The University of Pennsylvania Orthopaedic Journal

Volume 32 June 2022

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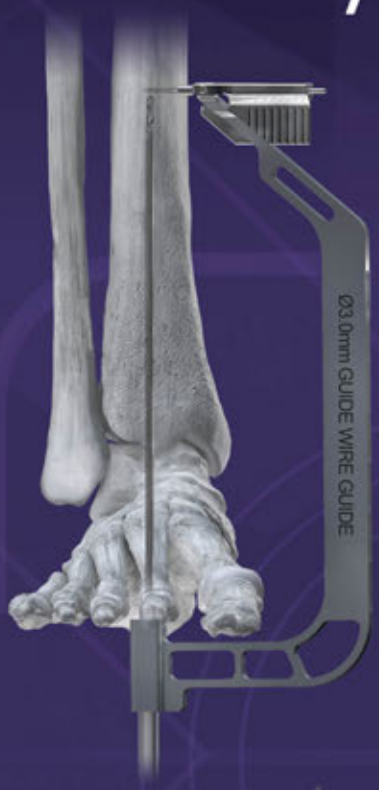

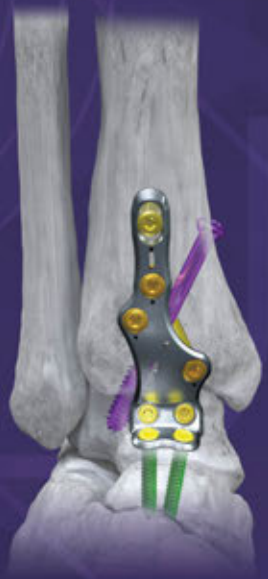

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Volume 32, June 2022

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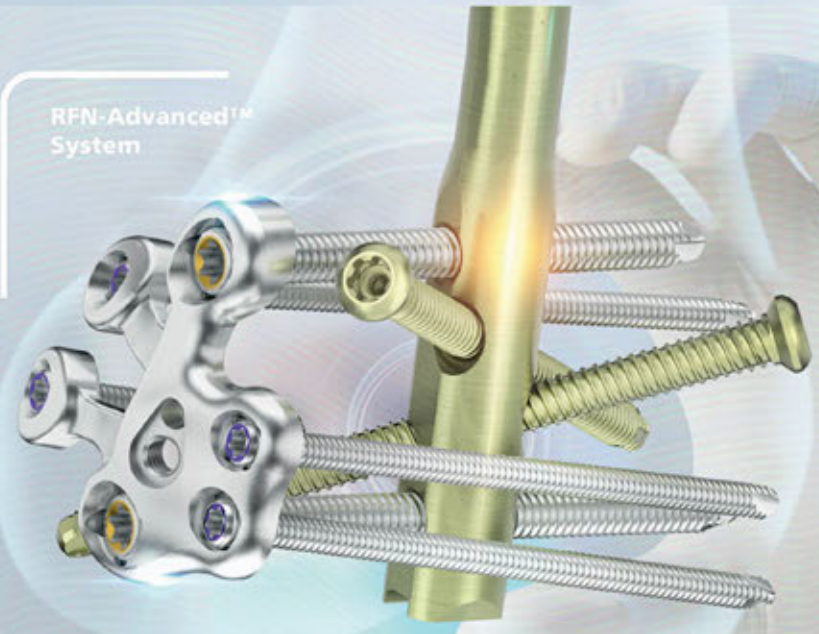

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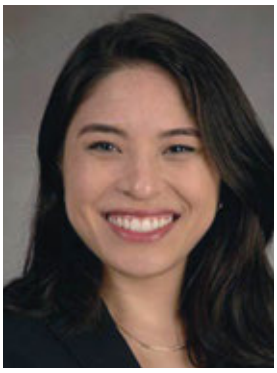
Letter from the Editors: Orthopaedic Surgeons as Leaders

Kendall M. Masada, MD and Jordan S. Cohen, MD



Welcome to the 32nd edition of the University of Pennsylvania Orthopaedic Journal (UPOJ). Founded in 1986 under the guidance of Dr. Carl T. Brighton, the UPOJ remains a testament to the department's commitment to basic science and clinical research. This year, we reached a new milestone marking these efforts: the Department of Orthopaedic Surgery at the University of Pennsylvania was ranked #1 in National Institutes of Health funding amongst all other orthopaedic departments in the country. We are incredibly proud of this achievement as it represents the tireless work, innovation, and collaboration of our team—always striving to gain new insights and seek better understanding of the musculoskeletal system, with the ultimate goal of providing the best possible care for our patients.

Healthcare is a dynamic field, which requires flexibility and adaptability among those who wish to continue to provide the highest quality of care to their patients. Some challenges we face today including an aging and less healthy population, pressures for cost containment and value-based care, and increased adoption of technology have been evolving for decades. Others, like how to care for patients in the midst of a global pandemic and incorporate virtual interactions into our patient care and professional workflows, are much more recent. However, it is indisputable that surgeons today must be leaders beyond their operating rooms and clinics if they hope to propel our field into the future. Leadership comes in many forms, and the special leadership section of this year's edition highlights some of the ways orthopaedic surgeons and other leaders in our field have risen to the challenge and demonstrated leadership locally, nationally, and globally. Their contributions span broadly, and we hope that our readership will enjoy learning from their narratives and find important takeaways that they can apply on their own leadership journeys.

We are honored to dedicate this year's edition to Dr. G. Russell Huffman. He served as a leader at Penn for 16 years prior to moving his family to Orlando, Florida. During his time at Penn, Dr. Huffman built one of the premier shoulder and elbow practices in the region. He committed himself to resident and fellow education as the director of Penn's Shoulder and Elbow Fellowship, published numerous book chapters and peer-reviewed scientific publications, and lectured nationally and internationally.

We are grateful for the leadership of our Chair, Dr. L. Scott Levin, for the support of the journal's advisors, Dr. Samir Mehta and Dr. Derek J. Donegan, and for the efforts of our resident section editors. As a fully resident-run publication, the UPOJ would not be possible without our team's contributions. We would also like to thank this year's industry sponsors whose generous financial support helps the journal continue to support the educational and research missions of Penn Orthopaedics.

This year's journal and prior editions are available for free online at www.upoj.org. We encourage everyone to subscribe to the journal at www.upoj.org/subscribe.

It has been our honor to serve as editors for the 32nd edition of the UPOJ. We hope you enjoy and learn as much as we did in the process.

Kendall M. Masada, MD
Jordan S. Cohen, MD

Letter from the Chair: Leadership is a Privilege

L. Scott Levin, MD, FACS, FAOA

Leadership is a privilege. For thirteen years, the missions of the Department of Orthopaedic Surgery have been my responsibility. As with all leaders, history will judge the effectiveness of my oversight using several different metrics including the increase in clinical and research faculty, year-over-year growth of the contribution margin to the health system, clinical program development, and research funding, just to name a few. It is fair to say that our clinical care is respected locally and nationally. Our educational programs are highly regarded both at the residency and fellowship level in multiple orthopaedic disciplines. Recently, we were notified that Penn Orthopaedics is ranked #1 by the National Institutes of Health in terms of research funding in the United States. Since I began my term in 2009, getting to number one has been a team goal of the McKay Laboratory. I want to congratulate our entire research team, and particularly acknowledge Lou Soslowsky, Ph.D. who has been among the top 5 NIH funded investigators in orthopaedics for more than twenty years!

While the path has been challenging, the determination to improve our ranking is emblematic of our commitment to our research mission- creating new knowledge to benefit our patients. This achievement is a testimony to the brilliance and grit of our basic scientists and clinical faculty collaborators. I have espoused the acronym T.E.A.M. many times: TOGETHER EVERYONE ACHIEVES MORE! "Teamwork makes the dream work." This statement is attributed to American clergyman John Maxwell and our dream to become number one was realized based on teamwork, collaboration and Sir William Osler's formula for success: hard work. Our hats (and surgical caps) are off to recognize our research teammates.

While we are on the subject of long-term goals, I am delighted to report that our commitment to diversity, equity and inclusion has been manifested by an increase in women and underrepresented minorities in our resident and faculty ranks. Lorraine Boakye, M.D. will be joining our foot and ankle division this fall. She is an outstanding surgeon scholar and will be Penn's first African American woman to join our faculty. My intent is that she will not be the last! Women now lead two of our divisions- Cara Cipriano, M.D., M.Sc. has taken over the Division of Orthopaedic Oncology and is also directing medical student education. She has developed a unique "surgeon educator" track for our residency and has already transformed our footprint in the school of medicine by improving the orthopaedic surgery clerkship experience for our Penn medical students. Casey Humbyrd, M.D. is our new Division Chief of Foot and Ankle Surgery and is leading the exponential expansion of that division with skill and vision following the remarkable legacy of Keith Wapner, M.D.

Other faculty hires include T. David Tarity, M.D. and Jean-Claude D'Alleyrand, M.D. MSE. Dr. Tarity has joined the Division of Adult Reconstruction after completing his second joint replacement fellowship at the Hospital for Special Surgery. He has also served our country as an Air Force officer. Dr. D'Alleyrand will join our Division of Orthopeadic Trauma in the summer of 2023. He is the Director of Surgical Services at Landstuhl Medical Center in Germany. His responsibilities will include oversight of the V.A. Orthopedic Service as well as providing support for our PPMC trauma center.

While there have been many recent successes in the department, the COVID-19 pandemic has affected all of us. The recent surge severely impacted our ability to perform elective surgery during January. The lack of nursing and support staff has also compromised patient care throughout. Despite the emotional and logistical challenges of the pandemic, our team has "soldiered on." I could not be more proud of our entire team- our clinical faculty, residents, fellows and dedicated administrative staff led by Neil Ravitz, M.B.A. Mr Ravitz's extraordinary work ethic and commitment to our entire team must be commended. Other team leaders include Will Dyson and Andrew Kanoff who support our multiple clinic sites and operational needs.

I also want to recognize Daniel Farber, M.D., Vice Chair of Education, and Stephen Liu, M.D., Associate Residency Program Director, for their unwavering support of our residents. Virtual grand rounds, online visiting professors, and constant emails providing guidance and continuity for patient care have been seamless thanks to their 24/7/365 availability and responsiveness. Our chief residents Agnes Dardas, Yudi Kerbel and Liane Miller have adapted, improvised and conquered pandemic challenges and also must be recognized. I offer my gratitude and respect to all of the educational leaders for these extraordinary efforts.

One of our strongest assets over the years has been our ability and resources to provide an extremely robust visiting professor program for our faculty and residents. We have recently gone back to in-person meetings, which comply with university guidelines and the CDC. Edward Barksdale, M.D., Surgeon-in-Chief at University Hospitals Rainbow Babies and Children's Hospital, served as our inaugural DEI Lecturer and was outstanding. He shared his personal journey and inspired all of us. Our commitment to promote further diversity in our department was unanimously reaffirmed during his visit. In fact, our residents Brian Perez and Viviana Serra Lopez secured

funding to provide support for North10- a community center that serves inner city youth and disadvantaged families. We will provide sports physicals and other MSK health needs to this community. Giving back in this capacity is a joy and a responsibility. See *https://north10phl.org/* for more information about this organization. We will do more in the years to come.

David Helfet, M.D. delivered the Inaugural Dean Lorich M.D.-Hans Joerg Wyss Visiting Professor lectureship and provided a moving and impactful talk highlighting Dean's contributions to Orthopedic Trauma which are truly legendary and sustaining. I want to recognize the generosity of Hans Joerg Wyss and the Wyss Foundation for the generous support they have provided to the department for many years, and in many ways. The Lorich Wyss Trauma program is another example of their commitment to our missions of research and education.

In addition to Penn Medicine serving as the sole medical and Orthopedic Surgery provider for the Philadelphia Flyers ice hockey team, we entered a new and exciting agreement to serve as the sole medical provider to U.S. Squash. This extends our Penn brand globally and Penn Orthopedics will not only provide care for the athletes, but will benefit from our association with this world class organization.

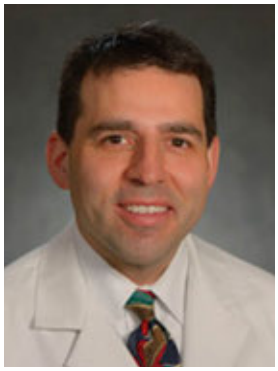
Finally, I want to share with you that I will be stepping down as Chair of Penn Orthopedics July 1, 2023 at the request of Dr. Larry Jameson and UPHS CEO Kevin Mahoney. They have asked me to assume the role of Vice President of the Penn Health System and Associate Dean of the Medical School for Resource Development. My second six-year term in the department was reviewed internally and externally, which is standard procedure in the school of medicine. External reviewers included Joseph Zuckerman, M.D. (NYU), Lisa Lattanza, M.D. (Yale), and Mitchel Harris, M.D. (MGH). Their outstanding review and report to Dean Larry Jameson, M.D., Ph.D. has provided a roadmap for continued success that includes our strategic plan (completed in 2021), which is well underway. The search for the new Chair of Penn Orthopaedics will begin this spring. I will be a great cheerleader for the next leader and do all I can to assure the continued the success of our great department.

My vision of building a new Orthopedic hospital across the street from our Penn MSK institute will become my goal after I step down. Architectural renderings show our institute connected to the new hospital by a bridge that crosses 38th street. Discussions have already started to make this a reality in the next few years. Stay tuned- our future is bright, our team is committed and strong, and our pride in Penn Orthopedics has never been stronger. Thanks for your continued support.

With best regards,
Scott

Letter from the Program Director

Daniel C. Farber, MD



It has been yet another eventful year for the residency program as the 2021-22 Academic year held nearly as many twists and turns as 2020-21. In June we welcomed our first virtually recruited intern class. Under the leadership of this year's chief residents, Liane Miller MD, Agnes Dardas MD and Yehuda Kerbel MD, we began the year with gradual resumption of some in-person education activities but travel and institutional restrictions had us continuing grand rounds as a virtual experience. The delta surge and then the omicron surge continued to gum up the works for in-person visitors but the past month has seen a number of visiting professors able to attend in person and impart not just their wisdom but their intangible personal touch to our educational events. Through all of this, the residents have mostly maintained in-person education sessions and we have also started back into the cadaver lab. With a brief hiatus for Omicron, the residents with the support of Samir Mehta, MD and others began a series of casual journal clubs off-site at attendings' homes, a brewery, and even "Top Golf!" Dr. Andrew Sobel, one of our new Hand attending staff, has begun a Friday morning "Hand Board" to review the week of consults with residents in person in what has quickly become a favorite educational conference. Plans are in place to extend this to trauma and other consults on a different morning.

With the introduction of the AAOS R.O.C.K. (Resident Orthopaedic Core Knowledge) curriculum and as a beta-tester for the program, the residents have contributed to the evolution of what will become a critical part of many orthopaedic programs' education. We were also excited to welcome back visiting students this year albeit all medical students were limited to 1 away rotation. We had another virtual recruiting session kicked off by the second year of a special webinar highlighting diversity and organized by our own Viviana Serra Lopez MD and Brian Perez MD. We interviewed a stellar and diverse group of applicants and anticipate another successful match. This coming year there are no away rotation limits and we look forward to getting to know sub-I's from many different backgrounds. Along the lines of medical student education, we welcomed Cara Cipriano MD from Washington University at St. Louis who will serve as the medical student director for Orthopaedics. She has already made great changes and enhancements to our interactions with the Perelman School of Medicine.

The residency program itself continues to evolve. This year marks the inauguration of the Faculty Advisor Program whereby individual faculty have volunteered to be responsible for either a PGY 1, 3, & 5 or PGY 2 & 4 resident. Faculty track these residents' performance, evaluations, and well-being to provide support and ensure their success progressing year to year to become excellent orthopaedic surgeons. The faculty also generously supported the purchase of surgical lead aprons for all the residents to keep them safe for years to come. We welcomed Angela Nieves as our second program coordinator, joining the inimitable Shannon Savelloni and enhancing the education team. We sadly bid farewell to Associate Program Director, Vince Moretti MD, who moved on to Texas but we were very pleased to welcome former Penn Ortho Alumnus and Penn Hand Surgeon, Stephen Liu MD, as the new Associate Program Director. Steve's familiarity with the program and can-do attitude have already brought great insight and program improvements.

The pandemic has had some silver linings for the program. Our newfound comfort with virtual interaction has allowed for the trauma team's interactive Sunday evening "Fracture of the Week" to include many attendings and residents from the comfort of their homes or the bunker. Virtual Subspecialty conferences allow for more global participation of residents and faculty no matter where they are seeing patients that day.

The incredible growth of our department has outstripped the ability of our residents to cover everyone. Thus, moving forward, we have revamped resident rotations to focus on consistent experience with specific attending surgeons to maximize the education benefit. We have created protected research time for the residents to enhance their ability to contribute to the research mission and accomplish their research requirement for graduation. We look forward to more educational enhancements as the years progress.

Of course, none of these achievements would be possible without the assistance of our amazing attending staff who dedicate themselves to resident and student education. We also appreciate the unwavering support of our Chair, L. Scott Levin MD. A big thanks as well to our outgoing Academic Chief Residents mentioned above and a hearty congratulations to the incoming Academic Chiefs, Ryan DeAngelis MD, George Fryhofer MD, and Gregory Minutillo MD. Finally, further congratulations to our graduating PGY5s who are all headed to fantastic fellowships.

We wake up every morning looking for ways to continue to improve the educational mission at Penn Orthopaedics and if you want to support this mission, please feel free to donate to the Penn Orthopaedic Education Fund. All donations directly benefit the residents and support everything from educational resources, resident instructional courses, and academic travel to the occasional resident happy hour that helps boost morale. Please contact Allyse Orsini at aorsini@upenn.edu or 267-788-0975. Also check out our Instagram page at Penn.Ortho!

Wishing everyone a happy and healthy and productive 2022-3 Academic year!

2022 Dedication: G. Russell Huffman, MD, MPH

Sachin Gupta, MD and David Glaser, MD

G. Russell Huffman, MD, MPH

"What we do is very difficult, not for the faint of heart." Dr. Huffman was and will always be cherished as a gem of our institution. It is with the utmost honor that we humbly dedicate this year's edition of the University of Pennsylvania's Orthopaedic Journal to Dr. G. Russell Huffman MD, MPH, former Director of the Shoulder and Elbow Fellowship Program and Associate Professor of Orthopaedic Surgery.

Dr. Huffman's interest in orthopaedics began early on at Duke Medical School where he sought out world renowned mentors including Dr. Urbanik who was chair of the department at the time. He recalls being so impressed with what a gentleman Dr. Urbanik was, ranging from the extraordinary care with which he treated his patients to his profound clinical expertise. He knew that orthopaedics was the right field for him based on the ability to directly impact the quality of life for patients of almost any background. In addition, Dr. Huffman found it fascinating one could operate from "anywhere in the body from the spine to the ankle or foot." At the end of the day, like most of us, he found it to be one of the most fulfilling specialties and one in which the residents and attendings had the best personalities. Dr. Huffman recalls, "I originally wanted to save patients' lives, and found that in orthopaedics, rather than save lives I could profoundly improve the quality of lives. Needless to say, of all the specialties, those colleagues in orthopaedics were the most fun to work with."

Contrary to what one might believe, medicine was not always the end-goal. Dr. Huffman, in college, began his studies in political science and at first had thoughts about enrolling in law school. However, his grandfather, great grandfather, uncle, and cousins were all physicians and had a tremendous influence on him. Spending a summer in Africa, he found that this was a field in which he could really impact people in a tangible way. While thoughts of entering the ministry intrigued Dr. Huffman, it was really medicine where he felt he could make a difference.

It was January 3, 2005 when we were lucky enough to court Dr. Huffman away from UCSF where he had completed his residency. Dr. Huffman found that Penn had opportunities to teach young orthopaedic surgeons and participate in groundbreaking research; it was one of the most comprehensive job opportunities that he had encountered. After meeting with Dr. Sennett who had recently established the sports center at Weightmann Hall at the time, and Dr. Glaser, who met with him at the local favorite White Dog Café, Dr. Huffman knew that this was the right fit for him. What he most cherished about Penn was the people. "It's easy to fall in love with a place because of the support and quality people who work at Penn." He really enjoyed taking time to get to know the residents. "They would read and publish articles, ask questions, and constantly challenge me." In addition, he enjoyed getting to know the fellows and developing relationships with his future colleagues as they worked closely with him. Dr. Huffman recalls Dr. Levin being tremendously supportive, seeing him as family rather than an employee. He states," the biggest thing I'm going to miss is the people. There's something special about working at Penn and especially training residents and fellows. It's a mentorship model which you don't get at a lot of places."

Dr. Huffman was our fellowship director for the shoulder/elbow division for 12 years. Throughout his tenure, he was both nationally and internationally recognized as an expert in the field of shoulder and elbow surgery. Dr. Glaser describes him as "one of the most creative surgeons you've ever seen." The creativity and complexity of his elbow cases that he tackled were unparalleled, garnering the respect of other shoulder and elbow specialists worldwide. He often received referrals from many well-respected surgeons given his ability to take on such difficult cases. He trained 12 fellows, all of whom have developed into accomplished surgeons with several starting their own fellowship programs.

Dr. Huffman's dedication to his fellows did not go unnoticed. Several of his prior fellows shared their praises of Dr. Huffman with us.

- Mohit Gilotra, MD (Associate Professor of Orthopaedic Surgery, University of Maryland Medical Center, Baltimore, Maryland): "Although I learned about surgical techniques in the lateral position for capsular release and labrums etc, what I learned most about was how to teach in the OR: how to have high demands on perfect technique but still keep a collegial nurturing atmosphere. Harder to do then it sounds."
- Christy Piper, MD (Signature Orthopaedics, St. Louis, Missouri): "Dr. Huffman's humility and dedication to his patients are just a few of his attributes that I strive to emulate in my own practice. He is always available to discuss difficult cases or offer sage words of advice. I feel so privileged to have spent fellowship year learning from him, and to now call him my friend and mentor."

- Venkat Seshadri MD (Premier Orthopaedic and Hand Center, Flossmoor, Illinois): "I'm proud to have had Russ and Dave as mentors and friends. I remember my fellowship year at Penn as one of the best years of my life personally and professionally."
- Chad Myeroff, MD (Twin Cities Shoulder and Elbow, Minneapolis, MD): "Dr. Huffman is a masterful clinical narrator, but I learned even more from his actions than his words: always honoring his duty to give each patient the benefit of the doubt and calling on creativity and sound principles to solve each unique problem for each unique patient, always available, and always with a smile."

Furthermore, Dr. Huffman was able to circumvent many challenges especially during COVID-19, which was undoubtedly frustrating especially for attendings and trainees alike. Nevertheless, he persevered and sought ways to improve the fellowship. "COVID-19 made us creative about how we presented ourselves; we were able to put together videos from past fellows and do a better job showcasing the program than most fellowships in the country especially with such short notice."

Despite having over 100 peer-reviewed publications, multiple NIH grants, and outstanding surgical prowess, Dr. Huffman describes his biggest accomplishment as being a father of four children. He feels he is still striving to discover the balance in his life between his busy, robust academic career and family life. In the coming years, he is eager to spend time with his father, who still resides in Orlando, Dr. Huffman's hometown, taking walks and eating ice cream with all three family generations together. Meanwhile, he also looks forward to building high-quality specialized care in an untapped growing market in Florida and hopes one day to train international visiting surgeons in addition to creating a destination training location for Penn fellows. Humble, innovative, and caring, Dr. Huffman exemplifies what we all strive to be as orthopaedic surgeons and most importantly humans. It was truly an honor to work with him and he will be missed. Nevertheless, Dr. Huffman will always be part of the Penn family.

Reflections of a Chairman: What I Wish I Had Known Then That I Know Now

L. Scott Levin, MD, FACS, FAOA

One of my most avid hobbies is studying leadership. The windowsill in my office is filled with books on leadership, leaders and leading. The concept of being born a leader or evolving into a leader can be debated indefinitely. I believe that effective leaders continually work on improving their leadership capabilities and acquiring new skills that are needed to confront the constant challenges of their organization and their ever-changing environment.

Often, whenever there is a transition in leadership in a department, there is a period of uncertainty within the organization regarding the new leader. If the current leader has been effective, it is because he or she has built trust and gained the confidence of those that are led. For example, when I arrived as the new Chairman of Penn Orthopedics - I made it a point to meet the residents my first day on the job at 6 am. That day was July 1, 2009. Twelve hours later- at 6 pm I met with the faculty- in person. My discussion with the residents centered around my expectations of them with regards to professionalism and patient care. I insisted then- and I do to this day that *appearance matters*. They are required wear a clean white lab coat. All men must wear a tie and be clean shaven at all times. No beards allowed. While this surprised many- it set standards so that there would be no guesswork regarding my expectations. I spoke to the faculty and said this: "You do not work for me. My job is to work for you!" If I succeed in helping you fulfill your career goals- our team will succeed. I often say to a faculty member- at the scrub sink, in the hospital corridors or on rounds- "is there anything that I can do for you?" I believe that question is rarely asked to faculty in academic medical centers. Asking such questions is not enough. Following through on requests is what counts- and a rapid definitive response is better than a protracted waiting period for an answer that is nebulous. As a leader, you can either deliver or not deliver. If you cannot- share that you tried and what was requested cannot be delivered and explain why. That approach builds trust.

I will comment on five main topics that summarize the last 13 years at Penn. First- I'd like to comment on what I believe are ***our*** team's major accomplishments. There is no "I" in the word team. Our major accomplishments center around the people that we have recruited and developed. This includes our clinical faculty, our research faculty, our residents, fellows and administrative staff. When I arrived at Penn, there were not defined vice chair roles, which are essential in a highly matrixed organization. I immediately appointed Dr. Brian Sennett as vice chair of clinical operations. His keen understanding of our department at every level has been an invaluable resource for me personally and has accelerated our growth as a department. Recruitment of Dr. Kristy Weber also was a huge step forward in raising the bar of our academic mission as well as our commitment to diversity at every level. Dr. Weber's profile nationally and internationally has provided the foundation for us to create unprecedented opportunities for women, underrepresented minorities and those from the LGBTQ communities. Appointing Dr. Louis Soslowsky as the vice chair for orthopedic research was long overdue. I believe that the model he and I have established in academic orthopedics can be designated "best in show." Fiercely promoting translational research ultimately impacts patient care. As the responsibilities and intricacies of graduate medical education have exponentially increased, the need for a vice chair of education became apparent. Dr. Daniel Farber serves as vice chair of education. He has educational oversight of Penn Orthopedics and is supported by Dr. Cara Cipriano (Director of Medical Student Education) and Dr. Stephen Liu (Associate Residency Program Director). The number of fellow positions has increased over the years commensurate with our clinical volume and expansion of our faculty. Finally, with the support of the School of Medicine and the events that have occurred in our country over the last year or two- all of Penn Medicine has dedicated efforts to improve our institution's approach to diversity, equity and inclusion. Dr. Lawrence Wells is serving as vice chair of DEI until July 1, 2022 at which time a new Vice Chair will be named. His impact has been monumental.

Other accomplishments include establishing the Penn Medicine University City Musculoskeletal Institute, the Penn Orthoplastic Limb Salvage Center, the Penn Nerve Center, the Penn Human Performance Laboratory, the Penn Fresh Tissue Lab, the Penn Cartilage Center, the Penn VCA program and hand transplant program, and a combined and totally integrated Penn Hand Surgery Service (Orthopedics, Plastic surgery, Neurosurgery). These are new programs that have evolved over the last 13 years.

One of the key leadership principles is that leaders must lead from the front and not the rear. I've maintained an active clinical practice and take one week a call each month of the Children's Hospital of Philadelphia for pediatric microsurgical emergencies. The leader should never ask anyone that he or she leads to do something that they would not do. Being "in the trenches" with students, residents, fellows and faculty and performing surgery across our health system has provided "facetime" with our Penn orthopedic family. In fact, I recently signed on to be a VA staff physician to help with lower extremity amputation surgery if indicated for our veterans. I had previously served the VA WOC (without compensation) and will take a more active role at the VA in the future. I am a veteran and believe in the mission of providing the best care possible to our wounded warriors, and servicemen and women.

In anticipating the future needs and direction of the department, I believe it'll be essential that we create a Penn Orthopedic hospital to provide musculoskeletal care for the future. We already have architectural plans and renderings that connect our musculoskeletal institute to a 20-story building built on the corner of 38th and Market Street. This new inpatient home will provide care for adults as well as children. Discussions have taken place between CHOP, Penn Medicine and the Shriners hospital to create a new vision for pediatric care on our campus.

In addition to expanding our services downtown, it is clear with the shift from inpatient to outpatient surgery in specialties such as Spine and Adult Reconstruction that we will need to develop micro hospitals and expansion of our outpatient surgery facilities. We will expand to provide care where our patients live rather than have them come to us downtown.

My role in the future will be to serve as a cheerleader for Penn Orthopedics as well as a staunch supporter of my successor. One of the main strengths of Penn Medicine is our collaborative spirit and totally integrated model for academic medicine. While we may not know what the future holds with regards to value-based care, reimbursement, new technology and new methods for providing care to our patients, we know that we are as well prepared as anyone to meet the future head on, with enthusiasm and unwavering support for continued excellence and achievement across all missions.

Developing Resident Leadership Skills: Implementation of a Formal Leadership Training Curriculum

Matthew K. Stein, MD, Stephen R. Barchick, MD and John D. Kelly IV, MD

What is the purpose of leadership training during a five-year intensive process dedicated to training doctors in orthopaedic surgical expertise? We would argue that it is to improve the lives of patients, peers, and other healthcare professionals beyond our interactions in the clinic and operating room.

If one wishes to leave the planet better and implement true and lasting positive change, leadership skills are *essential*. The best intentions can languish if not coupled with a skillset which will bring worthy goals to fruition.

Some argue: 'leaders are born, not made.' This is not true. Indeed, some individuals possess innate talents that predispose to influencing others positively. However, a great body of research demonstrates that leadership skills can be taught, learned, and developed.[1]

Leadership skills are not only for the few. In fact, ***everyone*** can benefit from training in the principles, methods, and skills necessary to lead.

Effective leaders can turn a vision to reality, create positive cultures, and guide others to the realization of their full potential. These skills are necessary to become effective at work, at home and in the community. Take a moment and consider areas of dysfunction in your daily lives, whether it is a poorly run restaurant or an inefficient surgical suite, while there may be many contributing factors, there is undoubtedly some failure of leadership. Conversely, thriving offices, companies, and homes uniformly are the result of effective and principle-based LEADERSHIP. Leadership is not management. Managers do things right. Leaders do the right thing and can help others morph from 'good to great'.[2]

Whether providing direction to one's family, place of worship or community, leadership skills will permeate into all aspects of our lives.

The University of Pennsylvania Department of Orthopedic Surgery has a rich tradition of training future leaders in both academic and community practice settings. In order to ensure that our graduates were equipped to handle the challenges that the contemporary practice of orthopedic surgery entails, a 'Leadership Strategy Team' was assembled in 2017, consisting of Drs. Levin, Donegan, Kelly and DeMaio. We fully recognized that the University of Pennsylvania had access to the renowned Wharton McNulty Leadership Program, led by Mike Useem and Jeff Klein. Both Mike and Jeff immediately demonstrated their exceptional generosity and benevolence to help create the Michael P. Kelly Sr. Penn Orthopedic Leadership Academy.

Orthopedic Surgeons are Leaders Inherently

Orthopedic surgeons are leaders of the musculoskeletal care team in the clinic, operating room and research arena. Clinically, they are called to direct patient care as many treatment decisions are dependent on the surgeon's judgment. Surgeons must recognize that they are called to lead health care teams toward the singular goal of quality musculoskeletal care. Surgeons are not 'heroes'; they are 'healers' whom the health care team will look to for direction and guidance.

In surgery, Orthopedists are indeed the 'Captain of the Ship' when executing a surgical procedure. The Surgeon Leader will dictate the 'culture' of the entire operating room. The surgeon leader who treats staff with kindness and dignity and communicates effectively while not losing sense of purpose, will be rewarded with a sense of teamwork and cooperativity which will translate to excellent outcomes. Leaders create safe and secure environments where workers can let their God-given talents flourish. Fairness and honesty are the order of the day, and every worker knows that they will be treated justly and compassionately.

In the research realm, orthopedists are often called to lead clinical investigations to ensure relevance to patients. For example, if research is conducted on the biomechanics of an implant which is technically difficult to employ, it behooves the surgeon leader to inform the research team that the study of other more 'user friendly' implants would be more meaningful. By keeping the research collaborators in line with the clinically relevant aspects of the particular study, the surgeon may ultimately lead the way to the solution of an important clinical problem.

Life Skills

Noted leadership guru, Steven Covey[3] emphasizes that self-mastery must precede the ability to truly influence others. In truth, Covey has noted that one cannot effectively lead others until mastery over one's life is attained. If a life true to timeless principles such as honesty, integrity and humility is attained, one can proceed effectively to influence others. For instance, imagine someone with an extreme egoic need for approval. Such a person will be prompted innately to promote the 'popular' decision rather than execute the 'right' decision.

Covey elaborates on the 'habits' of proactivity, adherence to a mission statement (begin with the end in mind) and adoption of executing around priorities (putting first things

first) to gain true self-mastery. Then, and only then, is the ability to lead truly unleashed.

More importantly, self-mastery will greatly lessen the incidence of burnout, an all-too-common plague of our beloved vocation.

Indeed, the same virtues necessary for strong leadership are also essential for a peaceful, powerful, and integrated life. Psychologists for many years have noted that the most joyful and self-actualized human beings are also the most kind, compassionate and moral. Leadership skills are synonymous with 'life skills.'

The study and incorporation of effective leadership skills and traits will allow each of us to pursue lasting and meaningful self-growth.

Penn Orthopedic Leadership Academy

The Michael P. Kelly Sr. Penn Orthopedic Leadership Academy was conceived in the hope to teach tried and true principles of real leadership to residents, students, junior faculty and all interested members of the health care team.

A consortium of leaders from the Wharton School of Business, the Penn Perelman School of Medicine, industry, and sports convey to attendees' key principles necessary to lead others to a common good. Chief elements of the curriculum are lessons in integrity, selflessness, decisiveness, organization, benevolence, vision, ingenuity and innovation–skills which all exemplary leaders share.[4] The Academy is predicated on four unique and synergistic programs:

1. ***Leadership Retreat***
   Every spring, residents are treated to a day long program administered by professors from the Wharton School. A rotating curriculum has been devised covering diverse aspects of leadership development including consensus and team building, negotiation, integrity emphasis and resilience training.
2. ***Individual Coaching***
   PGY-4 residents are assigned a personal Wharton professional coach, who meets with the assigned resident regularly. The resident and his/her mentor discuss life management, decision making and advice on career building.
3. ***Leadership Fellowship***
   Each year four Penn Ortho Leadership Academy Fellows are chosen by committee and enjoy a lifelong curriculum of coaching, didactic training from an assigned mentor, and advice on a yearlong project. Projects are directed at improving the culture of the program and improving the quality of life of current residents. This year's projects include a dedicated course on mindfulness training, a treatise on the value of a clinical database, an examination of communication deficiencies during surgery, and an evaluation of the self-awareness of residents.
4. ***Leadership Curriculum***
   Dedicated time has been apportioned to lectures devoted to leadership development as well as a leadership directed journal club. Articles and books ranging from self-help to the establishment of a healthy culture at work are discussed in detail.

The responsible practice of orthopedic surgery as well as effective living demands leadership acumen. It will become a fruitful exercise to study what makes great leaders great and implement these skills in daily practice.

In conclusion, the Michael P. Kelly Sr. Penn Orthopedic Leadership Academy is dedicated to developing the most effective and peaceful next generation of leaders. Armed with superlative orthopedic training, coupled with priceless leadership skills, University of Pennsylvania Orthopedic Graduates are poised to effect positive quantum change and effectively lead others in our most beloved vocation.

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Lessons as a Surgical and Leadership Trainee

Lauren M. Boden, MD, David P. Falk, MD, Gregory T. Minutillo, MD, MPH, and Matthew K. Stein, MD, MS

Introduction

When thinking of leaders, who comes to mind? Political leaders? Department heads? An attending? A chief resident? The head nurse? Teams and leaders are all around us. As physicians we are all leaders. Our patients look to us for help as we fix or mitigate their concerns. In the operating room and clinic, we lead a team of ancillary personnel to accomplish our goals of improving the lives of our patients.

Everyone on the team has a role and an opportunity to lead. Leadership is a skill, and just like the skills of taking a good history, completing a good exam, or completing a surgical procedure require training and practice, so too does leadership. The formal leadership training provided by the Penn Orthopedic Leadership Academy is designed to jumpstart those leadership skills with one on one mentoring, completion of a leadership project, and conveyance of knowledge gained to our peers.

Project Summaries

Lauren Boden

Physician burnout and stress are prevalent within the medical and surgical communities. Mindfulness techniques have shown benefits in anxiety, stress, and burnout, however traditional techniques are time intensive and not practical for use by surgical residents. With the mentorship of Drs. Mike Useem, David Casper, and John Kelly, we have initiated a pilot study for an application-based Mindfulness program for orthopedic surgery residents. The app is customizable to the individual resident and can be used at their convenience. We will measure burnout, stress, and anxiety over the course of an 8-week program that culminates in a mindfulness retreat. If successful we hope to expand the program in the future.

Dr. Useem's expertise with leading through disruption has helped reinforce the qualities of a good leader and how leaders outside of medicine approach problems. Working on identifying a common goal and setting a leadership style has increased my leadership skills in times of adversity.

David Falk

Through my project working with Dr. Preston Cline, Co-Founder and Director of Research and Education at Mission Critical Team Institute, along with othopaedic trauma attendings Dr. Samir Mehta and Derek Donegan, we identified that surgical residents transition from the controlled environment of medical school to the chaotic environment in the operating room without much preparation for the transition. Instead of learning in lectures and the library, residents take on a more apprenticeship-based role with the goal of mastering technical skills. Given the new environment and new goals, we are working to identify possible solutions to improve resident understanding of this new learning environment to promote more rapid skill acquisition and growth.

Preston's experience working with professional athletes and Navy SEALs provides a unique perspective, and one that I never would have been exposed to without the Wharton Leadership Program. Beyond the bounds of our project, working with Preston has allowed me to get a better understanding of how high-performing individuals outside the medical field communicate and lead in high pressure situations.

Gregory Minutillo

Penn does a large volume of hip and knee arthroplasty. One would think that we had an institutional registry in order to study joint replacement, but we do not. My project was to see if there was an association between an institution having a joints registry and the number of publications it produced in the journal with the highest impact factor over the last decade.

We looked at every arthroplasty publication in the last 10 years of JBJS and looked at which institution each publication came from. We then surveyed each institution to see which ones had joints registries and which did not to determine this association. After analysis, it was demonstrated that institutions with a joints registry published more than those without.

The motivation for this study was to initiate a joints registry at Penn and show that it could add to our ability to produce more research.

Matthew Stein

The question of accurately knowing oneself, and how to obtain that self-knowledge if it is lacking stretches beyond the field of orthopaedics and medicine. Yet, as we learn more about the deficiencies of physicians' ability to communicate with patients, coupled with the well documented issue of burnout, a comingling of ideas began to bring forth the concept of self-awareness and its benefits into medicine. Could it be our lack of self-awareness leads to more complicated and frustrating encounters with patients and colleagues? That our inability to learn what we truly value and discover what drives us leads

to burnout, lack of thriving, and overall unhappiness. Inspired by and in collaboration with Tasha Eurich, the author of the book *Insight*, we developed a study to assess self-awareness in residents.

Our main study goal was to determine if residents own perception of themselves, their internal self-awareness, reliably matched up with how others perceived them. Secondarily, we wanted to assess if this correlated with a residents' feeling of thriving in life and ability to avoid the well-known symptoms of burnout. This was made possible by Dr. Eurichs' validated self-awareness survey.

This idea was important to me as I believe the problem of burnout has been very well described, and yet there are still so few solutions that have been discovered. My hope is to carve a new path towards physician self-realization in the hope that we become purposeful and joyful in the challenging path we have chosen.

Conclusion

It has been an honor and a privilege to be selected as the inaugural Penn Ortho Leadership Academy fellows. We would like to thank our formal mentors Dr. John D. Kelly IV, Dr. Derek Donegan, Dr. Marlene DeMaio, Mike Useem, and Jeff Klein along with the additional department members who assisted with our projects for their support over the last year. The lessons learned from our mentors and projects will help us be successful leaders now and throughout our careers. Choosing to develop these skills while concurrently being a surgical trainee has helped highlight the fact that you can lead from any position on a team. Leading up is just as important as leading from the top and can be an effective way to create positive change. We are excited to see where this program goes in the future and hope to see a more formal leadership curriculum open to all residents.

A Decade-long Journey to the Gender Tipping Point and Beyond in the Penn Orthopaedic Program

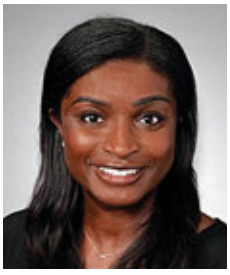
Kristy Weber, MD

The Department of Orthopaedic Surgery at the University of Pennsylvania (Penn Ortho) has a long history of women as clinical and scientific faculty, residents and leaders. However, until recently, it has not achieved a critical tipping point of female faculty and residents. Thirty percent is the number generally agreed at which an underrepresented group changes the conversation in a department or organization. With our 2022 resident class, including five women of eight residents, we are incredibly proud to have reached 38% (16 of 42) female and SGM residents at Penn Ortho (Figure 1). As a department, we value diverse voices and consider ourselves a leader in gender diversity in the areas of clinical practice, basic science research, and residency training.

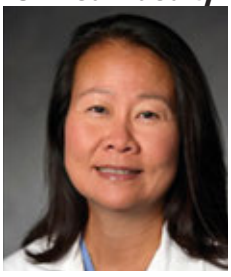
Dr. Mary Ann Keenan (Chief - Neuro-Orthopaedics–retired 2012) was the only female clinical faculty at Penn during this millennium until Dr. Wen Chao (Foot/Ankle) was recruited to the practice in 2012 and Dr. Kristy Weber (Orthopaedic Oncology) was recruited as Vice Chair of Faculty Affairs in 2013. Since that time, Dr. Marlene DeMaio (VA chief) and Dr. Kate O'Connor (Foot/Ankle) were recruited and subsequently moved to other cities. More recently, seven women have been recruited to the clinical faculty at Penn and the Children's Hospital of Philadelphia (CHOP) including Dr. Susan Harding (Trauma–2019), Dr. Kathleen Maguire (CHOP Sports–019), Dr. Hannah Lee (Hand–2020), Dr. Casey Humbyrd (Chief, Foot/Ankle–2021), Dr. Cara Cipriano (Chief, Orthopaedic Oncology–2021), Dr. Christine Goodbody (CHOP Deformity–2022), and Dr. Lorraine Boakye (Foot/Ankle–2022). (Figure 1).

Growth of research faculty has been steady over time with six funded faculty members leading robust musculoskeletal research programs including Dr. Sarah Gullbrand (degenerative disc disease), Dr. Sherry Liu (bone aging, diseases and therapies), Dr Foteini Mourkioti (muscle homeostasis and regeneration), Dr. Ling Qin (skeletal development, homeostasis, aging, and disease, Dr. Ernestina Schipani (cartilage and bone development, hypoxia) and Dr. Eileen Shore (rare genetic diseases of heterotopic ossification) (Figure 1).

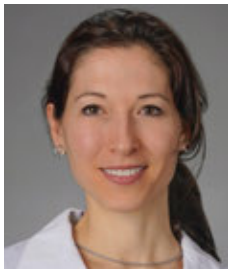
Clinical Faculty



Lorraine Boakye, MD
Assistant Professor
Foot & Ankle Surgery



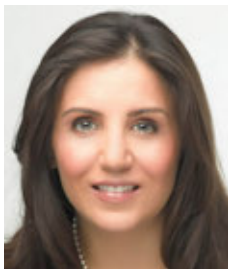
Wen Chao, MD
Penn Medicine Clinician
Foot & Ankle Surgery



Cara Cipriano, MD, MSc
Chief, Ortho Oncology
Associate Professor

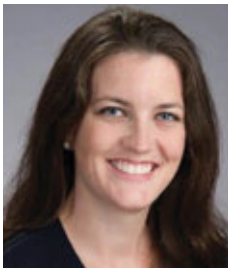
Christine Goodbody, MD
Assistant Professor
Pediatric Orthopaedics

Susan Harding, MD
Penn Medicine Clinician
Orthopaedic Trauma

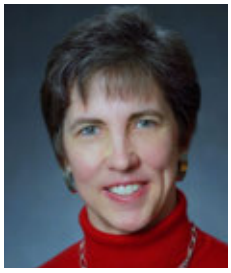


Casey Jo Humbyrd, MD, MBE
Chief, Foot & Ankle Surgery
Associate Professor

Hannah Lee, MD, PhD
Assistant Professor
Hand Surgery



Kathleen Maguire, MD
Assistant Professor
Pediatric Orthopaedics



Kristy Weber, MD
Vice Chair,
Faculty Affairs Professor
Orthopaedic Oncology

Laboratory Faculty

Sarah Gullbrand, PhD
Assistant Professor

X. Sherry Liu, PhD
Associate Professor

Foteini Mourkioti, PhD
Assistant Professor

Ling Qin, PhD
Associate Professor

Ernestina Schipani, MD, PhD
Professor

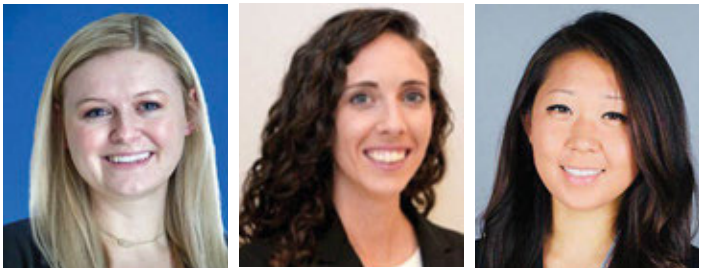
Eileen Shore, PhD
Professor

Current Orthopaedic Residents & Fellows

Caroline Granruth, MD
PGY-1

Erin Kelly, MD
PGY-1

Sand Mastrangelo, MD
PGY-1



Ashleigh Bush, MD
PGY-2

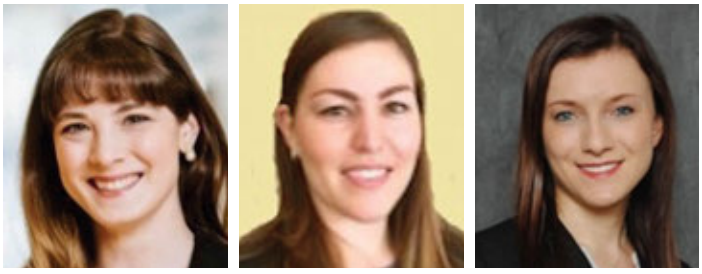
Kathleen Collins, MD
PGY-2

Dainn Woo, MD
PGY-2

Kendall Masada, MD
Research Year

Kelsey Young, MD
PGY-3

Lauren Boden, MD
PGY-4



Kelsey Bonilla, MD
PGY-4

Viviana Serra Lopez, MD
PGY-4

Sarah Blumenthal, MD
PGY-5

Agnes Dardas, MD, MSc
PGY-5

Liane Miller, MD
PGY-5

Jamie Grossman, MD
Sports Fellow

Incoming Orthopaedic Interns

Anna Blaeser, MD

Rachel Flaugh, MD

Lisa Friedman, MD

Emily Stabnick, MD

Alyssa Thorman, MD

Figure 1. Composite of the women and gender nonbinary residents and clinical/scientific faculty at Penn Ortho and the Children's Hospital of Philadelphia (CHOP)

The female faculty and residents organize a regular "Ortho Gals Night Out" to gather socially and create an informal forum to discuss professional and personal topics as they relate to orthopaedic surgery (Figure 2). They will be welcoming the five new female interns in June 2022. Penn Ortho will wish the graduating class well as they move on to fellowship training. Of the chief residents in the graduating class, two of the three were female. Penn Ortho also supports the Perry Initiative (www.perryinitiative.org), regularly hosting programs for female/SGM high school and medical students interested in orthopaedic surgery. Our recent Spring 2022 Perry Initiative program hosted medical students from six surrounding medical schools (Figure 3).

