon mechanics and ankle joint function have not previously been made. Therefore, the objective of this study was to quantitatively define and compare the effects and relative impact on tendon properties and ankle function of the three Achilles tendon injury models. We hypothesized that animals receiving a complete tear would have inferior mechanical properties and ankle function compared to those receiving a partial tear, and that immediate loading after a partial tear would improve post-operative mechanical properties and ankle function compared to immobilized tendons.

Methods

144 adult male Sprague-Dawley rats (400-450 g) were used (IACUC approved). Animals underwent either full-thickness, blunt complete transection and repair of the right Achilles tendon[3] (with one week of post-operative plantarflexion immobilization (CT+IM, n = 48) or full-thickness, partial-width transection (1.5 mm biopsy punch in center of tendon) without repair[4] (with one week of post-operative plantarflexion, PT+IM, n=48, or without IM, PT-IM, n = 48). Animals were sacrificed at 1, 3, or 6 weeks (n = 16/group/time point). Animals in 6 week groups underwent longitudinal in vivo ambulatory and passive ankle joint mechanics assessments[3]. At sacrifice, the Achilles-calcaneus complex was dissected out (n = 6/group/time point) and processed for histological analysis. All other animals (n = 10/group/time point) were frozen at -20°C and thawed for dissection prior to cross-sectional area measurement using a custom laser device and mechanical testing using a load controlled fatigue testing protocol (including frequency sweeps at 0.1Hz, 1Hz, 5Hz, and 10Hz, and fatigue cycling from 5 to 35N cycles at2 Hz until failure)[3]. Post-test, tendons were scanned using μCT at a 21μm resolution to assess for presence of heterotopic ossification (HO) within the healing tendon. Statistical comparisons were made between the CT+IM and PT+IM group and between the PT+IM and PT-IM group at each time point. Comparisons for mechanics, functional assessments, collagen fiber organization, and μCT metrics were made using one way ANOVAs with Bonferroni post-hoc tests. Histological comparisons were made using Kruskal-Wallis tests.

Results

Mechanical Properties

At 3 and 6 weeks post-injury, cross-sectional area was larger for CT+IM tendons compared to PT+IM (Figure 1A). PT+IM modulus was significantly greater than CT+IM at 1 and 6 weeks, but was significantly lower than PT-IM at 3 weeks (Figure 1B). Similar differences were also seen in stiffness (Figure 1C). Dynamic frequency sweeps at 0.125% strain also determined similar differences in dynamic modulus at all tested frequencies (data not shown). PT-IM tendons withstood significantly more fatigue cycles before failing than PT+IM tendons at 3 and 6 weeks, and only PT−IM tendons were able to produce a reliable fatigue response at 3 weeks (Figure 1D,E). Tissue modulus (Figure 1E) and both secant and tangent stiffness (data not shown) measured during fatigue testing were greater in PT+IM tendons than in CT+IM at 6 weeks, but there was no difference between PT groups in these metrics at this time (Figure 1E).

Histology

No differences were determined in cell number (cellularity), nuclear shape, or collagen organization. μCT: The presence of heterotopic ossification was observed in almost all samples in all groups at all time points (no differences between models, data not shown). Bone volume was significantly higher in CT+IM tendons than PT+IM tendons at six weeks (Figure 2A);