There has been an intentional effort to recruit senior women clinical faculty leaders over the past decade. Creating a more gender diverse department benefits the care of patients, role modeling for residents and students, and recognition of Penn Orthopaedics within the institution as well as in national organizational arenas. Penn and CHOP Ortho boast the highest number of faculty over the years who have served as RJOS presidents (Figure 4). Dr. Casey Humbyrd serves as a Division Chief as well as being visible at the AMA, the AOFAS Board of Directors and directs the Penn Surgical Ethics and Health Policy program. Dr. Cara Cipriano serves as a Division Chief and is visible at AAHKS, MSTS and is transforming the experience of the Penn medical students as they rotate through the Department of Orthopaedics. Dr. Kristy Weber serves as Vice Chair of Faculty Affairs and has been visible as past president of AAOS, MSTS, RJOS and current president of the International Orthopaedic Diversity Alliance (IODA).

The faculty and leadership in Penn's Department of Orthopaedic Surgery is committed to mentoring all residents

Figure 2. Ortho Gals Night Out 2022.

Figure 3. Perry Initiative Program at Penn (April, 2022) **3A.** Medical student program **3B.** Dr. Kendall Masada (R3) instructing on placement of a femoral nail.

and faculty and promoting their diverse careers. L. Scott Levin, MD, FACS, Chairman, Department of Orthopaedic Surgery, leads this commitment. He is visibly supportive of female and SGM members of the department and is a member of RJOS and IODA. The department's value of diversity, equity, and inclusion is reflected in the 5-year Penn Orthopaedics

Figure 4. Penn and CHOP past presidents of the Ruth Jackson Orthopaedic Society (RJOS). Dr. Mary Ann Keenan (1990), Dr. Helen Huntsman - CHOP (1988), Dr. Kristy Weber (2015) and Dr. Marlene DeMaio (2019).

Strategic Plan, which focuses on culture as it relates to these issues. We are proud of our reputation for gender diversity at Penn Ortho and acknowledge that we have more work to do to create an inclusive and equitable environment for everyone. My personal hope is that we intentionally make decisions over the next decade to create a culture of inclusion for every member of the Penn Ortho community; one where individuals have a sense of true belonging and being valued for their unique identities.

Training Tomorrow's Physicians: Undergraduate Medical Education in Orthopaedic Surgery

Cara A. Cipriano, MD, MSc

It is a great honor to return to Penn more than fifteen years after I was introduced to the field of Orthopaedic Surgery here as a medical student. Since then, I've been fortunate to participate in medical education in various roles at different institutions. Based on these experiences, I have developed a vision of medical education in which teaching, mentorship, and inclusion are actively supported throughout our department. As the Director of Undergraduate Medical Education, and with the collaboration of our dedicated residents and faculty, I am working to achieve this by focusing on four goals:

1. ***Provide all students with a fundamental understanding of musculoskeletal diagnosis and treatment.***

   Musculoskeletal complaints are widespread and common, so all physicians should graduate with a basic understanding of conditions such as fractures, degenerative disease, and nerve compression syndromes. In order to accomplish this goal, we have increased our department's presence in the medical school curriculum through faculty and resident participation in gross anatomy lab, lectures, and problem-based learning sessions. We are further collaborating with the School of Medicine on initiatives such as the Anatomy Task Force, which is dedicated to innovating and integrating anatomy throughout the four years of medical school.

   As every Penn Med student participates in the one-week Ortho 200 course, we have focused on this opportunity to teach them the fundamentals. The clerkship now features a problem-based learning curriculum, developed by rising PGY5 Ryan DeAngelis, with cases selected to introduce essential musculoskeletal concepts.

   In the next academic year, my goal is to broaden our offering of musculoskeletal electives. The current Ortho 300 courses are all sub-internships: focused, immersive experiences intended for students who have decided to apply for orthopaedic surgery residency. The new electives will be designed for students who wish to gain more exposure to musculoskeletal medicine as they prepare for careers in specialties such as family medicine, emergency medicine, and pediatrics.

2. ***Prepare students to apply, match, and succeed in orthopaedic*** surgery residencies.

   With the increasing competitiveness of our specialty, students benefit not only from clinical teaching, but also from research opportunities, guidance about the application process, and general mentorship. The Ortho 300 sub-internships are excellent opportunities for students to experience a subspecialty in depth, develop relationships with residents and faculty, and gain support for their application. Additionally, in partnership with the Leo Leung Orthopaedic Society, we have started holding group advising sessions for students at critical times during the application process. Both faculty and residents participate in these gatherings, lending valuable perspectives on topics from selecting an away rotation, interviewing, and ultimately forming a rank list. Next, we will be developing a formalized near-peer mentoring network for our students.

3. ***Promote an inclusive culture.***

   We are all acutely aware of the staggering lack of diversity in the field of orthopaedic surgery. As the physicians of the future, medical students represent an opportunity to diversify the pipeline of orthopaedic surgeons. A welcoming attitude and inclusive culture are needed to help minority students feel that their unique attributes are valued. Given the widespread stereotypes about orthopaedic surgeons, students come to medical school with formed opinions about our field and whether they fit (or don't fit) within it.[1] As educators, we have the opportunity and responsibility to reverse these preconceived notions through our interactions with the students.

   Our increased presence in the pre-clerkship curriculum, as described above, is an opportunity for us to demonstrate the diversity within our department as well as an inclusive attitude toward students. We are also fostering extracurricular engagement through the Leo Leung Orthopaedic Society and other student interest groups. So far this year, members of our department have collaborated with the Elizabeth Blackwell Society, the Association of Women Surgeons, the Agnew Society, and Penn Global Health. Our interactions with students who have not already selected orthopaedic careers is especially critical, as this will help counteract stereotypes and attract more diverse students to our field.

   Lastly, with support from the department and the School of Medicine, we have created the Inclusive Orthopaedics Scholarship at Penn. Every year, this program will provide three visiting students from other medical schools with funding to offset the financial

burden of an elective rotation at Penn. Applicants are selected by members of the Culture Committee, with approval from the Vice Chair of DEI, on the basis of academic achievement and the unique perspectives that they would bring to our program. We are pleased to report that three very accomplished students have been selected as the inaugural Inclusive Orthopaedics scholars.

4. ***Develop residents as educators.***

For medical students, residents are compelling role models and valued teachers. Many residents are passionate about education, leading them to consider academic careers. The medical educator track, which is being introduced in 2022, is an opportunity to develop the skills and experience needed to launch a career in education. Residents will become familiar with principles of adult learning, as well as develop and execute research or quality improvement projects related to medical education. They will graduate with an understanding of how to advance in this career path and a portfolio that will make them competitive in the academic job market. They will also be better prepared to evaluate opportunities, negotiate for support, funding, and protected time, and begin practice with an intentional focus.

Developing resident educators will benefit medical students on many levels. The insight, ideas, and dedication that our residents already contribute will only be increased with the support of the Med Ed program. Moreover, the projects they undertake will grow the educational impact of our department on an annual basis.

As faculty and residents, we interact with medical students at a time when they are encountering their first patients, discovering the field of orthopedics, and deciding on their future careers. For many of them, this may be their first exposure to surgery: the process of physically opening the human body to address a problem. They often bring a beginner's mind and a sense of awe for the world that has become routine to us over the years. Teaching them is a refreshing reminder of that fascination, and an opportunity to pay forward the gifts we received from our own educators and mentors.

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Expansion of a Healthcare System: Establishing Orthopaedic Care at CHOP's New Hospital in King of Prussia

John (Jack) Flynn, MD

Over the past 25 years, CHOP has become a victim of its own success. When I joined CHOP Orthopaedics in 1996, it was the 4th best pediatric orthopaedic practice in the Philadelphia area—far behind DuPont/Nemours, and weaker than St. Christopher's and Shriner's Hospital of Philadelphia. Our practice was small, local, and financially fragile; it was supported mostly by part-time faculty. But, at that moment in CHOP's history, the first of two visionary, transformative strategies were underway.

The first strategy was surrounding CHOP with a large community network of pediatricians—the Kid's First practices. It was a win-win, because CHOP got referrals, and the large, connected network of referring primary care doctors benefitted from CHOP's scale, at a moment in American healthcare history when "managed care" was transforming healthcare finances, and crushing many 20th century private practices. CHOP's network grew the hospital far past Nemours and St. Christopher's, and allowed many specialties like Orthopaedics to thrive.

The second strategy led to even more explosive growth at CHOP, and the need for The King of Prussia Hospital (KOPH). CHOP's clinical and business leaders began to recognize a transformation of America's pediatric healthcare in the early 21st Century: the need for tertiary/quaternary pediatric hospitals to care for the sickest of the sick, and the rarest of the rare conditions impacting children. Although Boston Children's had a bit of a head start, CHOP quickly caught up, attracting regional, national and international families with programs like The Center for Thoracic Insufficiency, The Center for Fetal Medicine, the Brain Tumor program, and many medical programs. These were backed by huge science investments, attracting hundreds of physician thought-leaders in many specialties. The rapid clinical growth in the past 15 years also created a hospital capacity crisis at CHOP: the inpatient census was often beyond 100%, elective admissions were halted and surgery cancelled. Post-ops sometimes spent their whole inpatient stay in the PACU. Meanwhile, not a single new inpatient OR room has been built since 2009. CHOP built some ASCs, but that was no help for the explosive growth of programs in Orthopaedics, Neurosurgery, or Cardiac Surgery. A victim of its own success, CHOP leadership recognized a new hospital was needed—a pediatric hospital with a "community model" that could offload primary and secondary care to make room for the most complex care at the Philadelphia Campus.

In early 2017, I was asked by the Chief of Surgery at CHOP to lead all the surgical services at the new KOPH. There was excitement about the new capacity - new ORs, ICU and inpatient beds, etc. But there was great concern among CHOP surgical leaders about the community model: most had never practiced in a hospital without residents and fellows on call. How could this new APP workforce possibly handle all the consults in 6 different surgical specialties? How will all the fracture reductions and other ED procedures be performed safely? Who will assist in the ORs? To learn and be able to respond to these concerns, I did lots of research. I traveled to Texas Children's Hospital, which has 2 community hospitals like KOPH. I learned how to train APPs in pediatric surgical specialty care, make a call schedule, and create lines of communication with on-call teams at the main hospital to assure consistent standards of care. CHOP hired this APP workforce in 2021, and I engaged Bev Teti and other surgical APPs to train the workforce. Our rotating residents, working with Todd Lawrence, did an incredible job with fracture training. Dr. Lawrence did a "Board Exam" of every APP in the Fall of 2021 to assure they met standards. The APP team was ready for KOPH Opening Day on 1/26/22, and the results have been outstanding. Open only 2 months, KOPH is already at 80% capacity, with more than 100 children/day seen in the ED. It is attracting families from all over Pennsylvania, and even Delaware and New Jersey.

In addition to the unfamiliar community APP model, the second big challenge has been covering two hospitals. CHOP's explosive growth is a stress to our culture in Orthopaedics. When I arrived in 1996, I was the 3rd full-time orthopaedic surgeon—now we have 28 Faculty members, including 18 full-time surgeons. We have to cover 8 sites in PA and NJ, and now we suddenly cover a whole new hospital, meaning a completely separate attending on-call schedule. We were already stretched thin, and it was challenging our unity and close "family" culture. Necessarily, some surgeons had to move most of their practice to KOPH to free OR space in Philadelphia for cases that cannot yet be done at KOPH: spine, CP, tumors, etc. There was a risk of creating "two practices", which would be unacceptable. I made these issues the focus of our FY22 Strategic Plan and the theme of our annual Faculty Retreat. I appointed Alex Arkader as our new Director of Culture, with funding for happy hours and dinners, CHOP Ortho swag, etc. Our VP in 2020, Professor Covid-19 (Wuhan, China), taught us many ways to stay more connected virtually. Our Wednesday morning case conference will now always be hybrid, allowing input from Faculty covering KOPH and other satellites. Our monthly CHOP Ortho Newsletter is a virtual way to celebrate our people with pictures, stories, and shout-

outs for accomplishments. Much more work is needed, but the progress is palpable on our team.

Enlightened humans recognize that the only constant is change; modern American healthcare is particularly impermanent. Clinical leaders need great vision to see and plan for that different future, along with the humility to understand we can't precisely predict it. We need the compassion to understand that the future will hurt some colleagues while helping others. When systems get bigger, healthcare workers become more anonymous. The risk is a "plug and play" model with interchangeable "providers." We won't let that happen in CHOP Ortho, even though we are 6x bigger than when I arrived. We will never forget that great healthcare is about the people, not the buildings. We must keep our workforce happy, engaged, inspired and appreciated. It's a never-ending battle, but one that is worth the huge time, energy and money needed to fight it.

Building a Young Adult Hip Preservation Center: Reflections and Lessons from the Last 13 Years

Wudbhav N. Sankar, MD

In 2009, we established the young adult hip preservation program at the Children's Hospital of Philadelphia, which later became intimately associated with the hip preservation center at the University of Pennsylvania. We've learned a lot through the process, and the following are some thoughts and reflections on our journey thus far.

Have a Vision

Before you can build anything, you have to know what it is you want to build. This seems obvious but too often we jump into action planning without considering the overall framework and direction. Starting a clinical center is no different. As we developed the Young Adult Hip Preservation Program at CHOP and later the hip preservation center at Penn, we needed to "begin with the end in mind". We sought to develop a "one stop shop" for pediatric, adolescent, and young adult hip disorders, where patients from all backgrounds would be welcomed, appropriate diagnostic work-ups could be conducted, targeted and effective treatment could be administered, and patients could be followed long term to gauge the real outcomes of our work. We wanted to develop a national reputation that drew patients from beyond the local region. From start to finish, we obviously wanted patients to get excellent clinical care. But rather than just performing high quality surgery, we wanted to deliver a comprehensive clinical experience that was rewarding to the patient.

In 2009, the field of hip preservation was fledgling (and some would argue it still is). This represented an opportunity but also a concern. A bit like the Wild West, lots of surgery was being performed for variable indications and many surgeons were in the steep part of their surgical learning curve both in the region and nationally. In contrast, we were committed to providing evidence-based care whenever possible, and principle-based care in situations where high quality data was lacking. Furthermore, we wanted to both direct and contribute to evolving research in the field with the goal of elucidating hip pathophysiology, clarifying surgical indications, refining surgical technique and optimizing patient outcomes.

Know the landscape

When you're starting from scratch, you need to know the environment. As I had trained in the area, I had some pre-existing sense of the market. I was hopeful that CHOP and Penn would support the programmatic development, but recognized that there are several other health centers in the region that also desired to care for some of these patients. From the start, we presented our center not as a threat to local surgeons, but rather as an outlet for challenging clinical situations. We worked hard with our marketing and public relations team to get the message out that we would accept anything and everything regardless of insurance status, social situation, or medical complexity.

Primarily centered at CHOP, especially in the early years, one of our biggest challenges was changing the perception that CHOP was just for kids. This represented a real paradigm shift. Certainly, the precedent had been somewhat established, with many congenital cardiac patients continuing their care at CHOP well into middle age, but seeking out new patients who had already reached adulthood and getting them to come to CHOP for the first time was totally different. Again, we worked tirelessly with our marketing team to try (at that time) a novel strategy for a children's hospital. Instead of targeting referring physicians (i.e. pediatricians), we recognized that the target population (men and women in their 20s and 30s) would certainly not be seeing a pediatrician and would likely not even have a primary care physician. Instead, we devoted the limited resources afforded by the general orthopaedic division at CHOP to create a high quality patient centered video that was pushed out through YouTube and social media streams in an effort to reach patients directly. In addition to a more modern advertising campaign, we also needed to change the culture within the walls of CHOP itself. This started with phone schedulers who were used to turning away adults and extended to front desk staff who were unfamiliar with a thirty-year-old woman arriving without a child. It was a slow and pain-staking process at times, but eventually treating adults became well accepted at CHOP. The care of older adults with medical comorbidities was greatly improved when the partnership with Penn was strengthened several years ago so that high quality services could be provided at both centers.

You're only as good as your team (so collaborate)

A single surgeon does not make a center, regardless of the talent or the dedication that he/she may have. In order to deliver high quality clinical care and perform meaningful investigations, you need a team of professionals. As the old adage says, "it takes a village…" In order to build a great team, you need to develop personal relationships. This requires foresight, planning, direct communication, and thoughtful follow-up. In the early years we had several in-person meetings with physical therapy, inpatient nursing, anesthesia, radiology, and sports medicine. We identified champions in each area who would be invested in developing care

pathways, imaging protocols etc, and we took care to cultivate these relationships by returning gratitude and including the wider team in publications. Within the orthopaedic realm, developing expertise at the physician assistant and nursing level is crucial to providing an outstanding patient experience. The more knowledgeable and experienced the entire care team, the safer and smoother the clinical course. As we grew, we enlisted a nurse navigator who could facilitate out of state referral—this was another key step in building a true national reach. Under the leadership of Jack Flynn, MD and L. Scott Levin, MD, the relationship between Penn and CHOP was strengthened which allowed improved partnerships with the likes of John Kelly, MD and Kate Temme, MD and others who had been providing excellent clinical care within the University of Pennsylvania Health System for years. For those patients who were no longer amenable to hip preservation, we enlisted the expertise of the adult reconstruction faculty at Penn. Neil Sheth, MD in particular took special interest in the care of the very young patients who required total joint arthroplasty.

On the clinical research front, we were invited to join high caliber national research groups like ANCHOR, which improved our capacity for prospective multi-center research. It was important to represent CHOP and Penn at these meetings to establish us as a legitimate center of excellence. Locally, our clinical collaborations organically supported the development of multi-disciplinary research. Working with radiology, anesthesia, and Penn engineering provided opportunities to publish on modern imaging techniques, optimized recovery pathways, and anatomic modeling. Again, it takes a village.

Keep one eye on the future

Any great clinical center needs to evolve with the times and expand its clinical reach, while keeping an eye towards the future. By maintaining our commitment to clinical research and our presence on the national stage, we sought to keep CHOP/Penn on the leading edge of the modern hip preservation movement. Several years ago, we recognized the growing trend of hip arthroscopy as the primary surgical modality for femoroacetabular impingement and recruited Kathleen Maguire, MD to CHOP to provide additional expertise in this area. Along with John Kelly, MD, and Charles Nelson, MD this expanded our ability to provide arthroscopic services to adolescents and young adults at both centers. In 2019, we were able to recruit Chris Anthony, MD to join the faculty as the co-director of hip preservation at the University of Pennsylvania. Chris brought an impressive research pedigree along with outstanding clinical training at University of Iowa (residency) and Washington University in St. Louis (fellowship). Since his arrival, Chris has greatly expanded the clinical volume in hip preservation with skills in hip resurfacing, hip arthroscopy and open hip preservation.

Reflecting back on 13 years, it's amazing how far we've come and how much we've grown. While we've had some success, we remain restless to do better. Future goals include improved biomechanical modeling and potential navigation for hip osteotomies—and of course clinical expansion. The village is strong, and so is the future of the hip preservation program at CHOP and Penn!

Serving the Community: Experience Establishing an Orthopaedic Clinic for Underserved Patients

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Exposure to a wide variety of pathology and a diverse patient population is essential in any medical training program. In the Department of Orthopaedic Surgery at the University of Pennsylvania, we are fortunate to have access to both. However, there is still a large population of underserved patients in the surrounding area who do not have access to routine medical care; these patients often present to our Emergency Department (ED) where it can be challenging to find a reliable and expedited way for them to obtain the necessary follow-up and care. In addition, there are patients who are referred for non-urgent orthopaedic evaluation and for multiple reasons are not able to establish care. Seeing this need, orthopaedic surgery residents from the class of 2021 established a clinic where those in need of orthopaedic care could be evaluated and directed to the appropriate channels for care.

In 2016, Dr. Jon Morris, a general surgery attending at Penn, along with a group of residents launched the Center for Surgical Health (CSH) to help vulnerable patient populations in Philadelphia gain access to surgical care. One of the community centers CSH works with is Puentes de Salud (Puentes), which provides primary and specialty care to the Latino immigrant population in South Philadelphia. Several surgical specialties had already established clinics in this setting, and this is where Penn's Orthopaedic Surgery Department joined in the efforts to support vulnerable communities in our area.

In the Fall of 2020, Penn's Department of Orthopaedic Surgery began to have monthly clinics. Through these clinics, residents had a chance to evaluate patients under the supervision of an attending and develop an individualized treatment plan. To this date, 30 patients have been evaluated at the orthopaedic surgery clinic at Puentes, and 13 have undergone surgical intervention, while the remaining patients have either been treated non-operatively with appropriate follow-up or are in the process of applying for emergency medical assistance (EMA).

It is worth mentioning that none of this is possible without a strong support team. Puentes and CSH are supported by an incredible group of medical students that serve as personal patient navigators (PPNs) and assist in various tasks from helping patients apply for EMA to accompanying patients to their medical appointments and surgeries. In addition, an integral part of the success of this program has been our faculty's unwavering support in helping us care for these patients.

Our experience at Puentes has helped us hone many of our skills including physical exams, identifying surgical indications, and developing treatment plans. We have been fortunate to be exposed to the complex social needs that are sometimes required to get patients the care they need. This may range from coordinating childcare and transport so patients can attend appointments, to providing translators to help patients with paperwork. The clinic at Puentes de Salud has also become a way for the orthopaedic department to provide follow-up for the uninsured patients who we have seen in the ED. In addition, we further develop our teaching skills by interacting with the medical students that serve as PPNs while we evaluate the patients.

The most important aspect has been gaining the trust of a new patient population, who we hope to serve for years to come. Future directions include expanding the number of patients we reach at Puentes and establishing similar free clinic models in other communities in Philadelphia.

We are grateful for the support of the Penn community and the orthopaedic surgery leadership in establishing and maintaining this clinic.

Health Policy: Current Issues and Orthopaedic Surgeon Involvement

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In any game, the agreed-upon rules are of prime importance in the play and final outcome. In Monopoly, for example, will you get an extra $500 bill for landing on free parking, or just the taxes that have collected? Life is but a game. In healthcare, the agreed-upon rules come from our government, our payers (both federal payers and the private payors that manage the vast majority of payment transactions), medical interest groups deciding on codes and coding packages, hospitals, and providers.

Before dice are rolled in a board game, presumably, all players agree to specific rules. But when starting a medical career, surgeons assume that because they are entering the game late, the rules are set in stone, and they must be followed without question or modification. They are wrong, notwithstanding the reality that there are a trillion other important things competing for a young surgeon's focus, including actual patient care

Health policy is the perpetual discussion of the rules. Nothing is set in stone. Other superfluous stakeholders chronically debate and change the rules. Without surprise, the participants in those discussions benefit. And that benefit comes at the expense of the players absent to that discussion.

Perhaps you have remained absent from health policy discussions. If so, you are playing in a game that is designed for you to lose, to become burned-out, to not shine in the craft you invested 10+ years to hone. Voting is not enough; we have seen broken promises and failure of relief from both major political parties. A quiet wheel will not get greased.

But the fix can be easy. Involvement can be as simple as financially supporting your representatives to these discussions. Contributing to the Orthopaedic Political Action Committee (PAC) is a bare minimum (stop reading this and do it now!). The trial lawyers mobilize PAC support at nearly 100% participation; hospitals and insurance companies do as well. Orthopaedic surgeon participation hovers between 20-30%.

Deeper involvement in health policy generates even deeper effects. Surgeons should meet and support their elected officials and share stories of the incredible improvements in patients' lives. Encourage patients to champion the treatments that keep them mobile. Go to Congressional fundraisers (the PAC will pay your way) and build meaningful relationships that you can call upon later. Join your surgical society trips to Washington DC to deliver clear and simple asks of your representatives. We are the experts in musculoskeletal care and elected officials need access to our expertise.

Today's health policy discussions, like yesterday's and tomorrow's, revolve around money, either directly or indirectly. Top on the minds in Washington, DC lives the persistent and now predictable *annual* assault on payments for our work. Year-on-year, the complexity and challenges of orthopaedic surgery are consistent. If anything, the work gets harder as we raise the bar incrementally and accept fewer complications, fewer dissatisfied patients, and fewer outliers. Despite this, and despite being successful at reducing complications and dissatisfaction, and while dramatically improving the quality of life and functional productivity of patients, we get paid less today than yesterday.

Surgeon fees account for about 5% of the total episode cost in total joint arthroplasty, but the bullseye remains on our backs. For example, the 2021 Medicare Physician Fee Schedule (PFS) reduced wRVU for THA and TKA by 5.3% from 20.72 to 19.6 units. This was explained by the fewer number of post-op visits documented with modern arthroplasty (i.e., less work over the 90 days). This may not even be true, but if it is, it is a result of improved outcomes and pre-surgical optimization efforts that were stimulated by earlier bundle models. On top of that, there is a PFS conversion factor that multiplies the overall RVU to determine surgeon payment. In 2022, we faced a proposed cut in the PFS conversion factor from 34.89 to 33.59 (3.7%); ultimately the cut was "only" to 34.60 in the final rule. These cuts in wRVU and conversion factor combine to decrease payments from around $1,415 to $1,270 for a joint replacement.

For years, the recurrent strategy from payers has been to propose deep cuts and then compromise on a smaller cut. We sigh in relief from a smaller cut, but let's not forget that we are still worse off than the year before. Advocacy and our collective involvement can be thanked for the smaller cut. Greater bargaining power, from universal involvement (imagine our clout if we enjoyed 100% participation in our PAC), meaningful relationships with elected officials, and a clearer narrative focusing on patients and surgeons, might stop these recurrent cuts. To really dream big, an increase to match inflation could occur one day. Or—gasp!—an increase, like a raise, even after paying for higher annual labor and other expenses of a practice.

In the Budget Control Act of 2011, Congress passed a 2% sequestration clause in Medicare payments. The CARES Act in 2020 provided relief from that cut to help cover costs from the pandemic. As of April 1, 2022, 1% of that sequestration has returned, with the remaining 1% reduction planned to start

on June 1, 2022. The downward pressure on payments is ever present.

Stronger participants in the health policy discussions have not fared the same as surgeons. Hospitals have enjoyed annual increases in payments for DRG 470 (lower extremity arthroplasty without major medical complications or co-morbidities) since 2019. The 2022 payment is $11,675, which is $252 (2.2%) more than in 2021 and $265 more than in 2020. Recall that surgeons are paid around $145 less per case compared to 2020. Sitting on the sidelines of this game is not working out for us.

Private payers are in the game. Surgeons accustomed to reading financial reports should read the most recent UnitedHealth Group (UNH) quarterly report ending March 2022. An easy way to understand profitability is to look at how $80 billion in *quarterly* revenue trickles down to individual shares. By law, at least 80% of revenues have to pay for actual health care, so that leaves $16 billion for salaries, costs, and shareholders. In the full year, UNH expects to profit around $20 per share. They have almost a billion shares "floating" out there. Though we love capitalism, it is hard to cheer for this $20 billion drainage from the healthcare system. Adding the profits of Anthem, Aetna, CVS, and other private insurers, even a capitalistic society must ask whether scarce healthcare dollars really ought to end up in investment accounts.

Health policy agendas go beyond perennial payment concerns. A major contemporary issue, and one that undoubtedly contributes to the profitability of UNH and others, is the impediment to patient care known as "prior authorization." This is the modern implementation of private payer oversight of medical decision making. An insurance representative, often lead by a medical director, reviews submitted documentation to determine if the indication for a surgical procedure is met. This is a cost-control tactic, and its use has increased significantly in recent years. Congress and the Department of Health and Human Services are aware of the problems of prior authorization, in particular because patient care is disrupted and delayed, but also because of the burdens placed on medical practices.

One major concern from hip and knee surgeons is the lack of evidence for some of the criteria used by insurance companies and third-party reviewers like eviCore. An internal AAHKS membership survey found that prior authorization denials never or rarely followed clinical practice guidelines and evidence-based medicine 55% of the time. For example, eviCore requires a documented range of motion spanning greater than 50 degrees before approving knee replacement. On the contrary, when performed by experienced hands, arthroplasty restores function and improves the lives of patients with such severe motion limitations.

Other health policy agenda items are wide ranging, including restoring surgeon discretion for site of service, namely performing surgery as a hospital in-patient versus hospital outpatient or ambulatory care center, shaping bundle payment models, and advocating for federal research support for orthopaedic diseases.

As the foremost experts in musculoskeletal care, orthopaedic surgeons have a duty to patients that expands beyond the clinic and into the halls of Congress and several agencies in Washington. At a minimum, participation in the PAC is as easy as setting up auto-pay for your cell phone bill. Going further, attending fundraisers and engaging with elected representatives helps patients and our profession.

Orthopaedic Surgery in a Global Context

David A. Spiegel, MD

Orthopaedic surgery is a "contextual" field, and the most appropriate treatment is crafted at the site of service delivery. Whether the solution involves an individual patient, or organizing service delivery within a health system, a number of variables are important and differ considerably when comparing high income countries (resource unconstrained, over-resourced) with low and middle-income countries (LMIC, resource constrained or challenged, under-resourced). Deficiencies in access to surgical care result from economic or political fragility/instability, armed conflict, geospatial constraints (terrain, road infrastructure, transportation), lack of availability of services, inability to finance services, and cultural acceptability. Timely access to "essential" procedures, for example drainage of an abscess or irrigation and debridement of an open fracture, which are often performed by non-surgeons or general surgeons (task shifting or sharing), are cost effective and can prevent the need for more complex treatment strategies. Health systems aspire to provide universal access to these essential orthopaedic services at primary referral level facilities, while at the opposite end of the spectrum tertiary services are usually available in the major cities at large public hospitals or teaching hospitals. These centers often have more advanced imaging technologies (image intensifier, CT/MRI), availability of advanced anesthesia services and also access to a variety of surgical implants. They typically have training programs as well.

How can surgeons trained and practicing in a high-income country contribute in a meaningful way to orthopaedic service delivery in these resource challenged environments? We must be sensitive to contextual differences in the pathology, resources available, health system, and sociocultural milieux. The visiting surgeon will be exposed to the common presentation of conditions which they rarely see at home, for example tuberculosis or the sequalae of polio or untreated hip sepsis. They are also exposed to the uncommon presentation of familiar conditions for example a displaced supracondylar humerus fracture presenting three weeks after injury, tibial osteomyelitis with a sequestrum protruding through the skin, or an adult with an untreated clubfoot. These late presenting cases require more complex interventions for which the outcomes are predictably inferior versus the same condition presenting acutely. Modifications of the treatment plan are commonly required when resources are limited, and always have one or more back-up plans. Newer techniques for minimally invasive fracture fixation, especially in the pediatric age group, cannot be considered without reliable access to an image intensifier and/or implants. Imaging for a bone lesion may be limited to plain radiographs. Surgical care becomes essential for source control in cases of hematogenous osteomyelitis when antibiotics are unavailable, as disease-free survival requires wide resection of all contaminated tissue. Don't forget honey when addressing challenging wounds. Sociocultural variables often impact the choice of treatment. Don't assume that an adolescent female with an untreated clubfoot is having pain or seeking treatment for gait disturbance, the problem may be the social stigma; she may be unable to have a marriage arranged unless her club feet are corrected. While an amputation maybe the best treatment option to salvage a mangled extremity or provide palliation for a large and painful malignancy, some patients may still refuse to have their limb removed. These decisions must be respected.

There are multiple avenues for surgeons to become involved, at an international venue and/or the virtual world. Some choose to participate in service-oriented experiences, for example mission trips, in which they provide direct patient care, often bringing a team with implants and the appropriate resources to perform procedures such as total joint arthroplasty or correction of spinal deformities. Others prefer to be involved in capacity building through teaching/training, research, advocacy/policy related initiatives, with or without a component of direct patient care, or more than one of these. Virtual platforms for didactic learning and interactive experiences offer an opportunity for those who are unable to travel. Some elect to become involved as an individual, while others work with non-governmental organizations, academic institutions, or others. Some service opportunities require us to step back from our typical practice patterns, for example the principles of trauma management in disaster relief or war surgery have been informed by extensive experience in the field, are focused on provisional stabilization and reducing complications, and are reflected in protocols by organizations such as the International Committee of the Red Cross (ICRC). Surgeons can become involved in disaster relief and/or war surgery must understand these concepts, for example open reduction and plating of a closed pediatric femur fracture has a very high risk of being complicated by infection when performed in an environment with limited sterility, for example in mobile surgical unit following an earthquake. These patients should all be placed in traction or have external fixation applied during the early phases of their care.

A few general principles should be considered prior to engaging in any of these activities. Think of yourself as a guest in someone's home. It's useful to listen before we speak, to gain an understanding of the local context. Emphasize your "software", thought process and approach to solving problems, and in general avoid the temptation to bring "hardware" unless these items can be maintained or

restocked locally. Solve problems with what is available locally. Research efforts should emphasize building local capacity by teaching local surgeons and their trainees to ask appropriate questions, answer them, and then publish their findings. Local students and providers should always be authors on projects completed in their center. Surgeons involved in service missions need to consider who will manage the patient when they have left, especially any complications. They should also be aware of what resources are available for rehabilitation, and whether orthotics and/or assistive devices are available. It is important to realize that there can be untoward effects on the local health ecosystem. For example, visiting surgical teams caring for well to do members of a community and therefore undercutting the income of the local surgeons who often need to supplement the meagre income they receive from practice in the public sector by having a private practice in the late afternoon or evening, after their government service. We must recognize the importance of interactions between colleagues practicing in resource challenged environments, through local or regional conferences, exchanges, journals, and training activities. Perhaps the greatest impact can occur with establishing networks involving individuals and institutions in both high and low-income environments.

Orthopaedic surgeons who have had the opportunity to explore their field in another context will likely agree that there is enormous educational value, and that the experiences enhance their perception of disease, awareness of deficiencies in access to health services, and the importance of context when developing treatment strategies. A sensitivity to the local context is essential if we are able to contribute in a meaningful way to enhancing the delivery of orthopaedic surgical care in resource challenged environments. The greatest opportunities may lie in forging relationships between individuals and institutions, and this model of cross fertilization should enhance both training and patient care, a win-win situation for all involved. The pandemic has made most of us familiar with technologies which make it easy to engage colleagues around the world, and innovative educational platforms can add value to these relationships. There are innumerable ways in which individuals and institutions can work together, it's a matter of figuring out how we can incorporate these global activities within the many commitments we have at home. Building global activities into the culture of an academic orthopaedic department can enhance the educational program and open the eyes of our faculty and trainees to the vast world of orthopaedic surgery.

Expanding Access to Orthopaedic Surgical Services in Northern Tanzania: Creating a Durable Strategy to Reach the Most Underserved

Neil P. Sheth, MD, FACS

Interest in Global Health–My Mentors

In 2003, as an Intern in the Department of Orthopaedic Surgery at the University of Pennsylvania, Dr. Enyi Okereke was assigned to me as a faculty mentor—a Foot and Ankle surgeon that had been on staff at the Hospital of the University of Pennsylvania (HUP) for 13 years. We met periodically to discuss clinical rotations, research, career goals, and keys to being a successful Penn resident. It wasn't until 2005, as a PGY-2 on the HUP trauma service, that I learned of Dr. Okereke's global health efforts. We were routinely prompted by the OR staff to hand over all removed implants to be re-sterilized for Dr. Okereke's next teaching trip to Nigeria.

Dr. Okereke traveled to Nigeria 4-5 times annually to treat patients with orthopaedic lower extremity deformities—his focus was on changing the system so that the local team could treat their own patients in a timely fashion. I was interested in accompanying him on his next trip—at the time, I was the first resident to make such a request. He offered me to join him when I was a more seasoned resident—so we went to Nigeria for 10 days in January 2007 when I was on his rotation as a PGY4. The experience was life changing! As an adjunct to my inaugural global experience, I benefitted locally from the guidance and wisdom of Dr. David Spiegel and Dr. John Esterhai—Penn Attendings with a keen interest and deep understanding of global surgery.

Focusing on Tanzania

In November 2008, Dr. Okereke tragically passed away in Nigeria from a myocardial infarction due to a lack of the appropriate medications to resuscitate him—he was age 54. Although utterly shocked, I was honored to be selected to deliver a part of his eulogy at his memorial service. That day, I made a pledge to continue his work life's work—***building capacity in underserved countries through creating sustainable systems***. Following his demise, I traveled to Nigeria twice in 2011. During our last visit, we were confronted by a group of individuals that threatened our security - that was my last trip to Nigeria. In June 2012, I was invited to be a part of the first Operation Walk to Africa in Arusha, Tanzania. I fell in love with the country and the people—this was the right place for me to immerse myself in global health as so many people were in need of help.

Changing the Paradigm

At the conclusion of the Operation Walk trip, the team was ecstatic and felt good about what we had accomplished—50 total joint replacements in 4 days. But for some reason, I didn't feel great. I returned to Tanzania in February 2013 and spent time with Dr. Kabira, the local Orthopaedic Surgeon in Arusha. What he said to me changed my entire thinking and was the impetus for our current project. He stated that his team was not very happy when we had visited during the prior year. We were technically excellent and could treat a lot of patients in a short period of time, but we left him with problems that he could not handle. Four total knee replacements had gotten infected and one total hip replacement was chronically dislocating. More importantly, after we left, he had no patients for three months—patients came to his hospital during our trip for free care from US surgeons. Following our departure, patients were unwilling to pay for care from an African surgeon, until they realized that the US team wasn't returning anytime soon.

It was clear to me that the traditional approach of blitz surgery had to change. Even with the best intentions in mind, parachute medicine has untoward, unintended consequences in the host country, which we would never understand without asking the right questions. As a result of my conversation with Dr. Kabira, I spent the next two years scouring the globe to learn about existing global health care models throughout the developing world. I learned a great deal and interfaced with several people through this process, and I was able to envision a solution that would mitigate the effects of one-off orthopaedic trips to developing nations.

The Foundation for an Orthopaedic Center of Excellence - Studying Your Target Market

In 2014, we started a relationship with Kilimanjaro Christian Medical Center (KCMC)—the largest medical, nursing, therapy, and allied health school located in Moshi, Tanzania. Prior to pitching a potential solution, I sat down with two orthopaedic surgeons at KCMC and asked what the three major barriers were to delivering timely orthopaedic care. Without hesitation, they delineated that the barriers were: (1) lack of capacity (this included space (only one orthopaedic theater) and work force (only four orthopaedic surgeons)); (2) an absence of a consistent supply of orthopaedic implants (they relied heavily

on donated implants); and (3) patients didn't have the ability to readily pay for orthopaedic care.

These barriers formulated the foundation for our project in Tanzania and set the stage for collecting data regarding the current state of affairs – market research is critical when creating a system within a system. Guatemala or Cambodia are different than Tanzania – failure is guaranteed if data from one market is extrapolated to another on the basis of population size without understanding the nuances of the specific target market.

Starting in 2015, students from across Penn's campus (Perelman School of Medicine, the Wharton School, Leonard Davis Institute of Economics, and the School of Public Health) joined our team to start conducting research remotely and on the ground in Tanzania. Our research has focused on the burden of orthopaedic disease, defining systems issues that prevent care delivery, the finances and economics of care delivery, and increasing care access for patients that are unable to pay. These research endeavors have served as the foundation for a new orthopaedic center of excellence and have resulted in several publications which have helped to define the current landscape in Tanzania.

Progress Towards Implementation

Over the past six years, a plan has been devised to address the three major barriers identified by the local team. We are embarking on building an orthopaedic center of excellence in conjunction with KCMC on their campus – a center with four operating theaters and 100 beds. Twenty-five university orthopaedic programs from around the globe have joined the University of Pennsylvania to donate 2-weeks per year to cover the center, work with the local team at KCMC, and participate in 2-way education/knowledge transfer at every level. We have partnered with Nebula Surgical, an implant company based in India with a distribution center in Tanzania, that can provide orthopaedic implants at 1/9th the cost of what is encountered here in the US. Through a robust collaboration with GE Healthcare Africa, GE Capital, and the Wharton School, a financial plan has been created to treat all patients. This plan allows for the delivery of democratized care – care that is independent of the patient's ability to pay, and paying patients would help cross-subsidize non-paying patients.

Challenges due to the COVID Pandemic

The global pandemic has presented significant challenges for this project. Over the past two years, the President of Tanzania as well as one of the former orthopaedic residents passed away due to the coronavirus. The inability to travel to Africa has prevented students from across Penn's campus from continuing to perform research locally in Tanzania. Funding that had been secured to build the center of excellence has been repurposed for COVID. But with the hopes of travel re-starting and the continued support from our critical partners, opportunities continue to be present to secure additional funding and get back on track.

Delivery of Orthopaedic Care Abroad: Leadership Exemplified

Luke A. Lopas, MD

To some extent, everyone in medicine feels the proverbial call to help those in need. Certainly, when it comes to orthopaedic care, especially orthopaedic trauma care, there is a substantial and well documented burden of trauma and musculoskeletal disease in low- and middle-income countries (LMICs)[1,2]. Trauma disrupts the ability to physically navigate the world which can mean not only personal disability for a patient, but potentially poverty for the entire family if the injured member is the primary provider.

Regardless of where in the world an injury occurs, the same basic tenets of care are required for a successful patient outcome. Namely, accurate and timely diagnosis, and patient centered shared decision making ultimately leading to patient and culturally appropriate treatment with adequate rehabilitation and follow up through healing. The ethics of participating in medical care in LMICs is complex and viewed differently when stratified by hosts and visitors[3]. It's easy to go and do a bunch of complex surgeries and reconstructions, but what does that mean for the patients left behind? How do you avoid leaving behind a wave of complications and destruction? How do you truly serve the population(s) that you are trying to help?

I was fortunate enough to witness first-hand what it looks like to live this mission of service and how leadership in this context is embodied. As a chief resident, one of my co-residents (Dr. Kristin Buterbaugh) and I had the opportunity to join our own Dr. Samir Mehta as well as a group from Rush University, lead by Drs. Monica Kogan and Stephanie Crane (Figure 1), on a mission trip to the Dominican Republic. I had the privilege of seeing what two decades of effort and service could build. Dr. Crane has been working in the Dominican Republic for more than 20 years, first starting an NGO (Community Empowerment) to develop a water purification and distribution system (Figure 2). She then leveraged this infrastructure and income to partner with the local community in Peralta to create primary care clinics staffed by local providers. After investing in the training and leadership of these clinics for two decades, Community Empowerment turned over full ownership of these clinics to the local community in 2018. As if this wasn't enough, she continues to work towards these goals with surgical and emergency medical care. The partnerships she has fostered are clearly built on mutual admiration and respect which yields an impressive collaborative effort (Figure 3). Dr. Crane

Figure 1. Members of the medical mission trip from Community Empowerment, Rush University, and the University of Pennsylvania.

Figure 2. Members of Community Empowerment, including Dr. Stephanie Crane (center) who are the driving force behind the infrastructure required to successfully complete a medical mission trip.

Figure 3. Minyetti, head of the sterile processing department at the hospital, partners with Community Empowerment to provide care for the local community.

spends much of the year, physically present in the community, truly epitomizing a servant leader.

Fortunately, there is more than one way to lead in international orthopaedic care. Drs. Kogan and Mehta not only give time and energy to lead surgical missions but spend hours writing grants to secure implants or equipment, as well as take advantage of relationships to secure donations and collections for use not only during the mission, but critically to build local capacity. Observing and participating in this experience continues to be one of the most inspiring and meaningful experiences in medicine I've had and serves as a fundamental reminder of the central feature of successful care regardless of location – the people and the relationships.

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Creating a Social Media Presence as an Orthopaedic Surgeon

Yelena Bogdan, MD, FACS, FAAOS

Introduction

Social media is a powerful tool for communication and connection in modern society. Orthopaedic surgeons can harness this power for patient communication, promotion of their practice, or educational activities (the lattermost of which is my area; for advice on the former two, alternative sources should be used). It is important to understand that involvement in social media is completely optional, may require a significant time commitment, and has certain pitfalls and limitations.

Goals of Social Media

I initially started my social media account to share evidence-based medicine, and then developed it into an educational platform to share "bread and butter" tips and tricks in orthopaedic trauma, many of which were taught to me by my mentor, Paul Tornetta, and others that I developed myself. My primary audience consists of other surgeons who do not practice trauma as a subspecialty. My cases help them understand the nuances of the specialty and provide easy-to-use mini-lessons to help their cases flow more smoothly. Every surgeon will have his/her own goals, and establishing a clear focus of one's account is the most important factor for success on social media.

Impact of Social Media on my Practice

I am an educator at heart, and everything I do in my professional life aims to disseminate high-quality orthopaedic trauma information. Social media has had a great impact on my ability to share information with other subspecialties, particularly once it grew. As of this writing, I have 17,000 followers from all subspecialties and all over the world. The term "Twitter fellowship" has been used to describe learning that occurs in bite-sized chunks via tweetorials or other twitter interactions; for example, I have picked up tips on hand surgery from colleagues on Twitter, people I would have never interacted with otherwise. This communication enriches us all. The growth of my social media presence has led to invitations to conferences and journal clubs as well, further enabling the spread of information and education. Various societies, such as the OTA and AAOS now have robust presences on social media, and the ability to serve as an ambassador on their behalf has opened my network even further.

Challenges Encountered

A very active social media presence is a part-time job. It is built with near-constant engagement, daily posts, and answering questions from followers. I do not take any days off Twitter, and having enough time to create thoughtful and educational posts can be difficult, given other clinical and personal responsibilities. There is also an element of screen addiction, and social media can easily take over all free time if allowed to do so. Creating a good balance of the "online world" and the "real world" is challenging.

Advice for Starting on Social Media

1. Build a brand of what you are good at: whether it is providing educational material, sharing cases, or something else, a concrete goal for the account will allow the audience to understand what they will get out of following you.
2. If sharing cases, always deidentify and always get written patient consent: while truly deidentified imaging may not meet HIPAA requirements (I gave a lecture about this at the OTA that is available on my account), the safest practice is to get a written consent for anything you share on social media. You can add further layers of deidentification with techniques such as posting "out of time" (not the same day of the surgery), not using age or sex (saying "elderly" not "83" if age is important to the educational point you're making), and others.
3. Don't become obsessed with likes or followers: social media is not a contest, and it takes time to grow an audience (sometimes years of consistent posting). Many "popular" accounts buy followers, and it is important to remember that popularity does not equal quality.
4. Remain professional: refrain from insults, arguing extensively, negative political commentary (that your patients could see), and similar activities. Muting or blocking is a great way to avoid stress on social media.
5. Don't give specific medical advice (beyond providing general information): in some instances, giving direct advice to a patient constitutes a physician-patient relationship and opens you to legal liability. If you are on social media to promote your practice, direct the patient to make an appointment in person.
6. Don't perform medutainment: the term refers to posting material (that may involve patient information) that has no educational purposes but is done purely for entertainment. Examples include posting gruesome injuries for likes ("look how gnarly this is"), or posting a case you did without any educational point or explanation ("look what a great surgeon I

am"). Everything you do on social media should serve your audience and/or your patients in some way. Use the "TV rule:" if you are not comfortable with the post broadcasted on live television, do not post it.

The Future of Social Media and Orthopaedics

As our field continues to grow and evolve, I see social media becoming an important adjunct for collaboration of both individuals and societies. Important articles (such as the FLOW trial) had a significant press and social media release, and I foresee journals using social media increasingly as a tool to reach younger surgeons who may not read paper journals. I also suspect that other web 2.0 tools will be incorporated, along with social media, into residency curricula across the country.

Creating a New Category—A Disruptive Journey

Derek J. Donegan, MD, MBA

"You miss one hundred percent of the shots that you don't take." Wayne Gretzky could not have spoken truer words. In the tech boom we are currently living through, most industries are prime for disruption. Healthcare is no different. In the simplest of terms, a disruptive technology is any innovation that creates a new market and disrupts an existing one. As some of you who are reading this know, I have been on the journey of creating a new category and trying to disrupt an old one for the last 4 years. I am often asked how to do this. The truth is, I have no idea. The path seemed to happen so organically that it is difficult to give a set of guidelines or rules to guarantee success. The only certainty is that if the idea remains only an idea, it will never be successful. As a friend of mine recently said to me, "we all talk about it, but you are actually doing it." The "it" referring to taking an idea and turning it into a reality.

So, how did this all come about? The experience of being a busy orthopaedic trauma surgeon combined with formal education getting my MBA proved to be my personal disruptor. There were back-to-back classes in business school on "Managing Information in the Enterprise" and "Disruptive Leadership." As the class names depict, they focused on information technology and strategy and how to lead through disruption. These critical experiences started to transform my thought process. I developed an understanding that information is a major economic good and that technology could be leveraged to transform organizational and system readiness. Systems that can receive, process, and respond to information quickly tend to gain advantage and those that do not fall behind. The goal is for the system to work toward the most effective way to complete the processes, not in the silo fashion that our system currently exists. Mapping information technology to value requires realizing that: automation equals operational efficiency; controls lead to better checks and balances; better and quicker access to information empowers decision making; and collaboration generates creativity and leverages the power of the group. This ultimately led to my vision of a digital platform that connected the entire process of performing surgery.

In the backdrop of this educational experience, I began talking about building a consulting business in the medical device world with a longtime friend of mine, Tim Donnelly. Tim, at the time, had been working as a medical device consultant for about a decade. After my experience with these two classes, I suggested that we dive into software instead to help improve the orthopedic operating room process. Donnelly, while on a phone call with me, did a quick test and asked iPhone's Siri a specific question about which size drill bit was needed for a 3.5mm cortical screw. When Siri pulled up the exact manufacturers webpage that had the answer, we knew enough underlying technology existed to support our idea. So, we started out on our journey to build a platform that would revolutionize the surgical process to ensure the successful delivery of surgical care (Figure 1).

As we began to assemble our team, we started to identify the specifics of the problem that we set out to address. Our team was made up of what we liked to call "insiders," so we were developing our solution from the inside out. In comparison, this digital solution space for healthcare was filled with many outsiders seeking solutions to problems that they had never experienced. With many years of actual clinical experience in the OR, we quickly identified four main gaps in the existing process: 1) the ability to select the right equipment; 2) access to mission critical information; 3) experience handling the equipment; and 4) ability to record accurate data. We knew that far too often the equipment delivered to the OR for surgery was wrong, incomplete, or unnecessary due to fragmented and outdated surgical processes, increasing complexity of surgical equipment, and the knowledge gaps of less experienced staff (Figure 2). With these problems in mind, we built ORtelligence to create cutting-edge software fix

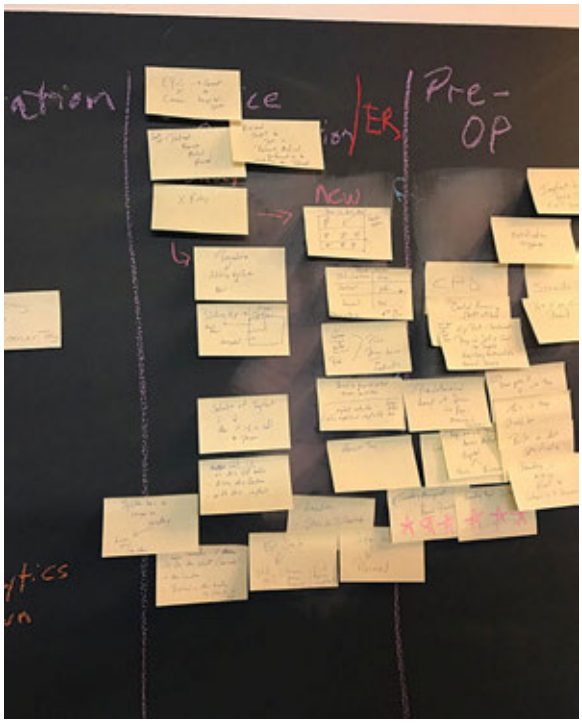

Figure 1. Picture of blackboard from early planning sessions.

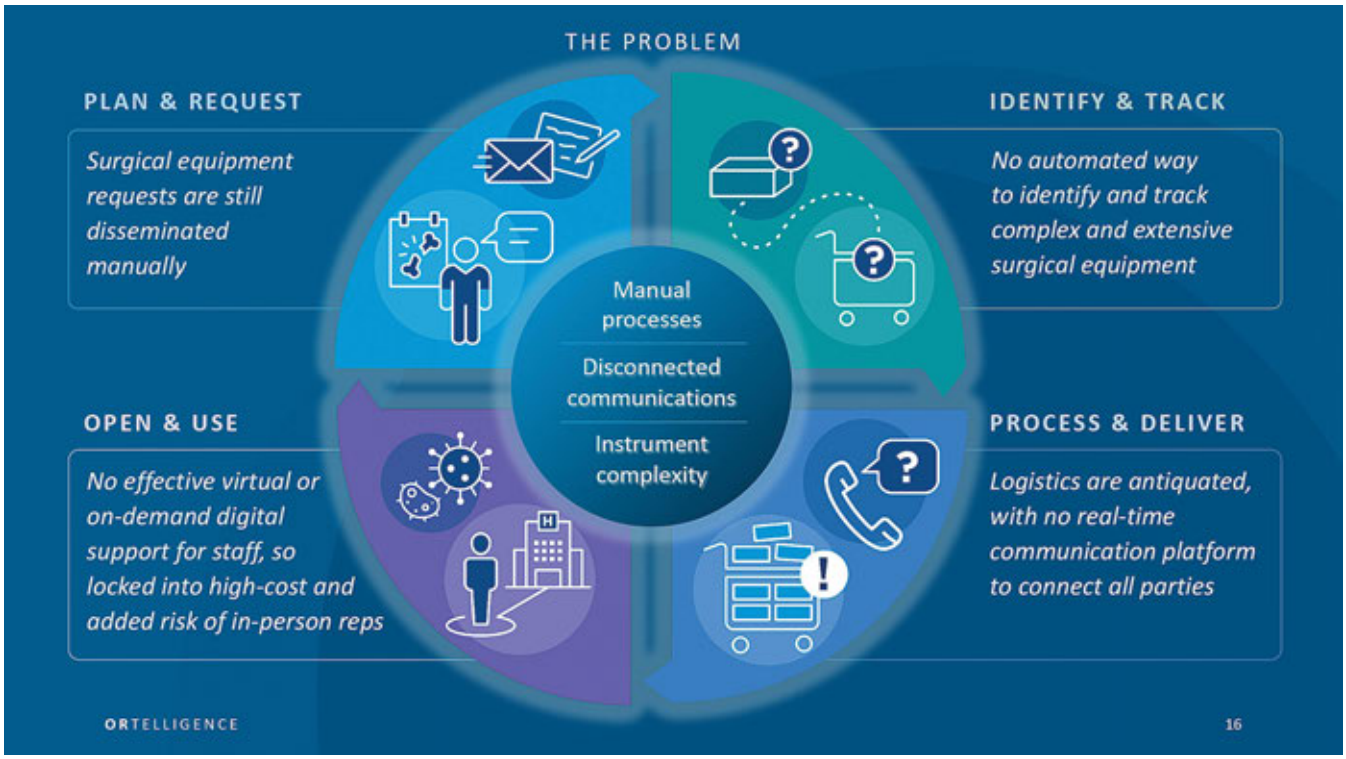

Figure 2. Problem slide of the surgical process.

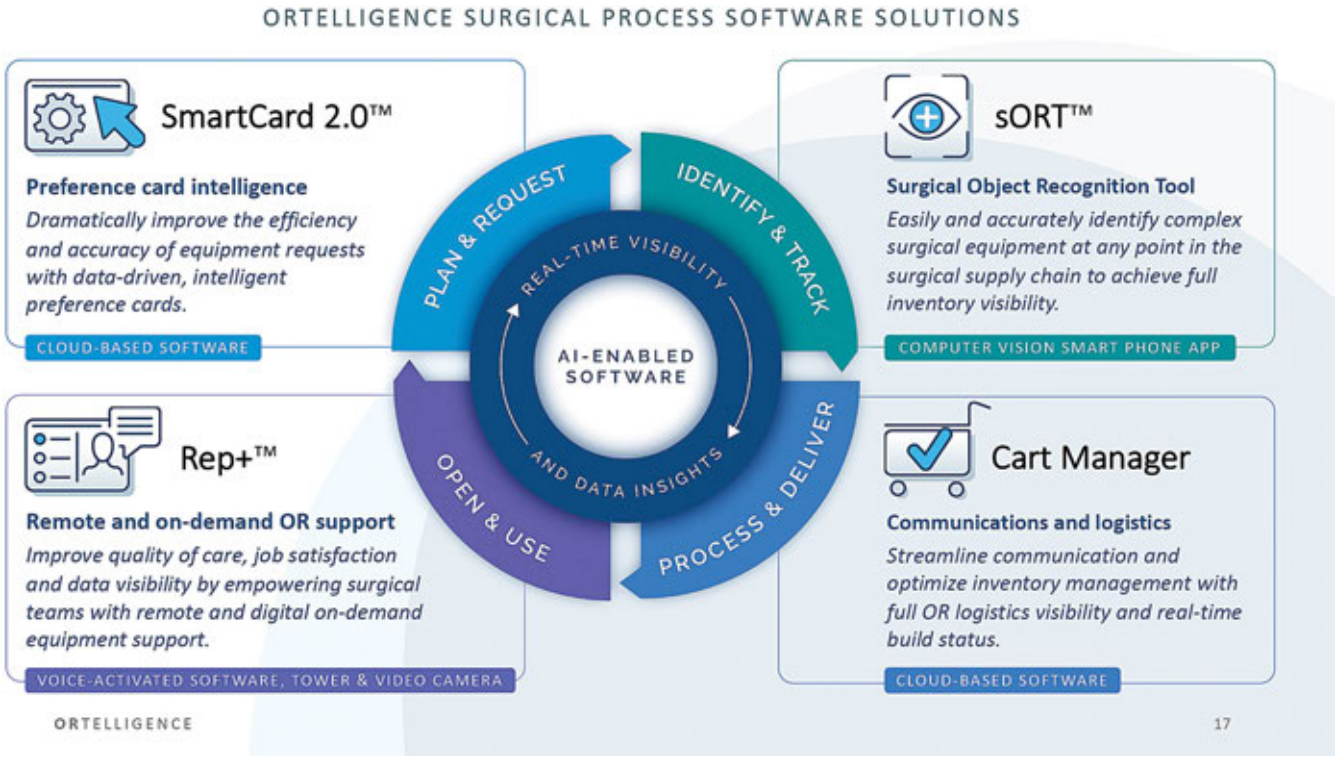

Figure 3: ORtelligence solutions.

these gaps and align surgical teams with the right information, equipment, and support to deliver the best possible surgical care.

ORtelligence ("ORT") is a technology company that creates surgical process software and technological solutions that are designed to optimize the surgical process by identifying and tracking all surgical equipment, bridging the gaps in operating room team communication, and allowing for remote, on-demand expert support in the operating room. The patented technology is designed to complement both the electronic

healthcare record and existing technologies to harness the information into a powerful, transformative tool. The comprehensive end-to-end solution is built from three core technical competencies:

1. Data management and taxonomies;
2. SaaS software; and
3. Artificial Intelligence and Machine Learning.

The platform consists of four separate, but interconnected products that allow for real-time visibility and data insights (Figure 3):

1. ***Smartcard 2.0™:*** An AI-enabled planning tool based on surgeon preferences and facility contracts. Designed as an intuitive "shopping cart" interface optimized for user preferences, this dramatically improves the efficiency and accuracy of equipment requested by replacing static preference cards and disjointed communication with data-driven, intelligent SmartCards.
2. ***Cart Manager:*** A communications and logistics tool designed for case cart preparation. Cart manager is designed to streamline communication and optimize inventory management by replacing siloed, manual processes with full OR logistic visibility and real-time build status.
3. ***Rep+™:*** An AI-enabled interface with image recognition and a natural-language user interface to provide remote and on-demand OR support. Rep+™ is designed to improve quality of care, job satisfaction and data visibility by empowering surgical teams with remote and digital on-demand equipment support.
4. ***Surgical Object Recognition Tool (sORT™):*** A patented, computer-vision smartphone app utilized to identify equipment and set contents and create alerts for missing items. sORT™ is designed to easily and accurately identify complex surgical equipment at any point in the surgical supply chain to achieve full inventory visibility.

What has the path been like so far? The entrepreneurial path is often likened to a roller coaster with many ups and downs. This journey has been no different. What started as a concept has developed into a fully functional business with multiple product offerings. The company has grown from a team of three to ten full time employees, an executive board, and multiple partners who complement the vision and mission of the company. There have been two formal funding rounds and countless pitch decks (roughly 50). Failing early and often is more of a way of life rather than a catchy saying. Although, with the early failures have come evolution and growth. The growth has opened significant opportunities for us in the future to pursue our vision of revolutionizing the surgical process to ensure the successful delivery of surgical care.

In conclusion, the road of a start-up company is an exciting one. In my opinion, there is no one right answer on how to be successful. The truth of the matter is that most start-ups are not successful with 90% failing. In fact, we still have roughly a 50% chance of failing understanding that less than 50% of start-ups are still in existence after five years. With that said, every day we are still living our vision is another day we have the opportunity to succeed. What if you decide to follow in these footsteps? Well, deciding to take on this endeavor will prove to be challenging but rewarding. It is most likely more about timing and luck than anything else, but a good business sense and a good idea worth acting on can go a long way. While I might not have the answers on how to do "it" successfully, here are some guiding thoughts:

- **The business opportunity:** What problem are you solving or need you are filling? How did you identify or recognize this opportunity, problem, or need?
- **Describe the service:** Need to state exactly what it does and how it does it. What are the strengths and weaknesses of the idea? Are there any remaining unknowns and what are the assumptions that need to be tested?
- **Innovativeness and Uniqueness:** How is your product different than others that solve the same problem or fulfill the same need? Or in other words, why will people want to purchase it? Is it easier, more fun, faster, cheaper, more functional, better performing, a cooler design, more convenient, safer, more environmentally friendly, etc? This is often referred to as the "competitive advantage."
- **Competitors and Substitutes:** Who/what is the direct competition (products that perform the same function and compete against each other, such as iPhone vs. Android smart phones)? Who/what is the indirect competition (products that are close substitutes but perform the same or similar function)?
- **Target Customer:** Who will use and/or purchase your product? Describe your typical customers. If selling to consumers: describe age, income, ethnic group, geography, use/lifestyle profile (amateur athletes, heavy TV watcher), etc. If selling to a business: what industry/industries, size of business by sales or number of employees, geographic location, etc.
- **Value Proposition:** A simple statement that summarizes why your target customer would choose your product and the value your product would provide. A clear, concise statement communicating the clearest benefit of your product by the customer.
- **Pricing:** Product market fit. What is the market willing to pay for your product?
- **Team:** "Build a big tent."
- **Investment Structure:** How are you going to fund the endeavor? Funding while maintaining ownership/control?
- **Strategy and Operational Plan:** What are you going to do with the funding to achieve success? What is success? How do you measure success? Where are you now and where are you going to be in the future?

Surgeon-Industry Partnership: My Experience Working with Industry

Frank A. Liporace, MD

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Introduction:

The relationship of Orthopedic Surgeons and Industry has evolved significantly in the last two decades. The foundation of this relationship should be looked upon as a positive way to advance and develop technology to be disseminated throughout the population and improve patient care. This can be enhanced by collaborative efforts in unbiased research and education. As a result, practicing Orthopedic surgeons and trainees are introduced to the latest offerings and direction that Orthopedic care is moving. The input of surgeons on design teams to work with engineers and marketing executives can synergistically advance the usability, practicality, quality, and exposure of new devices and technologies that are being brought to market.

We are all well aware of the scrutiny by the DOJ (Department of Justice) that brought these relationships to the public's attention nearly 15 years ago. As a result, polarized views have been developed. Some believe that this helps with transparency on the amount and reason for physician reimbursement while others look at reforms as a "roadblock" to progress. In this manuscript, we will not editorialize the current climate but rather focus on the existing field, what it means to be involved, how to get involved, and what justifies that partnership.

Initial interest and how I got started:

Typically, there are some commonalities amongst surgeons that are involved with industry in the two main roads that are not mutually exclusive. These are 1-Design and 2-Research / Education. Both roads require the individual to appreciate the merits and exposure to ideas that industry can facilitate.

Early in my training and career, I was fortunate to have mentors that were deeply involved in both. I was awestruck by the fact that I was being trained by those that have influenced the direction our field was going and were the main engine to the advancements, technology, and progress. This was my initial spark to emulate my predecessors.

To get involved, it's important that it's justified. Let's never assume that "pay to play" or surgeon product usage should influence involvement. Justification to be intimately involved with industry is important, specific, and required. The three main foundations of publishing, podium presence / experience, and clinical experience are pivotal to justify involvement. Relationships with those in the field can "open doors" but will not have you walk through the threshold in a meaningful or lasting manner.

Publishing on topics of interest, topics that are commonly confronted or commonly viewed as challenging, and new concepts all spark interest. Peer-reviewed journals, specialty society publications, AAOS publications, and textbooks are all time-proven, unbiased, and indisputable quality methods of publishing. Podium presentations at AAOS and subspecialty society meetings are graded by the audience, attended by industry partners, and a great way to highlight the type of education you can offer. Also, these opportunities allow you to build relationships with leaders in our field, get insights on how to lecture more effectively, and provide you with personal growth and education. Once again, this highlights justification for industry involvement.

As I grew in the above and developed relationships, opportunity was presented to educate with industry, design, and be involved as a KOL (key opinion leader) on topics and techniques that happen to correlate exactly with what supplied the justification for my involvement.

Barriers, experiences, career impact:

The greatest barrier is impatience. Most of the reason we are impatient is out of ignorance in process, necessity, regulation, and impact of not "following the rules." The following brief description of the general processes are necessary to understand when joining a design team or independently presenting a design idea to an industry partner.

As with surgeon selection by industry, the investment of resources in a project for a specific product / technology design comes with the need for justification. A market analysis must be done (frequently transcending worldwide markets) based on comparison of existing market share of the company, competition, market need, cost-analysis and ability to sell the final product at a sustainable yet affordable margin.

If a project is put "in the cue" then industry assignment of appropriate R&D (research and development) and marketing resources must enter a business plan. Budgets for engineers, design surgeons, resources, lab time, testing, FDA filing, etc. must be allocated and approved in advance to avoid as many predictable problems and delays down the road as possible. If approved, scheduling of meetings that go through the pre-approval analysis, goals / scope and needs with all team members are necessary in the "kick-off" phase. Only, at this juncture can the actual design meetings dedicated to instrument and implant design commence. With that, considerations in brand "look and feel", compatibility, production capability, usability and ease in the clinical setting based on surgical approach, etc. must all be considered. When "agreement" on each of

these is reached for every instrument, piece of implant, and packaging then the next phase begins. Research into the IP (Intellectual Property) field and pre-existing patents that may impinge the production of what the team has designed must be done and "worked around" to ensure no violations of IP are present. Labs to confirm the usability and function with follow-up meetings and design adjustments must be done. This allows the milestone of "Design Freeze". Along the way toward Design Freeze, limited mechanical testing had to be done and production quality instruments and implants created for appropriate team confirmation. All this requires machine time which requires re-tooling of machines for production and testing that are multi-purpose. Then final mechanical testing, sterilization and packaging testing, and FDA / 510K submission must commence. Each of the above steps can result in repeating prior steps to "get it just right".

After this multiple year journey, limited set release for in vivo / clinical alpha and beta testing by design surgeons and KOLs must be done for clinical data acquisition and may result in further adjustments. This has variable impact on where the algorithm is re-run.

Finally, strategic regional and worldwide release targets of sets of instruments and implants must be formulated based on a market that has changed over the years of the design process. Resources must be allocated including machine time and outsourcing vendors for production that can meet the specifications that were approved.

Typically, surgeons are reimbursed for time of meetings and travel while performing design team meetings. Many opportunities offer royalties on sales of SKUs (stock keeping units) produced during development for a defined time period after product release. All this must be defined within the contract between the physician and industry partner. Rates of reimbursement are based on FMV (Fair Market Value) and DOJ guidelines.

That is a brief overview of what I've learned about "Industry Driven" Product Development. Certainly, many surgeon leaders approach industry with product ideas at various stages of development and concept inception. This forms in two realms: institutionally employed physicians and independent private physicians. The key difference with institutionally employed physicians is navigating the waters with the employer on what freedoms are afforded to them. Some employment contracts mandate a "split" with the employer of all IP and associated profits that were developed by the employed physician during the time of employment. This can be addressed with the institution's leadership and hopefully be broken down to the categories of using institutional time / resources or not. Full transparency by the employed physician is necessary. Inclusion / exclusion criteria of the institution sharing in royalties and industry reimbursement for travel / meetings / educational events must be fully documented in an employment contract Appendix to avoid potential misconception and litigation.

Once the assignment of profit is satisfied then the steps of presenting product ideas to industry become similar for both groups. The days of "signing a napkin or self-addressed, sealed, dated envelope with drawings" are over. These are not binding ways of protecting IP and should not be relied upon. Based on the stage from idea inception through patent / product development that the surgeon presents to industry will correlate with the amount of profit sharing with industry that the surgeon will yield.

A few following definitions will be important as an overview but consultation with a patent attorney is strongly recommended. None of this manuscript represents any legally binding information, is based on personal experience through my career, and is an ever-changing landscape.

- Provisional Patent: a provisional application is a legal document filed in the United States Patent and Trademark Office (USPTO), that establishes an early filing date, but does not mature into an issued patent unless the applicant files a regular non-provisional patent application within one year.
- Non-provisional patent: a non-provisional application requests the United States Patent and Trademark Office (USPTO) to issue a utility patent. This type of patent protects intellectual property rights for anything novel, useful, and non-obvious:
    - Machines
    - Manufactures
    - Processes and systems
    - Chemical compounds or compositions of matter
    - Improvements on pre-existing patents
- Also known as a utility patent application, a non-provisional patent application leads the way to a utility patent issue.
    - Can cover electrical, mechanical, or chemical inventions.
    - Can protect an inventor's rights to make, use, and sell an invention.
    - Can serve as public notice of innovation and intellectual property ownership

If the process is brought to full maturity and a Full Patent is issued, this is quite valuable if it sparks interest by an industry partner, is expensive, time consuming, and needs to be considered for a World-Wide Patent application with multiple filings necessary based on country.

How I see the surgeon-industry partnership evolving:

One of the most important things to realize is the need for justification and validation are important in every step of the process from person selection, market needs, design, and product release. The processes in the United States and different parts of the world to allow the use of new products and technologies is ever changing and becomes more specific overtime. A similar regulatory necessity to our FDA / 510K in Europe is the CE Marking Certification. CE Marking Certification is essentially a declaration by manufacturers that a product meets all applicable legal provisions set by the European Union under the CE Marking requirements. Recent changes indicate a certain amount of clinical evidence of new product usage and prospective following of results to attain

a CE mark. It would not be unexpected if this transcends to other arenas.

Partnering with industry to be a central data collection center and publishing on the results of new products is a creative way to help with research support and critical evaluation of newer methodologies. To remove bias, setting up research relationships with unrestricted grants or retrospective reimbursement for research resources used to publish manuscripts on new designs compared to historical treatment controls takes the perceived bias of industry influencing research results out of the equation. This promotes objective evaluation of new releases and allows the research engine to strive forward. Surgeons with clinical research interest will be invaluable as this process matures and standardizes.

Due to supply chain issues, production issues, and personnel issues, many larger Orthopedic Companies have acquired smaller ones that were solely dedicated to one aspect of Orthopedic Surgery. This has proven beneficial for these privately-owned manufacturers to be acquired and has created efficiencies for the major Orthopedic Implant suppliers to avoid all of what was outlined above for the multiple products and product lines that they supply. This allows for a great "footprint" of exposure for the smaller manufacturers to achieve worldwide exposure and is a potential avenue for additional surgical involvement with design.

All too often, we think of Orthopedic advances in terms of implants and instrumentation. Many manufacturers are looking toward real-time tracking of patient performance, rehabilitation goals, compliance, healing rates, and function. The implants are being looked as a conduit for entering this next realm as it develops as well as a conduit for avoiding complications such as infection. Computer apps, data tracking devices within implants, and "coated" implants are what many believe will bring our field to the next level. Those with experience and interest in such arenas will be very useful as our field evolves.

Conclusions and how future surgeons may consider getting involved:

Without a doubt, Orthopedic Surgery has been one of the subspecialties with the highest rate of technologic advancement and design in recent decades. The above outline on how to reliably, transparently, and appropriately get involved with industry will most likely not change in the near future. We have gone from a field of suspected "pay to play" to one that is looked upon as a leader in medicine on how to "do it right" through justification and following the tenants of EBM (evidence-based medicine). This makes us proud and motivated to continue leading the charge with technologic advancement and setting the gold standard on how to do it appropriately. Mentorship and learning from the experiences of our predecessors are the drivers to the next generation.

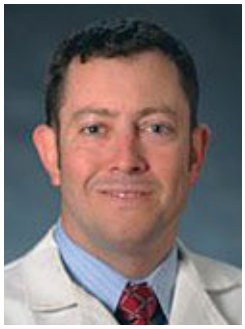
Involvement comes in many forms that are intimately related and extremely important. They range from: industry driven design team members, surgeon driven designers, key opinion leaders, researchers, podium speakers, technique instructors, and clinicians. None of the above in isolation holds meaning without all the counter parts as we drive toward delivering our collective patients the best and most predictable care that technology can offer. Without industry, surgeons cannot perform and without surgeons, industry cannot produce.

Orthopaedic Trauma and Fracture Service Division "Your Pace or Ours"

Samir Mehta, MD

Orthopaedic Trauma Faculty

Samir Mehta, MD



Derek Donegan, MD, MBA

Susan Harding, MD

The Division of Orthopaedic Trauma & Fracture Surgery continues to be an exceptionally busy and dynamic subset of Penn Orthopaedics. The orthopaedic trauma service, now well settled into its new home at Penn-Presbyterian Medical Center, practice at the highest volume Level 1 trauma center in the Delaware Valley performing nearly 2000 cases annually. The case diversity is expansive, ranging from ankle and distal radius fractures through complex pelvic and acetabular injuries, peri-articular fractures, and managing multiply injured polytrauma patients (Figure 1). The division frequently collaborates with other subspecialties, including plastic surgery for complex revisions and wounds; neurosurgery for spondylopelvic disruptions; and geriatric medicine, for optimal care of our geriatric hip fracture population. In addition to strong surgeon leadership, the division succeeds due to the relentless efforts of dedicated advanced practice providers in both the inpatient and outpatient settings, who facilitate management of acute injuries, as well as run an outpatient fracture clinic daily to ensure that new and follow-up patients are seen in a timely and consistent manner. Additionally, orthopaedic trauma is supported by excellent social workers, case workers, physical therapists and nurses who enable our trauma patients to receive optimal care during what is often one of the most challenging times of their lives. However, the life-blood of the orthopaedic trauma program is the resident complement, who continue to support the service line through tireless effort. The trauma program resident compliment now includes a PGY-1, two PGY-2s, a PGY-3, a PGY-4, and a PGY-5 as chief resident on the service. Clinical roles and responsibilities are divided amongst all the residents on service with a focus on graduated responsibility and autonomy. Lastly, the trauma service is only able to provide 24-7-365 coverage thanks to the non-trauma faculty who sacrifice time from their family and additional obligations to take call nights and weekends to divide the workload. Because of their sense of responsibility and dedication, our call faculty facility the ability of the trauma service to function at a high-level at all times.

Innovation in patient care occurs contemporaneously with upholding longstanding division traditions. For example, the trauma division has worked closely with geriatric and emergency medicine to develop a state of the art geriatric hip fracture program, whereupon relevant members of the care team are immediately notified of a geriatric hip fracture patient

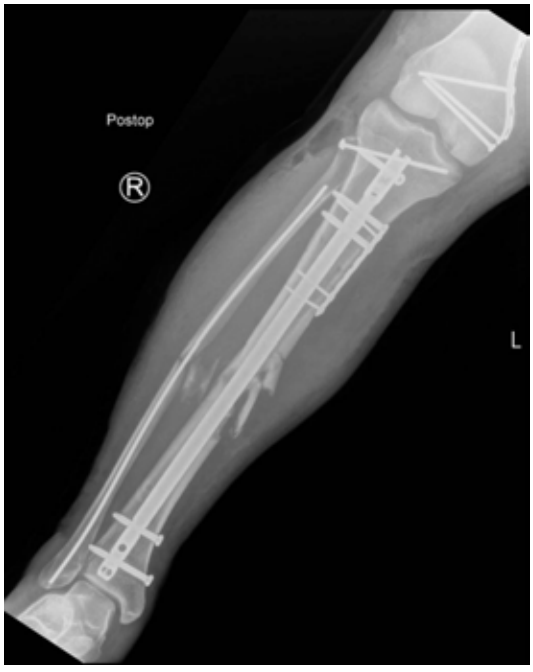


Figure 1.

upon their arrival to the hospital so that the teams can mobilize to provide the patient with streamlined care from ambulance to OR. Geriatric Hip Programs, like that at Penn, have been shown to improve the outcomes of patients suffering from these life-changing injuries. In fact, our geriatric fracture program was recently awarded "Premier Status" by the International Geriatric Fracture Society. Additionally, the orthopaedic trauma service through the support of Dr Levin and the Health System has been diligently working in increase the breadth and depth of the Penn Orthopaedic Limb Salvage Center (POLSC). The orthopaedic trauma service offers several limb salvage and reconstruction opportunities including repair of complex fractures using ring fixation. We have also started the TALLER program – Total Aesthetic Limb Lengthening and Extremity Reconstruction to increase stature. In addition, the division is using 3D printing technology to salvage extremities (Figure 2).

The division's presence extends beyond the region and beyond medicine, at large. The orthopaedic trauma faculty are involved with the AO Foundation and the Orthopaedic Trauma Association. Both organizations are geared towards advancements in fracture care. The Penn Orthopaedic Trauma faculty have chaired national and international courses which attract hundreds of residents and faculty to learn and to teach the principles of basic and advanced fracture care. The impact of COVID-19 altered the delivery of this academic content, but not the ability to do so. While international outreach came to a halt from 2020 through 2022, there are plans to continue our efforts in the Dominican Republic starting in 2023. Our interantional experiences can be followed on Instagram at @ pennots.

Clinically, the Division continues to extend its areas of expertise focusing on "elective" orthopaedic trauma care. The Division has a distinct interest in peri-prosthetic fractures, complex arthroplasty, robotics and navigation, infection (osteomyelitis), malunions, and non-unions (Figure 3). The division utilizes advanced technology to facilitate the care of these complex patients including ring fixation and lengthening nails. By collaborating with our colleagues within the department, such as shoulder and elbow, adult reconstruction, foot and ankle surgery, orthoplastics, hand, spine, and oncology, the orthopaedic trauma division can provide the highest level of care. Additionally, the division has done several cases utilizing 3D printing of implants in an effort to salvage extremities in patients with severe injuries.

This year has been one of recovery and enhancement. We have emerged from COVID-19 having continued to provide orthopaedic trauma care throughout the entirety of the pandemic. Dr Susan Harding, who was at Hahnemann University, has transitioned successfully to Penn Orthopaedics without missing a beat. She has built a tremendous orthopaedic trauma presence at Cape Regional Medical Center and also continues to support the trauma service at Penn Presbyterian Medical Center. We are extremely fortunate to have an individual with Dr Harding's enthusiasm and experience be part of the Penn Orthopaedic Trauma family. The orthopaedic trauma service has continued to our Sunday night weekly fracture conferences that were a direct result of our desire to stay connected with our learners during the pandemic.

The trauma division remains a cornerstone of the residency program's education. Every resident spends 6 to 12 weeks of their year as a member of the busy trauma service, and the rotation is a favorite amongst most residents, regardless of ultimate career goals, due to the high yield learning environment with faculty who value teaching and education. Drs. Donegan, Harding, and Mehta all participate in resident morning lectures, department grand rounds, as well as the General Medical Education Committee (GMEC).

In conclusion, the expertise and diversity of the Trauma and Fracture Division continues to grow, and, despite the challenges (of COVID) and the changes that lie ahead, we are looking forward to another momentous year of patient care, innovation, research, outreach and education.

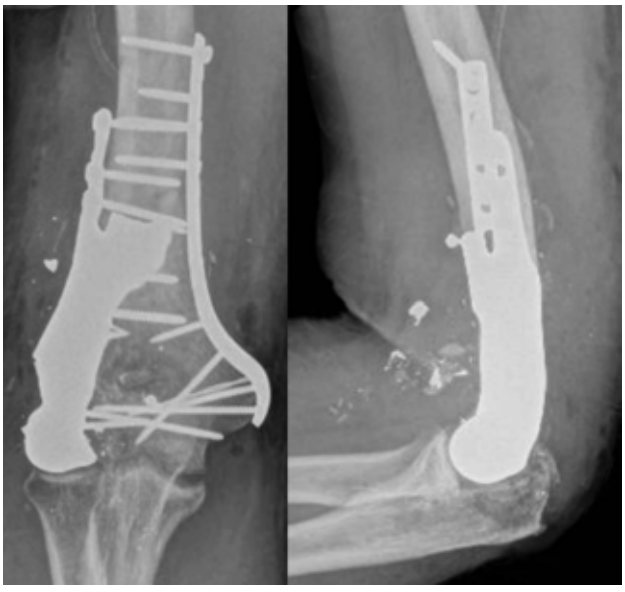


Figure 2.

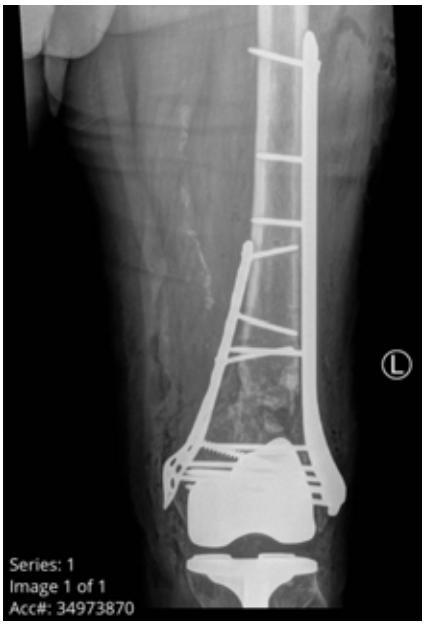


Figure 3.

Spine Division

Harvey Smith, MD

Spine Faculty


Harvey Smith, MD


Vincent Arlet, MD


Amrit Khalsa, MD


David Casper, MD


J. Rush Fisher, MD

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

Clinical Growth

Over the past year we have continued our clinical growth and expanded our satellite clinics to new locations.

Research

Our division has been established 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, developing the first *in vivo* large animal tissue-engineered total disc replacement. Our clinical research division is led by Dr. David Casper. Dr. Casper is investigating outcomes for our complex deformity patients as well as all adult spine patients. Dr. Khalsa is continuing his research interests in evaluating cost-effectiveness and risk adjustment models in spine surgery. Dr. Arlet continues his role as an international thought leader in complex spinal deformity. Our division members have multiple federal, society, and industry grants to support our research program.

Academic Productivity

Penn Ortho Spine has been represented in over 25 peer-reviewed publications, abstracts, and book chapters. Multiple faculty have been visiting professors for Grand Rounds and have also presented at the Seattle Science Foundation three times this past year. Our faculty chair committees with the North American Spine Society, and have organized Instructional Course Lectures at national and international 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. Dr. Khalsa maintains an ongoing outreach program in South America. Due to the 2020 COVID-19 pandemic, there was a pause in our international work. It is with great excitement that Dr. Arlet resumed his outreach in Trinidad this year.

Spine Fellowship

Our spine fellowship is entering its sixth year of partnership with the Shriners Hospital of Philadelphia. Our complex spinal deformity fellowship is unique in that it offers a combined adult and pediatric complex deformity experience. This past year we added an additional fellowship position.

Penn Sports Medicine Division

Brian Sennett, MD

Sports Medicine Faculty


Brian Sennett, MD


James Carey, MD, MPH


John Kelly, MD


Miltiadis Zgonis, MD


Kevin McHale, MD

Like much of the world, the Sports Medicine Division at Penn Orthopaedics was challenged with the pandemic as youth, college, and professional sports moved to the sidelines for an extended period of time. However, as we have all learned to live with COVID, athletics have returned to the community and organized sports. The Broad Street Run returned in October 2021 and will return to its normal spot on the calendar on the first Sunday of May this year. Penn Sports Medicine has been and will continue to be the medical providers to this fantastic event. Drs. Alexis Tingan and John Vasudevan serve as the Medical Directors of the Broad Street Run. In addition, they are Co-Directors of the Running and Endurance Sports Program. This collaboration between Penn Sports Medicine and Good Shepherd Penn Partners is tailored to the specific needs of endurance athletes (runners, cyclists, swimmers, etc.) through a combination of medical care, physical therapy, surgical treatment, and connections throughout the Philadelphia community. In addition to the Broad Street Run, Drs. Tingan and Vasudevan have served as Medical Directors for the Penn Relays, Philadelphia Distance Run (formerly Rock 'n' Roll Half-Marathon), LOVE Run Half-Marathon, and Philadelphia Triathlon, and bring experience and expertise to help endurance athletes optimize performance and both treat and prevent injury. This program will expand the services offered by Penn Sports Medicine and aspires to be a unique clinical service in the region. In addition, Dr. Tingan has been selected to serve as the team physician for USA Track and Field at the World Junior Track and Field Championships in Cali, Colombia in August 2022.

In addition to the vast amount of running events, the Division of Sports Medicine has continued to provide medical coverage for Penn Athletics, Drexel University, the University of the Sciences, and many local high schools. In addition, Penn Medicine provides medical and orthopaedic care for the Philadelphia Flyers and medical care for the Philadelphia Eagles.

Medical and orthopaedic care for the Philadelphia Eagles has been provided primarily by Drs. Gary Dorshimer, Brian Sennett, and James Carey. The medical care for the Philadelphia Eagles has continued to be delivered by Dr. Arsh Dhanota who serves as both the Head Team Physician and Chief Medical Officer of the Philadelphia Eagles.

A new addition to Penn Sports Medicine and Philadelphia has been US Squash. US Squash moved to a new home in Philadelphia, opening a new state of the art complex. Upon relocating, US Squash quickly engaged Penn Medicine to become its official health system to keep the organization's world-class players fit and healthy.

As the official health system of US Squash, Penn Medicine will also be the official health system of the United States' national team, the U.S. Open Squash Championships, and the newly opened Arlen Specter US Squash Center in Philadelphia – the world's largest community squash center.

Our organizations share values of excellence, integrity, diversity, teamwork, and also the City of Philadelphia. The combination of the two top-tier organizations won't just be mutually beneficial, but it will also hold great value for the surrounding communities.

The three-year agreement designates Penn Medicine as the official health system of US Squash. Penn Medicine personnel will also serve as the official team physicians – and official orthopaedic providers – of the United States' national squash team. Athletes from US Squash will also benefit from Penn Medicine's Sports Science Optimization services to both improve their play and keep them healthy. The next three U.S. Opens, the most prestigious professional championships in the country and all at the Specter Center, will also be sponsored by Penn Medicine.

In addition to the on-the-court and in-the-clinic benefits, Penn Medicine and US Squash will combine to strengthen the US Squash Community Initiative. This effort seeks to expand access to the sport across many different communities and bring new athletes to the sport who previously had been unable to experience it. This includes no-cost clinics for new

players, open court access to the public, and the creation of new public school squash teams in partnership with the Philadelphia School District. SquashSmarts, an intensive out-of-school academic and athletic mentoring program, will operate its West Philadelphia programs at the Specter Center's Lenfest Learning & Innovation Center. All of these programs are designed with the mission of positively impacting social determinants of health including opportunities for physical activity and educational access.

Education and research have always been cornerstones of the Division. Dr. James Carey continues to serve as Director of the Penn Cartilage Center and serves as Associate Editor of the American Journal of Sports Medicine. In August 2021, Dr. Carey took over for Dr. Sennett as the Program Director for the Orthopaedic Sports Medicine Fellowship, which trains two fellows per year with faculty at Penn and at CHOP.

It has been an extremely busy time in the Division of Sports Medicine as the top athletic programs in town continue to reach out to Penn Medicine to provide the best medical care for their athletes.

Hand Division

David Bozentka, MD

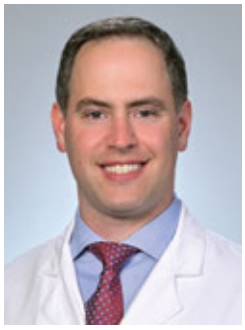
Hand Surgery Faculty


David Bozentka, MD


David Steinberg, MD


L. Scott Levin, MD, FACS


Hannah Lee, MD, PhD


Robert Carrigan, MD


Robert Carrigan, MD


Apurva Shah, MD, MBA


Stephen Liu, MD

The Penn Hand and Upper Extremity Service has emerged the Covid-19 pandemic stronger in our clinical, research, and educational programs.

We congratulate our chairman, L. Scott Levin MD, who was awarded the Kappa Delta Elizabeth Winston Lanier Award through the American Association of Orthopaedic Surgeons. The prestigious award recognizes research in musculoskeletal disease or injury with the potential to advance patient care. Dr. Levin was chosen for his work in the evolution of microsurgery and the development of the orthoplastic approach and microsurgical reconstructive ladder for extremity reconstruction. Dr. Levin performs many critical roles within the health system, including Vice President and Associate Dean for Resource Development, the Paul B. Magnuson Professor and Chairman of the Department of Orthopaedic Surgery, and Professor of Surgery in Plastic Surgery at the University of Pennsylvania School of Medicine.

In addition to his busy clinical practice at Chester County Hospital and Pennsylvania Hospital, Dr. Stephen Liu has been named Associate Program Director for the Orthopaedic Surgery Residency Program for the University of Pennsylvania Department of Orthopaedic Surgery Perelman School of Medicine. In this role, Dr. Liu will help oversee the implementation and evaluation of the educational program for over 40 orthopedic surgery residents. With his exceptional motivational skills and passion for teaching, we know Dr. Liu is the ideal person for the position.