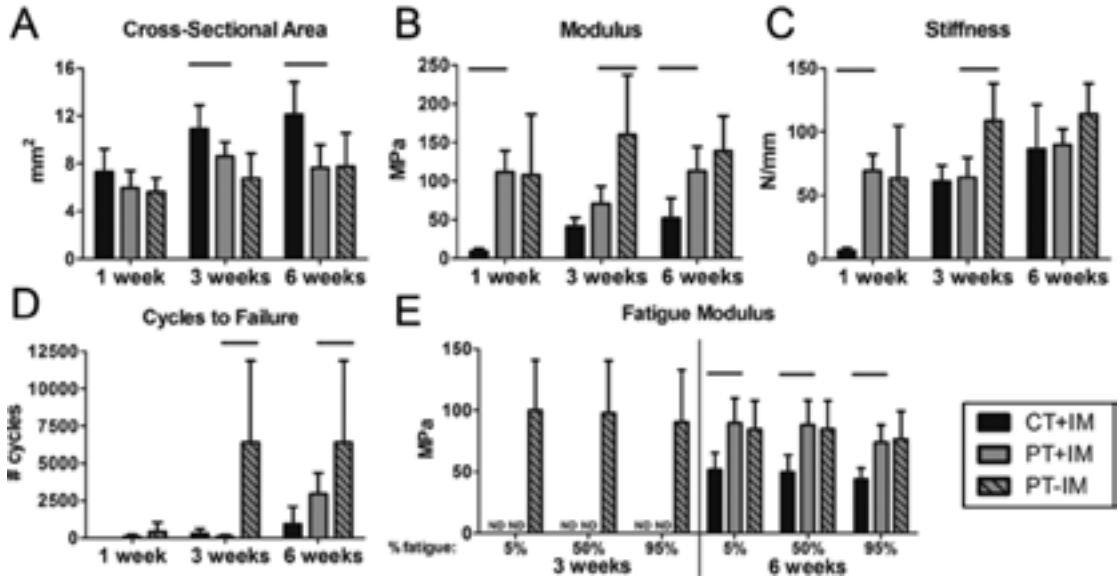


Figure 1. Mechanical Properties**.** Injury model affects **(A)** tendon cross-sectional area at 3 and 6 weeks; both injury mode and IM alter **(B)** tissue modulus and **(C)** tendon stiffness; immediate load bearing improves **(D)** cycles to failure at 3 and 6 weeks; and CT decreases **(E)** fatigue modulus at 6 weeks. ND: data was not able to be collected. Bars: $p < 0.025$.

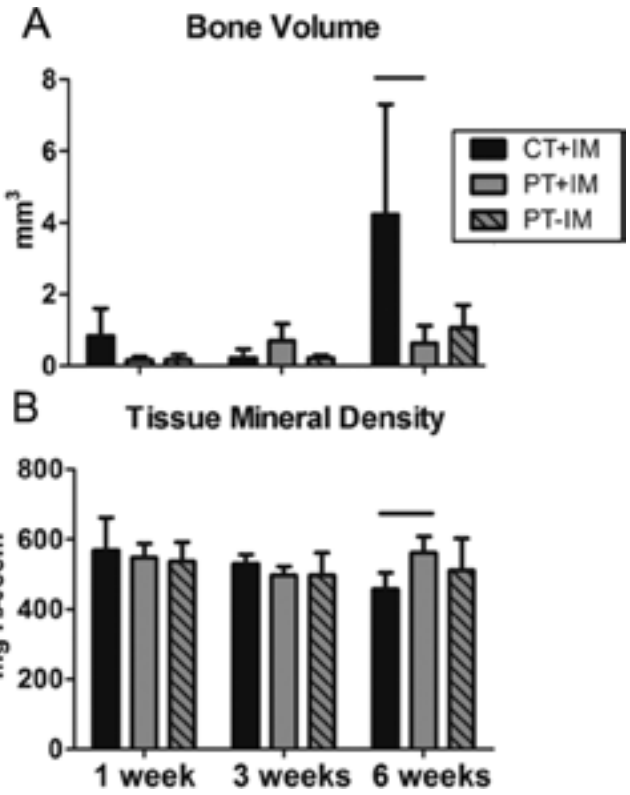


Figure 2. uCT Properties. **(A**) CT+IM showed **(A)** increased heterotopic bone volume but **(B)** decreased tissue mineral density at 6 weeks post-injury. Bars: $p < 0.025$.

however, this mineralized tissue had decreased tissue mineral density (Figure 2B).

Functional Assessments

Ankle joint stiffness and range of motion (ROM) through dorsiflexion were significantly altered in CT+IM and PT+IM groups (Figure 3A,B).Ankles from complete tendon tears were stiffer than both partial tear groups at 14 days post-injury, but by 6 weeks, were only stiffer than the PT−IM group (Figure 3A). In contrast, CT+IM and PT+IM groups had similarly diminished dorsiflexion ROM (~60% decrease) at 14 days (Figure 3B). PT+IM joints regained significantly more ROM by 6 weeks, while CT+IM joints did not recover (Figure 3B). Few differences existed in plantarflexion parameters (data not shown). CT+IM animals also had significantly slower rate of loading (Figure 3C) and longer stance time (data not shown)