We are fortunate to have added Dr. Andrew Sobel to our Penn Hand Surgery Section. Dr. Sobel obtained his undergraduate degree in biomedical engineering at Duke University and medical school training at State University of New York at Buffalo. He completed his orthopedic surgical residency at Brown University Rhode Island Hospital and his hand surgical fellowship from Washington University in Saint Louis at Barnes Jewish Hospital. Before arriving at Penn, he developed a busy hand and upper extremity practice at St. Luke's University Health Network. Dr. Sobel has hit the ground running taking on the role of Director of Hand Surgery Clinical Research. Dr. Sobel's clinical practice is based at Pennsylvania Hospital and Penn Medicine at Valley Forge. In addition, he has expanded the hand surgical education program leading the Friday morning Hand Board to review weekly consults and hand surgical concepts with the residents and fellows.

The most recent Penn Hand Surgery family member is Evan Park Lee, born on October 3, 2021. Mom and clinician-scientist Dr. Hannah Lee notes that Evan spends the vast majority of his day admiring the intricacies of his hands, especially their taste. Dr. Lee is rising quickly in the academic ranks as the American Society recently awarded her the Goldner Pioneer Award for Surgery of the Hand. The award is bestowed upon

the highest-ranking research grant, which is highly innovative and far-reaching to the hand surgical membership.

The hand surgery fellowship has excelled under the leadership of David R. Steinberg, M.D. as the director and Ines Lin, M.D. as the associate program director. Our hand surgery fellows have had a solid clinical and academically productive year. Dr. Charles (Chris) Jehle, who hails from Kansas, completed his plastic surgery residency at Brown University Hospital and Rhode Island Hospital. He will be returning home to the University of Kansas, Department of Plastic, Burn and Wound surgery, in the Division of Hand, Peripheral Nerve and Microsurgery. Dr. Kareem Hassan completed his plastic surgery residency at the University of Chicago. After completing his fellowship year, Dr. Hassan will be joining the practice at Phoenix Children's Hospital.

Although elective clinical work was curtailed at the height of the pandemic, the hand section continued to treat urgent traumatic injuries and care for patients virtually through telemedicine. The new robust telemedicine platform has become a consistent part of the clinical practice despite the declining number of covid cases. The education program also advanced through the pandemic as it converted to a virtual format. Currently, hand surgical conferences take place on Tuesday evenings, with the online design allowing members throughout the country to attend. We welcome all alumni to join the virtual meetings and add to our educational sessions.

The hand and upper extremity research team continue to thrive with solid support. Annamarie Horan, Ph.D. is the Director of Orthopedic Clinical Research, and Mary Dooley has been named Clinical Research Program Manager. The team has been instrumental in advancing the numerous ongoing clinical research projects.

The hand transplant team has successfully performed bilateral upper extremity allotransplantation for four patients with quadra-membral amputations. Unfortunately, the listing of patients has been on hold due to the Covid pandemic. Despite the covid restrictions, the group has met virtually and in the human tissue lab performing cadaveric rehearsals and honing the procedure checklists in preparation for when our fifth bilateral upper extremity allotransplantation is listed.

The hand and upper extremity service could not function without the outstanding support from our superb advanced practice providers, nurses, and administrative assistants. With this exceptional support and collaboration, the future looks bright for the hand surgery section.

Shoulder and Elbow Division

David Glaser, MD

Shoulder & Elbow Faculty

David Glaser, MD

Andrew Kuntz, MD

Gabe Horneff, MD

We emerge from the pandemic with greater strength and focus in all three missions. With continued commitment to manage of the most complex cases, the section's tertiary referral network has continued to increase, along with the complexity of cases. In FY21, the group performed over 11,000 visits and performed over 1,000 surgical cases with revision shoulder arthroplasty and elbow surgery seeing increased volume.

Gabe Horneff, a former administrative chief resident, superior surgeon, researcher and educator, who joined us from The Rothman Institute during the pandemic, immediately took ownership of resident education for our division. Gabe has now stepped seamlessly into our practice at PAH. Our indications conference which was expanded during the pandemic has continued and includes a nationwide group of our past fellows, our therapy team, and regional shoulder and elbow providers. Jeff Abrams and Brian Galinat have been welcome additions to our educational mission. Through a virtual platform, the group of talented sub-specialists re-unite monthly to discuss complex cases, opportunities for research and to catch up on important life events.

Andy Kuntz is leading our research effort, setting a high standard for both scientific methods and clinical outcomes. We would like to recognize Andy for his continued focus as a clinician-scientist, providing world class clinical care, while contributing to all aspects of our research mission- clinical, translational and basic science. He was recently awarded a Merit Grant to further support his research. Alongside Andy, Gabe has helped expanded our clinical research program, mentoring several medical students and residents with their academic endeavors. In close collaboration with Lou Soslowsky and others in the McKay Research Laboratory, we helped advance the McKay lab to #1 in National Institutes of Health funding. We are currently rolling out an integrated research platform that will be able to seamlessly unite clinical and research activities, providing a much-needed tool for data collection, while improving two-way clinical communication with our patients. Through his leadership, we have helped complete enrollment in the first stemless reverse IDE study and begin another. We are working on several sponsored clinical trials including a multi-center trial, which is the direct result and translational follow-up to basic science research performed in the McKay Lab. The multimodal pain protocol for outpatient shoulder surgery that we developed is now being utilized at other Penn sites and has made our transition to outpatient shoulder arthroplasty seamless. For Andy's efforts, he continues to serve on the Orthopaedic Research Society (ORS) board of directors and has served on the ORS membership committee and Community Council while also being active in the ASES.

The fellowship has continued to thrive, attracting the most competitive candidates. Despite Russ's departure, this year's candidate pool was as competitive as prior years. Our program is unique in that the fellow has exposure to four different surgeons, with complementary philosophies, who use an extreme range of devices and approaches. John Kelly has added an additional opportunity to fellows interested in creative arthroscopic approaches to manage complex shoulder and elbow pathology. Additionally, now in its fifth year, and in collaboration with our French colleagues, we offer our fellow an opportunity to visit world leaders in shoulder surgery. Current fellow Brandon Romero (F'22) will follow Christy Piper (F'21), Greg Gomez (F'19), Josh Rogozinski (F'18), and Chad Myeroff (F'17), and spend three weeks visiting academic centers in Europe. As our international relationships grow, Brandon is planning to visit Spain, Monaco, Germany and France. We have consistently matched our top choices. Past fellow, Mohit Gilotra (F'15) won the 2018 ASES Charles Neer award and several prior fellows participate in resident education including Chad, Ben Widmer and Dan Doty.

We will continue to leverage our internal cohesiveness, therapy partners (superstars Brian Leggin, Joseph Kearns, and Marty Kelly) and recent collaborations with non-Penn shoulder and elbow providers, to bring success to our division, in all three missions.

Adult Reconstruction Division

Charles Nelson, MD

Arthroplasty Faculty

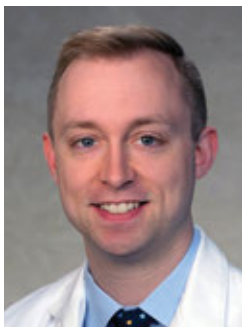
Charles Nelson, MD

Craig Israelite, MD

T. David Tarity, MD.

Christopher Anthony, MD

Neil Sheth, MD



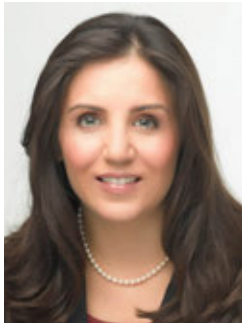
Christopher Travers, MD

This past academic year has been a productive one for the Penn Orthopaedics Adult Reconstruction Division. Despite many of the challenges with the ongoing COVID pandemic, the adult reconstruction division has maintained a high surgical volume and provided high quality care for a wide spectrum of patients. We continue to care for both healthy and high-risk patients with innovative strategies to minimize complications and optimize quality in the high-risk patient cohort. In addition to clinical excellence, our faculty have remained active in making scientific contributions and clinical education nationally and internationally, as well as serving in leadership and volunteer positions within most of the important national orthopaedic organizations including: the American Academy of Orthopaedic Surgeons; The Hip Society, The Knee Society, the American Associaton of Hip and Knee Surgeons, the American Orthopaedic Association, and the American Board of Orthopaedic Surgeons. Our faculty participated in several dozen peer reviewed publications, scientific presentations and invited lectures in 2021. The division continues to remain active in clinical research with substantial federal and industry funding. The adult Reconstruction faculty members currently include Professor Charles L. Nelson, MD, Associate Professors Eric Hume, MD, Craig Israelite, MD and Neil Sheth, MD and Assistant Professors Christopher Travers, MD, Christopher Anthony, MD, and T. David Tarity, MD.

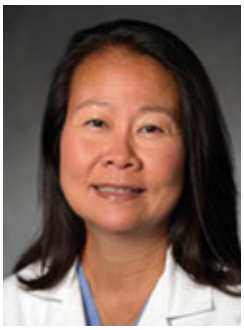
Foot and Ankle Division

Casey Humbyrd, MD

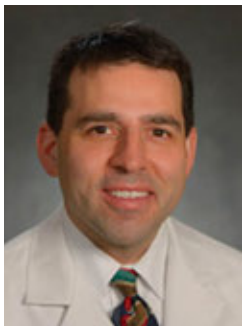
Foot & Ankle Faculty



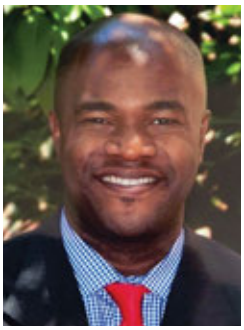
Casey Humbyrd, MD



Wen Chao, MD



Daniel Farber, MD



Anthony "Bobby" Ndu, MD

Keith Wapner, MD

This year was filled with transitions for the foot and ankle team.

Dr. Keith Wapner stepped down as foot and ankle chief, transitioning that role to Dr. Casey Humbyrd. Dr. Wapner had his last OR day on January 20, 2021. He is continuing to see patients on a part-time basis, three days a week for two weeks a month, a slow transition to retirement after a busy and successful career.

The division also said a difficult goodbye to Dr. Kathryn O'Connor, as she moved to the Washington, D.C. area for family reasons. Dr. O'Connor and her husband recently welcomed a baby boy in September 2020. Before leaving Penn, Dr. O'Connor had a busy clinical practice as well as her work with Josh Baxter, PhD on Achilles tendinopathy.

Dr. Casey Humbyrd assumed the chief role in January 2021. She came from Johns Hopkins University, where she was the chief of the foot and ankle division. Dr. Humbyrd completed residency at Johns Hopkins, fellowship at Mercy Medical Center, and a Masters in Bioethics at the Bloomberg School of Public Health. Dr. Humbyrd's academic interests focus on ethical issues in orthopedic surgery, and she has published broadly in this area. She has a column "Virtue Ethics in a Value-Based World" in Clinical Orthopaedics and Related Research. Dr. Humbyrd serves as a reviewer for Foot and Ankle International, the Journal of the American Academy of Orthopaedic Surgeons, and Clinical Orthopaedics and Related Research. She is also a board member of the American Foot and Ankle Society, an AAOS representative to the American Medical Association and Chair of the Orthopaedic Section Council, and a member of the Committee on Ethics and Outside Interests of the AAOS. She was recently elected as a new member to the Association of Bone and Joint Surgeons and the Orthopedic Foot Club.

Dr. Humbyrd is excited to build the foot and ankle division in clinical work, research and teaching components. To that end, she and the Department successful recruited Dr. Anthony "Bobby" Ndu who will be joining the division in May 2021. Dr. Ndu is a graduate of the Yale University medical school, as well as Yale's Master's in Business Administration program. He completed his residency at Yale as well. He is a former foot and ankle fellow at Penn, completing his training in 2013. His interests include resident and fellow education as well as quality improvement.

Dr. Daniel Farber has continued to lead the educational mission of the department as Vice Chair for Education and Residency Program Director while maintaining a busy clinical practice. He serves on the education committee of AOFAS and has helped with the development and rollout of the AOFAS fellowship accreditation program. Dr. Farber is involved in the chronic Achilles instructional course lecture for the AAOS, which is being converted into a piece for the Instructional Course Lecture book. He is also Chair of the AAOS resolutions committee. He has continued his participation in the industry "Lapiplasty" study, as well as basic science research efforts in collaboration with Lou Soslowsky, PhD and the McKay lab resulting in a recent publication in AJSM simulating chronic Achilles rupture treatment in a rat model. He is also a collaborator with Josh Baxter, PhD of the Human performance lab on his recent K01 and R01 awards exploring Achilles pathology. He also continues to work on research involving the weight-bearing CT scanner here at Penn, specifically investigating hallux valgus deformities.

Dr. Wen Chao continues to be the orthopedic foot and ankle consultant to the Pennsylvania Ballet since 2001. She also serves as a member on the Public Education Committee for AOFAS, as well as reviewer for Foot and Ankle International and Foot and Ankle Orthopaedics. She is a member of AAOS, AOFAS, AOA and the Orthopaedic Foot Club. Dr. Chao is working on research projects, including investigating the accuracy of ultrasound and MRI with intraoperative findings in peroneal tendon pathology, as well as the long-term follow-up after FHL tendon transfer.

2020 had a notable success for the division with the nomination of the Cartiva MAUDE study for the Roger Mann

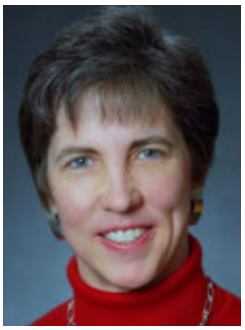
Award at the 2020 AOFAS Annual Meeting. Moving forward, we plan to deepen our work in Achilles tendon research in collaboration with the McKay Lab. We also hope to expand our collaborations with medical students and residents. Additionally, Dr. Humbyrd is transitioning her research projects from Johns Hopkins to Penn, including projects on the ethical use of opioids in orthopedic surgery, equity in bundled payment programs, and shared decision-making for in ankle surgery.

As we look to the future, the foot and ankle team hopes to recruit more phenomenal residents into foot and ankle as well as continuing our excellent fellowship program. We also plan to expand our reach in the Philadelphia area, including increased presence in New Jersey and the Philadelphia Suburbs. While the year has been full of transitions, we anticipate emerging stronger together, building on the tremendous legacy of Dr. Keith Wapner and finding new opportunities for growth in our tripartite focus of clinical care, research and teaching.

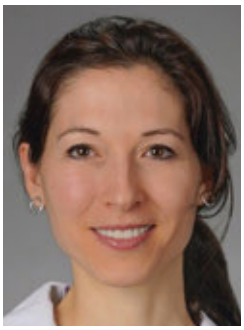
Orthopaedic Oncology Division

Cara Cipriano, MD, MSc

Orthopaedic Oncology Faculty



Kristy Weber, MD, FACS



Cara Cipriano, MD, MSc

2021-22 was a year of transition for the Orthopaedic Oncology service at Penn, with exciting changes to both our team and surroundings.

In September 2021, Dr. Cara Cipriano joined Penn Orthopaedics as the Chief of Orthopaedic Oncology and Director of Undergraduate Medical Education. Dr. Cipriano attended the Perelman School of Medicine here at Penn, followed by residency at Rush University. She completed fellowships in Musculoskeletal Oncology at the University of Toronto and Adult Reconstruction at Virginia Commonwealth University. She earned her master's degree in Clinical Investigation and practiced for seven years at Washington University in St. Louis, where she was the Director of Medical Student Education for the Department of Orthopaedics. Her clinical focus is on primary and secondary tumors of the musculoskeletal system, as well as primary and revision joint replacement. In addition to seeing patients at PCAM, she is building a practice at Radnor to improve access.

Dr. Kristy Weber continues to run a busy clinical service at PCAM and serves as the Vice Chair of Faculty Affairs. In 2021, she completed her term as First Past President of the AAOS while dedicating a tremendous amount of energy to her division and department here at Penn. As the Director of the Sarcoma Program at the Abramson Cancer Center, she leads the multidisciplinary sarcoma team, including medical oncology, radiation oncology, pathology, radiology, and neurosurgery. The group meets weekly for virtual multidisciplinary tumor board to ensure optimal coordination and care for our patients.

PA Kate Barrie remains an essential member of the team. Kate not only plays a large role in managing the service, but also sees patients independently. Kate exemplifies dedication, compassion, and clinical excellence, for which she is beloved by patients and colleagues alike. Our prior administrative coordinator, Sasha Mendez, and ambulatory nurse, Chrissy Vanella, have moved on to other roles, and Chrissy continues to help in a temporary capacity whenever possible as we build our new team.

In October, we also experienced a physical transition with the opening of the Pavilion hospital. The building features panoramic views of the city, large screens in every patient room, and elevators without buttons. We marvel at the innovation and still sometimes get lost in its 1.5 million square feet. We operate and consult on oncology patients in the new building, while our postoperative patients remain comfortably lodged in the familiar surroundings of Rhoads 4. With the support of HUP leadership, we are increasing collaboration with social work and other inpatient services to further improve the care of our patients.

The past year has seen an increased focus on clinical research in our division. Through collaborative projects with radiation oncology and neurosurgery, we are currently investigating strategies of local disease control, including surgical and nonoperative treatments. These projects are designed to address the unanswered questions we encounter in our own practices, with the goal of providing answers that will improve patient care beyond our institution.

Our basic and translational science team continues to maintain impressive extramural funding and push the envelope of modulating the immune environment in soft tissue sarcoma and identifying targets for the prevention and treatment of sarcoma metastasis to the lung. We have strengthened our collaboration with the Children's Hospital of Philadelphia with collaborative clinical trials across the full age span led by Drs. Patrick Grohar and Robert Maki. Overall, the portfolio of available clinical trials for a variety of bone and soft tissue sarcomas as well as aggressive benign conditions has more than doubled over the past year at Penn.

We would like to extend our heartfelt thanks to our patients, their families, and other supporters who continue to make our research possible through philanthropic generosity.

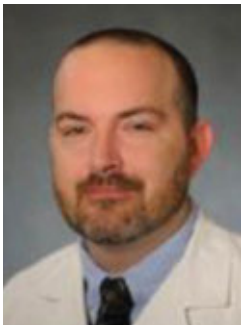
Upcoming Events:

After two years of postponing due to COVID-19, we look forward to hosting Dr. Carol Morris, Chief of Orthopaedic Oncology at Johns Hopkins University, as the Penn Orthopaedic Oncology Visiting Professor in September 2022. Our 8th annual Steps to Cure Sarcoma event is scheduled to take place in person on May 22, 2022 (www.stepstocuresarcoma.com). We hope to see you there!

Neuro-Orthopaedics Division

Keith Baldwin, MD, MPH, MSPT

Neuro-Orthopaedic Faculty



Keith Baldwin, MD, MPH, MSPT

David Spiegel, MD

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 Orthopedics at Penn and is one of a handful of orthopedic surgeons nationally who cares for the spectrum of neuromuscular disorders in both adults and children. Dr. Baldwin works alongside Brian Fletcher, 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 and has recently been joined by Chrissy Goodbody, 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, Jessica Staschak, and Suzanne Manzoni 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, the Orthopedic Oncology Service, the Sports Medicine Service and the Trauma Service. The adult Neuro Orthopedic Service was also invited to provide clinical training to the Penn and CHOP Physiatry program

Our partnership with the Philadelphia Shrine continues to grow and evolve, with many of the Penn/CHOP neuro orthopedic services' gait studies being performed by the Shriner's hospital. Dr. Baldwin continued his work giving a talk at this year's virtual Orthopedic Rehabilitation association meeting along with Emeritus Chief of Neuro Orthopedics Mary Ann Keenan who gave a wonderful tribute to Dr. Jacquelin Perry. One of our outstanding medical students Ariana Meltzer-Bruhn working with a CHOP fellow Matthew Landrum won the Vernon Nickel award at that meeting for their work on nutrition consultation in patients with neuromuscular spinal deformity. The service has also given talks or presented papers nationally and internationally including the SLAOTI virtual meeting, the AAOS, and will be presenting in the next month at the SEHA conference teaching pediatricians about gait problems in Abu Dhabi.

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. The research program in neuromuscular orthopedics was busy with publications in neuromuscular spine published in the Journal of Pediatric Orthopedics, Spine Deformity, and Journal of Bone and Joint Surgery. Ongoing research in neuromuscular hip surgery, multicenter studies on neuromuscular foot reconstruction and neuromuscular spine surgery have increased the profile of the program and its thought leadership nationally. We have faced the challenges of the COVID-19 pandemic to bring care to this disadvantaged and often forgotten population of patients in a safe and effective manner, and look forward to continuing to provide them care to aid in functional recovery in the years to come.

Orthoplastic Limb Salvage Division

Meghan E. Wilson, RN, Christine McAndrew PA-C, Stephen Kovach, MD, L. Scott Levin, MD, FACS, and Samir Mehta, MD

Orthoplastic Limb Salvage Faculty

Stephen Kovach III, MD

L. Scott Levin, MD, FACS

Samir Mehta, MD

The Penn Orthoplastic Limb Salvage Center (POLSC) continues to grow strong after four years since its official launch in 2018. Limb reconstruction has been around for ages, but the POLSC officially combines the close collaborative efforts of both orthopedic and plastic surgery into one program to deliver efficient and streamlined care for patients. Dr. Stephen Kovach, Dr. Scott Levin, and Dr. Samir Mehta continue to be at the forefront of innovative strategies to salvage and reconstruct upper and lower extremities. The close collaboration of care between both orthopedics and plastic reconstructive surgery is key in the successful outcomes in patients and restoring limb function. The addition of a nurse coordinator has helped guide patients through the web of appointments, referrals, surgeries, therapies, post-operative appointments, home care, etc. Advanced Practice Providers on our team are performing the complex care management of this patient population. The APPs are at the forefront providing high quality care throughout the continuum of care for our patients.

Since the launch of the program, there have also been two orthoplastic fellowships that have come through the program designed specifically for a year of hands-on experience for limb salvage procedures. Both previous fellows have gone back to their homes in Canada and Israel to work on limb salvage centers for their own. Although the position went vacant this past year, we are happy to have another orthoplastic fellow joining the program this upcoming summer. Dr. Linden Head will join us from Canada. Linden completed medical school at the University of Ottawa (2012 – 2016). He then completed a Plastic and Reconstructive Surgery residency program at the University of Ottawa (2016 – 2021). Following residency, he completed a fellowship in Hand and Upper Extremity Surgery at the University of Pittsburgh (2021 – 2022). We look forward to Dr. Head joining our team as our orthoplastic and limb salvage fellow.

Another addition to POLSC is the use of bi-weekly operating room block time at Presbyterian Medical Center specifically dedicated for the use of the use of combined orthoplastic cases. This has given us more time for the urgent reconstructive cases that need to be added into the already full OR schedule. It has also made scheduling these cases easier as coordinating OR time between the two services can be difficult due to conflicting schedules. The POLSC continues to expand and grow, and has even begun to treat international patients for limb salvage procedures.

Microsurgery is a huge component of the Orthoplastic Limb Salvage Center. Vascularized free tissue transfers are preformed frequently to give patients adequate soft tissue coverage. Patients with extensive limb injuries will not perform well if there continues to be exposed bone and hardware. A wide variety of free flaps are performed at Penn Medicine on a regular basis. Post-operative flap care has been established with dangle protocols. In addition to soft tissue coverage, free vascularized bone transfers are also frequently used to treat non-unions, malunions, avascular necrosis and bone defects in the case of the free vascularized fibula graft (FVFG) and the medial femoral condyle (MFC) flaps. FVFG are used for several reconstructive surgeries, including our hip preservation surgery for patients with AVN of the femoral head without collapse. Orthoplastics at Penn Medicine is ever evolving and continues to look at outcomes to improve the patient experience.

Penn Medicine continues to be at the forefront for the latest advances in extremity care. In addition to the highly skilled microvascular vascularized free flaps that are frequently

performed to provide adequate soft tissue coverage, there are many other advances in surgical procedures utilized within POLSC. On the orthopedic side, Dr. Samir Mehta is utilizing specialized implants to improve outcomes. The limb lengthening nail is implanted into patients' femurs or tibias for limb length discrepancy. The surgery typically involves preforming an osteotomy in the mid shaft of the bone which allows the patient to use an external hand held magnetic device in the convenience of their own home that pairs to the implanted nail to turn the rod. Patients will use this device at home with a prescription for a lengthening program which is set into the machine to bring lower extremities out to length to improve overall gait and function. Dr. Mehta is also using 3D printing technology to take contralateral images of a patient's talus to create a total replacement implant. Several patients have had successful outcomes from the total talus replacement surgery.

On the plastic reconstructive and microvascular side are advancements in Targeted Muscle Reinnervation (TMR). In not always an unfortunate manor, patient's seeking limb salvage end up with an amputation. Amputations can help free patients from long-standing wounds, chronic osteomyelitis, chronic pain and the inability to ambulate and get on with their lives. However, amputations done to alleviate these symptoms are not without their own complications. Amputations are notorious for residual and phantom limb pain, which leads to complex chronic pain and inability to ambulate in a prosthetic. TMR is a nerve transfer that takes the distal end of the nerve, removing any neuromas present, and connecting it to a proximal motor branch. These motor branch nerves are found by using a biphasic nerve stimulator. This technique of TMR helps reduce and eliminate phantom and residual limb pain.

In addition to limb saving procedures is our hand transplant program. Penn Medicine has performed four successful bilateral hand transplants (3 adults and 1 child). Although the global pandemic has put a slight pause on the program, we continue to work and care for our past transplant patients as well as our candidates pending donors. We received heartwarming news from one of our previous bilateral hand transplant female patients who successfully delivered a healthy baby girl in the last few months. She is the first hand transplant patient to deliver a baby after her transplant. She was overly joyed to be able to hold and care for her baby, and despite being on lifelong immunosuppression, had an otherwise healthy pregnancy. Due to the pandemic, one of our international transplant candidates had to put a pause on active donor offers. However, despite travel restrictions, Dr. Stephen Kovach and Dr. Scott Levin went overseas to Switzerland last spring to treat our patient with microvascular surgery to his bilateral lower extremities. The patient underwent bilateral free flaps to his lower extremity amputations for chronic fissuring and wound issues. This permitted our team to better prepare our patient for his upcoming bilateral hand transplant.

POLSC continues to have a presence on social media to promote our accomplishments. Posts include patient testimonials, surgical highlights, and physician spotlights. The goal of the POLSC social media presence is to engage other patients and healthcare facilities to share progress and innovative surgical procedures we have at Penn Medicine to continue to restore function to limbs.

The POLSC continues to grow and expand on future plans. Osseointergration is a procedure on the horizon that is currently being worked on to bring to Penn Medicine. This advancement in amputation care helps amputates improves mobility (control of the prosthetic leg), improves proprioception, reduces nerve pain, and eliminates common problems associated with sockets. Although this is not currently being performed here at Penn Medicine, it is something we hope to have the ability to perform in the near future. The Penn Orthoplastic Limb Salvage Center is making huge strides to save and salvage functional limbs, as well as restore function and mobility to patients who have undergone amputations.

Case to highlight:

We present the case of a 38-year-old who had a left below the knee amputation with residual painful neuroma. The patient initially suffered a traumatic injury of his left lower extremity in an industrial accident. He initially underwent an attempt at

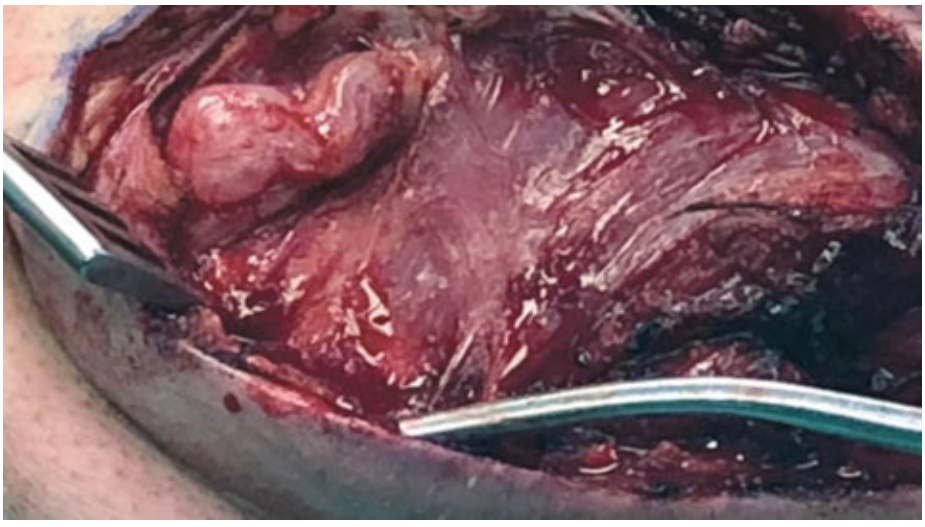


Figure 1. Dissection over the anterior compartment demonstrating large neuroma of the deep peroneal nerve.

limb salvage including microvascular free flap reconstruction of his extremity. He developed recurrent osteomyelitis and elected for a below knee amputation. He was initially able to ambulate in a prosthesis, but developed debilitating pain in the distribution of his peroneal nerve, resulting in inability to wear his prosthesis and pursue his desired functional and recreational activities. Physical exam confirmed the presence of a palpable, exquisitely tender mass overlying his anterior compartment consistent with a neuroma of the deep branch of the peroneal nerve. He underwent a block of his common peroneal nerve with Marcaine™ with complete relief of his pain. Secondary to the complete pain relief with anesthetic blockade, he ultimately decided to pursue TMR for his symptomatic deep peroneal nerve neuroma.

The patient was seen in follow up and is pain free after years of a symptomatic neuroma. He is now back in his prosthesis and has returned to his physical activity without pain.

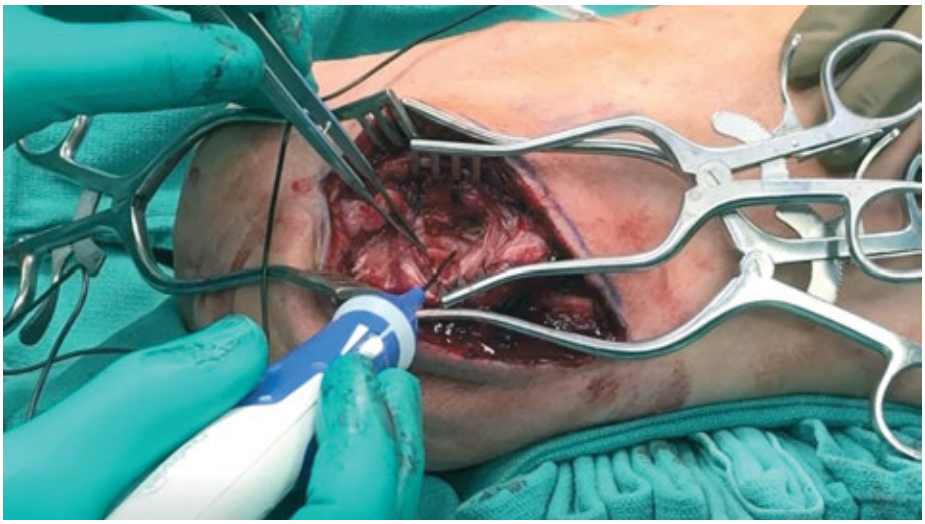


Figure 2. After dissection and definition of the neuroma of the deep peroneal nerve, the Checkpoint® nerve stimulator was used to map and identify the motor branches. Demonstrated is confirmation of proximal motor branches of the deep peroneal nerve with branches to extensor digitorum muscle body.

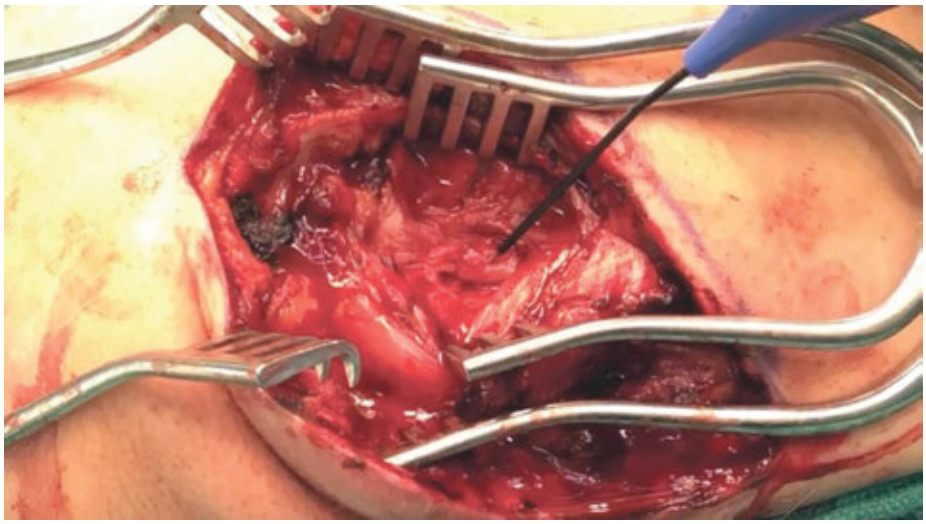


Figure 3. After resection of the neuroma, the proximal deep peroneal nerve is coapted to the motor branch to the extensor digitorum in an epineural fashion with 8-0 nylon with loupe magnification. Shown is the activation of the motor branch with the Checkpoint stimulator by stimulating the deep peroneal nerve proximal to the nerve coaptation demonstrating an intact nerve coaptation and conduction. This is possible due to the close proximity of the target muscle and stimulation through a coaptation to motor nerve recently transected.

Children's Hospital of Philadelphia

John (Jack) Flynn, MD

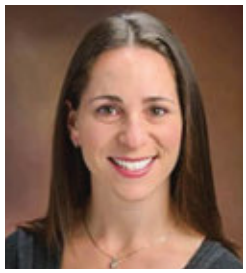
Pediatric Faculty


John Flynn, MD


Jason Anari, MD


Alexandre Arkader, MD


Keith Baldwin, MD, MPH, MSPT


Naomi Brown, MD, FAAP, CAQSM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Benjamin Chang, MD, FACS


Richard Davidson, MD


Vincent Deeney, MD


Malcom Ecker, MD


Theodore Ganley, MD

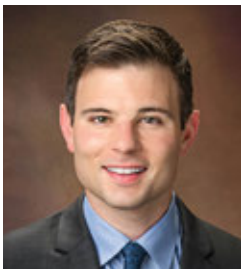

B. David Horn, MD


J. Todd Lawrence, MD, PhD


Ines Lin, MD


Kathleen Maguire, MD


Christina Master, MD, FAAP, CAQSM, FACSM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Apurva Shah, MD, MBA


David Spiegel, MD


Brian Vernau, MD, FAAP, CAQSM


Kristy Weber, MD, FACS


Lawrence Wells, MD


Brendan Williams, 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 pediatric musculoskeletal care in the nation/world, we have continued to expand our clinical, research, and teaching programs despite challenges due to COVID-19 pandemic. Again in 2021, *US News and World Report* ranked CHOP Orthopaedic Surgery 1st in the nation in pediatric orthopaedic surgery.

In 2021, CHOP Orthopaedics welcomed a new sports medicine pediatrician to our team, participated virtually and in person at national and international conferences, maintained enrollment of three FDA Phase IIIb investigational drug trials and a feasibility device trial, published more than 200 articles, and obtained significant extramural funding from major funding agencies such as National Institutes of Health (NIH), Department of Defense (DoD), and National Science Foundation (NSF).

Clinical Program

Our Orthopaedic faculty continues to expand and is currently comprised of thirty members: eighteen specially trained pediatric orthopaedic surgeons (including three transition-to-adult care faculty), four non-operative physicians, six sports medicine-trained pediatricians, and two collaborating plastic surgeons. In March 2022, we welcome Dr. Chrissy Goodbody (Figure 1), who will join us as an Attending Surgeon in pediatric limb deformity, foot/ankle and neuromuscular disorders. She completed her medical degree at the University of Pennsylvania, her residency at the Hospital of Special Surgery, her Pediatric Orthopaedic Fellowship at CHOP, then a sub-specialty fellowship at the Baltimore Limb Deformity Center. Our division also welcomed faculty member, Dr. Edward Re (Figure 2). He earned his medical degree at Brown University in Providence, Rhode Island. Dr. Re completed an internship in Emergency Medicine at the Hospital of the University of Pennsylvania before joining CHOP as a pediatric resident, then a primary care sports medicine fellow. He joins our program as a new sports medicine pediatrician.

Figure 1. Chrissy Goodbody, MD

Figure 2. Edward Re, MD

Education Program

CHOP Orthopaedics currently funds four one-year clinical fellowships. The 2021-2022 clinical fellows are Brett Lullo, MD (Figure 3); Joseph Yellin, MD (Figure 4); Raghav Badrinath, MD (Figure 5); and Alex Gornitzky, MD (Figure 6). The 2020-21 research fellow was Dr. Soroush Baghdadi, MD from Iran (Figure 7). While at CHOP, Dr. Baghdadi focused his research efforts on basic science projects related to cartilage regeneration and clinical research focused on pediatric trauma, neuromuscular conditions, and sports injuries. We are excited to have Dr. Baghdadi join our team as a clinical fellow in August 2022.

Figure 3. Brett Lullo, MD

Figure 4. Joseph Yellin, MD

Figure 5. Raghav Badrinath, MD

Figure 6. Alex Gornitzky, MD

Figure 7. Soroush Baghdadi, MD

To celebrate the graduation of the 2020-2021 clinical fellows, the Division hosted the Nicholson Visiting Professor Program and Fellows Graduation & Reunion in June 2021. This year's Visiting Professor was Dr. Steve Frick, Professor of Orthopaedic Surgery and Vice Chairman—Education at Stanford University School of Medicine Department of Orthopaedic Surgery, and Chief of Pediatric Orthopaedics at Stanford Children's Health. He is a nationally recognized expert in clubfoot and foot/ankle disorders, trauma, osteogenesis imperfecta, hip dysplasia, growth, leadership, professionalism, and graduate medical education.

The 2021 Drummond Rising Star Visiting Professor was Ben Shore, MD, MPH. Dr. Shore is an Associate Professor of Orthopaedic Surgery at Harvard Medical School and Boston Children's Hospital. He serves as the Director of the Orthopaedic Fellowship Program at Boston Children's Hospital and Co-Director of the Cerebral Palsy and Spasticity Center. He gave excellent talks on hip surveillance in cerebral palsy, Legg-Calve-Perthes disease, and all things related to trauma. 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.

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 continues to solidify its standing with research work from Dr. Fanxin Long and Dr. Veronique Lefebvre. 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. They focused on pediatric pathologies including Multiple Hereditary Exostoses (MHE), Fibrodysplasia Ossificans Progressiva (FOP), Temporomandibular Joint dysfunction, Lamb-Shaffer syndrome, Hjadu-Cheney syndrome, and spondyloarthritis. The research program is currently supported by 14 RO1 grants from the National Institutes of Health and generous donations from private foundations.

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 in collaboration with Medical Image Processing Group were awarded a NIH R01 grant to develop novel dynamic functional metrics for TIS patients by establishing a comprehensive normative database of dMRI images and anatomic and functional models and metrics, and to translate these to develop biomarkers of TIS and of its corrective-surgery outcomes.

With the generous philanthropic support, Dr. Campbell's legacy was strengthened with the establishment of *Wyss/ Campbell Center for Thoracic Insufficiency Syndrome*, enabling CHOP to discover countless more breakthroughs in research and care for TIS children.

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, Tibial Spine fractures (TSF) 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.

Clinical Research

The Division of Orthopaedic Surgery is currently conducting more than 236 IRB-approved clinical research projects. This includes more than 100 prospective and observational studies. CHOP Ortho faculty are also members of a number of multicenter study groups, including the Harms Study Group (HSG), the Pediatric Spine Study Group (PSSG), Research in Osteochondritis Dissecans of the Knee (ROCK), SCFE Longitudinal International Prospective Registry (SLIP), Tibial Spine Prospective Cohort (TSF-PC), 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), Children's Orthopedic Trauma and Infection Consortium for Evidence based Studies (CORTICES), Congenital Upper Limb Differences Registry (CoULD), Research in Osteochondritis of the Elbow (ROCKET), Sports Cohort Outcomes Registry (SCORE), and International Perthes Study Group (IPSG). Investigators within the division have been awarded funding from both internal and external sources to conduct these studies. In 2021, the Division published over 226 articles in major orthopaedic journals, including *JAMA, JBJS, Lancet, JPO*, and *CORR*. Members across our division presented more than 140 presentations at international and national conferences last year alone.

Our Benjamin Fox Research Fellowship for medical students between 3rd and 4th years welcomed Patrick England (Washington University School of Medicine in St. Louis.), Sara Kiani (Icahn School of Medicine at Mount Sinai) and Nathan Houlihan (Sidney Kimmel Medical College at Thomas Jefferson University) (Figure 8-10).

Figure 8. Patrick England

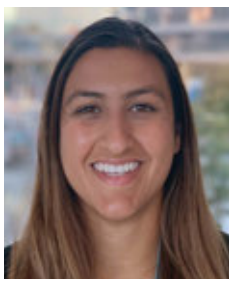


Figure 9. Sara Kiani

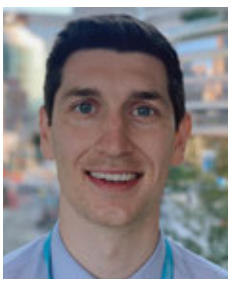


Figure 10. Nathan Houlihan

Recognition and Achievements

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

Jason Anari, MD served as international faculty member at the Salzburg Medical Seminar in Pediatric Orthopedics in Salzburg, Austria. Dr. Anari also received a new grant as PI from Pediatric Orthopaedics Society of North America (POSNA) titled, "*Managing failure to lengthen in MCGR: Best practice guidelines"*.

Alexandre Arkader, MD was the Vice Chair for the Pediatric Orthopaedic Society of North America (POSNA) Educational Course Committee. He also serves as sub-committee chair for Global Courses. 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, Journal of Pediatric Orthopaedics B and Journal of Children's Orthopaedics*. He continues to serve as Co-PI on RSNA Research & Education Foundation Seed Grant titled "*Osteosarcoma Imaging with UTE MRI: Validation and Optimization with CT and Histopathology Correlation*." Dr. Arkader is an active member of CORTICES study group.

Keith Baldwin, MD, MSPT, MPH is the Associate Director of Orthopaedic Trauma in the Division of Orthopedic Surgery. He currently serves as a reviewer for several journals including the *BMC Medical Education, BMC Musculoskeletal Disorders, BMJ Open, Journal of Pediatric Orthopaedics, Annals of Internal Medicine, Journal of Bone and Joint Surgery—American*, and the *American Academy of Pediatrics*. He also serves as an 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 and CORTICES Research Committee. He also received the prestigious *Standard Research Grant* from Scoliosis Research Society.

Patrick Cahill, MD started his term as Board of Director for Pediatric Cervical Spine Study Group. He serves as Chair for Health Policy Committee and member of Governance Council at Scoliosis Research Society. He is also 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, Pediatric Spine Study Group, and Fox Pediatric Spine Deformity study group, which are multi-center groups prospectively researching care improvements for complex pediatric spine deformities. Dr. Cahill received a new grant as co-PI from Scoliosis Research Society titled, "*New Strategies for Pulmonary Assessment in Spinal and Chest Wall Deformity*". He is the Director for *Wyss/Campbell Center for Thoracic Insufficiency Syndrome*.

Robert Carrigan, MD continues to serve on the ASSH Fellows Conference 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, completed his term as the Vice President of the American Board of Orthopaedic Surgery and began serving as President of the Pediatric Spine Study Group/Pediatric Spine Foundation. He also was selected to serve on the JBJS Board of Trustees. Dr. Flynn is a co-editor of *Lovell and Winter's Pediatric Orthopaedics, Rockwood's Fractures in Children, Operative Techniques in Pediatric Orthopaedics*. Dr Flynn serves on the Editorial Board of *Journal of Spinal Deformity*. He is a site leader for *Hospital-Based Cluster Stratified Randomization Control Trial* where 21 national sites are participating to compare 6-week lengthening interval compared to a 16-week lengthening interval on spinal growth in EOS patients undergoing treatment via Magnetically Controlled Growing Rods.

Theodore Ganley, MD is the Sports Medicine Director at CHOP was the second VP of the Pediatric Research in Sports Medicine (PRISM) group, co-founder and executive board member as well as President 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*. He is leading a nationwide initiative on Tibial Spine prospective study group with 14 sites currently participating and it was funded by *Arthur H. Huene Memorial Award* from POSNA. 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). Dr. Ganley also serves as the site PI for recently NIH funded grant "*IMPACCT: Infrastructure for Musculoskeletal Pediatric Acute Care Clinical Trials*".

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. Dr. Lawrence is an active member of sports medicine multicenter research groups such as PLUTO and he leads a 12-site study group MEMO, which is the largest group studying medial epicondyle fractures and injuries. He continues to serve as a reviewer for the *American Journal of Sports Medicine (AJSM)* and *Journal of Shoulder and Elbow Surgery (JSES)*. Dr. Lawrence continues to serve as a co-PI from NIH titled "*A Low-Cost, Collaborative Tool for the Tracking of Youth Activities to Reduce Risk of Physical Injury*" and site Co-PI

for recently NIH funded grant "*IMPACCT: Infrastructure for Musculoskeletal Pediatric Acute Care Clinical Trials*".

Kathleen Maguire, MD is our new faculty member continuing her work at our Sports Medicine Performance Center. She is an active member of AAOS Emerging Leaders Program.