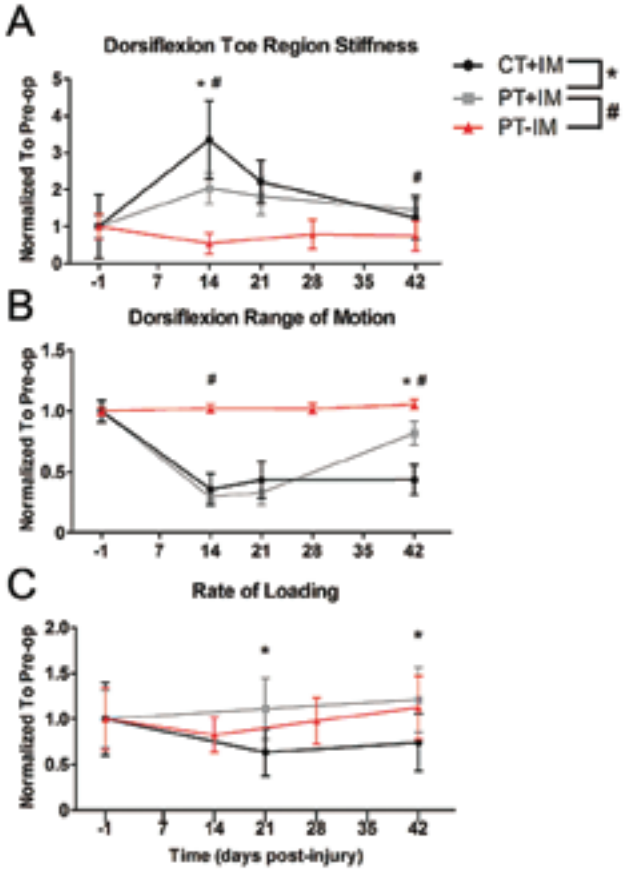


Figure 3. Functional Assessments. Passive joint testing demonstrated that **(A)** dorsiflexion stiffness was increased and **(B)** dorsiflexion ROM was decreased for CT+IM group post-injury. Ambulatory analysis showed that **(C)** rate of loading was decreased in the CT+IM group. post-injury. Sig difference notations labeled in legend ($p < 0.025$).

during ambulation than PT+IM, even though overall speed was increased at 6 weeks (data not shown).

Discussion

This study investigated differences in ankle function, tendon mechanics, and HO in three different models of Achilles injury. All models were reproducible and had distinct effects on measured parameters. Injury severity (CT vs PT) had a drastic influence on tendon healing, with complete tear causing diminished ankle mobility and decreased tendon mechanics throughout post-injury time points compared to partial tears. Changes in loading rate and stance time of the injured limb indicate that CT animals are altering ambulation patterns more severely, which may be due to loss of function or increased pain[5]. CT tendons also contained significantly more HO than PT tendons. However, differences in bone density between groups suggest that the mechanisms of HO development or maturation may vary between models. One week of plantarflexion IM had a strong effect on animals receiving a partial-width injury. Most notably, tendons in the PT+IM group failed extremely early during fatigue cycling 3 weeks post-injury (113 $\pm$ 85 cycles), prohibiting fatigue analysis. Surprisingly, a partial tear injury without immobilization had no effect on ankle range of motion through dorsiflexion at any time point, while PT+IM animals demonstrated diminished function at all post-injury time points. Together, these results indicate that even short-term immobilization may impair healing and increase ankle stiffness in partial Achilles tears in rats. Future studies will investigate long-term effects of these models.

All three models of Achilles injury could be useful for tendon healing investigations, chosen based on the prospective applications of a potential therapeutic. This work also sheds light on the universal occurrence of heterotopic ossification after surgically-induced injury in a rat Achilles tendon, as well as the potentially detrimental effects of complete immobilization/unloading on partial Achilles tears.

References

1. Barfod KW *et al.* *J Bone Joint Surg*, 2014.
2. Hast MW *et al.* *Bone Joint Res*, 2014.
3. Freedman BR *et al.* *J Orthop Res*, 2016.
4. Boorman-Padgett J *et al.* *Trans ORS*, 2018; 1454.
5. Caro AC *et al.* *J Am Assoc Lab Anim Sci*, 2014.

Ultrasound Echogenicity is Associated with Fatigue Damage of Achilles Tendon in a Cadaveric Loading Model

Elaine C. Schmidt
Todd J. Hullfish
Michael W. Hast
Josh R. Baxter

Department of Orthopaedic Surgery
University of Pennsylvania

Introduction

One in twenty patients with tendinopathy sustain an Achilles tendon rupture[1]. Clinical diagnoses currently rely on patient-reported symptoms of pain, a reduction in ankle range of motion, and tendon swelling. However, by the time Achilles tendinopathy becomes symptomatic, many degradative changes to the tendon have already been initiated[2]. Detecting markers of pre-symptomatic tendinopathy may lead to better treatment and improved outcomes for patients. This study sought to determine the efficacy of quantitative ultrasound imaging to explain in vitro fatigue-induced degradation of Achilles tendon mechanical properties.