Wudbhav Sankar, MD is the Director of the Young Adult Hip Preservation Program at CHOP. Dr. Sankar currently serves as 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 (IPSG). 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 continues his tenure as the Director of Clinical Research. He continued to serve as co-PI on the grant from Orthopaedic Trauma Association titled, "*Opioid utilization after rotational ankle fractures*". He continues to serve as the team leader and traveled to Sigua Tepeque, Honduras for a pediatric hand surgery medical mission. Dr. Shah is currently a reviewer for the *Journal of Bone and Joint Surgery* and *Journal of Pediatric Orthopaedics*. Dr. Shah continues to serve as the PI for Angela S.M. Kuo Memorial Award from POSNA for his research project "*Opioid vs. Non-Opioid Analgesia in Pediatric Supracondylar Humerus Fractures.*" He also serves as the site Co-PI for recently NIH funded grant "*IMPACCT: Infrastructure for Musculoskeletal Pediatric Acute Care Clinical Trials*".

David Spiegel, MD continued his work with the Children's Hospital of Philadelphia Global Health Pilot Grant. He currently is the chair for the International Scholars Program at AAOS. 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. Dr. Wells currently serves as the President of Board of Directors for the Philadelphia Orthopaedic Society and as Vice Chair for Inclusion, Diversity and Equity at the Perelman School of Medicine.

Brendan Williams, MD continued his work at our Sports Medicine Performance Center. Dr. Williams serves on POSNA Educational Courses Committee and AAOS Emerging Leaders Program. He continued his tenure as Board of Directors for Children Beyond Our Borders.

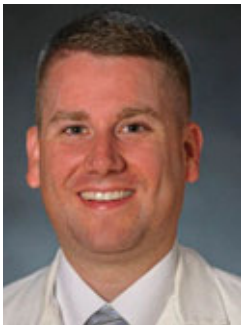
Corporal Michael J. Crescenz Philadelphia VA Medical Center

David Steinberg, MD


Joseph Bernstein, MD


L. Scott Levin, MD


Eric Hume, MD


Andrew Kuntz, MD


Hannah Lee, MD, PhD


Harvey Smith, MD


David Steinberg, MD


T. David Tarity, MD

After dedicating the past two years to improving musculoskeletal care for our veterans, Dr. Richard E. Grant stepped down as Chief of Orthopaedics. Under his leadership, we saw the expansion of orthopaedic clinical care beyond Philadelphia, including a greater presence at the Wilmington & Coatesville VA campuses, and the installation of a state-of-the-art arthroscopy simulator (procured by his predecessor, Dr. Marlene DeMaio) to advance the education of our residents and fellows. As an Air Force veteran, Dr. Grant understood our veteran population and was able to connect with them in a way no other could. With Dr. Grant's transition, David Steinberg has again assumed the role of Acting Chief of Orthopaedic Surgery, in addition to his responsibilities as Chief of Hand Surgery.

After spending four years on the faculty at the VA and Penn, performing total joint arthroplasty and trauma surgery, Dr. Vincent Moretti has relocated to Texas. To assist in caring for our veterans after Dr. Moretti's departure, Dr. T. David Tarity has stepped up to the plate, carving some time out from his growing practice at Penn to help Drs. Hume and Bernstein manage patients with hip and knee arthritis. While he has always been an influential presence at the VA, guiding the evolution of the orthopaedic division and educating the residents, Dr. L. Scott Levin has officially joined the ranks of the clinicians. He will be able to more directly offer his expertise in the orthoplastic management of veterans with both upper and lower extremity pathology.

We are excited to announce the anticipated arrival of two additional faculty over the next three to twelve months, which will expand our services in joint reconstruction and orthopaedic trauma. Timothy Costales, MD completed an orthopaedic residency at the University of Maryland/Shock Trauma and is currently training in adult joint reconstruction

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at Massachusetts General Hospital/Harvard Medical School. Colonel Jean-Claude D'Allyerand, MD, MSE is an orthopaedic traumatologist and Associate Professor of Surgery at USUHS, who is currently serving as Deputy Hospital Commander for Surgical Services at Landstuhl Regional Medical Center in Germany. He will assume the role of Chief of Orthopaedic Surgery at the VA after completing his tour of duty with the US Army.

We continue to offer general orthopaedic and subspecialty services to our veterans, under the guidance of our dedicated faculty, including Drs. Eric Hume, Joe Bernstein, David Steinberg, Harvey Smith, Andy Kuntz and Hannah Lee, as well as the aforementioned Drs. Levin & Tarity. Over a twelve-month period, over 6000 visits were recorded for the outpatient Orthopaedic Surgery Clinics, only slightly below our pre-COVID data. We offer surgical services four days weekly and performed over 440 operative procedures last year. We would not be able to provide comprehensive orthopaedic care to our patients without the dedication of our residents, hand fellows, our orthopaedic nurses (Alex David & Mary Manattu), the other clinic staff, and our PA's. Special recognition is needed for our two exceptional orthopaedic physician assistants, Mitchel "Chip" Staska, MP-C and Thomas Bialkowski, MPAS/PA-C. They form the backbone of the clinical arm of orthopaedics, providing a seamless journey for our patients, from initial referrals and consultations through outpatient evaluations, both in-person and via telemedicine. They assist the residents and faculty in managing patients, ordering appropriate diagnostic tests & consults, and scheduling surgeries; Chip & Thomas teach us how to efficiently navigate through a complex medical system.

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. Kuntz, Steinberg, Lee, and Smith have each applied for or been awarded research grants through the Veterans Administration and outside funding sources. Working alongside Drs. Mauck, Soslowsky, Scanzello, Dyment, Cullen, Dodge, Gullbrand, & L Smith, they investigate many facets of the musculoskeletal system, focusing on the repair & regeneration of tendon, cartilage, meniscus, nerve, & the intervertebral disc. These studies have resulted in presentations at numerous national and international conferences, and publications in premier orthopaedic and biomedical research journals (including *Tissue Engineering*, *J Biomechanics*, and *J Orthopaedic Research*). While basic science research has always been one of our strong suits at the VA, we are increasing our clinical research efforts as well. Dr. Bernstein recently received a grant to study hip fracture decision-making. Other clinical studies by the faculty and residents in total joint arthroplasty and Dupuytren's disease were presented by Dr. Masada to the Association of VA Surgeons and by Dr. Nypaver at the annual meeting of the American Association of Hand Surgeons, respectively.

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 have expanded our educational efforts. This includes weekly resident conference with Dr. Kuntz, quarterly Chairman's rounds with Dr. Levin, and the recent acquisition of the arthroscopic simulator.

With the team effort of our orthopedic family, and in collaboration with other services at the Veterans Administration Medical Service, we strive to provide our veterans with exceptional health care, by providing compassionate patient care, advancing medical knowledge through world-class research, and educating our next generation of health care providers.

Pennsylvania Hospital

Neil Sheth, MD

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.

Education is at the forefront of our focus at PAH. Residents are typically in the operating room three to four days per week, with dedicated clinic time in multiple sub-specialties. Video conferencing continues for conferences historically held at PMUC, and weekly sub-specialty specific conferences for spine and foot and ankle continue to be coordinated virtually.

The administration at Pennsylvania hospital continues to be extremely supportive of the expanded presence of orthopaedic faculty and residents. The hospital system has further 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 and additional attendings are added to the faculty. These efforts have allowed PAH to maintain its reputation in the region as a first-class hospital.

The Department of Orthopaedic Surgery at the University of Pennsylvania now staffs 20 attending surgeons and non-operative providers 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. Andrew Sobel (hand surgery) has been newest addition to the roster at Pennsylvania Hospital. Dr. Sobel increases our complement of providers across several sub-specialties.

With the continued increase in operative volume, PAH continues to be staffed by a PGY-1, PGY-2, PGY-4 and complemented by a team of nurse practitioners and physician extenders that assist with patient clinical care and floor work. The Orthopaedic Intern spends a portion of the week in the operating room or across various outpatient clinics and also assists the PAH team with patient care issues on the floor.

With the continually changing healthcare environment, we continue to grow the outpatient total joint arthroplasty program which started four years ago. We have implemented and continue to refine the dedicated rapid recovery program – the 9th floor extended stay unit opened in October 2019 and now services nearly 60%+ of the orthopaedic patient volume coming through PAH. In addition, new robotic platforms are being offered at Pennsylvania Hospital. Pennsylvania Hospital is poised to be successful in the region as we continue to evolve.

Penn Center for Musculoskeletal Disorders

Louis J. Soslowsky, PhD

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 were pleased that in 2021, we were renewed again for five more years. We remain 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 1) CT 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, and 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 200 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 60 affiliate faculty members for more than 17 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

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. There are more than 135 full- and part-time staff and trainees now in the labs (an increase of 105% since 2008). McKay is an active, thriving research and educational community committed to advancing basic and translational musculoskeletal research.

The McKay labs have recently completed a transformation both in terms of physical space and faculty. Our home, Stemmler Hall, underwent a >$120 million renovation, completed in late 2019, which resulted in a fully modernized facility (>110% increase) in which to grow our laboratory space, faculty, and research and training endeavors. Since 2008, our faculty have grown from 7 principal investigators (PIs) to 19, an increase of more than 170%. Working in conjunction with the newly formalized departmental strategic plan, we are excited to continue to support our existing faculty and strategically grow the faculty in the coming years to spur new innovations in musculoskeletal research and education.

With respect to funding, current research expenditures in support of our McKay research programs are >$15M USD annually, a number that has grown by >172% since 2008, despite flat and/or decreasing NIH pay lines over that time frame. Indeed, **for the first time in more than 30 years, the Department of Orthopaedic Surgery at Penn is ranked #1 in NIH funding** in the nation. While the department has been ranked in the 'top five' of orthopaedic research programs for more than a dozen years, reaching the top position of all programs in the US represents the culmination of years of effort, strategic recruitments, and the hard work of all our faculty, staff, and trainees. Among those contributing to this ranking, Dr. Soslowsky has ranked in the top 5 individually for over a decade, and six of our faculty members are now ranked in the top 50 in the field in terms of NIH funding. Our McKay Lab and research division is 1 of only 2 programs in the nation to be positioned in the top five over this time period, and Dr. Soslowsky is the only investigator to consistently rank in the top five over the last decade.

Notably, a number of our younger and/or newly recruited faculty have been very successful in establishing and growing their research funding base as well. For instance, Drs. Joeng, Heo, Boerckel, Mourkioti, Baxter and Dyment (all Assistant Professors) together have brought in 8 new NIH R01 awards as PI to the Department over the last two years, and the recruitment of Dr. Schipani brought an additional 3 R01s. At the same time, existing faculty have renewed and/or added many additional NIH R01s, R21s, VA Merit Awards, and other federal funding to further support and grow the research base. Just as importantly, we have continued to support our young faculty towards 'K'-type Awards from the NIH and Career Development Awards from the VA, with two K01s (Baxter, Heo), one CDA-2 (Gullbrand), and one K25 (Hast) over just the last three years. As these new research programs continue to mature, we expect that the Department will continue to rank very highly among all programs nationwide. Finally, our Penn Center of Musculoskeletal Disorders (PCMD), located within the McKay Labs and supported by an NIH P30, was **renewed in 2021 for another five years (years 16-20)!** This Center is the longest running P30 in the nation, and serves as a critical hub for musculoskeletal research at Penn. In addition to the above-mentioned new grants this year awarded to our faculty, each of the McKay Laboratory faculty members remains well-funded through ongoing and newly awarded research grants from federal agencies and industrial sponsors.

Our McKay faculty and trainees also continue to represent the department at major international meetings and via national and international recognitions and high impact publications. For example, Dr. Robert Mauck was awarded the Van C. Mow Medal from the American Society of Mechanical Engineers. Dr. Sarah Gullbrand was awarded the JOR Spine Early Career Award at the 2022 ORS Meeting and Dr. Lachlan Smith was elected President of the ORS Spine Section. Our trainees also won numerous awards and prizes over the last year, including multiple Section Awards and New Investigator Recognition Awards at the 2022 Orthopaedic Research Society Meeting, Young Investigator Awards at the 2021 American Society for Bone and Mineral Research Annual Meeting, and multiple PhD and Masters' Competition selections at the 2021 Summer Bioengineering Conference, to name just a few (for more, please see: https://www.med.upenn.edu/orl/news/). Dr. Foteini Mourkioti and Dr. Ling Qin were also recently awarded the prestigious PSOM Dean's Innovation Award, in recognition of their cutting-edge research. Faculty and trainees also regularly publish high profile papers in the leading journals of our field, and these accomplishments are regularly promoted in the lay press.

Growing musculoskeletal research in the Department of Orthopaedic Surgery and across the Penn campus has been a primary objective for our program. Towards this end we have, over the last dozen years, more than doubled in terms of lab faculty, lab personnel, lab space, and research expenditures. Over the last two years, we also initiated two new sub-committees within the McKay Labs. The first is the McKay Diversity, Equity, and Inclusion Committee. This committee (https://www.med.upenn.edu/orl/mckay-dei-committee.

html) organizes activities aimed at increasing awareness and engagement of all McKay members to broaden our vision and expand diversity and equity in our research community. This committee has been very active, organizing book clubs, outreach events ('Learning on a Limb'), and conference grants to support, recruit, and retain a diverse trainee population in orthopaedic research. Likewise, our Mckay International Outreach Committee (https://www.med.upenn.edu/orl/international-outreach-committee) is working to help the McKay Lab present a welcoming face to our international trainees and collaborators, and to promote cultural awareness across McKay and share knowledge with members of the international community joining the group. Finally, to promote and expand our educational mission we hold a monthly internal seminar series, the 'McKay Young Investigator' Seminar, highlighting the outstanding work from our trainees. This event provides an opportunity for trainees to present their work to the entire group and develop presentation skills. We are so proud of the hard work that McKay members are doing to promote orthopaedic research and build community, here at Penn and across the globe.

The goal of our collective work in McKay remains the same as when the laboratory was founded more than 40 years ago, to carry out the most cutting edge fundamental and translational research in the field of orthopaedics, to train the next generation of scientists and surgeon-scientists, and to improve the health and quality of life of those who suffer from musculoskeletal conditions. With our 40 years of leadership, training, and scientific contributions to musculoskeletal research and building a vibrant and inclusive community of scholars, we are excited for what the future will bring.

Corporal Michael J. Crescenz VA Medical Center's Translational Musculoskeletal Research Center

Carla R. Scanzello, MD, PhD, and Robert L. Mauck, PhD

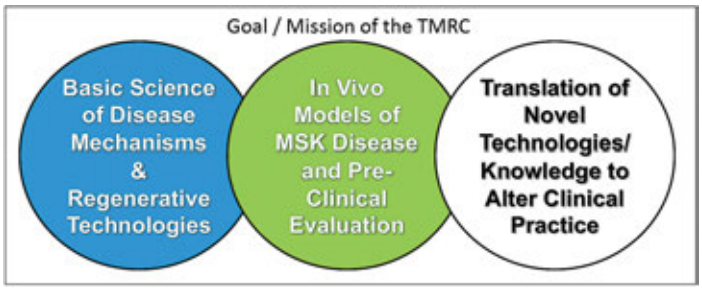
Musculoskeletal (MSK) conditions are part of normal life and aging however occur more frequently in individuals after a variety of injuries. MSK conditions and joint diseases, such as osteoarthritis, spine and disc degeneration also may arise as a consequence of the high-risk physical activity typical of military service and combat trauma. In fact, Veterans are disproportionately affected by MSK diseases and related disabilities compared to the general population. While improvements in armor and "in theater" medical care have 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 their response to common injuries. In 2014, the VA created an enterprise located at the Corporal Michael Crescenz VA Medical Center (CMC VAMC) with a focus on developing novel technologies and therapies to enhance musculoskeletal tissue repair, regeneration, and function. This was named the Translational Musculoskeletal Research Center (TMRC), which has grown over these past 8 years to be a research enterprise comprised of 21 Principal Investigators, 11 VA employees and more than 35 WOC employees (Figure 1). The PI's of the TMRC have been awarded over 10 million dollars in VA-funding and over 45 million dollars in NIH awards.

This growth has transformed the TMRC into a truly multidisciplinary enterprise, where individuals with expertise in Orthopedics, Rheumatology, Rehabilitation Medicine, Neurosurgery, Cell and Tissue Engineering, Cell Biology and Immunology, working together with colleagues from the University of Pennsylvania in these disciplines, collaborate on projects with the goal of improving Veteran musculoskeletal health. These last several years have seen a dramatic growth in VA-sponsored MSK research across the nation, with one of the largest increases occurring at our CMC VAMC in Philadelphia as a result of TMRC investigator efforts. Currently there are more than 15 VA-funded research projects being carried out within the TMRC focused on the injury and repair of MSK tissues, including tendons, ligaments, disc, bone, meniscus, and cartilage, as well as treatment of arthritic conditions.

Critical to our research mission is to keep the research we do focused on the outcomes that relate to improving regenerative and rehabilitative approaches that ultimately will translate into improving the lives of Veterans. To carry out our mission, we are an integral part of the Department of Research & Development at the CMC VAMC, including the Shared Instrument Core which is comprised of high tech-state of the art imaging and analysis instrumentation. Physically, we all under one roof, in approximately 9,000 sq. ft. of renovated research space. Drs. Carla Scanzello and Robert Mauck co-direct this enterprise with input, advice, and support from a joint CMC VAMC / Penn TMRC Advisory Committee and local and central office leadership. As a result of his reputation and productivity, including the establishment and growth of the TMRC, Dr. Mauck was awarded a VA Career Scientist Award in 2021, the first such award at our CMC VAMC to a PhD. This past year has also seen several new grants from both VA and NIH sources including an R21 to Drs. Nathaniel Dyment and Andrew Kuntz to study tendon-to-bone repair, a VA SPiRE award to Dr. Edward Bonnevie to study cellular mechanosensing in synovial fibrosis, a Merit award to Dr. Carla Scanzello to study pattern-recognition in osteoarthritis, a new Merit Award to Dr. Andrew Kuntz to study tendon healing, a renewal of a Merit Award to Dr. Harvey Smith to further develop engineered disc replacements, and funding for a VA multi-center clinical trial for Veteran patients with knee osteoarthritis (the MOVE-OK trial) awarded to Dr. Joshua Baker, MD MSCE. VA grant funding at the VA TMRC totals more than $2.5 million dollar in direct costs yearly.

The ultimate goal of the TMRC is to develop a focused, internationally recognized research center at the CMC VAMC (Figure 2). The TMRC continues as a center for MSK translational research both at the VA along with partners and collaborators at Penn, CHOP, Drexel and Temple Universities. We will continue to focus on Veteran MSK issues and do so by bringing new resources and regenerative technologies to

all service members, past and present. Overall, the TMRC is on an upward trajectory, with a vibrant multi-disciplinary team of investigators and significant new funding directed towards new discoveries in musculoskeletal repair and regeneration and 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.



Clinical Research

Annamarie D. Horan, MPA, PhD

Historical Perspective on Clinical Research.

In the nearly 12 years since I joined the Department, and 18 years since I formally transitioned from bench work to Clinical Research, I have enjoyed the work tremendously and am continuously grateful for the opportunity to be engaged in it. Strangely, fewer people than expected typically think of Human Subjects Research when they think of the broad topic of "science."This could be in any context from a private conversation, to a scene from a movie, all the way through even to an academic setting. In fact, even in my own field, I have never heard a young person express the desire to grow up and become a "clinical researcher". Until I was hired into my earliest role in this discipline, I too never knew it existed. At almost 2 decades, it is almost comical.

When the topic of Clinical Research does come up, sadly, the tragic failures of the past often drive the discussion and distract from the value of the bigger story. Undeniably, we all routinely purchase and use products that might or might not be safe or trustworthy if it were not for an unknown number of actual experiments performed with an uncountable number of participants over literally millennia. Millennia? Yes. It has been proposed, and I share with you, as a matter of interest, that the first true clinical research experiment was a nutrition study, performed, under conditions outside our current regulatory framework by the Prophet Daniel while captive in Babylon. The full story, interpreted as a research study is cited below.[1] Its impact was rather profound.

On more recent fronts, the National Institutes of Health (NIH) has defined as its own core mission as follows:

> *"NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability."*[2]

Similarly, the Food and Drug Administration (FDA) is similarly aligned in mission with NIH:

> *"The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation."*[3]

Independent of funding source, focus on living humans vs. large deidentified data sets, size of study, whether or not there is publication potential or payment for services rendered, research involving human subjects or data from human subjects, clinical research is an intriguing and important part of the entire research world, a part of discovery itself. It is work which we do with pride and for which we should have some reverence to those who participate, usually with no benefit to themselves. For all the beautiful discoveries in all branches of science of which Clinical Research is one part, I am honored again to provide this year's update.

Adult Reconstruction

Adult Reconstruction remains highly productive with 11 active funded studies. The myMobility study (NCT03737149) led by Dr. Israelite hit a significant milestone this year when we enrolled our 200th patient. The Medacta Masterloc study (NCT03168750), led by Dr. Sheth, reached its full enrollment goal of 50 patients and continues to follow-up with those enrolled. Dr. Nelson is having continued success with the PCORI funded PEPPER study with ongoing enrollment and about 50 Subjects in active follow up. Dr. Travers maintains his involvement in DePuy ACTIS and Biomet Perfuse and has taken on an important relationship with Drs. Michael Ashburn and John Farrar as a co-Investigator in the NIH funded EN20-01 Centrexion Knee OA Study. In this capacity, Dr. Travers plays a key role in strengthening Penn's position as a both a HUB and an active study site in the UPENN HEAL- Pain Clinical Trial Network Specialized Clinical Center (U24NS115691-Farrar/Ashburn, NINDS). Dr. Hume continues his activity on two DePuy funded studies of Ceramic on Ceramic Hips one of which successfully closed and the other is fully enrolled and nearing the end of follow up. Lastly, we are very sad to recognize the pending departure of Dr. Lee who has been a tremendously active PI on many studies over the years with about a dozen different Sponsors. Dr. Lee has been extremely collegial and collaborative and has often been the first to step up to assist his partners with enrollment in their studies.[1] We will miss him and wish him well!

Staff in Adult Recon has undergone some growth. We acknowledge the steadfast dedication of Helena Moses who has been supporting Adult Recon since her first day in Orthopaedic Surgery. We welcome the arrival of Abigail Watson to the team. Abby has propelled the myMobility study enrollment forward and restored Penn's standing among other sites. We also welcome back Warren Harding who has returned to our team. Warren is currently assisting with myMobility and PEPPER and has become our mobile CRC, traveling to our satellite sites to ensure enrollment and follow up activities are accomplished.

Foot & Ankle

Foot & Ankle has wrapped up industry funded studies recently, with Dr. Farber's Treace ALIGN3D study (NCT03740282) being the only active industry funded study currently in the follow-up stage. We look forward to continuing the successful partnership with Treace and initiating another study, MINI3D, in the coming year. We also look forward to additional projects in Foot & Ankle discussed elsewhere in this volume, led by Dr. Josh Baxter and others.

Fibrodysplasia Ossificans Progressiva (FOP)

The Penn FOP clinicians continue to advise industry sponsors on ongoing and upcoming clinical trial design, and their expertise shapes the direction of clinical research in this disease and prioritizes the safety of the FOP community they champion. Dr. Mona Al Mukaddam continues to serve as the PI on the ongoing multi-center industry sponsored clinical trials for FOP while Dr. Kaplan serves as a site sub-investigator and the global PI for these trials. Drs. Emily Chu (Dermatology) and Staci Kallish (Medicine) provide invaluable collaborative work as sub-investigators on FOP clinical trials. The FOP team completed a successful twelve-day FDA audit of 3 studies in their Palovarotene clinical trial program (NCT02322255, NCT02279095, and NCT03312634) over the summer of 2021. In addition to no inspection findings, the FDA auditor complimented the PI and her team on how well they executed the studies and on their thorough and complete record-keeping. Of important note, this FDA audit was the first performed in the Department in over 12 years. The success of this experience reflects very positively on the entire program and is testimony to the dedication and expertise of the FOP Team.

The ongoing Phase II and III clinical trials will come to an end in 2022 and active subjects will be given an opportunity to enter into a new Phase III roll-over study for continued IP access (NCT05027802). A new investigational product, IPN60130, will be studied in a Phase II study set to open at Penn in the spring of 2022 (NCT05039515). Study start-up is underway for a Phase II study of another new investigational product, INCB000928 (NCT05090891). The FOP Program is still supported by Katherine Toder, Project Manager, and Kamlesh Rai, Clinical Research Assistant. The team is excited to welcome two new Clinical Research Coordinators this year, Hongshik Park and Allison Bautista.

Hand Surgery

Hand Surgery has been successfully wrapping up groundbreaking and investigator-initiated studies. The results of Dr. Steinberg's Digital Tomosynthesis study (NCT03856450) are being prepared for presentations and publications. Dr. Levin's DOD-funded Hand Transplantation Qualitative Research Study (W81XWH1820067) has completed the critical milestone of 1st Manuscript submission. The impact and importance of this achievement cannot be understated. Dr. Levin and his co-PIs, Dr. Tulsky (University of Delaware) and Dr. Tintle (Walter Reed National Military Medical Center) and the respective teams at each site have worked tirelessly to lead those involved in Composite Tissue Allotransplantation to a truer understanding of the entire patient population and patient experience. We look forward to the publication of this groundbreaking work that will assist all providers and patients in the future. The Hand Division welcomed Dr. Andrew Sobel as the Director of the Hand Surgery Clinical Research Program, and he is already making excellent contributions to the Division.

Shoulder & Elbow

Shoulder & Elbow continues its strong Clinical Research presence over the past 10 years with 5 industry funded studies ongoing. We welcomed Dr. John G. Horneff to the Shoulder & Elbow Division, and he brought multiple ASES studies to the Division. This Division has also diversified its energy and expertise by adding quality improvement initiatives to improve patient experience. We are also saddened by the departure of Dr. Huffman during this year but wish him the best in his new location. Dr. Huffman, like Dr. Lee, was very active in Clinical Research at Penn and will be missed. Dr. Tamara Rial has supported this Division successfully as CRC and we appreciate all her hard work, attention to detail, and diligence across this active and productive faculty.

Spine

Spine successfully initiated the new STRUCTURE study (NCT04294004). This project is a Phase II study enrolling patients undergoing single level transforaminal lumbar interbody fusion. This study is led by Drs. George Dodge and Harvey Smith. In the next year, we also look forward to beginning an investigator-initiated study led by Dr. Casper that has received a grant from Cerapedics focused on mindfulness techniques for residents. We welcomed Ellen Stinger as a CRC for this Division and she quickly adapted to not only assisting with Spine studies but also with ongoing projects in the Foot and Ankle and Hand Divisions. Ellen also has been serving as an asset to the entire Clinical Research Team in various capacities and always does so with an enthusiasm and a smile.

Sports Medicine

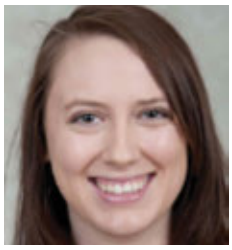
Sports Medicine continues to have a robust repertoire of active funded projects. Dr. Carey continues in his role as the Local and Global PI on the Vericel sponsored PEAK study (NCT03588975) and also participates in a Vericel sponsored retrospective study. Drs. Kelly and Dodge's study investigating the impact of Kenalog injections on metabolic syndrome biomarkers was also initiated. The recognition and regulation of the pre-diabetic state in the orthopaedic population is anticipated to be very impactful and we look forward to the success of this and similar projects. We recently welcomed a new CRC to this Division, Mounika Ponakala. We are happy to have her as part of the Team.

Ortho Trauma

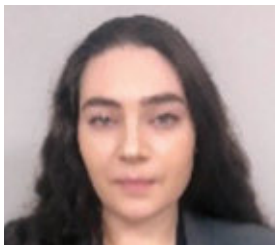
Ortho Trauma is in a phase of expansion. One of Dr. Mehta's grant funded projects, PREPARE, is wrapping up while another, investigating the relationship of infections, transcriptome, and microbiome in the trauma population, is quickly ramping up enrollment. We look forward to initiating 3 or more industry studies in this Division in the coming months. Linda To joined our team as the Trauma CRC and has swiftly adapted to the unique trauma environment. Linda had previously worked with us during two terms as a Drexel co-op student. We are glad to have her return to us! Dr. Mehta also serves as the Medical Director of Clinical Research and we thank him for the outstanding job he does of supporting our Team.

Farewell

On a final note of both hearty congratulations, sincere thanks, and farewell, we say goodbye to Dr. Mary Dooley who is leaving our team to joyfully expand her family. We thank her from the bottom of our hearts for her outstanding work and wish her and her family health, prosperity, and success. Thank you.



Mary Dooley
Project Manager



Katherine Toder
Project Manager

Allison Bautista
FOP

Warren Harding
Adult Reconstruction

Helena Moses
Adult Reconstruction

Hongshik Park
FOP

Mounika Ponakala
Sports Medicine

Kamlesh Rai
FOP

Tamara Rial
Shoulder Elbow

Ellen Stinger
Spine, F&A, Hand

Linda To
Trauma

Abigail Watson
Adult Reconstruction

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

Annamarie Horan, MPA, PhD
Director of Clinical Research
Orthopaedic Surgery and Anesthesiology & Critical Care

1. Weingarten S. (2018). Food in Daniel 1:5-16: the first report of a controlled experiment? JLL Bulletin: Commentaries on the history of treatment evaluation.

2. National Institutes of Health (2017). Mission and Goals. National Institutes of Health Website.

3. U.S. Food & Drug Administration (2018). What We Do. Food and Drug Administration Website.

Do Not Let the Hard Times Get You Down

Neil Ravitz, MBA

Chief Operating Officer
Chief Administrative Officer, Musculoskeletal Service Line

As we come up on two years of the COVID-19 pandemic, it is hard to remember a time in which COVID was not affecting our lives or our department. As it waxes and wanes, we find ourselves continuing to tackle operational and financial challenges in the department. Regardless of those challenges, we continue to expand, invest and innovate to keep the department functioning at the highest levels possible. Our new faculty provide the growth and fresh ideas to help us expand. Our investments in the sports arena help us rebuild our sports volume and build brand awareness. Finally, our investments in technology and automating the way our patients get access to our clinical team pave the way for future growth and a better patient experience.

First, several new clinical faculty members joined the Department in the past year. In the Adult Reconstruction Division, we welcomed Dr. David Tarity in September 2021. He completed a fellowship in adult reconstruction and joint replacement at the Hospital for Special Surgery in New York City before joining their clinical faculty for several years. Dr. Tarity is now practicing at Penn Presbyterian Medical Center. The Hand Division also added a new faculty member with Dr. Andrew Sobel joining us in September 2021 from St. Luke's in Allentown. Dr. Sobel and is dual fellowship trained in hand and microsurgery as well as trauma and sees patients at Pennsylvania Hospital and Valley Forge. We continue recruitment efforts to replace faculty members who departed for other opportunities in the divisions of Adult Reconstruction, Ortho Trauma, and Shoulder & Elbow. All of these recruits are key as we look to grow our presence across our region and increasingly, the nation.

The department has also made significant investments in the last year to increase our provision of sports care in the Philadelphia market. In the professional sports arena, we continue our status as the official healthcare provider of the Philadelphia Flyers, which has been in place since January 2020. As the NHL has finally resumed a "normal" season in 2022, it's been great to see Penn Medicine's name on the boards and on the ice! Additionally, US Squash has also partnered with Penn Medicine as its official health system after moving to its new home in Philadelphia at the world's largest community squash center. On the collegiate level, Penn Medicine was recently named the official orthopaedic provider for Drexel University Athletics, providing medical care for nearly 500 student athletes across 18 different teams. Finally, at the local level, Penn Medicine is excited to have signed on as the official medical partner of the Blue Cross Broad Street Run, the nation's largest ten-mile race. The race will return to the first weekend in May in 2022 for the first time since 2019, and we know Penn Medicine will be well represented!

Our third strategic investment is the expansion of our digital presence in the Philadelphia market. Traffic to Penn Orthopaedics' website is up over 200% in the last two years, due in part to the addition of services like online scheduling and increased provider reviews. As a consumer-driven specialty, orthopaedics patients tend toward convenience and access when scheduling appointments. Our investment in the DocASAP platform allows for just that – patients can choose to schedule an appointment online for a given location, body part, or provider with as few clicks and calls to the Access Center as possible. We can also leverage this platform to route patients toward our new faculty and advanced practice providers with more availability to grow their patient panels. We have also invested in online reputation management services to ensure that our providers have as many fair, verified reviews as possible available through search engines like Google.

Musculoskeletal and Rheumatology Service Line Update: Continued Agility During COVID-19

Hannah Lacko, MA

Director, Quality and Patient Safety, Musculoskeletal and Rheumatology Service Line

As the pandemic continues to surge and abate, the Musculoskeletal and Rheumatology (MSKR) Service Line, spanning Orthopaedic Surgery, Rheumatology, Pain Medicine, Physical Medicine & Rehabilitation, and Musculoskeletal Imaging, has remained steadfast in its mission to align care delivery and optimize clinical quality outcomes across the six entities that comprise our health system. It has been a tiring two years; but to focus only on what we have lost would minimize the success realized in capitalizing on momentum, growing market share, and most importantly continuing to provide safe, valuable musculoskeletal care to the Penn Medicine community.

MSKR's work is driven through disease teams: multidisciplinary partnerships across departments, divisions, clinicians, and administrators. Our disease team structure and the regular meetings for each provide a road map for achieving our annual goals. In setting our goals for 2022, we sought to optimize new processes established during the pandemic, and to expand our expertise to include new patient populations including Bone Health and Spondyloarthritis.

Clinical Quality Goals

We aligned this year's clinical quality goals to support the health system's key initiatives including discharge to home, surgical site infection reduction, and patient access. We continue to strategize about where opportunity for maintaining momentum exists across initiatives like discharge to home and same-day discharge through better partnerships with caregivers, setting clear expectations pre-operatively, and ensuring consistent communication across the continuum of care. Patient access has proven to be an ongoing challenge for the entire health system, and we remain indebted to our providers across the service line who have adapted frequency of telemedicine utilization in line with the virus's presence in our community. We have honed other approaches to creating access, by leveraging an automated texting platform to match patients with the right site of care, and by optimizing in-house capture of ultrasound-guided injections. We have also added a new disease team to our complement to address the many opportunities related to bone health, starting with osteoporosis education and follow-up. The development of a fragility fracture registry will also aid in identifying these vulnerable patients through collaboration with our Trauma & Fracture Disease Team.

Cost & Efficiency Goals

Financial stewardship across MSKR saw continued effort to standardize implant shelf pricing across vendors for all entities within our health system. The effort has been expanded beyond major lower joints this year to include fixation to treat traumatic fractures. We have also expanded our efforts around same-day discharges, combining upper and lower extremity arthroplasty into one cohesive same-day pathway across all five sites where the procedures are performed. We continue to work through needs around consistent patient identification and resolving confusion and dissonance as an increasing number of our surgeries are deemed "outpatient" by insurance agencies.

We are energized by this next phase of the pandemic, where we learn to live alongside the virus. We are proud of the innovations that have been put into place that will be harnessed for the long term, and of our agility in pivoting to the needs of our patients, employees, and faculty.

Advanced Practice Provider

Christine McAndrew, PA-C

Penn Orthopaedic Surgery Advanced Practice Providers (APPs) have been fundamental members of the Orthopaedic team for years. They deliver care to Orthopaedic patients on all levels of the care continuum. Our APPs work with the interdisciplinary care team to coordinate smooth transitions in care and work to provide patient and family centered care. They serve as key educators and train the future workforce of orthopedic APPs by precepting physician assistant students and lecturing.

Over the last year, our teams have continued to treat our patient population through the ongoing pandemic while adapting to the ever-changing policies in healthcare. Through this unprecedented time, the APPs continued to provide consistent quality care in a time where stability is not necessarily guaranteed.They continue to assist the department in increasing our volumes and access to care in a safe manner. The APPs have found ways to continue to utilize telemedicine where applicable while providing the majority of our patient care with in-person visits.They provide a constant presence in the patient care experience all while balancing their personal lives and some enduring life changing events such as marriage or children. I admire our APP team for their perseverance, commitment and loyalty to our departmental mission through this trying time.

Patient safety and quality improvement is a continuous goal for our advanced practice provider group. They have a strong collaboration with our clinical care teams to decrease readmission and mortality rates. APPs have worked over the last year to improve communications between our outpatient and inpatient teams to decrease mortality rates by increasing awareness of comorbid conditions pre-operatively. We have added a smart phrase into our history and physical template which clearly defines clinical predictors of cardiac risk. This initiative from the APP's has provided increased cognizance of surgical risk to not only our own providers but to anesthesia and our inpatient teams.

Our advance practice provider team continues to grow year by year as we expand our department and recruit additional faculty members. We currently have 39 advanced practice providers within our department. In the past year, we have added several APPs to our group. Lisa Kelly PA-C joined our spine team to support Dr. Sheriff for our PMMG group. Talore Hooker PA-C joined our spine team as Dr. Rush Fischer's physician assistant. Talore came from Penn State Rehabilitation Center with 3 years of experience as a spinal cord injury PA. Rachel Jackson PA-C joined our spine team as a new graduate to serve as Dr. David Casper's physician assistant. Alissa Norris PA-C (new graduate) then joined as an additional spine PA who supports Dr. Harvey Smith. We are thrilled to not only have a full APP team in the spine division but an excellent one at that!

This past year we also hired Kaitlin Freeswick PA-C to our shoulder and elbow team to support Dr. Gabe Horneff. Kaitlin comes with a couple of years of experience in orthopedics. Benjamin Chartier PA-C joined our foot and ankle division to support Dr. Ndu. Ben comes with several years of experience in Orthopaedic surgery. In addition, we added Megan Mellon PA-C as a new gradate to serve as Dr.Travers physician assistant. Claire Maxted PA-C also joined our team as a new graduate supporting Dr. David Tarity. Michael Colucciello PA-C is a new graduate who we have recently recruited to join our trauma division in the near future. We are all so excited to welcome our new APPs who have all been a great addition to our team!

In addition to new hires, we have also had some role changes within our APP group. With the recent departure of Dr. Huffman, Allison Huss has accepted a new role as an independent general Orthopaedic physician assistant. The new role aligns with her goals to be more autonomous and expand her knowledge in other fields of orthopedics outside of shoulder and elbow. Brian Fletcher continues to serve as an independent joints physician assistant but has also transitioned to support Dr. Keith Baldwin with his complex neuromuscular practice.

The Orthopaedic APPs continue to support the health system initiative of NPV access as well as general access to care. The majority of our APPs all run independent sessions which consists of post-operative patients, return and new patients; as well as minor procedures. Seeing the majority of the postoperative patient's allows the physician's more availability to see new patients to the practice. They are completing the history and physicals preoperatively and prepare the patients for surgery. In FY21 they saw a total of 4,085 new patients and 19,655 established patients for a total of 23,740 visits total. This number is very close to pre pandemic numbers which is outstanding!

In the face of a decrease in our resident and fellow numbers this past year, our APP's have stepped in to support our physicians in the operating room. All newly hired physician assistants are first assisting and covering the operating room with their attending physician.

The advanced practice providers of the Orthopedic surgery department are an exemplary group of practitioners. They go above and beyond each and every day to provide high quality care to our patients. I cannot thank this group of brilliant individuals enough and I look forward to another year of success with this incredible team!

Letter from the Administrative Chiefs

Yehuda "Yudi" Kerbel, MD, Liane Miller, MD, and Agnes Dardas, MD, MSc

Being chief residents this year has been a transformative experience. Between the ongoing COVID pandemic, the rapid growth of our faculty, and the day-to-day vicissitudes of running one of the largest residency programs in the country, this has been a year of continued challenges and achievements. It hasn't always been easy, but it's been a fantastic opportunity for us to develop our leadership skills and forge closer relationships with our faculty and co-residents, and we're extremely grateful for the experience. We would like to thank Drs. Levin, Farber, Liu and Moretti for their support and guidance throughout the year. We wish Dr. Moretti the best of luck in his new position in Texas and welcome Dr. Liu, who stepped in to seamlessly guide the program forward as the new assistant program director. His longstanding experience as a former resident and current faculty member is incredibly valuable and we are lucky to have him as part of the leadership team. We would also like to thank all of the rest of the faculty and all our co-residents for their tireless hard work and drive to make Penn orthopaedics better every day.

We have achieved several notable new initiatives this year to make this an even better residency program. After the lull of COVID restrictions, we have resumed our in-person cadaver labs and are gradually returning to a full schedule, including both grand rounds and extracurricular labs. We began an exciting educational partnership with Stryker, who are using our residency as one of only 3 pilot programs across the country to create a robust extracurricular educational schedule. To date, we have had multiple labs focusing on arthroscopy and arthroplasty with upcoming sessions on trauma, spine and upper extremity scheduled for the remainder of the academic year. These labs have given us a chance to forge deeper relationships with our co-residents and faculty outside of the formal work setting and obtain more hands-on time learning surgical techniques and approaches. We are grateful to the faculty who have volunteered their time to teach us at these sessions.

Additionally, we were able to resume our in-person visiting professor curriculum and learn from the best and brightest minds in the field of orthopaedics. Our speakers travelled from all over the country to educate us not only on the latest surgical developments, but also on important issues in leadership and diversity, areas in which Penn continues to blaze at the forefront of the orthopaedic community. We are grateful to all of the amazing educators who came to visit our department and share their knowledge.

Speaking of leadership, our department continued to innovate by establishing the inaugural Wharton Leadership Coaching program for selected PGY4 and 5 residents. This initiative paired residents with an executive coach from the Wharton School who helped us grow as leaders during the year. This program was transformational for our residents and is yet another unique way in which Penn Orthopaedics helps its residents grow both personally and professionally during their training. We would like to thank all of the involved Wharton faculty and staff, and Dr. John Kelly in particular, for spearheading this program and raising the funds necessary to maintain it for next year as well.

As we hand over the reins to the next class of chief residents, we'd like to extend sincere gratitude to our co-residents and faculty who make every day a rewarding learning experience at Penn. We hope we have served you well during this year and are honored to have been included among the pantheon of chief residents at this program. We are optimistic about the continued growth of the residency and look forward to continuing to participate as alumni as we move on to fellowship and beyond.