Methods

Achilles tendons were harvested from 3 fresh-frozen cadaveric feet. The calcaneus was potted in PMMA and the tendons were cut into dog-bone shapes to ensure failure at the mid-substance. Tendons were tested with a universal test frame and a custom tank that included a temperature controlled PBS bath (Figure 1). Tendons were cycled between 10-20 MPa at 1 Hz until complete mid-substance failure. An ultrasound probe was fixed in place and images were acquired were recorded every 500 cycles. At these times, 2 cycles were performed at 0.25 Hz to allow for thorough image analysis. images were post-processed using custom MATLAB image analysis algorithm.

Results and Discussion

Mean echogenicity decreased when tendon fatigue damage increased. This decrease in ultrasound image intensity was most apparent after 95% of fatigue life (Figure 2A). For all three specimens, mean echogenicity plateaued during the second phase before decreasing rapidly proceeding tendon failure. From 50% fatigue life to failure, mean echogenicity decreased by 2.5 ± 0.4%. In two of the three specimens, changes in mean echogenicity increased with increased fatigue damage (Figure 2B).

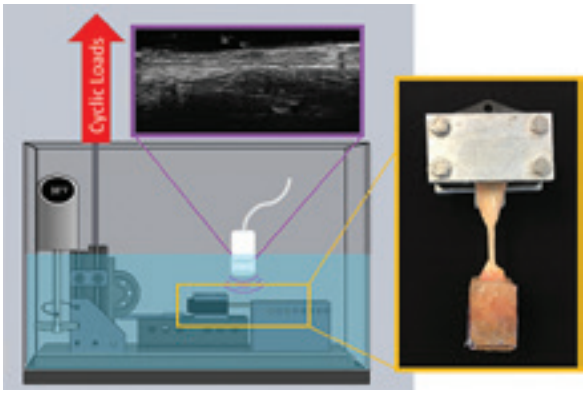


Figure 1. Tendon specimens were cyclically loaded in water bath while images were acquired using an 18MHz ultrasound probe

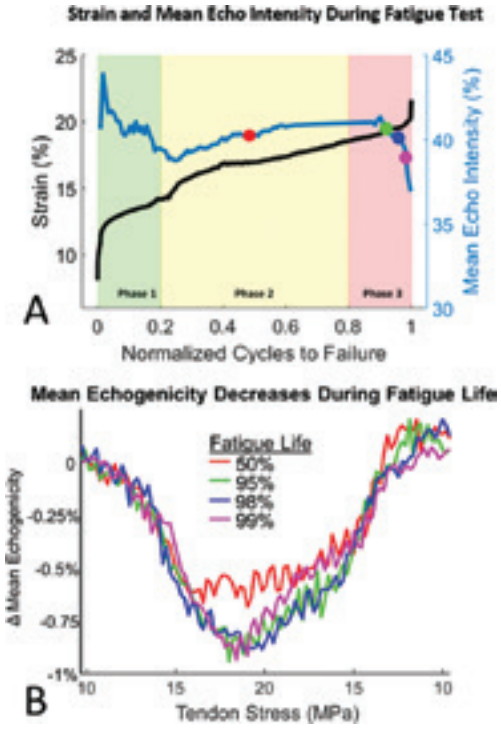


Figure 2. Change in strain and mean echogenicity during the three phases of fatigue life for Specimen 1 **(A)**. Change in mean echogenicity during one cycle at different points of fatigue life **(B)**.

Conclusions

Mean echogenicity is a promising marker for quantifying fatigue damage in Achilles tendons. Our ongoing work is focused on developing computer-based predictive tools to assess Achilles tendinopathy risk in physically active adults.

References

1. Yasui *et al.* *Biomed Res. Int.* Epub 2017 Apr 30
2. Sunding *et al.* *Knee Surg Sports Traumatol Arthrosc.* 2016. 24.6: 1988

THE UNIVERSITY OF PENNSYLVANIA ORTHOPAEDIC JOURNAL VOLUME 29