Current Residents

Clinical Year 5 Resident Spotlight

Sarah Blumenthal, MD
Fellowship: Trauma, Hospital for Special Surgery
Medical School: University of California - Los Angeles
Undergraduate: Harvard University

Martin Griffis, MD
Fellowship: Hand, New York University
Medical School: Drexel University
Undergraduate: Temple University

Matthew Counihan, MD, MS*
Fellowship: Sports, Boston University
Medical School: Drexel University College of Medicine
Undergraduate: University of Richmond

Brandon Haghverdian, MD
Fellowship: Foot and Ankle, Duke University
Medical School: University of California, Irvine
Undergraduate: University of California, Irvine

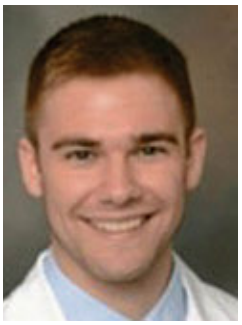
Agnes Dardas, MD, MSc
Fellowship: Hand, Harvard Brigham & Women's
Medical School: Washington University in St. Louis
Undergraduate: Harvard University

Yehuda (Yudi) Kerbel, MD
Fellowship: Adult Arthroplasty, Rush University
Medical School: Drexel University
Undergraduate: La Salle University

*Indicates Resident is in the 6-year Research Track

Liane Miller, MD*

Fellowship: Sports, University of Pittsburgh Medical Center
Medical School: University of California, San Francisco
Undergraduate: University of California, Santa Barbara



Ivan Zapolsky, MD, MS

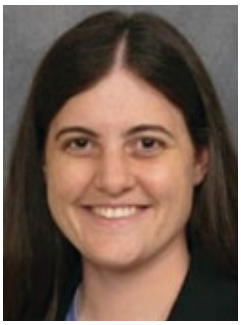
Fellowship: Spine, Mount Sinai
Medical School: Tulane University
Undergraduate: Tulane University

Eric Pridgen, MD, PhD

Fellowship: Sports, Washington University
Medical School: Stanford University
Undergraduate: University of Delaware

*Indicates Resident is in the 6-year Research Track

Clinical Year 4 Residents



Lauren Boden, MD

Undergraduate:
Pomona College

Medical School:
Emory University

Kelsey Bonilla, MD*

Undergraduate:
Rutgers University

Medical School:
Perelman School of Medicine at University of Pennsylvania

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

George Fryhofer, MD, MTR*

Undergraduate:
Harvard University

Medical School:
Perelman School of Medicine at University of Pennsylvania

Joseph Koressel, MD

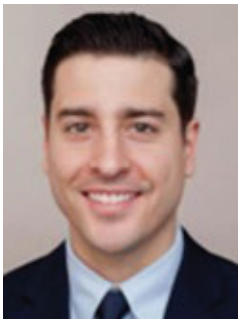
Undergraduate:
University of CA - Davis

Medical School:
Weill Cornell

Viviana Serra Lopez, MD, MS

Undergraduate:
Mass. Inst. of Technology

Medical School:
University of Puerto Rico



Gregory Minutillo, MD, MPH

Undergraduate:
James Madison University

Medical School:
Tulane University

Brian Perez, MD

Undergraduate:
Rutgers University

Medical School:
Albert Einstein

*Indicates Resident is in the 6-year Research Track

Clinical Year 3 Residents

Stephen Barchick, MD

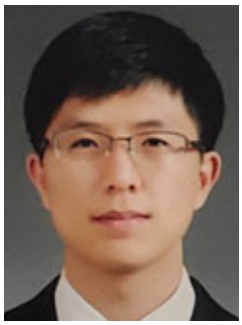
Undergraduate:
Harvard University

Medical School:
Duke University

Sachin Gupta, MD*

Undergraduate:
George Washington University

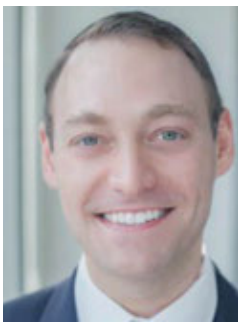
Medical School:
George Washington University



Joung (Richard) Kim, MD

Undergraduate:
University of Rochester

Medical School:
Icahn School of Medicine at Mount Sinai



Charles Lucas Myerson, MD

Undergraduate:
University of Southern California

Medical School:
Tulane University

Matthew Stein, MD, MS*

Undergraduate:
Univ. of Maryland

Medical School:
Georgetown University

Kelsey Young, MD

Undergraduate:
Cornell University

Medical School:
Cornell University

Steven Zhang, MD

Undergraduate:
Cornell University

Medical School:
Stanford University

Research Year

Kendall Masada, MD*

Undergraduate:
University of Texas

Medical School:
University of Texas Health Science Center

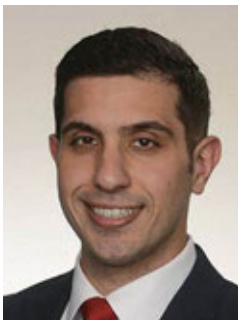
Jordan Cohen, MD*

Undergraduate:
University of Maryland

Medical School:
George Washington University

*Indicates Resident is in the 6-year Research Track

Clinical Year 2 Residents



Aymen Alqazzaz, MD

Undergraduate:
University of Maryland

Medical School:
University of Maryland

Ashleigh Bush, MD

Undergraduate:
Indiana University

Medical School:
Indiana University

Kathleen Collins, MD

Undergraduate:
Morehouse School of Medicine

Medical School:
Virginia Polytechnic Institute and State University

Bijan Dehghani, MD*

Undergraduate:
Albany Medical College

Medical School:
Boston University

Mitchell Hallman, MD*

Undergraduate:
Perelman School of Medicine at the University of Pennsylvania

Medical School:
Washington University

Cody Hansen, MD

Undergraduate:
University of California San Diego

Medical School:
University of Denver

Brian Velasco, MD

Undergraduate:
Geisinger Commonwealth School of Medicine

Medical School:
Franklin & Marshall College

Dainn Woo, MD

Undergraduate:
New York University

Medical School:
The City College of New York

*Indicates Resident is in the 6-year Research Track

Clinical Year 1 Residents

Mohammed Abdullah, MD*

Medical School:
The University of Texas Medical Branch
Undergraduate:
The University of Houston

Caroline Granruth, MD

Medical School:
Tulane University

Undergraduate:
University of Virginia

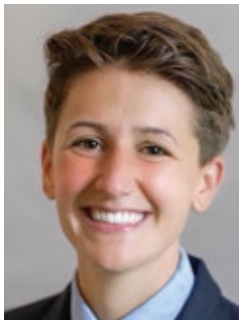
Jaret (Mac) Karnuta, MD, MS

Medical School:
Case Western Reserve

Undergraduate:
Duke University

Erin Kelly, MD

Medical School:
Wake Forest School of Medicine
Undergraduate:
Wake Forest University



Sand Mastrangelo, MD

Medical School:
Dartmouth
Undergraduate:
Brown University

Bradley Osemwengie, MD

Medical School:
Texas Tech
Undergraduate:
University of North Texas

Eric Schweppe, MD*

Medical School:
Columbia University
Undergraduate:
United States Military Academy

Weston Smith, MD

Medical School:
University of Utah
Undergraduate:
Brigham Young University

*Indicates Resident is in the 6-year Research Track

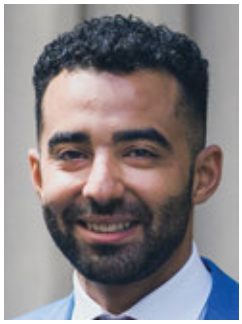
Current Fellows

Aaron Gebrelul, MD
Adult Recon – Joints

Jonathan Tran, MD
Adult Recon – Joints

Henry Yu, MD
Adult Recon – Joints

Brandon Romero, MD
Adult Recon – S/E



Kareem Hassan, MD
Hand

Charles Jehle, MD
Hand

Xun Li, MD
Spine

Colin Whitaker, MD
Spine

Michael Boniello, MD
Sports Medicine

Jamie Grossman, MD
Sports Medicine

Penn Medicine Orthopaedic Surgery Residency Intern Class 2022-2023

Ellis Berns, MD

Brown University

Anna Blaeser, MD

Albany Medical College

Rachel Flaugh, MD*

Harvard Medical School

Lisa Friedman, MD*

Case Western

Samuel Oduwole, MD

Quinnipiac University

Emily Stabnick, MD

University of Massachusetts

Alyssa Thorman, MD

University of Utah

Thompson Zhuang, MD

Stanford University

Visiting Professor Lecture Series

Jordan S. Cohen, MD

June 17, 2021: Raymond G. Tronzo, MD Visiting Professor Lectureship

Wayne G. Paprosky, MD, FACS

Professor, Department of Orthopaedic Surgery at Rush University Medical Center

Wayne G. Paprosky, MD, FACS, graduated the University of Western Ontario and McMaster University School of Medicine. Following an orthopaedic surgery residency at the Henry Ford Hospital, he completed an adult joint reconstruction surgery fellowship at New England Baptist Hospital. Dr. Paprosky is a clinical professor of orthopaedic surgery at Rush University Medical Center.

Dr. Paprosky was one of the first surgeons to perform total hip surgery with cementless implants, which is today's standard. He developed the Paprosky Classification, which is now used worldwide to assess acetabular bone loss when performing revision hip surgery. Dr. Paprosky co-developed and implanted the first gender specific hip for women 15 years ago. These concepts have led to the development of today's gender specific implants for active females. In addition, Dr. Paprosky performs minimally invasive total hip and knee surgery enabling patients to go home within 24 hours.

He is an active member and leader in many societies including the American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons, the Hip Society (President 2008), and the International Hip Society.

Figure 1. Wayne G. Paprosky, MD, FACS

The University of Pennsylvania Department of Orthopaedics was honored to welcome Dr. Paprosky virtually for the Raymond G. Tronzo, MD lectureship (Figure 1). In his lecture, Dr. Paprosky offered a retrospective on the field of revision hip arthroplasty. He then engaged in a lively, interactive case-based discussion with the residents and fellows where he provided his expert insights on challenging cases encountered within our own health system.

October 7, 2021: Inaugural Dean G. Lorich, MD Memorial Lectureship

David L. Helfet, MD

Professor of Orthopaedic Surgery, Cornell Medical College; Chief Emeritus of the Orthopaedic Trauma Service, Hospital for Special Surgery, New York Presbyterian Hospital

Dr. Helfet is Chief Emeritus of the Orthopedic Trauma Service (OTS) for HSS and NY Presbyterian Hospital, professor of Orthopedic Surgery at Weill Cornell Medicine, and is annually ranked as one of Castle-Connolly's publication, "America's Top Doctors."

Dr. Helfet is a world-renowned orthopedic surgeon and has served as member of the Board of Directors of Synthes, Chairman of AO Clinical Investigation and Documentation, President of the OTA, member of the AAOS, and examiner of the ABOS. Dr. Helfet is globally published and received numerous honors including the Presidential Guest and Watson-Jones Memorial Lecture of the British Orthopaedic Association, HSS Lifetime Achievement Award, and the Inaugural Award of the Society of Honorary Police Surgeons of the City of New York. He recently was inducted into the Johns Hopkins Society of Scholars and is currently designated as Orthopedic Trauma specialist for the Fire Department of New York, the New York Police Department, and New York State Police.

Dr. Helfet received a BSc in Biochemistry, M.B.CH.B from the University of Cape Town, completed internship at Edendale Hospital in Pietermaritzburg, South Africa, surgical and orthopedic residencies at Johns Hopkins University, Trauma fellowship at the University of Bern/Insel Hospital in Bern, Switzerland, and Sports Medicine Fellowship at UCLA. Under Dr. Helfet's direction, the orthopaedic trauma service (OTS) has multiple ongoing research studies. Over the past five years, the OTS published 19 articles per year in peer reviewed journals. OTS research is presented nationally and internationally. Most recently, nine OTS studies were presented

at the AAOS Annual Meeting. Dr. Helfet's research initiatives are supported by numerous grant awards.

We were excited to welcome Dr. Helfet for the first in-person grand rounds since the beginning of the COVID-19 pandemic (Figure 2). Dr. Helfet began the morning with a lecture entitled, "Inaugural Dean Gerard Lorich, MD Lecture: An Enduring Legacy of Excellence." He described Dr. Lorich's surgical excellence, devotion to research, and profound contributions within the field of orthopaedic traumatology. Joined by his colleagues David Asprinio, MD, and David Wellman, MD, Dr. Helfet then hosted a trauma case discussion with involvement from our orthopaedic residents and orthopaedic trauma attendings. The variety of perspectives and expert insights obtained during the case presentations made them extremely valuable to all who were able to attend.

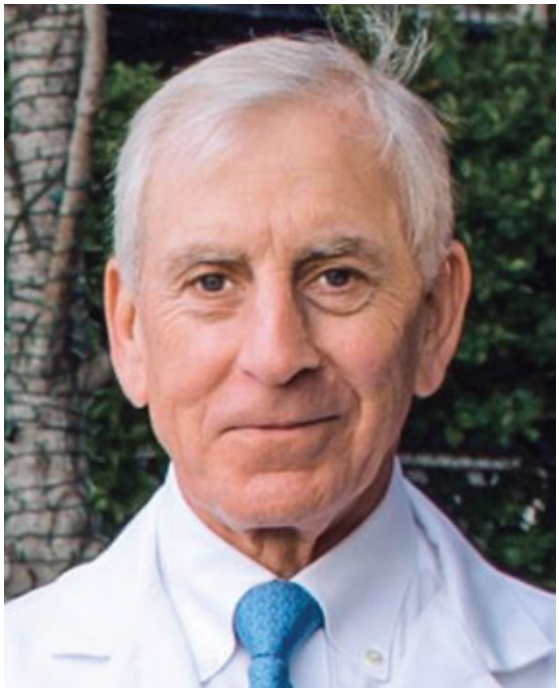


Figure 2. David L. Helfet, MD

January 6, 2022: R. Bruce Heppenstall, MD Visiting Professor Lecture

James R. Ficke, MD, FACS, FAAOS

Colonel (retired) US Army; Robert A. Robinson Professor, Orthopaedic Surgeon-in-Chief, The Johns Hopkins Medical Institution

Dr. James R. Ficke is the Robert A. Robinson Professor and Chair of the Department of Orthopaedic Surgery at The Johns Hopkins Medical Institution (Figure 3). He has an active surgical practice in the Johns Hopkins Hospital. He currently also serves as a member of the Committee on Trauma and Chair of the Disaster Committee, American College

Figure 3. James R. Ficke, MD, FACS, FAAOS

of Surgeons, and the Board of Directors for the American Academy of Orthopaedic Surgeons. Dr. Ficke completed his BS degree in Engineering at West Point, MD at Uniformed Services University, and residency in orthopaedic surgery at Tripler Army Medical Center in Honolulu. He completed an AO fellowship in Trauma in Munich, Germany as well as a Foot and Ankle fellowship in Dallas, Texas.

Retired after 30 years of service in the United States Army, his last military assignment was Chair of the Department of Orthopaedics and Rehabilitation at San Antonio Military Medical Center at Fort Sam Houston, Texas. He also served the U.S. Army Surgeon General as the senior advisor for Orthopaedic Surgery and extremity injuries for seven years. While on Active Duty, he deployed to Iraq as senior orthopaedic surgeon-in-country and Deputy Commander for the 228th Combat Support Hospital. He also served as the Chief of Staff for the Surgeon General's Dismounted Complex Blast Injury Task Force, and the Army Lead for the DoD/VA Extremity Trauma and Amputee Center of Excellence Development Group. He served as Chair or Co-Chair of the Steering Committee for the DoD Peer Reviewed Orthopaedic Research Program for 8 years. He currently holds research grants with DoD and NIH and his primary research focus areas are clinical outcomes in post-traumatic ankle arthritis, National Trauma Systems Development, Resident Research Training (T32), and Disaster Response Improvement.

He has received the Society of Military Orthopaedic Surgeons' COL Brian Allgood Memorial Leadership Award as well as the Surgeon General's Major General Lewis Aspey Mologne Award for excellence in military academics, education, and clinical care. He is a Legionnaire in the Infantry Order of St. Michael, and a Distinguished Member of the Army Medical Regiment. In 2018, he received the Johns Hopkins Award for Advancement of Women in Science and Medicine,

and the Boy Scouts of America Leaders in Healthcare Award.

Dr. Ficke hosted Grand Rounds virtually due to the omicron wave of COVID-19. In his first lecture entitled, "High Energy Lower Extremity Trauma: Development of METRC & Current Best Practices," Dr. Ficke discussed the evolution of thought concerning the management of severe lower extremity trauma, including both operative and nonoperative aspects of care including prostheses and bracing. He discussed his extensive experience managing mangled extremities as well as ongoing research in the area, including his involvement in the Major Extremity Trauma Research Consortium (METRC). After this lecture, Dr. Ficke gave another fascinating lecture, "Leadership Development in Changing Times: Saying Yes to Opportunity (Perspectives as Director of the Largest & Longest COVID Hospital)." It was impressive to hear about how he had used lessons learned from his military experience to direct the Baltimore Convention Center Field Hospital and expand hospital capacity to meet the rising demand for hospital care among those from the Baltimore area suffering from COVID-19. Following these lectures, he hosted a journal club for the residents where he provided his perspective on articles focusing on severe lower leg trauma, limb salvage, and lower extremity amputation.

February 17, 2022: Edgar L. Ralston, MD Endowed Visiting Professor Lecture Celebrating Diversity, Equity, and Inclusion

Edward M. Barksdale, MD

Surgeon-in-Chief Rainbow Babies & Children's Hospital/ University Hospitals, Case Western Reserve School of Medicine

Edward M. Barksdale, Jr. MD is the Robert J. Izant, Jr. MD Professor and Surgeon-in-Chief at Rainbow Babies and Children's Hospital/University Hospitals and Case Western Reserve School of Medicine. An All-American Athlete and Honors graduate of Yale University (1980), Dr. Barksdale received his medical degree from Harvard University (1984). He completed a residency in General Surgery at Massachusetts General Hospital (1991) and fellowship training in Pediatric Surgery at Children's Hospital Medical Center in Cincinnati (1994). He began his academic surgical career at the Children's Hospital of Pittsburgh (1994-2007) and was recruited to Rainbow/UH in 2007.

Dr. Barksdale has been widely recognized and awarded by colleagues and communities for his service to his various missions. A member of numerous national medical/surgical organizations, where he has also held leadership roles, Dr. Barksdale is the current President of the American Pediatric Surgery Association. He currently works at the nexus of academia, clinical surgery, medical education, public health, and social justice as a passionate advocate for child health and healthcare. He endeavors to invest his academic, clinical, and service efforts to inspire individuals and transform communities at the precipice of hope. In Cleveland, he has been devoted to building programs to address health disparities particularly in fragile populations of children. He is the co-founder of the Antifragility Initiative, a novel holistic, person-centered, pediatric violence intervention funded by the Victims of Crime Act (VOCA). He is a proud husband and proud father of four adult children. His life and career have been guided by the strong humanistic and Christian values he learned from his family and his community growing up in Lynchburg, VA during the dynamic 1960's.

In a riveting session, Dr. Barksdale presented a presentation titled, "A New Paradigm for Building Diversity in Surgery and Healthcare" (Figure 4). In this session, he reframed the popular understanding of diversity as a destination, discussed the importance of empowering people from all groups and providing an environment where all people fee

l valued, reviewed the limitations of current strategies to improve diversity, and discussed his philosophy on how to recruit, retain, and promote talent within an organization. His message encouraging true inclusivity that "leaves no group" behind was inspiring to all. Additionally, he hosted a leadership-themed journal club and answered residents' questions regarding mentorship, sponsorship, and leadership in medicine.

February 24, 2022: Leo Leung Visiting Professor Lecture

Ranjan Gupta, MD

Professor of Orthopaedic Surgery, Anatomy & Neurobiology, and Biomedical Engineering, Chief of Shoulder Surgery, Councilor for the Zeta Chapter of Alpha Omega Alpha Honor Society, University of California, Irvine

Ranjan Gupta, MD received his undergraduate degree from Rensselaer Polytechnic Institute, and his medical doctorate degree from Albany Medical College through the Accelerated Six Year Biomedical Program. He completed a general surgery internship, residency in Orthopaedic Surgery, and an NIH Post Doctoral Research Fellowship at the University of Pennsylvania. Subsequently, Dr. Gupta completed fellowship training in hand surgery/ microsurgery at the University of California, Los Angeles, followed by an AO Fellowship in hand surgery/traumatology/shoulder at the University of Berne in Switzerland. He served in the role of Department Chairman for the University of California, Irvine from 2006 to 2015. He is the Principal Investigator for the UC Irvine Peripheral Nerve Research Lab that has been funded with extramural grants from numerous foundations (OREF, ASSH, OTA, Aircast) and the NIH. His lab is focused on Schwann cell control of neural injury and the pathogenesis of motor endplate degradation after traumatic nerve injury.

Figure 4. Dr. Barksdale as Ralston/DEI VP. Left to right: Dr. L. Scott Levin, Dr. Agnes Dardas, Dr. Edward Barksdale, Dr. Larry Wells

He has published over 100 manuscripts and has been recognized by his peers with the NIH Career Development Award from the National Institute for Neurologic Disorders & Stroke (2000), the Marshall Urist Young Investigator Award from the Association of Bone & Joint Surgeons (2005), the Kappa Delta Young Investigator Award from the American Academy of Orthopaedic Surgery and the Orthopaedic Research Society (2006), the Sterling Bunnell Traveling Fellowship from the American Society of Surgery of the Hand (2008), the American-British-Canadian Traveling Fellowship for the American Orthopaedic Association (2013), the Joseph H. Boyes Research Award from the American Society of Surgery of the Hand (2015), the Andrew J. Weiland Medal from the from the American Society of Surgery of the Hand to honor a surgeon-scientist who has contributed a significant body of research that has advanced the science and practice of hand surgery (2016), and the Charles S. Neer Award from the American Shoulder and Elbow Surgery (2019). He is particularly proud of receiving Faculty Teaching Awards (2016 & 2017) from his residents as well as serving as an oral examiner for the American Board of Orthopedic Surgery for eight years and the co-chair of the ASES education committee.

We were excited to welcome Dr. Gupta back to the University of Pennsylvania. In his first presentation, "The Lazarus Project: Preservation of the Neuromuscular Junction after Traumatic Nerve Injury," he discussed his extensive his research on the interplay between nerves and muscles and how surgical techniques could leverage these interactions to restore function in patients with neurologoic deficits. It was fascinating to hear about his innovative approaches to patient care and to learn from the cases he presented. Next, he presented, "Looking over Darwin's Shoulder: The Continuous Evolution of Shoulder Arthroplasty." This talk provided a

Figure 5. Dr. Ranjan Gupta in the human tissue lab with current residents and fellows

valuable historical perspective on the major advances that have improved shoulder prosthesis designs and ultimately patient outcomes. After his lectures, Dr. Gupta joined the residents in the Human Tissue Lab where he demonstrated nerve transfers including the AIN to deep motor branch of the ulnar nerve transfer, Oberlin Transfer, and partial radial nerve to axillary nerve transfer (Figure 5). He also taught the residents how to identify the spinal accessory nerve in the supraclavicular space and harvest intercostal nerves.

March 17, 2022: June C. Wapner Visiting Professor Lectureship

Robert Anderson, MD

Director of Sports Foot and Ankle, Titletown Sports Medicine and Orthopaedics; Associate Clinical Professor, Department of Orthopaedic Surgery, Medical College of Wisconsin

Robert B. Anderson, MD was born in Milwaukee, WI and attended the University of Mississippi where he was inducted into their Hall of Fame. He completed his medical degree at the Medical College of Wisconsin. He was the founding orthopaedic surgeon of the O.L. Miller Foot and Ankle Institute of OrthoCarolina in Charlotte, North Carolina, practicing there for 29 years. In 2017, he joined the Titletown Sports Medicine and Orthopaedic Clinic in Green Bay as Director of Foot and Ankle. Dr. Anderson is fellowship-trained in foot and ankle disorders, studying with Dr. John Gould in Milwaukee, WI in 1988. He served as a team orthopaedist to the Carolina Panthers from 2000-2017 and is now an associate team physician to the Green Bay Packers. He has served as the chairman of the Foot and Ankle Subcommittee for the NFL since 2003 and was appointed as the co-chair of the NFL's Musculoskeletal Committee in 2016, overseeing all orthopaedic injuries and research in professional football. He actively consults for a number of NFL/ NBA/ NHL/ MLB teams and colleges. He was named the NFL Physician of the Year in 2016.

A cofounder of the OrthoCarolina Foot and Ankle Fellowship program, he also served as Chief of the Foot and Ankle Service at Carolinas Medical Center from 1989-2015. Dr. Anderson is also a past-president of the American Orthopaedic Foot and Ankle Society. He is the co-editor of the 9th edition of Mann's: Surgery of the Foot and Ankle; former Editor-in-Chief of the journal, Techniques in Foot and Ankle Surgery; associate editor/reviewer for JBJS, JAAOS, FAI, AJSM and numerous other peer-review publications; and author/editor of numerous chapters and manuscripts.

We were privileged to welcome Dr. Anderson to the University of Pennsylvania this year (Figure 6). In his first talk, "Update on the NFL with Lower Extremity Injury Trends and Research Testing," Dr. Anderson discussed his firsthand experience working with the NFL on efforts to identify modifiable contributors to the injury burden in the league. In particular, he discussed his extensive work on the interaction between footwear and playing surfaces. He also discussed his other ongoing research projects and their potential impact on the players moving forward. He then gave a second lecture about foot and ankle injuries in the elite athlete. In this, he discussed common lower extremity injuries in football, his treatment algorithms, and the unique challenges associated with treating elite athletes. Finally, he led a journal club on the residents where he discussed his thoughts on articles dealing with relevant clinical problems including Lisfranc injuries, achilles tendon ruptures, turf toe, and syndesmotic injuries.

Figure 6. Robert Anderson, MD

April 14, 2022: Ernest J. Gentchos and Friend Visiting Professor Lectureship

Mark A. Frankle, MD

Chief of Shoulder & Elbow Surgery, Florida Orthopaedic Institute; Principal Investigator, Foundation for Orthopaedic Research and Education

Mark Frankle, MD has been with Florida Orthopaedic Institute since 1991 and received his fellowship training at Mayo Clinic in Rochester, Minnesota. He is board certified by the American Board of Orthopaedic Surgery and specializes in shoulder and elbow surgery. Dr. Frankle has authored more than two hundred articles in professional journals, maintains ongoing research projects and has presented his findings at various professional conferences. He has also been serving as a reviewer of the Journal of Orthopaedic Research. A shoulder implant designer, Dr. Frankle's replacement methods and instrumentations, like his reverse shoulder prosthesis,

have been utilized in several surgeries among many different orthopedic organizations.

Dr. Frankle currently serves as the Immediate Past President of the Society of American Shoulder and Elbow Surgeons. He is the director of the Biomechanical Shoulder and Elbow Research Lab at the University of South Florida College of Engineering. He is also the director of the Shoulder and Elbow fellowship program, a collaborative effort between Florida Orthopaedic Institute and the Foundation for Orthopaedic Research and Education. He received the prestigious Charles S. Neer award for Basic Science from the American Academy of Orthopaedic Surgeons. Dr. Frankle enjoys setting aside time for researching and finding new ways to innovate and progress orthopedics from a surgical perspective. His implementations continue to act as stepping stones that further improve overall orthopedic care.

We were honored to have Dr. Frankle to the University of Pennsylvania this year as a visiting professor. In his first talk, "The History of the Reverse Shoulder Arthroplasty—A Loonshot," he discussed the development of rTSA and his experience with early implant systems. He then discussed the evolution of rTSA implants over the years. Finally, he discussed cases of shoulder osteoarthritis, clinical considerations when performing shoulder arthroplasty, and his lessons learned from decades in practice. After his lectures, Dr. Frankle joined the orthopaedic residents, shoulder fellow, medical students, and Penn shoulder and elbow surgeons in the human tissue lab where he instructed the residents on how to perform TSA and rTSA using the DJO implant systems (Figure 7).

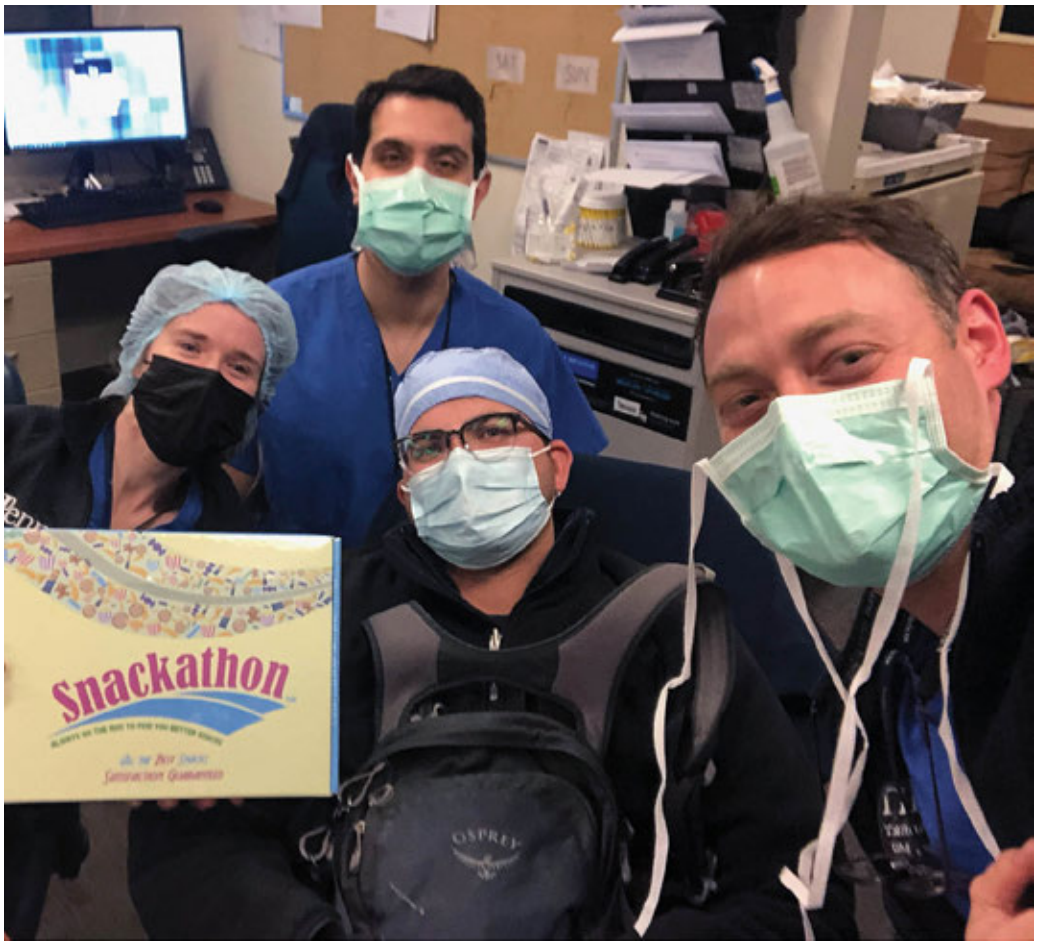
Figure 7. Dr. Mark Frankle with the orthopaedic residents, medical students, and Penn shoulder and elbow faculty in the human tissue lab

Resident Life

Kendall M. Masada, MD

Intern class hanging out on a Philly rooftop. Left to right: Eric Schweppe, Sand Mastrangelo, Mac Karnuta, Erin Kelly, Weston Smith, Mohammed Abdullah, Bradley Osemwengie, and Caroline Granruth.

Trauma team photo on the Presby helipad. Left to right: Aymen Alqazzaz (PGY2), Sand Mastrangelo (PGY1), Richard Kim (PGY3), Matthew Counihan (PGY5), Gregory Minutillo (PGY4), and Ashleigh Bush (PGY2).



Trauma team making sure the snack drawer in the bunker is stocked. Left to right: Liane Miller (PGY5), Aymen Alqazzaz (PGY2), Brian Perez (PGY4), and Lucas Myerson (PGY3).

PGY2 class in the PAH surgical amphitheater. Left to right: Aymen Alqazzaz, Brian Velasco, Dainn Woo, Ashleigh Bush, Bijan Dehghani, Mitchell Hallman, Cody Hansen, Kathleen Collins.

Residents and spouses welcome Dr. Andrew Sobel to Penn at Circa Green. Left to right: Andrew Sobel (Attending, Hand), Erin Kelly (PGY1), Jordan Cohen (Research PGY3), Kendall Masada (Resarch PGY3), Sand Mastrangelo (PGY1), Ashleigh Bush (PGY2), Kathleen Collins (PGY2), Kelsey Young (PGY3), Brian Velasco (PGY2), and Aymen Alqazzaz (PGY2).

Happy Thanksgiving! Mitchell Hallman (PGY2) in the CHOP call room with a turkey.

Trauma team photo on the Presby helipad. Left to right: Bradley Osemwengie (PGY1), Ashleigh Bush (PGY2), Aymen Alqazzaz (PGY2), and Weston Smith (PGY1).

Celebrating the end of the year. Left to right: Ryan DeAngelis (PGY4), Sachin Gupta (PGY3), Matthew Stein (PGY3), Viviana Serra Lopez (PGY4), Joseph Koressel (PGY4), David Falk (PGY4), and Lauren Boden (PGY4).

Touring the new HUP Pavilion in fashionable safety gear. Left to right: Eric Hume (Attending, Adult Arthroplasty), Ashleigh Bush (PGY2) and Sand Mastrangelo (PGY1).

Journal club at Dock Street. Left to right: Agnes Dardas (PGY5), Erin Kelly (PGY1), Ivan Zapolsky (PGY5), Steven Zhang (PGY3), Kendall Masada (Research PGY3), Jordan Cohen (Research PGY3), Lucas Myerson (PGY3), Sand Mastrangelo (PGY1), Kathleen Collins (PGY2), Ashleigh Bush (PGY2), Aymen Alqazzaz (PYG2), Kelsey Bonilla (PGY4), and Bijan Dehghani (PGY2).

Interns, (left to right) Erin Kelly, Eric Schweppe, Mac Karnuta, and Mohammed Abdullah, showing off their handiwork after their Intern Skills splinting/casting session.

Yudi Kerbel (PGY5) trying out virtual reality in the Human Tissue Lab.

PGY3 class hanging out on a Philly rooftop. Left to right: Richard Kim, Jordan Cohen, Kendall Masada, Stephen Barchick, Steven Zhang, and Lucas Myerson.

Trauma team photo on the Presby helipad. Left to right: Stephen Barchick (PGY3), Sand Mastrangelo (PGY1), Dainn Woo (PGY2), Ivan Zapolsky (PGY5), and David Falk (PGY4).

Interns, (left to right) Sand Mastrangelo, Bradley Osemwengie, Caroline Granruth, and Weston Smith, showing off their cast during the Intern Skills splinting/casting session.

Journal club at Top Golf. Left to right: Viviana Serra Lopez (PGY4), Lauren Boden (PGY4), Kelsey Bonilla (PGY4), Sarah Blumenthal (PGY5), Lucas Myerson (PGY3), Agnes Dardas (PGY5), Steven Zhang (PGY3), Ashleigh Bush (PGY2), Dr. Stephen Liu (PGY10, Attending, Hand), Aymen Alqazzaz (PGY2), Mitchell Hallman (PGY2), Cody Hansen (PGY2), Jordan Cohen (Research PGY3), Stephen Barchick (PGY3), Erin Kelly (PGY1), Sand Mastrangelo (PGY1), David Falk (PGY4), Ryan Deangelis (PGY4), and Bijan Dehghani (PGY2).

Enjoying a Philadelphia Flyers game. Left to right: Jordan Cohen (Resident PGY3), Mac Karnuta (PGY1), Steven Zhang (PGY3), and Stephen Barchick (PGY3).

Kendall Masada (Research PGY3) and Ivan Zapolsky (PGY5) completed the Penn-sponsored Gritty 5K run in costume.

Celebrating the new year with custom "I have a bone to pick with you shirts." Left to right: Liane Miller (PGY5), Agnes Dardas (PGY5), Kelsey Bonilla (PGY4), and Sarah Blumenthal (PGY5).

Group dinner. Left to right: David Falk (PGY4), Joseph Koressel (PGY4), Aymen Alqazzaz (PGY2), Bijan Dehghani (PGY2), Brian Perez (PGY4), Steven Zhang (PGY3), Kathleen Collins (PGY2), Stephen Barchick (PGY3), and Gregory Minutillo (PGY4).

Interns learning how to apply a coaptation splint during Intern Skills. Left to right: Bradley Osemwengie (PGY1), Ryan DeAngelis (PGY4), Mitchell Hallman (PGY2), Weston Smith (PGY1), and Sand Mastrangelo (PGY1).

Trauma team photo on the Presby helipad. Left to right: Weston Smith (PGY1), Kelsey Bonilla (PGY4), Eric Pridgens (PGY5), Steven Zhang (PGY4), and Kathleen Collins (PGY2).

"Ortho gals" get-together. Top row (left to right): Kristy Weber (Attending, Oncology), Caroline Granruth (PGY1), Sand Mastrangelo (PGY1), Kelsey Bonilla (PGY4), Liane Miller (PGY5), Erin Kelly (PGY1), Hannah Lee (Attending, Hand), Casey Humbyrd (Attending, Foot & Ankle). Middle/bottom row (left to right): Wen Chao (Attending, Foot & Ankle), Viviana Serra Lopez (PGY4), Sarah Blumenthal (PGY5), Ashleigh Bush (PGY2), Agnes Dardas (PGY5), Lauren Boden (PGY4), and Kendall Masada (Research PGY3).

Photo collage for the faculty thanking them for obtaining the residents personal lead. Top row (left to right): Stephen Barchick (PGY3), Matthew Counihan (PGY5), Cody Hansen (PGY2), C. Lucas Myerson (PGY3), Steven Zhang (PGY3), Agnes Dardas (PGY5), Ivan Zapolsky (PGY5). Middle row (left to right): Lauren Boden (PGY4), Yudi Kerbel (PGY5), Jordan Cohen (Research PGY3). Bottom row (left to right): Liane Miller (PGY5), Mitchell Hallman (PGY2), Gregory Minutillo (PGY4), Kelsey Young (PGY3), Ashleigh Bush (PGY2), Aymen Alqazzaz (PGY2), Kendall Masada (Research PGY3), Joseph Koressel (PGY4), and Dainn Woo (PGY2).

Class of 2012 Alumni Residents—Where are they now?

Kendall M. Masada, MD

Okechukwu A. Anakwenze, MD, MBA

Where did you go to fellowship?
Shoulder and Elbow, Columbia.

Where are you currently practicing? How would you describe your practice?
Duke University. Academics.

How has training at Penn impacted your practice?
Penn was a great foundation to build on. I learned how to do research, operate. Challenges at Penn allowed me to develop a more resilient disposition. My experiences as a resident guide my treatment of current residents.

What have you learned in your first decade of practice?
Don't let failure get to your head or success get to your head. This is an amazing field; it is one that will keep you humble. Leadership skills are critical for success. A leadership title doesn't make you a leader and vice-versa. EQ is more important that I thought of as a resident. What got you here won't get you there so continue to evolve.

What advice would you give to the current residents?
Enjoy it. OR skills and knowledge are critical but really try to hone your leadership skills. Every task is an opportunity. Find mentors early. It's okay (in many ways advantageous) to think differently. However, it's a team game, so think WE.

Ryan M. DeCoons, MD

Where did you go to fellowship?
Sports, UHZ Sports Medicine Institute (now Miami Orthopedics and Sports Medicine Institute).

Where are you currently practicing? How would you describe your practice?
Augusta, GA. Academic sports practice. Assistant Professor of Orthopaedic Surgery, Medical College of Georgia at Augusta University.

How has training at Penn impacted your practice?
Penn provided well-rounded orthopaedic training that has allowed me to adapt and excel in a variety of practice settings, including private practice (4 yrs, sports/general), locum tenens (1 yr, trauma/sports), and now academic practice (3.5 yrs, sports). Training at Penn also provides a great network of mentors and colleagues, with relationships that have extended well beyond residency training.

What have you learned in your first decade of practice?
The earliest and most important lesson I learned in practice was the importance of work-life balance, stress management, and avoiding burnout. Dr. Kelly has been a driving force in this area, speaking at numerous meetings as well as coming to share this message with our residents in Augusta. It may not seem as tangible during residency training, but mental health and personal well-being become very real under the stress of starting one's practice.

What advice would you give to the current residents?
I would advise current residents who are about to embark on their practice to define their priorities in life and find a job that allows them to stay true to them. For me, these are 1) family, 2) self, and then 3) my career/practice/patients, as I feel that I can only be my best for my patients when my family life and my own well-being are in order. Never feel "stuck" and just accept a bad job situation, and be open to exploring other opportunities or practice models that more align with your priorities.

Atul F. Kamath, MD

Where did you go to fellowship?

Adult Reconstruction, Mayo Clinic. Maurice Mueller Hip Fellowship in Europe.

Where are you currently practicing? How would you describe your practice?

Cleveland Clinic. Academics.

Ryan E. Moore, MD, PhD

Where did you go to fellowship?

Adult Reconstruction, Rothman.

Where are you currently practicing? How would you describe your practice?

Napa Valley, CA. 100 percent hip and knee arthroplasty, patients predominantly from rural parts of northern CA, good mix of primary joints, complex primary and some revision. I'm hospital-employed with 2 partners who also have 100 percent arthroplasty practices. To my surprise I've coauthored a few papers since going into practice, but overall my work is 95% patient care. I run 2 rooms with a PA assistant in each room and we are able to do 6-7 cases per day. Occasionally a medical student will rotate from a local DO program, but for the most part it's me and the PAs getting the work done.

How has training at Penn impacted your practice?

It was the solid foundation that allowed me to succeed in my joints fellowship at Rothman. I felt my class and the classes that preceded me at Penn were exceptionally good, my goal each day of residency was to try my best to keep pace with the rest of the program. Trying to reach that high bar each day helped me to build habits and develop a foundation of skill and knowledge which I feel have allowed me to be successful in my practice.

What have you learned in your first decade of practice?

If you hold yourself to the same standards that were present at Penn during our training, and remain committed to learning and improving every day, and remember to always put the patient first, you'll have a great practice at 10 years. Work gets easier every year as well.

What advice would you give to the current residents?

Put your best effort into your work each day, take the extra effort to prepare for your next day, every case, every consult is an opportunity to learn, and the better you prepare, the better you will learn. Your co-residents and faculty are great friends and resources in your first 10 years, keep that in mind as you work together through both the fun and also the tough times during residency.

Surena Namdari, MD, MSc

Where did you go to fellowship?

Shoulder & Elbow, Washington University in St. Louis.

Where are you currently practicing? How would you describe your practice?

Rothman Orthopaedic Institute - Thomas Jefferson as Professor of Orthopaedic Surgery, Fellowship Director, Co-Director Shoulder & Elbow Research.

How has training at Penn impacted your practice?

Residency training was 5 of the best years of my life. I use the lessons learned at Penn daily. Most importantly, I learned that, while excellence in research and teaching are important to building an academic career, the number one priority is superior patient care. Additionally, I was fortunate to leave Penn with great friendships with both co-residents and faculty. I lean on these people regularly for career and life advice.

What have you learned in your first decade of practice?

You forget about your success quickly but your failures stay with you. Complications happen, and it is critical to own them. Patients need to know that you are invested in helping them, even if things have not gone well. Those patients need more of your time and personal attention.

What advice would you give to the current residents?

There are only so many hours to be a resident. This is your opportunity to learn the principles that will make you successful in the future. There are no short-cuts and the hours that you invest now will pay dividends later. My advice is to arrive early, stay late, do the extra case, see the extra consult and enjoy the ride because it'll go by fast!

John A. Scolaro, MD, MA

Where did you go to fellowship?

Trauma, University of Washington/Harborview Medical Center.

Where are you currently practicing? How would you describe your practice?

University of California, Irvine Medical Center (Orange, CA). Level 1 Academic Medical Center.

How has training at Penn impacted your practice?

My time at Penn was priceless. I remain close to many of my co-residents and faculty who trained/mentored me. The Penn Orthopaedic network is incredibly strong and continues to be impactful in just about every aspect of my orthopaedic practice.

What have you learned in your first decade of practice?

1) Every patient can teach you something and the education never ends 2) Finding the right "balance" is not easy and is different for everyone 3) Utilize mentors and peers regularly when you have questions or need advice (specific case, job, family, etc.).

What advice would you give to the current residents?

It is easy to get wrapped up in the stress and challenges of finishing training and starting your practice. We have all been there. You will avoid most professional and personal pitfalls if you just work hard and remain honest, humble and compassionate.

Laura C. Wiegand, MD

Where did you go to fellowship?

Sports Medicine, Massachusetts General Hospital.

Where are you currently practicing? How would you describe your practice?

I am currently practicing in Pittsburgh, PA for the Allegheny Health Network. Currently, I am an employed physician, working with a small orthopedic group which is now affiliated with the larger orthopedic group within the larger network.

How has training at Penn impacted your practice?

The training I received at Penn has been invaluable to my current practice. My practice is general orthopedics with a focus on shoulder and sports medicine, so I rely heavily on techniques and training I learned throughout residency in all areas of orthopedics including trauma, hand, and joints in addition to sports/shoulder.

What have you learned in your first decade of practice?

Listen to your patients, they will help you make the right treatment decisions for them! Patient selection is extremely important. The practice of orthopedics is a life-long learning process. Techniques and implants will change over time, and you will need to adapt to these, while continuing to rely on basic diagnostic and technical principles you learned during training.

What advice would you give to the current residents?

Penn is a very special place with wonderful faculty. Take advantage of their expertise, and observe how they speak to patients and their families. Learning surgical technique is very important, however, the art of talking to patients and making decisions is equally as important. Do the best you can for your patients and you will succeed.

Miltiadis H. Zgonis, MD

Where did you go to fellowship?

Sports, Duke University.

Where are you currently practicing? How would you describe your practice?

The University of Pennsylvania. Academic adult sports medicine.

How has training at Penn impacted your practice?

In every way. The mentorship I received during training helped me become more efficient and much more organized, and the surgical training (and yes trauma plans!) has translated very well into some of the complex reconstructions we see come to Penn.

What have you learned in your first decade of practice?

Listen to patients - critically important for accurate diagnoses, and do not rely on other physicians to tell you what's wrong - particularly radiology (no offense!)

What advice would you give to the current residents?

Learn how to be as good as you can be at interpreting studies related to your specialty. Seek out instruction and continue learning. Find your work-life balance as soon as you can (and when you figure it out, let me know).

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1 Hatch D, et al. Foot & Ankle Ortho. 2020, 5(4): 1-8. 2 Dayton P, et al. J Foot Ankle Surg. 2016. 55:567-71. 3 Ray J, et al. Foot Ankle Int. 2019 Aug;40(8):955-960. 4. TMC Data on file. 5. TMC Data on file.

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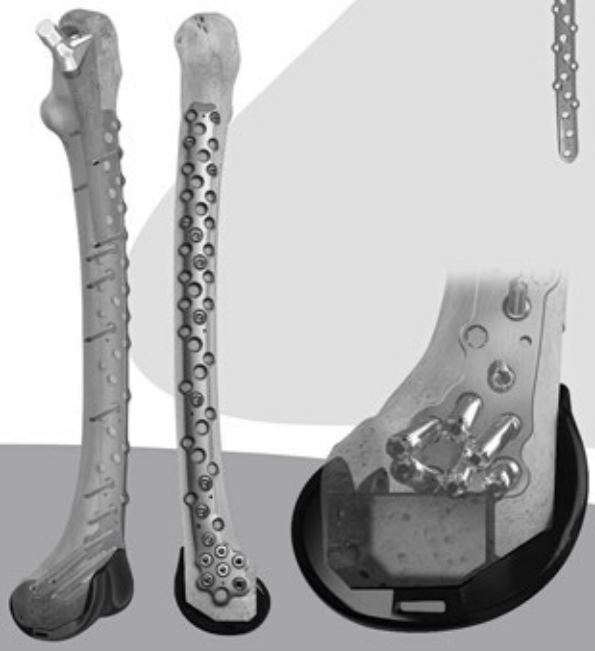

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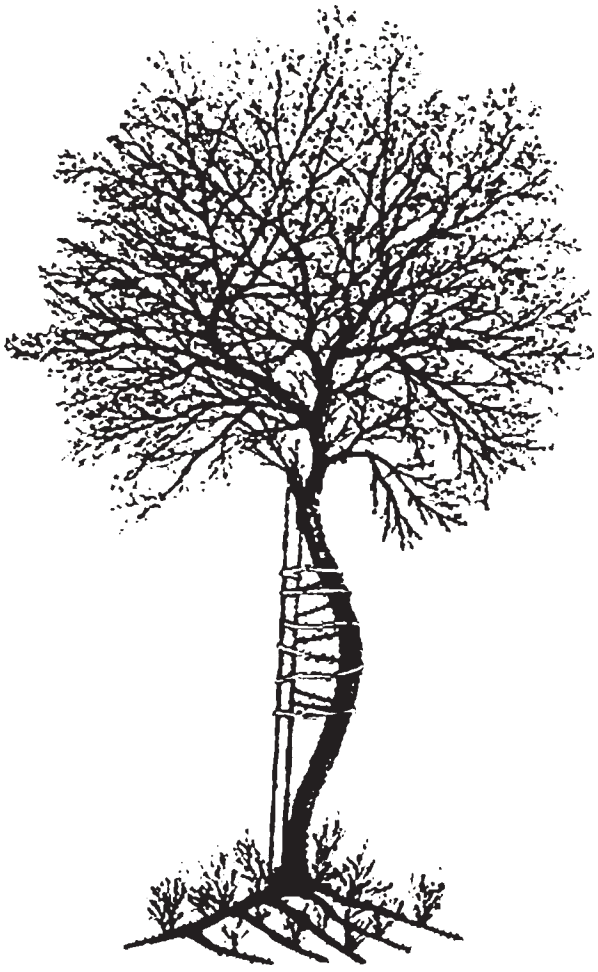

University of Pennsylvania Orthopaedic Journal

2021-2022 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, and the Philadelphia Veterans Affairs Translational Musculoskeletal Research Center. In addition to research, each clinical section is preceded with a "Tips & 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

Shoulder and Elbow

Adult Reconstruction

Foot and Ankle

Oncology

Orthoplastics

Pediatrics

Basic Science Research Sections:

Bone & Development

Cartilage, Meniscus & Disc

Muscle, Tendon, & Ligament

Trauma

U·P·O·J

Trauma Tips and Tricks: Current Concepts Review of Ballistic Injuries

Eric Schweppe, MD[1]
Matthew Bryan, BS[2]
Derek Donegan, MD[1]
Samir Mehta, MD[1]

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

2Harvard Medical School, Harvard University, Boston, MA

Introduction

Gun violence and ballistic injuries are serious public health problems in the United States that are associated with substantial morbidity and often require orthopedic expertise in treatment. The incidence of firearm injuries has increased in recent years. An estimated 134,000 nonfatal firearm injuries occurred nationally in 2017, an increase of over 50% from two years prior according to the Centers for Disease Control and Prevention.[1] The majority of these injuries occur in urban areas, like Philadelphia, which saw 2,266 shooting victims in 2020, nearly double the number from 2015.[2] Firearm injuries continue to rise with 354 shooting victims from Jan 1st–March 3rd 2022.[3] The violence predominantly affects males, those under the age of 35, and racial minorities. In Philadelphia, people of color comprised 95% of gunshot wound (GSW) victims in 2021.[2] Therefore, proper treatment of GSW injuries is an important component of health equity. This article reviews basic management of GSW injuries along with specific insights obtained from working at a high-volume urban Level 1 Trauma Center.

Guns, Ammo, and Ballistic Wounds

Current firearms can be classified in three basic categories: shotguns, rifles, and handguns. Shotguns are smoothbore with limited range, firing either multiple pellets or a single projectile (slug). Wadding is used to separate the propellant from the projectiles. Rifles are long barreled with parallel spiraling grooves along the bore, called rifling, which gives ejected bullets rotational spin. With this stabilization, rifles can fire powerful ammunition with increased range and accuracy. Handguns may also have rifling along their barrels but are typically less than 30 cm in length.[4] Handgun rounds are generally less powerful and less accurate. Exceptions to this rule, however, are increasingly relevant as rifle and handgun distinctions blur.

Bullets are typically lead alloy projectiles (Figure 1). Two key variations on a standard solid design include jacketed and partially jacketed bullets. Jacketed rounds are composed of a soft lead core encased in a harder metal alloy. Partially jacketed bullets, "hollow point," have an exposed tip which allows the projectile to flatten and expand on impact. This transmits more force and leads to more significant and complex injuries.

Ballistic wound character and severity are therefore heavily influenced by mechanism of injury as much as anatomic location. First, the kinetic energy (KE) of a bullet is greatly influenced by the projectiles speed ($KE = \frac{1}{2}*MV^2$). Conventional categorization relies on this characteristic in grouping injuries as either resulting from bullets at low-velocity ($< 2{,}000$ ft/s) or high-velocity ($> 2{,}000$ ft/s). However, actual energy transfer is an important

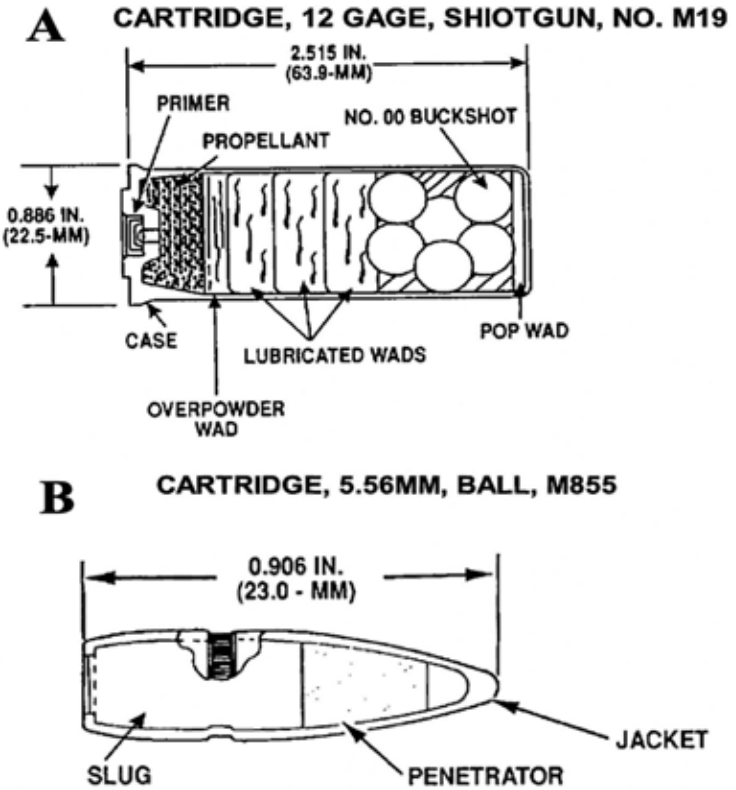

Figure 1.[20] **(A)** Schematic of a 12-gage shotgun round; **(B)** Schematic of a 5.56 millimeter, fully jacketed rifle bullet commonly used in military and civilian rifles

component of the injury. A bullet which comes to rest within the body will transfer its entire KE after impact, compared to the smaller fraction of a bullet which exits. Bullets create a permanent cavity through the tissue though often not in a straight path. Upon impact, the projectile experiences increased yaw, the angle between bullet axis and its initial trajectory, and after 15 degrees will begin to tumble. Bullet trajectory is further altered by fragmentation or striking bone. In high velocity injuries, tissues adjacent to the direction of travel of the projectile will undergo a rapid radial expansion. This expansion forms a temporary cavity with significant damage to small blood vessels and peripheral nerves, and may cause simple fractures.

Acute management

Death prior to arrival of first responders on scene is a major driver of firearm mortality. Philadelphia has sought to reduce prehospital time by allowing police to directly transport to trauma centers.[5] On arrival, patients are stabilized per ATLS protocols. In the trauma bay at Penn Presbyterian, airway, breathing, and circulation are rapidly assessed as the patient is fully exposed. All penetrating wounds are then identified and marked with taped paperclips (closed for anterior and open for posterior) to assist in trajectory identification (Figure 2). The presence of a single wound (or odd number) increases suspicion for a retained bullet. Wounded areas are assessed for pallor, gross contamination, joint effusions, exposed bones, and compartment swelling. Vascular examination using ABI/ABPIs are conducted in cases of poor perfusion or pulsatile bleeding with CT angiography available for continued concern. A neurologic exam documents baseline function. Tetanus prophylaxis is given and, time permitting, wounds are irrigated to remove gross debris, photographed, and dressed. Standard radiographs are taken for assessment of possible fractures, retained bullets, and joint injuries. The fracture is then reduced when necessary and splinted. Skeletal traction is applied for fractures of the acetabulum, femur, or if there are retained materials in the joint (Figure 3).

Treatment Overview

Low velocity GSW fractures can often be treated similar to closed injuries with the goal of restoring function and minimizing complication. Formal debridement is typically not required, and patients are treated with simple wound care and a short course of oral broad-spectrum antibiotics. Stable fractures can be managed conservatively with appropriate wound care. The ulna and tibia remain exceptions, with increased rates of infection stemming from their relatively subcutaneous position. These are treated as open fractures with operative irrigation, debridement, stabilization, and soft tissue coverage as needed.[6] Exploration for soft tissue bullet removal is not recommended due to the risk of damage to surrounding structures. Symptomatic subcutaneous bullets, however, should be removed.

High velocity GSW fractures require more complex treatment emphasizing life and limb saving procedures. Extensive soft tissue injury can include vital end organs which require management by general trauma surgeons. In cases of severe trauma, controlling bleeding is imperative to prevent the lethal triad of hypothermia, coagulopathy, and acidosis. Wound hemorrhage should be managed with direct pressure using a sterile dressing (Figure 3), followed by neurovascular

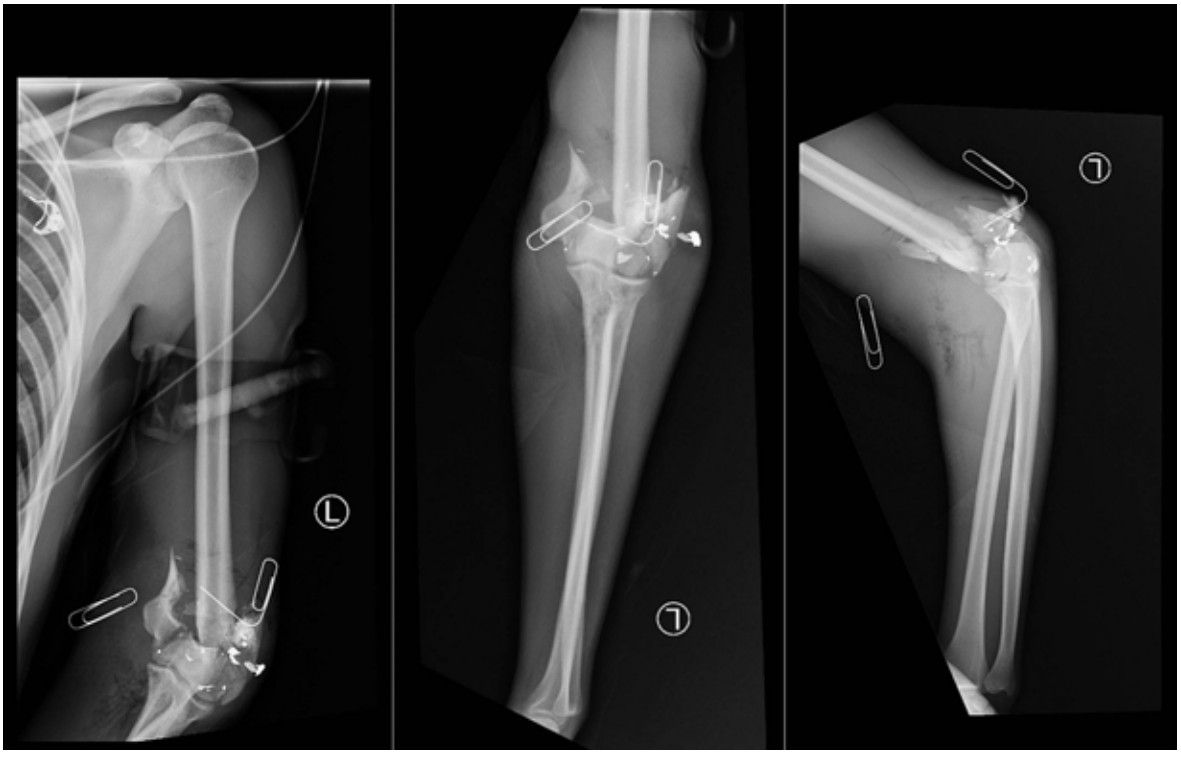

Figure 2. Portable radiographs of 20yo male in trauma bay demonstrating comminuted left distal humerus fracture with retained ballistic fragments.

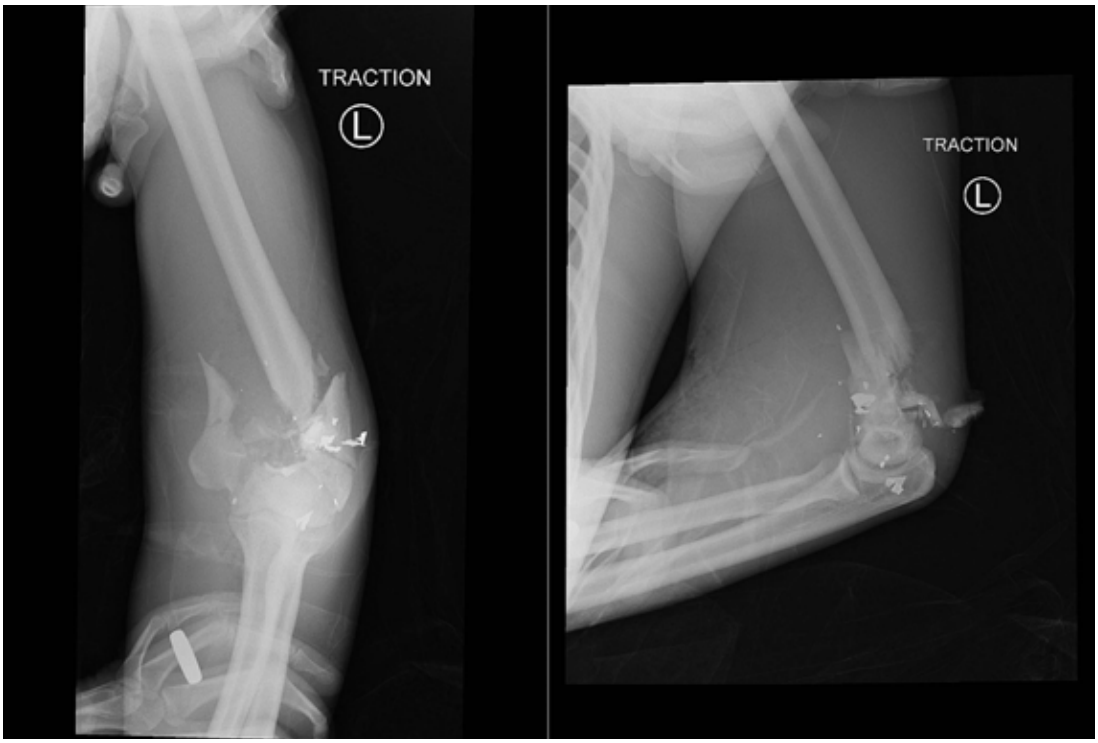

Figure 3. Traction views of comminuted left distal humerus fracture to evaluate for retained fragments

assessment of the limb with fracture reduction if possible. Tranexamic acid is administered to halt fibrinolysis if injury has occurred within three hours of arrival. The patient should be resuscitated as needed with blood products in 1:1:1 (platelets: fresh frozen plasma: packed red blood cells).[7] Serum lactate should be taken regularly to monitor adequate volume resuscitation. Additionally, calcium levels should be monitored and repleted to prevent coagulopathy. Hypothermia is corrected with active warming. Damage control surgery will prioritize hemorrhage control with the duration determined by the physiologic state of patient and definitive surgery deferred to a future date.

Intra-articular Injuries

Bullets retained within the joint space are associated with a high rate of infection, mechanical wear, and lead toxicity.[8] As such, intraarticular injuries with retained bullets should undergo I&D with bullet removal (Figure 4). The bullet or fragment should also be considered for removal if proximal enough to the joint to limit mobility and affecting neurovascular structures. However, cases in which the bullet passes through the joint space with minimal articular damage do not require surgical debridement unless there is high suspicion of contamination within the joint. Arthroscopy can be used for many cases of irrigation and debridement. For example, the arthroscopic debridement of the knee can assess soft tissue injuries while removing fragments of bullets and loose bodies.[9]

Antibiotics/Infection

Low velocity GSW fractures treated operatively are managed with standard perioperative antibiotics. Debate continues around the best antibiotic regiment for non-operatively treated GSW fractures. Not only is there no clear superiority between oral and intravenous antibiotics in recent meta-analysis,[10] but also some studies show no significant difference in infection rates in GSW fractures treated with antibiotics versus those that are not treated with antibiotics.[11] Furthermore, gram negative coverage is not necessary in operative or non-operative treated patients based on similar infection rates between first and third generation cephalosporins.[12,13] At Penn, a single dose of first-generation cephalosporin is employed to reduce the risk of microbial resistance and avoid antibiotic side effects.

High velocity GSW fractures are treated as open fractures and require early administration of antibiotics.[14] First generation cephalosporin are employed for 48–72 hours (potentially longer in cases of serial debridement) with no additional requirement for enhanced gram negative coverage.[15] In situations with significant bone loss, soft tissue injury, or both, antibiotic-impregnated polymethylmethacrylate (PMMA) beads can be added for dead space management and synergy with intravenous antibiotics.

Vascular Injuries

Vascular injury should be identified quickly as these patients are at risk of not only volume depletion but also associated nerve injury and infection. In lower extremity GSW injuries, ankle-brachial indexes should be obtained, where a ratio of < 0.9 necessitates further vascular assessment (e.g., vascular consult, CTA, MRA, angiography). In the event of vascular injury, proximal control should be obtained through either a tourniquet (distal injuries) or surgical vascular control (abdomen or pelvis). Surgical treatment includes shunting to restore blood flow, provisional or definitive bony stabilization,

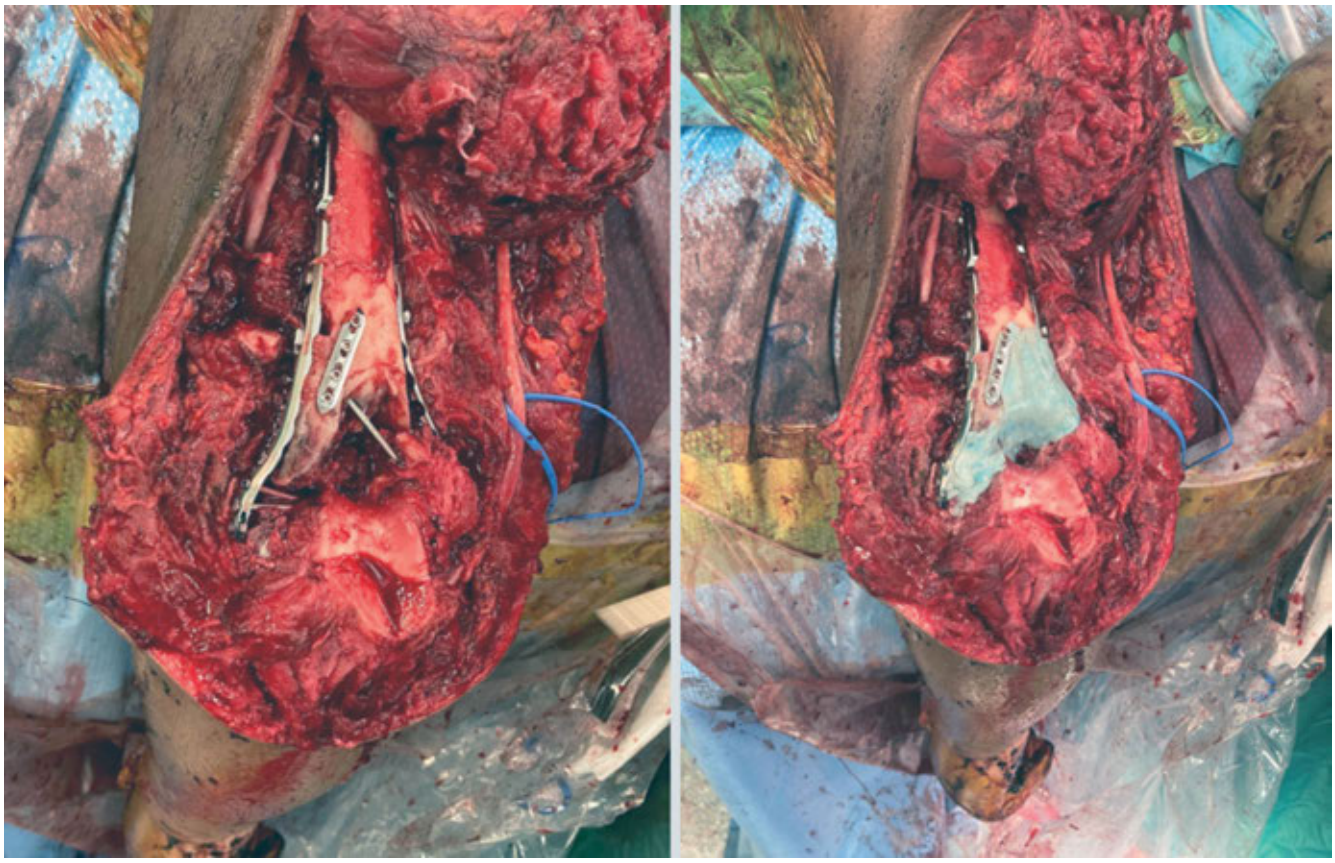

Figure 4. Intraoperative pictures of left distal humerus irrigation and debridement, open reduction internal fixation, and distal humerus reconstruction of cortical defect with cement.

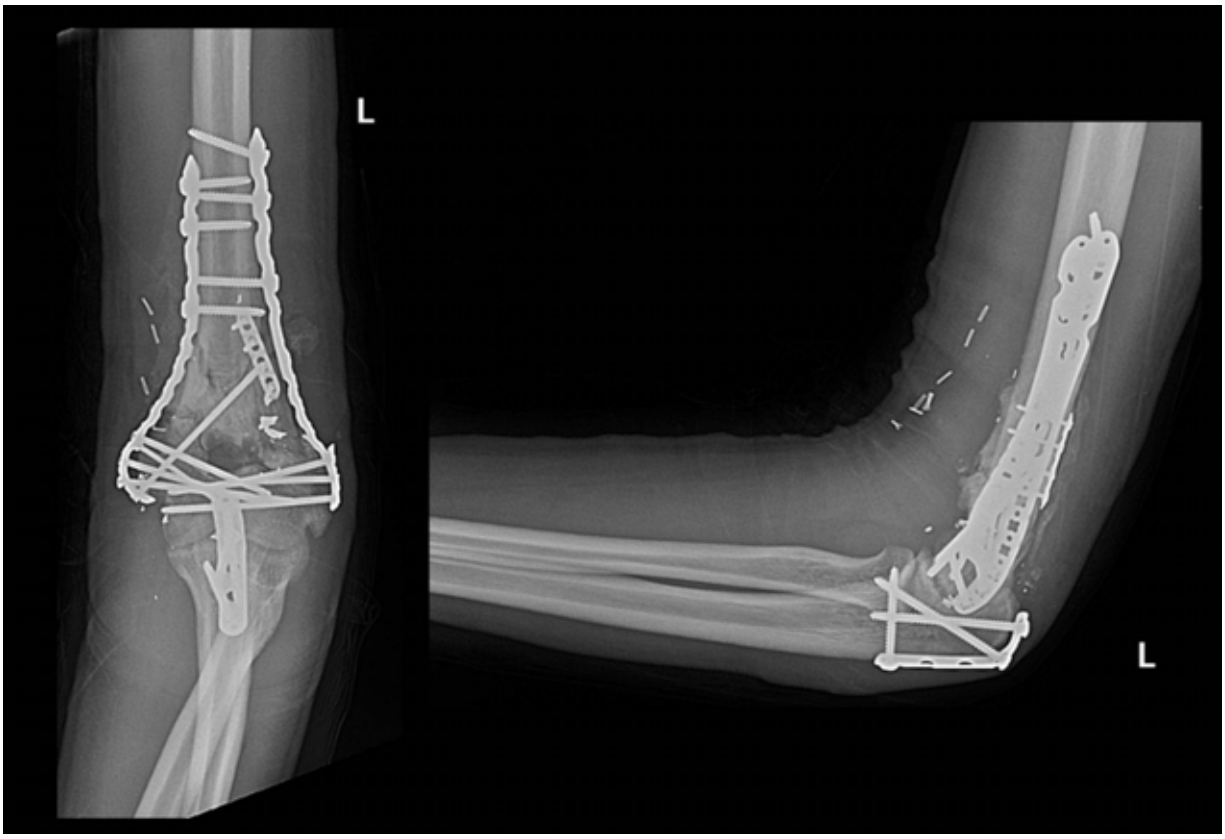

Figure 5. Three month post-operative AP and lateral radiographs with intact hardware. Patient's range of motion full supination/pronation, 45-110° flexion/extension.

vascular repair, and fasciotomies. GSW fractures with associated vascular injuries have a higher rate of infection and should be monitored closely.[16]

Nerve Injuries

Nerve injuries in GSW trauma should be identified early with a neurologic examination of the limb when able. A vascular injury should increase suspicion of a nerve injury because 71% of patients with an arterial injury will also have an associated nerve injury.[17] However, a nerve impairment does not diagnose neurotmesis (laceration). Nerves in the vicinity of a high-velocity GSW may sustain significant intraneural damage, axonotmesis.

In cases of nerve laceration, the ends should be tagged and repaired if the wound is clean. Nerve conduction studies should be conducted only in a delayed fashion (usually three or more weeks from time of injury) to allow for Wallerian degeneration signs to appear.[18] When patients show no signs of improvement three months after initial GSW injury, referral to a peripheral nerve specialist should be considered. Persistent neuropathic pain is often the result of severe scar tissue constricting an otherwise intact nerve. Creation of a healthy tissue bed is essential to nerve recovery which may require soft tissue coverage procedures like local soft tissue rearrangement or fasciocutaneous free tissue flaps. Mixed motor and sensory nerves such as the common peroneal, ulnar, and median nerve tend to have worse outcomes.[19]

Summary

Increasing gun violence in the United States has now brought ballistic injuries once exclusive to warfare to many civilian trauma centers. Management of GSW injuries is related to the amount of energy imparted to the receiving tissue. Life or limb threatening injuries are the priority of treatment which often require a multidisciplinary team effort (Figure 5). Low-velocity GSW fractures can be treated as closed injuries and often managed non-operatively according to standard fracture principles. Exceptions to this include injuries to the subcutaneous bones, like the ulna and tibia, and intra-articular retention. High-velocity GSW fractures require surgical irrigation, debridement, and fixation.

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Spine

Tips & Tricks: Lateral Lumbar Interbody Fusion: Preoperative Positioning for Success

Stephen R. Barchick, MD[1]
Bradley O. Osemwengie, MD[1]
Colin M. Whitaker, MD[1]
Amrit S. Khalsa, MD[1]

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

Background

Lateral Lumbar Interbody Fusion (LLIF) is a newer technique addressing lumbar spinal pathology which has the advantage of requiring a less invasive retroperitoneal dissection compared to more traditional approaches to the lumbar spine. This technique also allows for indirect decompression, restoring disc height and alignment while tensioning the surrounding ligamentous structures.[1] Furthermore, LLIF allows insertion of a large footprint cage which can span the more dense apophyseal ring of the vertebral body.[2] Initial descriptions recommended a left-sided approach to avoid the inferior vena cava, but either side can be utilized safely considering various anatomic considerations. The technique was described initially in 2006 via a two-incision technique but has been adapted to a single incision technique along the flank region.[3,4] Patient positioning is essential to safely accomplishing the goals of LLIF surgery. There are a multitude of positioning considerations entirely unique to the lateral position compared to supine or prone positioning.[2] This necessitates appropriate and rigid positioning to ensure the patient does not move throughout the procedure, as reliable orthogonal fluoroscopic imaging is essential. Like many newer procedures, LLIF presents a learning curve which is not limited to positioning but begins with understanding the nuances of patient positioning.[4]

Example Case

A 63-year-old female presented to our outpatient offices with a one-year history of progressive low back and radiating buttock and anterior thigh neurogenic claudication and pain as well as lower extremity numbness and weakness. She also had a history of a previous L4-L5 fusion without complication. MRI lumbar spine revealed severe central and lateral recess stenosis at the adjacent L3-L4 level. After failing appropriate conservative management, she was deemed a candidate for L3-L4 LLIF with anterolateral instrumentation via a left-sided lateral retroperitoneal approach.

Positioning

Supplies

Axillary roll—An axillary roll is placed to protect the shoulder joint. It will be placed 3-4 inches caudal to the axilla to avoid brachial plexopathy.

Overhead Armboard—An overhead armboard is placed slightly more cephalad than normal to minimize obstruction with the fluoroscope.

OR Table—A Skytron 6600 or equivalent OR table is reversed 180˚ and the head extension attached to the former foot of the bed. This allows for appropriate clearance of intra-operative fluoroscopy from the base of the table (Figure 1).

Sticky Rolls—Two Sticky Rolls are created to stabilize the patient's torso. These are made by

Figure 1. A Skytron 6600 bed reversed with headboard attached at the former foot of the bed.

rolling an OR blanket into a bump and wrapping with 3" tape. The first wrap of tape is down at one end circumferentially to hold the roll together, then the tape is twisted to expose the sticky side and wrapped from one end to the other (Figure 2).

Surgical Setup

Positioning

The patient is positioned so the anterior superior iliac spine is just caudal to the break in the bed. This is critical to optimize the operative retroperitoneal corridor between the ilium and the 12th rib when the bed is flexed (Figure 3).

The hips and knees are flexed to ensure the patient can be centered on the table while also relieving tension on the psoas musculature and the lumbosacral plexus to reduce the risk of traction neuropraxia during operative exposure.

The down arm is placed into the lateral arm board with the elbow extended to allow for IV access and blood pressure monitoring. The upper arm is placed into an overhead armboard with a mild flexion through the elbow to allow for both arm boards to remain as cephalad as possible while still providing physiologic positioning. This again minimizes risk of the arm boards obstructing the fluoroscopic imaging during surgery (Figure 4).

Two pillows are placed between the legs and the fibular head and lateral ankles are padded bilaterally. Sequential compression devices should be attached and plugged in throughout the surgery.

Sticky rolls are utilized to stabilize the patient in a manner similar to a beanbag positioner, while maintaining a lower profile for operative considerations. The first roll is wedged posteriorly along the back, the second is wedged anteriorly against the abdomen (Figure 5). These provided

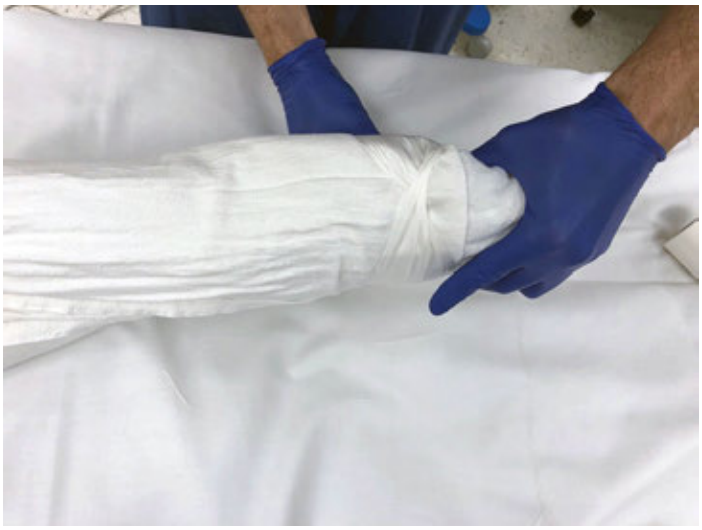

Figure 2. One of the two "sticky rolls" composed of tape and blankets that will assist with stabilization.

Figure 3. Posterior view of patient positioning with demonstration of ASIS below table break.

Figure 4. Armboard positioning demonstrated as Dr. Osemwengie simulates patient positioning.

Figure 5. Placement of the posterior sticky roll which will be wrapped in the table blanket.

additional stability to prevent rotational movement during instrumentation. This can be particularly helpful in more obese patients.

Taping

#1—Begin with 3" tape at the level of the greater trochanter / ASIS, wrap circumferentially around the patient and under the bed twice (Figure 6).

#2—Wrap around the thighs and legs. Start at the greater trochanter and wrap down the thigh toward the knee with foam crate along the fibular head (Figure 7). Continue taping below the bed aimed toward the feet, then circumferentially around the ankle, ensure the lateral malleolus is padded. Above the bed, continue the tape along the leg toward the knee and continue under the bed ending at the starting point for this roll of tape: the greater trochanter (Figure 8).

#3—Start another roll of tape along the rib cage, wrap circumferentially around ensuring the wrap allows for a wide surgical field for sterilization and draping (Figure 9). This provides stability to the proximal torso while allowing a wide field during the procedure.

Bed Angle

With the patient positioned appropriately, now break the bed approximately 10 degrees at the flank region to optimize access to the retroperitoneal space without abutting the ilium or rib cage. Given the bed is reversed 180˚, the operator will need to (1) Trendelenburg the bed and (2) reflex the bed (Figure 10).

Additional Reinforcement

Additional tape may be required to reinforce along the patient's hips and ribs once the bed is positioned at the appropriate angle.

Fluoroscopy

Position the C-arm on the ventral side of the patient, with the bed and patient appropriately positioned, the machine

Figure 6. Dr. Khalsa demonstrates wrapping the first band of tape at the pelvis.

Figure 8. The second roll of tape after including feet, legs with appropriate padding.

Figure 7. The second roll of tape starts at the greater trochanter and wraps around the table.

Figure 9. The third roll of tape wrapped around the torso, will allow access below the 12th rib.

should be orthogonal to the patient and maneuver from AP and lateral radiographs without any further adjustments of the fluoroscope and with the bed in a stationary position (Figures 11, 12). The C-arm will be placed parallel to the vertebral endplates of the planned surgical site in order to allow for achieving a true lateral and AP radiograph prior to surgery.

Assessment of true AP and lateral radiographs is important prior to preparation and draping. AP assessment includes assuring the spinous process in midline, the pedicles are symmetric and reside in the upper third of the vertebral body, and vertebral endplates are crisp and without double density. Lateral assessment includes assuring pedicles are completely overlapped and minimizing double density of the endplates in this plane.

Next, with the use of a T-tool, the posterior aspect of vertebral body is identified on a true lateral radiograph of the spine. Here we show an example of appropriate use of the T-tool at the L3-4 level, marking the posterior aspect of the operative disc space (Figure 13). This is marked with a permanent surgical marker on the patient's flank prior to prepping and draping. The eventual incision will completely parallel the operative disc space. After prepping and draping and surgical dissection, the appropriate start point allows for expedient insertion of instrumentation at the appropriate disc space and the final construct on lateral radiograph (Figure 14, 15).

Figure 10. With the bed flexed, appropriate patient positioning demonstrated with access to the operative corridor.

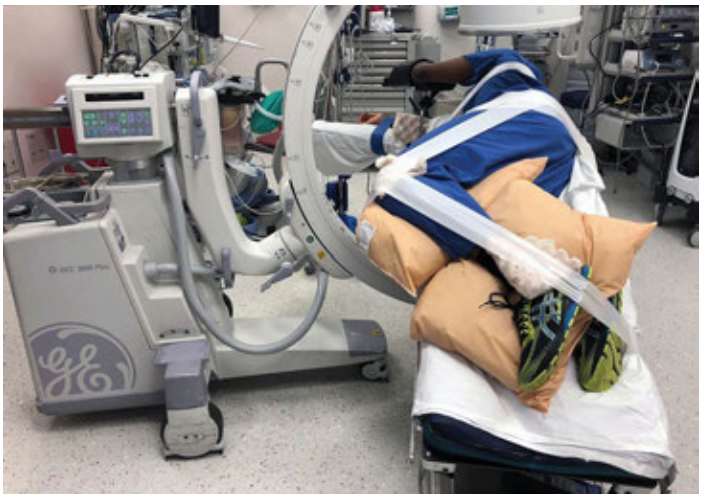

Figure 11. C-arm positioning is demonstrated for a lateral radiograph.

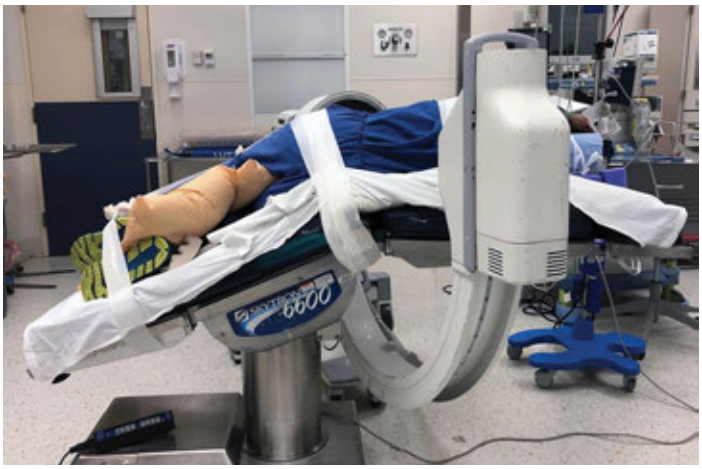

Figure 12. C-arm positioning is demonstrated for an AP radiograph.

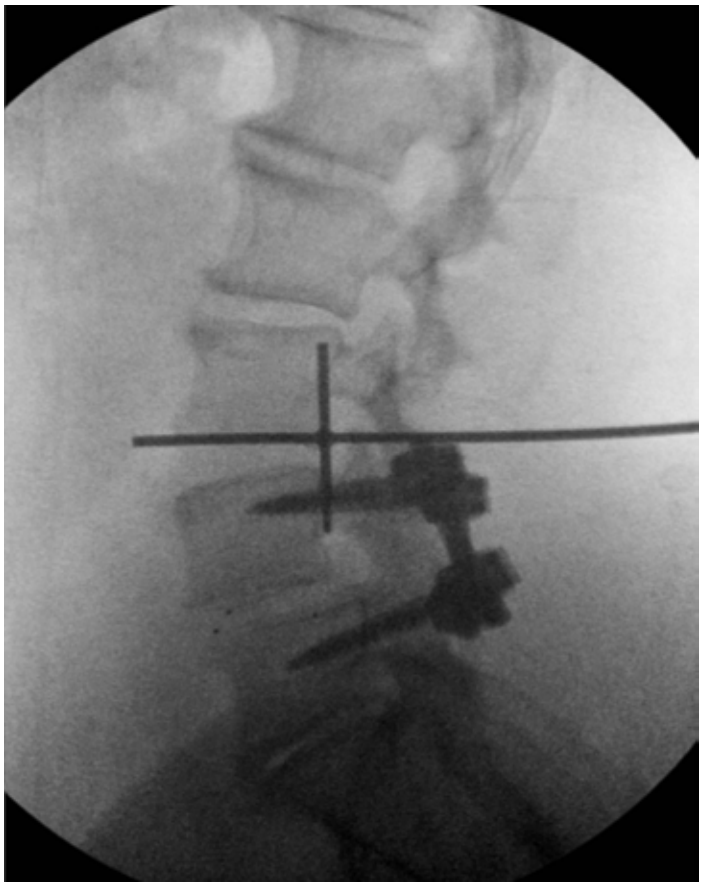

Figure 13. T-tool is aligned to the posterior aspect of the vertebral body on a true lateral radiograph.

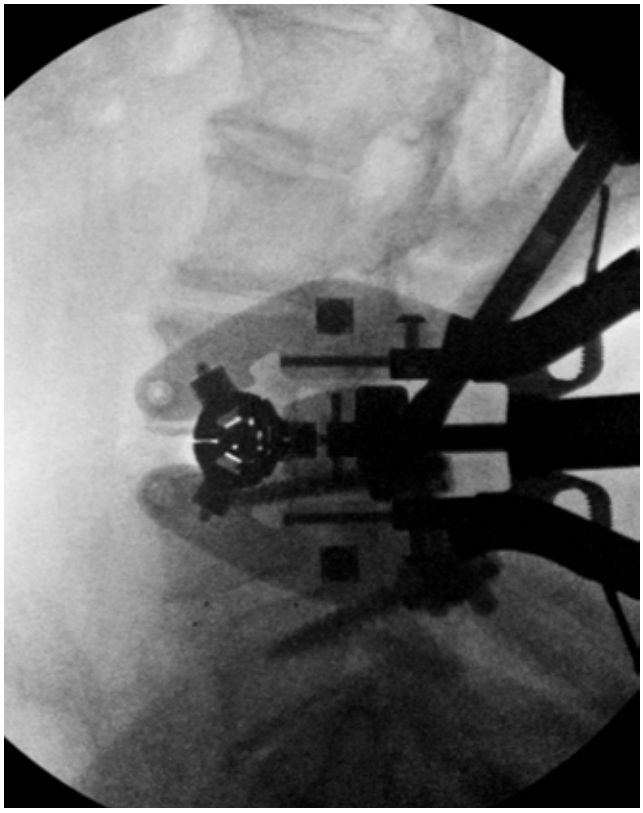

Figure 14. Radiograph demonstrating instrumentation insertion on a lateral radiograph.

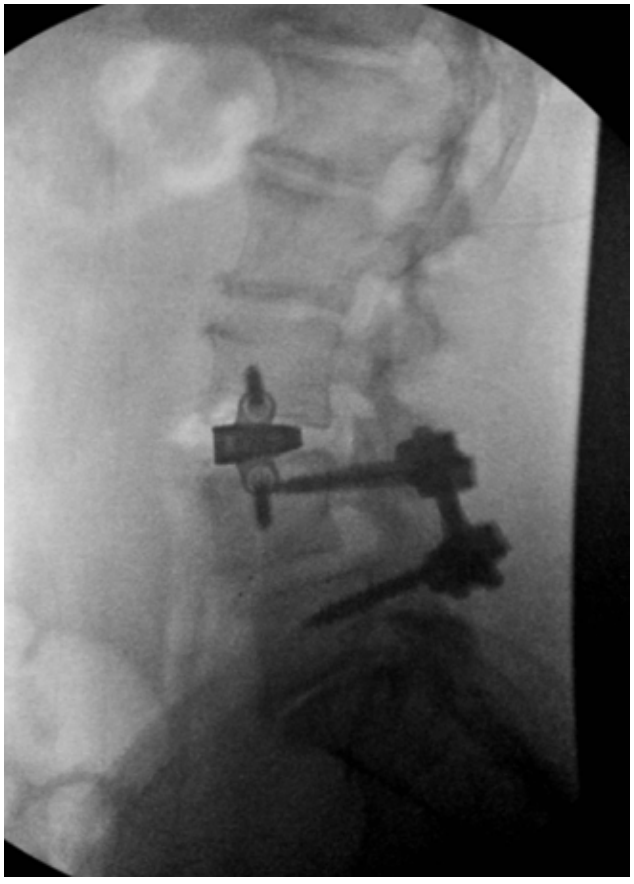

Figure 15. Final construct demonstrated on a lateral radiograph.

Additional Tips

Surgical stools should be readily available for the surgeon and assistant's use regardless of his/her height as the operative field is often higher given the position.

Discussion

Lateral lumbar interbody fusion is a newer technique gaining popularity in orthopaedic spinal surgery to address lumbar spine pathology. Effective use of the technique to help patients requires an understanding of how-to setup the operating table in a manner which maximizes patient stability and minimizes adjustment after the insertion of instruments. The process starts with proper bed selection and appropriate use of padding and support to stabilize bony prominences to position the patient with access to relevant lines while also allowing access to the surgical field. Positioning the pelvic girdle and shoulder appropriately aligned will minimize the need for adjustment while taping the patient to the bed. Stable, reliable positioning is absolutely essential to safely accomplishing the goals of this surgery. Here we demonstrate the method utilized by one of our senior spine surgeons which has been utilized with good success to allow efficient use of operating room time and to maximize intra-operative stability during instrumentation.

Please note that the patient fluoroscopic images have been anonymized and are used in conjunction with the photos of the physician modeling patient positioning for educational purposes.

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A Rare Case of Chronic, Atraumatic Atlantoaxial Rotatory Fixation in an Adult Treated with Halo Traction Suspension, Open Reduction and C1-C2 Fusion

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Introduction

Atlantoaxial rotatory fixation (AARF) is a rare condition in the adult population, with the vast majority being caused by trauma. Non-traumatic cases of AARF are even more rare, with only seven prior documented cases.[1–7]

Given the uncommon nature of this condition in adults, there is no consensus optimal treatment protocol. When diagnosed early, often AARF is treated successfully with non-operative measures such as traction with closed reduction. The diagnosis can be elusive as patients frequently present with normal neurologic exams and non-diagnostic cervical spine radiographs. In those with a delayed diagnosis of AARF, conservative treatment is less successful and patients generally require open reduction and C1-C2 fusion.

This is a case of an adult patient with delayed presentation of atraumatic atlantoaxial rotatory fixation. After informed consent and discussion with his surgeon, he was treated using halo traction suspension with open reduction and posterior C1-C2 fusion.

Case

Presentation

A 61-year-old male software developer with a past medical history significant for controlled type 2 diabetes mellitus, hypertension, nasopharyngeal cysts, and a history of deep vein thrombosis/pulmonary embolism previously treated with anticoagulation therapy presented to the outpatient spine clinic with a chief complaint of progressive torticollis over several years.

The patient was initially seen by physical medicine & rehabilitation in 2016 for left-sided neck tightness and paresthesias in the left ring and small fingers. He underwent a course of physical therapy and a series of cervical epidural steroid injections, with transient resolution of his symptoms. Despite completing multiple non-operative modalities, he continued to have left-sided neck pain and developed a noticeable head tilt. He was referred to see a spine surgeon, but was not seen in a surgical clinic until 2021 when he presented to establish care. At this point his torticollis had worsened. In addition to his complaint of atraumatic chronic neck pain, he endorsed mild tingling in bilateral small fingers without motor weakness. He denied changes in balance, or alterations in fine motor skills.

During examination, a tight left sternocleidomastoid was noted which caused the head to rotate to the right and tilt to the left (Figure 1). He had full strength and intact sensation in bilateral upper and lower extremities.

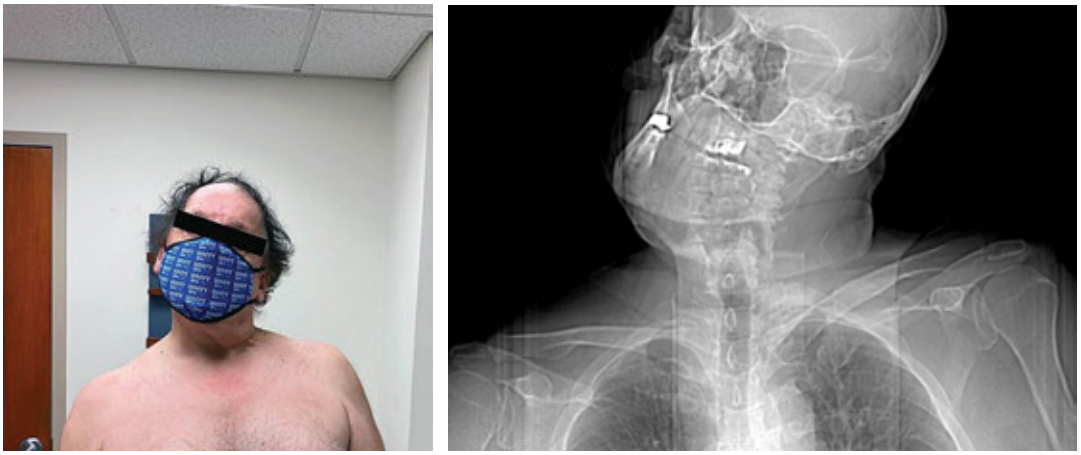

Figure 1. Pre-operative clinical photo and scout CT image demonstrating the classic "Cock-Robin" posture, with the head yawed to the right and rolled to the left.

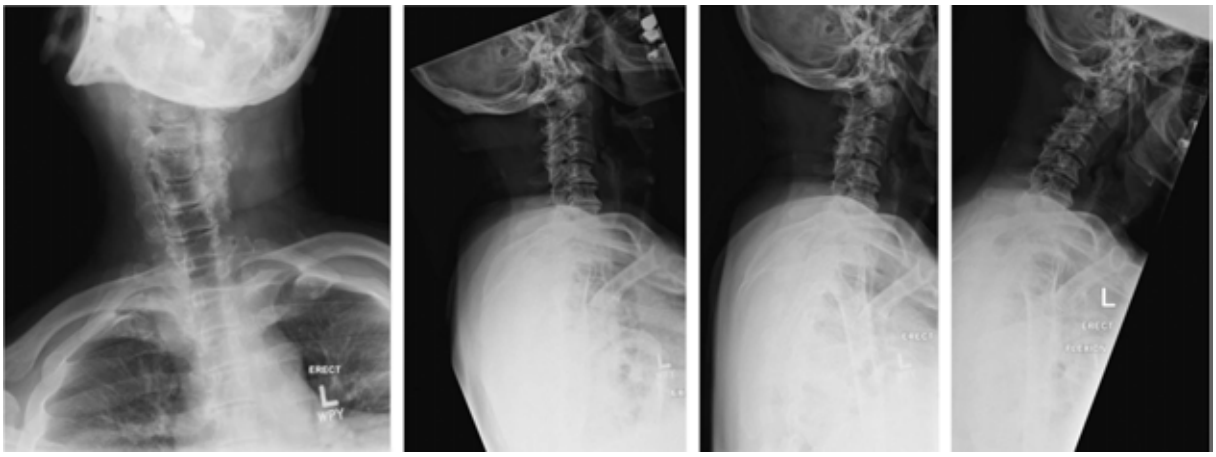

Figure 2. AP and lateral radiographs demonstrating head roll to the left associated with multi-level left-sided spondylosis. No instability is observed on flexion/extension views.

Antero-posterior (AP) and lateral radiographs of the cervical spine showed a head tilt to the left associated with multi-level left-sided spondylosis, without any evidence of instability (Figure 2). a CT scan obtained during evaluation at an outside institution the year prior demonstrated rotatory subluxation of the C1-C2 articulation without anterior displacement, consistent with Fielding Type I rotatory fixation (Figure 3).[8] An open-mouth odontoid view was unavailable for interpretation.

Given the patient presented with a five-year history of this issue and had failed physical therapy and injections, the senior surgeon felt that he would benefit from operative intervention. An MRI was obtained to determine the extent of the operative intervention given his ongoing bilateral hand symptoms. Additionally, a CT angiogram (CTA) was obtained to evaluate the vascular anatomy to plan safe placement of instrumentation.

The MRI showed multilevel cervical stenosis without severe cord compression and the CTA showed intact vertebral arteries without aberrancy. The patient was consented and scheduled for navigation-guided C1-C2 posterior spinal fusion with iliac crest bone graft.

Surgical Management

Following pre-operative optimization for glucose control, the patient was brought to the operating room. A halo was applied under general anesthesia while supine on a stretcher. He was then re-positioned prone on an open Jackson table. The halo was suspended and traction applied, using ten pounds for suspension and ten pounds for traction (Figure 4). A navigation array was then attached to the halo (Figure 5).

Through a posterior midline incision, dissection was carried out to the lateral masses of C1 and C2, taking great care to avoid the vertebral artery laterally in the setting of the patient's distorted anatomy. With fluoroscopy, the C1-C2 joint was localized. Bilateral C2 neurectomies were performed to improve access to the C1-C2 joint, allowing for better release and easier screw insertion later in the case.

To free up the C1-C2 segment, the facet joints were released using curettes and a small sharp Cobb elevator. Once the release was adequate, the halo device and head were manipulated to reduce the rotatory subluxation. With the traction suspension still applied, the reduction maneuver was performed by rotating the head to the left and tilting the

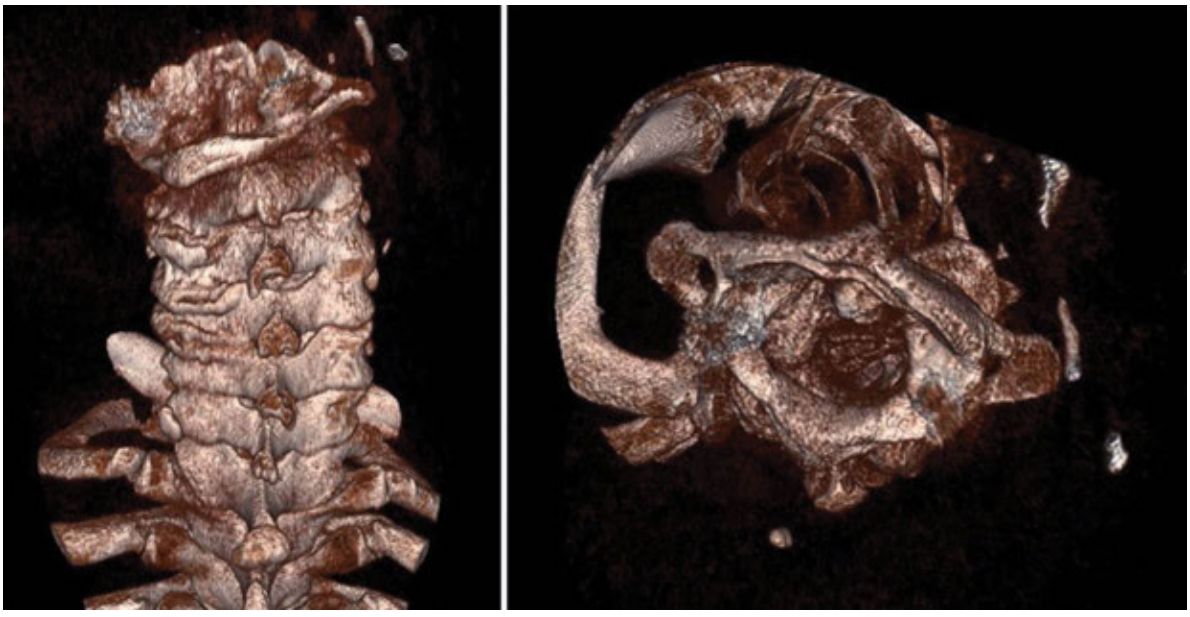

Figure 3. 3D CT reconstruction demonstrating Fielding Type I atlantoaxial rotatory fixation. The odontoid acts as a pivot point, with the left C1 facet subluxating anteriorly and the right C1 facet subluxating posteriorly. There is no anterior displacement.

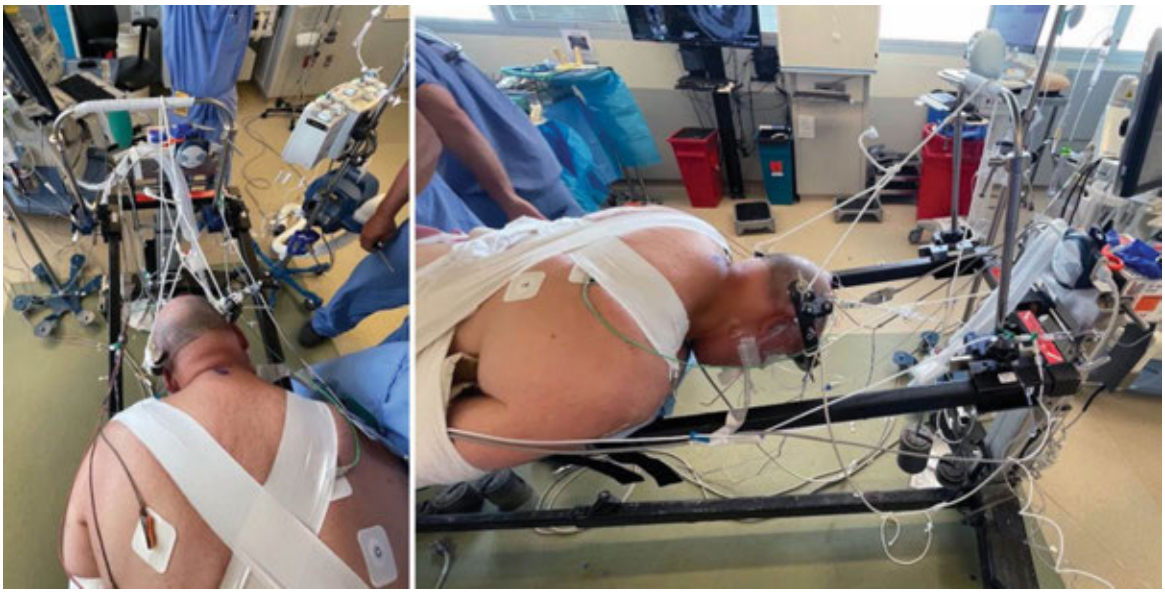

Figure 4. Intra-operative clinical photos showing the patient positioned prone on an open Jackson table with halo traction suspension applied.

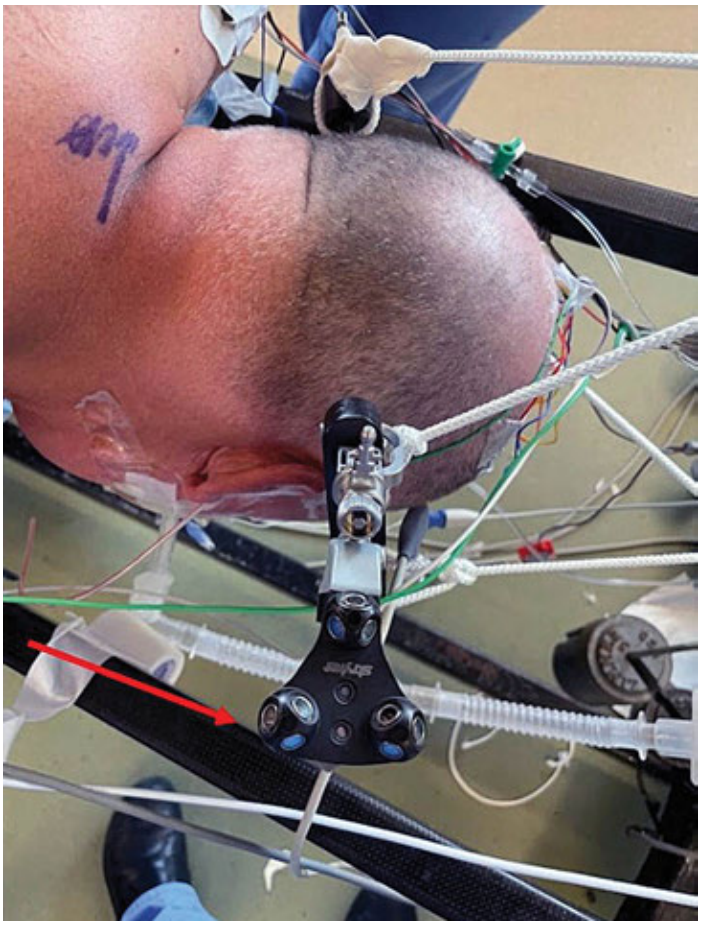

Figure 5. The navigation array shown attached to the halo (red arrow).

head to the right through the halo device. Reduction was visible along with an audible snapping sound. Fluoroscopic assessment confirmed appropriate alignment of the C1 and C2 vertebral bodies.

Unfortunately, the navigation array shifted during the reduction maneuver and the plan to navigate C1 and C2 screws was abandoned. Instead, fluoroscopic guidance was used for insertion of lateral mass screws into C1 and pedicle screws into C2. Rods were inserted. Distraction was applied on the left and compression on the right to further improve alignment of the cranium on the two superior vertebral bodies. A cross-link was applied at the caudal aspect of the construct to further limit rotation and prevent recurrent subluxation (Figure 6).

Next came bone grafting. After thorough decortication with a burr, iliac crest bone graft was harvested and laid between C1 and C2. The wound was then closed in a layered fashion. Drapes were taken down and a significant improvement in alignment was observed (Figure 7). The patient was re-positioned onto a hospital bed for removal of the halo and a hard cervical collar was applied. He was extubated in the operating room and transferred to the intensive care unit overnight for monitoring.

Post-Operative Course

Overnight the patient was stable and on post-operative day (POD) one, he was transferred to the floor. A CT scan was obtained, which confirmed safe placement of screws and appropriate reduction of the C1-C2 rotatory subluxation (Figure 8 & Figure 9).

Although the patient's alignment clinically was improved, he still had a slight persistent head yaw to the left (Figure 10). His left sternocleidomastoid contracture persisted. He elected to undergo left sternocleidomastoid tenotomy at the level of the clavicle on POD 3. He was then discharged home the following day on POD 4 in a hard cervical collar.

The patient was seen back in the clinic two weeks after discharge, at which time he reported 80% improvement in his symptoms (Figure 11). He remained in a hard cervical collar for ± weeks post-operatively. The patient returned to the office six months post-operatively and was satisfied with his alignment and range of motion.

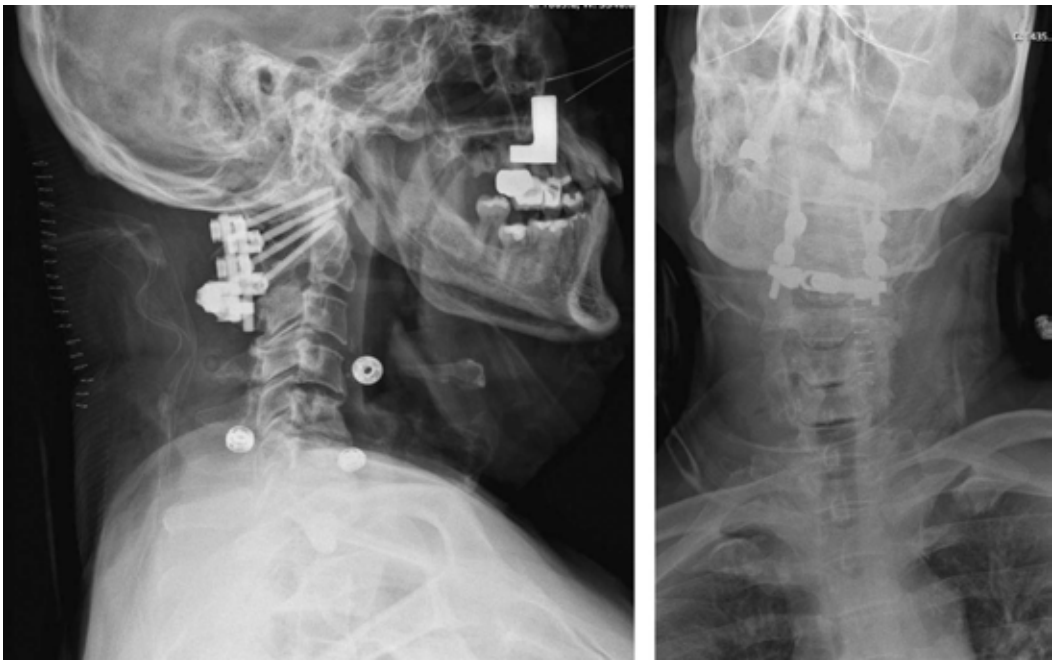

Figure 6. Lateral and AP radiographs showing the final construct, C1-C2 fusion with a cross-link at the caudal aspect of the construct.

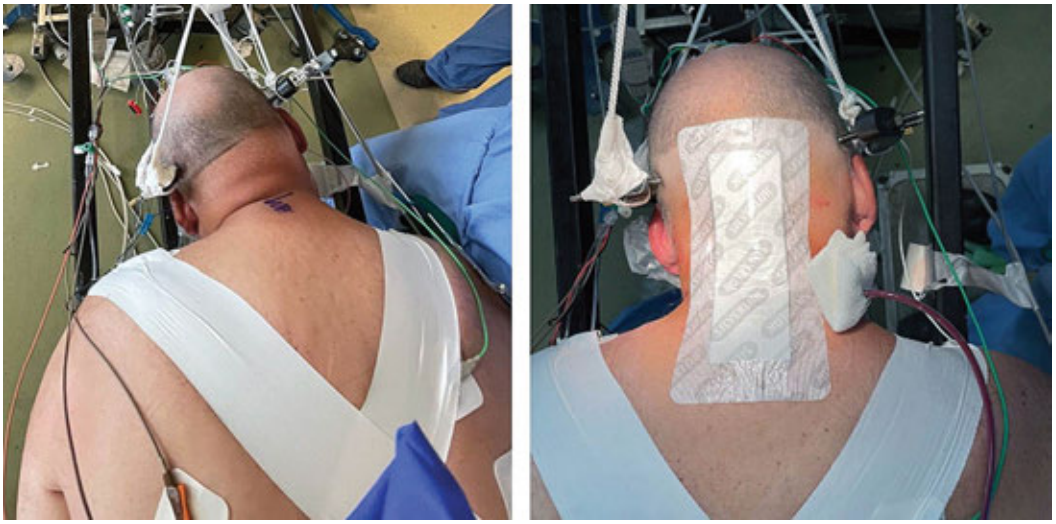

Figure 7. Intra-operative comparison of head alignment prior to **(LEFT)** and at the completion of **(RIGHT)** surgery while still in halo traction suspension.

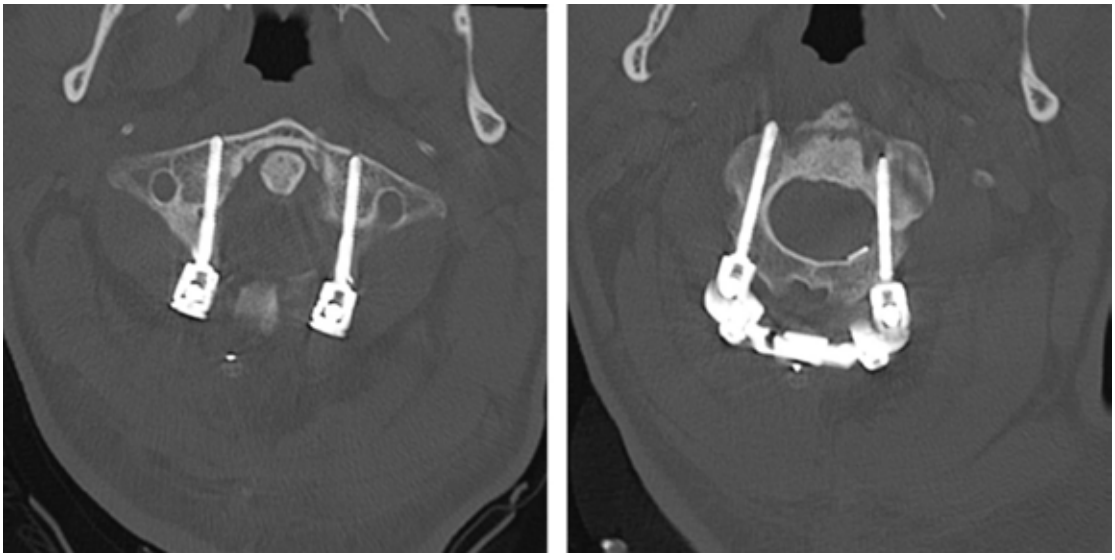

Figure 8. Post-operative axial CT images showing safe placement of C1 lateral mass screws **(LEFT)** and C2 pedicle screws **(RIGHT)**.

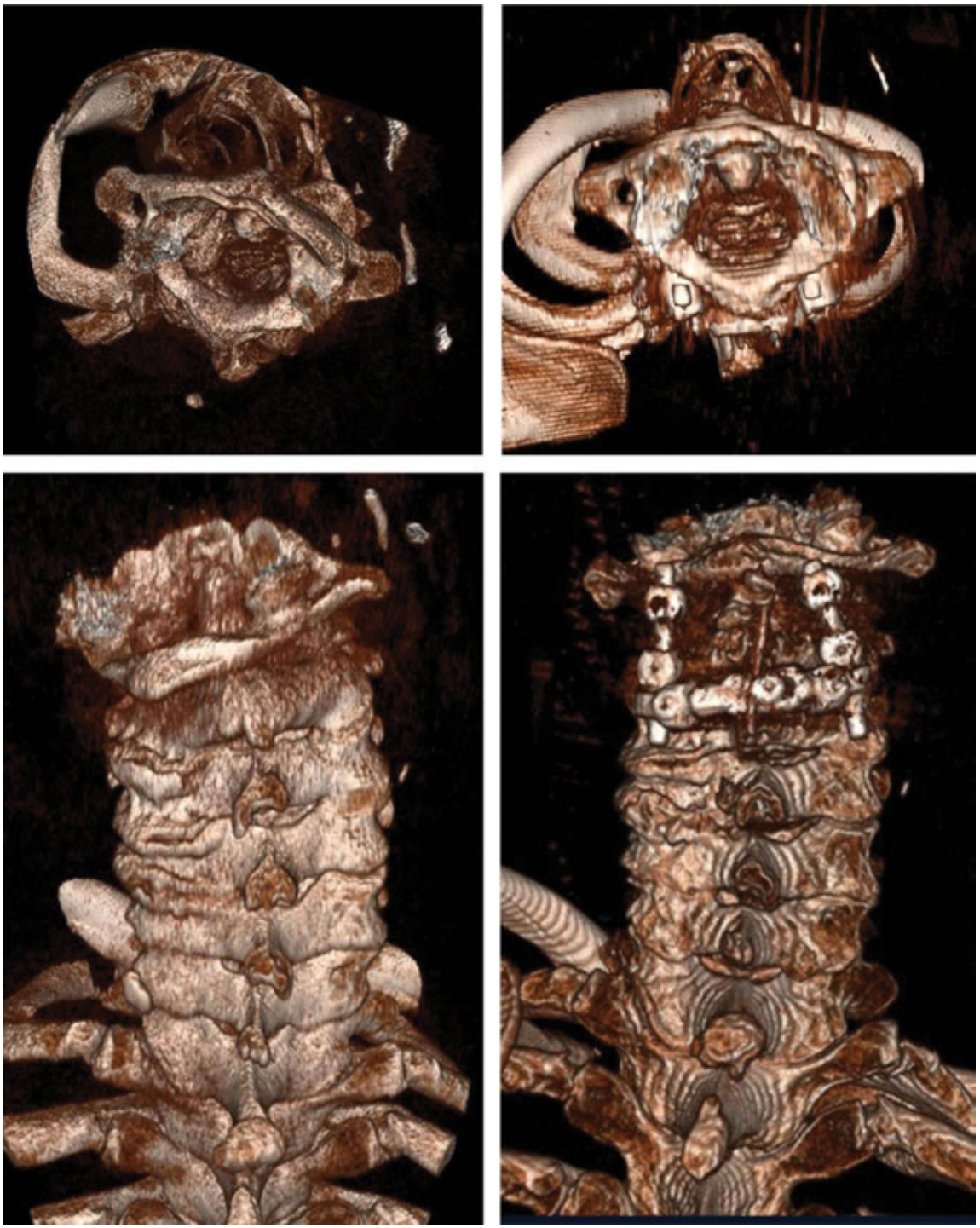

Figure 9. 3D CT reconstructions demonstrating interval reduction of C1-C2 rotatory subluxation (**LEFT:** Pre-Operative; **RIGHT:** Post-Operative).

Discussion

Atlantoaxial rotatory fixation (AARF) is a uncommon condition normally seen in the pediatric population and rarely seen in adults.[9,10] When it occurs in the adult population, AARF usually is caused by trauma, with case series citing automobile collisions, falls, and sport-related accidents as the most common etiologies.[10,11] Atraumatic AARF in adults, are even more rare, with only seven cases previously described in the literature.[1-7]

Regardless of the etiology, there is no consensus regarding the optimal strategy for managing this complex problem in adult patients.[12] Conservative treatment involves a trial of cranial traction with or without manipulation, generally followed by immobilization in a cervical collar or halo vest.[9,12] Additionally, there are varying expert opinions on the duration of conservative management.[12] In cases where no reduction is obtained with traction and manipulation, or in patients who experience re-dislocation, surgical treatment with C1-C2 fusion can be pursued.[9]

In the acute setting, conservative treatment has been successful.A recent literature review found that 25/31 patients who sustained traumatic AARF and initiated conservative

Figure 10. Clinical photos comparing head tilt before after the first stage of the procedure: **LEFT:** Head tilt pre-operatively before C1-C2 fusion.

RIGHT: Head tilt post-operatively after C1-C2 fusion, but prior to left sternocleidomastoid tenotomy.

Figure 11. Clinical photos at first post-operative visit, noting improvement in head alignment.

treatment within 1 month of injury successfully responded to traction and manipulation.[11]

Initially, AARF is often a missed diagnosis as patients can present with normal neurologic exams and non-diagnostic cervical spine radiographs, leading to delays in initiating conservative treatment.[13,14] For example, in a retrospective review of 26 patients treated for AARF at a single institution between 1988 and 2000, the authors found that it took an average of 15 months to establish the proper diagnosis of AARF.[9] Such a significant delay in diagnosis has major implications, as there is a correlation between time to diagnosis and failure of conservative treatment.[9,11] The same authors who found success with conservative treatment initiated within one month of dislocation also found that only 6/25 cases diagnosed after 1 month responded to conservative measures.[11] One possible explanation for this relationship is that muscle or ligamentous contractures may develop over time in response to the abnormal positioning of the C1-C2 joint.[11]

In these chronic cases where conservative treatment is unsuccessful or avoided entirely, open reduction with C1-C2 fusion can be performed. Multiple reduction strategies have been described, with several authors advocating for inserting temporary transverse rods at C1 and C2 as anchors to maneuver for reduction.[11,15]

Using a halo as the reduction tool, as in this case, has not previously been described in the literature. We feel this technique has multiple advantages relative to previously reported strategies. Use of a halo provides excellent rotational control of the head and allows manipulation of the device, making reduction maneuvers much easier. Compared to classic

head positioning with a Mayfield, the halo can be manipulated sterilely. When using halo traction suspension there is no need to have an assistant outside the sterile field to manipulate the Mayfield during attempted reduction maneuvers.

Although others have demonstrated success with the transverse rod technique described by Rajasekaran, the strategy relies on the strength of C1 screw purchase, which may not always be adequate to perform the reduction. This method place the C1 lateral arches at risk as the the screws can ploughing through them. Despite this theoretical risk, the transverse rod technique is an excellent adjunct if reduction maneuvers through the halo are not successful.

Conclusion

The diagnosis of atlantoaxial rotatory fixation is often missed in adults. Patients identified with the pathology early can be treated with nonoperative measures successfully. Delays in diagnosis are associated with failure of conservative treatment, and most patients with chronic AARF require posterior C1-C2 fusion.

Given the rarity of this condition in the adult population, controversy persists regarding therapeutic management, and multiple surgical techniques have been described. This case highlights the utility of halo traction suspension in achieving reduction of the C1-C2 joint in patients with chronic AARF.

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Combined Lateral Corpectomy with Posterior Instrumented Fusion for the Management of Post-Infectious Kyphosis

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Abstract

Although many surgical approaches have been described in the operative management of osteodiscitis, there is no consensus optimal technique. We present two patients who developed post-infectious kyphosis and were treated using combined lateral corpectomy with an expandable cage and posterior instrumented fusion. These cases highlight the utility of the lateral retroperitoneal approach in addressing post-infectious kyphosis.

Introduction

In recent years the incidence of spinal infections has been on the rise[1]. This finding has been attributed to improved diagnostic techniques as well as an increase in surgical volume[1]. Today, the most common form of spine infection in individuals over 50 years of age is bacterial infection of the intervertebral disc and adjacent vertebrae, known as osteodiscitis[2–4].

The disease process is characterized by deposition of bacteria from the bloodstream into the relatively avascular intervertebral disc[5]. The poor local vascularity of the intervertebral disc allows for bacterial proliferation, which can lead to invasion of adjacent structures and destruction of the vertebral endplates. Progressive destruction can culminate in spinal instability, deformity, abscess, and spinal cord compression[1].

The treatment of vertebral osteodiscitis is dependent upon the degree to which the infection. Antimicrobial therapy is fundamental to managing this condition and remains the first-line treatment. Indications for surgical intervention include progressive neurologic deficits, progressive deformity, instability, or persistent infection despite appropriate antimicrobial therapy[5,6].

When surgery is indicated, the decision regarding approach or technique is dictated broadly by the presence of deficits, the location of the infection within the spinal column, as well as the amount of bony destruction and deformity[1]. For patients with significant anterior and middle column destruction, anterior column reconstruction is often warranted[1,7].

Although anterior and posterior approaches are well-described in the literature in the surgical management of osteodiscitis, recently other techniques have utilized a lateral retroperitoneal approach. These include standalone lateral fusion with a plate as well as lateral reconstruction combined with posterior pedicle screw fixation[7–9].

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A combined lateral corpectomy with an expandable cage supplemented with posterior instrumented fusion can be utilized for the management of post-infectious kyphosis, as seen in these two cases.

Case 1:

A 61-year-old male with a past medical history significant for untreated Hepatitis C and cocaine-use disorder presented to the emergency room with one week of severe, progressive low back and bilateral lower extremity pain. His physical examination was notable for bilateral weakness in hip flexion. Radiographic and Magnetic Resonance Imaging (MRI) demonstrated a ventral epidural abscess at L3-4 with vertebral osteodiscitis extending from L3-L5 (Figures 1A & 1B).

Surgery

He underwent urgent operative L3-L5 laminectomy and decompression of the abscess. Operative cultures were negative, though blood cultures and urine cultures grew *E. Coli*. The patient's symptoms resolved post-operatively and he was discharged on post-operative day (POD) six with a peripherally inserted central catheter (PICC) line to complete a six-week course of targeted antibiotic therapy.

Despite initial improvements, he returned to clinic on POD 19 noting recurrence of low back and bilateral lower extremity pain with stable motor and sensory exam. Standing radiographs revealed interval collapse at L3-4 with focal kyphosis (Figure 1C).

The patient was brought to the operating room for a right-sided retroperitoneal approach

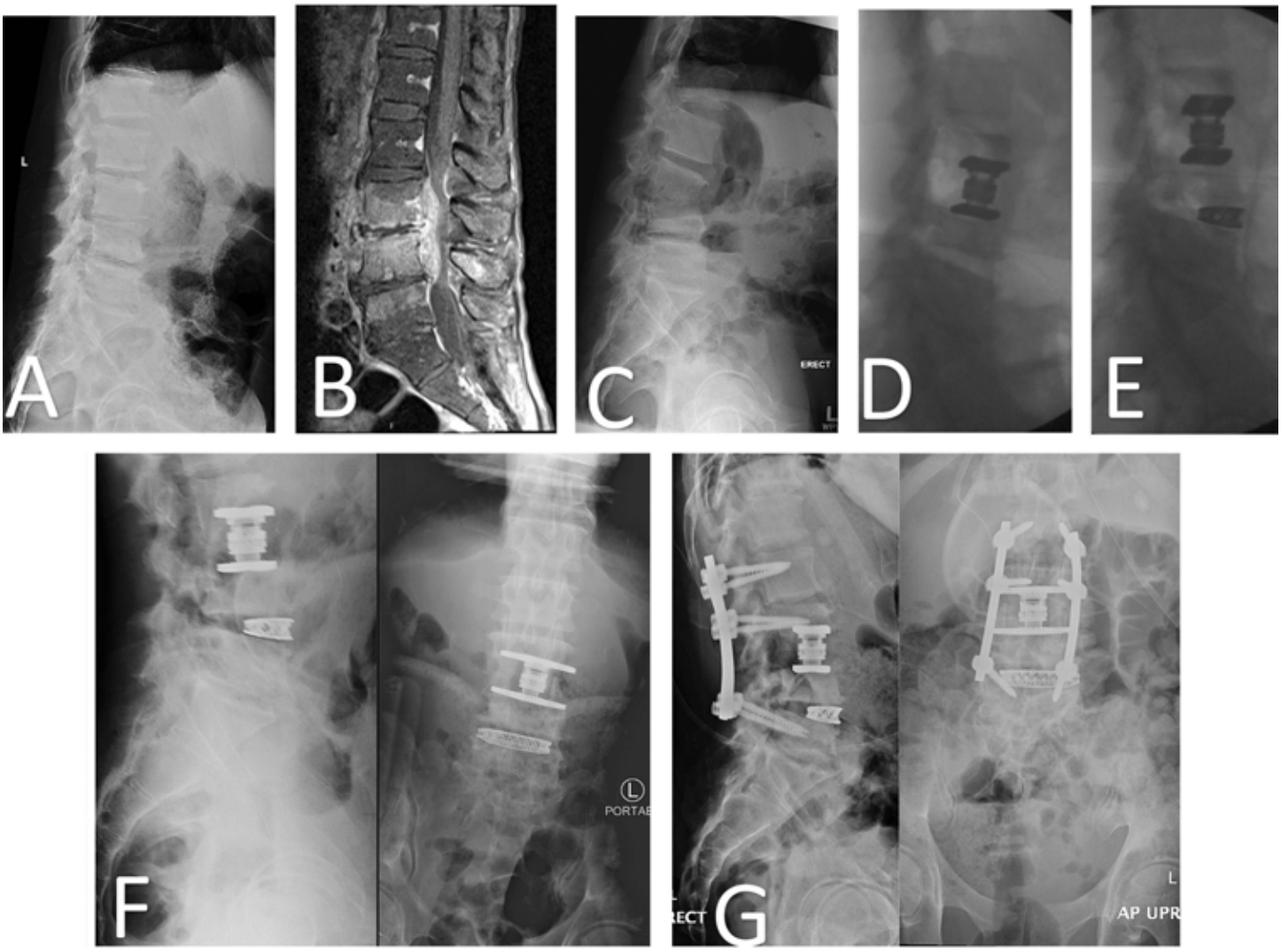

Figure 1A. Lateral radiograph of the lumbar spine showing loss of lordosis with multi-level degenerative changes. Endplate erosive changes are seen at L3-4 & L4-5.
Figure 1B. Sagittal T1 Contrast-Enhanced MRI demonstrating marrow and disc edema extending from L3-L5, in association with a large ventral epidural collection.
Figure 1C. Lateral radiograph of the lumbar spine illustrates the interval development of a focal kyphotic deformity at L3-4.
Figure 1D. Intra-operative lateral fluoroscopic image of the lumbar spine showing improvement in lumbar lordosis following insertion of the expandable interbody cage at L3-4.
Figure 1E. Intra-operative lateral fluoroscopic image of the lumbar spine following placement of an interbody cage at L4-5.
Figure 1F. Intra-operative lateral and AP radiographs of the lumbar spine demonstrating restoration of lumbar lordosis with an expandable interbody cage at L3/4 and an interbody cage at L4-5.
Figure 1G. Post-operative standing lateral and AP radiographs of the lumbar spine showing the final construct with posterior instrumentation L2-L5.

to the lumbar spine. Utilizing large osteotomes under fluoroscopy, a partial corpectomy of the L3 and L4 vertebral bodies was performed to debride residual infectious and necrotic tissue, followed by insertion of a large footprint expandable interbody cage packed with cancellous iliac crest autograft. The cage was expanded to restore native vertebral height and lordosis (Figure 1D). After, a complete lateral discectomy was performed through the same incision at L4-5 followed by insertion of an interbody cage packed with iliac crest autograft (Figures 1E & 1F). these incision were closed after completion of this portion of the procedure.

Next, the patient was repositioned prone and instrumented with bilateral pedicle fixation at L2, L3, and L5, skipping L4 due to the partial corpectomy. Cobalt chromium rods were then utilized to secure the segment.

Post-operative Period

Initially, the patient was managed in the intensive care unit (ICU) post-operatively. He was transferred to the floor on POD 2. He remained neurologically stable. Standing radiographs were obtained (Figure 1G).

The patient was discharged on POD ± to complete a 6-week course of additional targeted treatment guided by the infectious disease team. He returned to clinic on POD 39, reporting complete resolution of his pre-operative pain. Unfortunately, the patient was lost to follow up.

Case 2:

A 69-year-old male with a past medical history significant for tonsillar squamous cell carcinoma, intravenous (IV) drug use, hypertension, and a remote history of L1-2 osteomyelitis

treated with IV antibiotics presented to our clinic with progressively worsening low back pain and forward bent posture. His physical examination was notable only for a focal, tender prominence posteriorly over L1-2. Standing lateral thoracolumbar radiographs and CT scan demonstrated focal kyphosis at L1-2 with significant sagittal imbalance (Figures 2A & 2B). Given his progressive kyphosis with a history of infection with severe back pain and sagittal imbalance, he was indicated for reconstruction with a combined lateral corpectomy and posterior instrumented fusion.

Surgery

The patient was positioned in the left lateral decubitus position, The L1-2 disc space was localized fluoroscopically. The T10 rib was partially resected with attention to preserving the neurovascular bundle. The retropleural space was traversed carefully to gain access to the lateral vertebral bodies of L1 and L2. Retractors were positioned to allow complete discectomies at the T12-L1 and L2-3 disc spaces under fluoroscopic guidance. After, a corpectomy was performed at the L1 and L2 levels using large osteotomes. Then a large footprint expandable cage with local rib autograft was inserted to recreate native height and restore alignment. A lateral plate spanning T12-L3 was placed for additional fixation (Figure 2C). The incision was closed to allow for repositioning.

The patient was repositioned prone to allow a standard posterior midline approach. Bicortical pedicle screw fixation were placed from T11-L3 spanning the defect. A partial laminectomy and posterior column osteotomy at L1-L2 with instrumented fusion followed.

Post-operative Period

Post-operatively, the patient was managed in the ICU and transferred to the floor on POD3. He remained neurologically intact. Standing radiographs were obtained (Figure 2D). Operative cultures remained no growth and the patient was discharged on POD 6.

At his last follow up on post-operative day 57, the patient reported improvement in pain along with symptomatic improvement in his standing alignment. Physical exam remained stable. Standing AP and lateral radiographs of the lumbar spine demonstrated well aligned hardware with no evidence of subsidence.

Discussion

Although osteodiscitis is managed conservatively with intravenous antibiotics as a first-line treatment, patients with progressive neurologic deficits, progressive deformity, instability, and/or persistent infection should undergo operative intervention[5,6]. Despite the relative consensus on operative indications for refractory cases, the optimal surgical technique remains controversial. Multiple approaches have been described, including stand-alone anterior lumbar interbody fusion (ALIF), ALIF with posterior stabilization, and all-posterior constructs[7].

While high rates of infection clearance and fusion have been reported with these techniques, there are several challenges to consider with both anterior and posterior approaches[10]. The anterior approach inherently requires mobilization of the great vessels, often requiring additional resurce staffing with an access surgeon, which exposes patients to potential vascular complications and requires additional personnel to

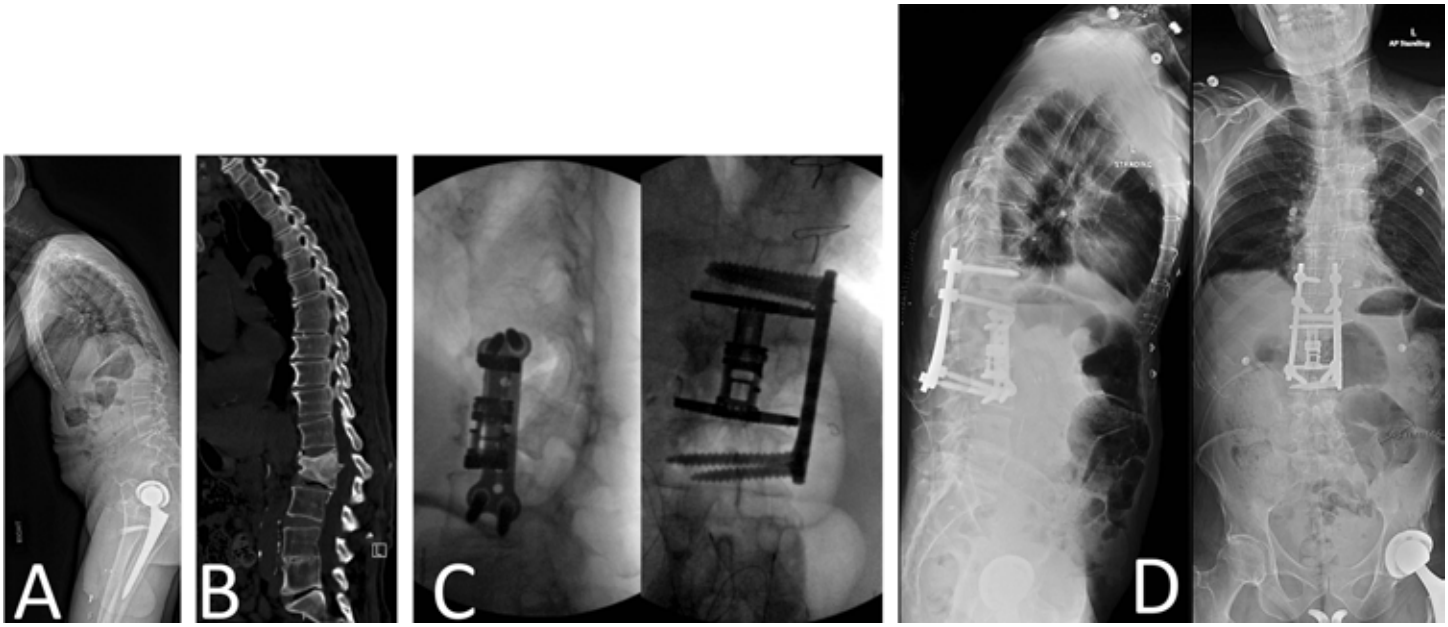

Figure 2A. Standing lateral thoracolumbar radiograph showing sagittal imbalance with severe anterior wedge compression deformity at L1-2 with focal kyphosis osseous fusion of the vertebral bodies

Figure 2B. Sagittal CT scan of the thoracolumbar spine further illustrating the compression deformity and fusion at L1-2 with focal kyphosis. Autofusion of L4/5 is noted as well.

Figure 2C. Intra-operative lateral and AP fluoroscopic images of the thoracolumbar spine demonstrating improvement in lordosis following insertion of the expandable interbody cage. The lateral plate with screws into T12 and L3 is also visualized.

Figure 2D. Post-operative standing lateral and AP radiographs of the lumbar spine showing the final construct, including the posterior fixation from T11-L3.

complete the surgical procedure. the possibility of vascular insult is relevant particularly in patients with osteodiscitis, as vascular adhesions are a concern in the setting of prior or active infection. Additionally, there are cardiopulmonary concerns with anterior exposure in the thoracic spine, and obesity can also limit ease of exposure with the anterior approach in general[7].

With a posterior approach, surgeons can decompress the spinal canal directly. However, adequate exposure of the affected intervertebral disc and vertebral bodies can be difficult with anatomic constraints limiting cage size for anterior column support[9]. Moreover, the posterior approach requires a laminectomy, which may destabilize a spine further. Given the disease process has already destroyed the anterior and middle columns, a laminectomy puts the remaining posterior column in a precarious situation.

Given these considerations with anterior and posterior approaches, some surgeons are utilizing the direct lateral retroperitoneal approach in the treatment of osteodiscitis, both as a standalone technique and with posterior supplemental fixation[7-9]. The lateral retroperitoneal approach is well-described and is used to treat a wide variety of conditions affecting the lumbar spine. Often, this approach can be extended into the retropleural space for access to thoracic and thoracolumbar junctional pathology.

In the setting of osteodiscitis with or without kyphosis, a direct lateral retroperitoneal approach has several advantages in comparison to the anterior and posterior approaches used to treat the same condition. Preservation of the anterior and posterior longitudinal ligaments affords stability while ligamentotaxis can provide indirect decompression of the spinal canal and neuroforamen. Ease of exposure with modern retractor systems provide a relatively facile and minimally invasive approach . Finally, large footprint cages can be inserted through the same lateral corridor, resulting in lower subsidence, more powerful anterior column support and correction than is possible through a posterior-only approach, while also mitigating the vascular and intra-abdominal risks associated with an anterior exposure[9].

Conclusion

Given the challenges associated with creating a randomized trial comparing the surgical techniques used in the treatment of osteodiscitis, case series have become the primary tool in the literature to explore techniques and their results.

These are two cases of patients with osteodiscitis who developed post-infectious kyphosis both treated with a direct lateral retroperitoneal approach. Although the first patient developed a kyphotic deformity acutely and the second patient's deformity developed over a period of years, both were treated with combined lateral corpectomy with an expandable cage and posterior instrumented fusion. These cases add to the limited literature describing the direct lateral approach in the surgical treatment of post-infectious kyphosis and demonstrate its advantages compared to well-recognized anterior and posterior techniques.

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Sports

Sports Tips & Tricks: Lateral Decubitus Positioning of Shoulder Arthroscopy

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Introduction

Shoulder arthroscopy has become a common orthopaedic procedure as it offers a minimally invasive surgical approach to treat a variety of shoulder pathologies. There are two patient positioning options: beach chair and lateral decubitus position. Both positions have certain advantages. The beach chair position provides a more anatomic, upright positioning with easier conversion to open procedures. The lateral decubitus position allows increased visualization of the glenohumeral joint with access to the posterior and inferior aspect of the glenoid. The following tips provide a general guide for a lateral decubitus positioning for shoulder arthroscopy. It is not meant to suggest one particular positioning over another, but rather a review for surgeons and trainees if a lateral decubitus positioning is decided for patient positioning in shoulder arthroscopy.

Surgical Consideration

Patient Positioning

The setup of the lateral decubitus position starts with the patient in a supine position on a beanbag (Olympic Vac-Pac, Natus Medical Incorporated, Middleton, WI). After the induction of anesthesia, the patient's eyes should be covered with tape or lubricated to prevent corneal abrasion, and sequential compression device placed on the lower extremities for deep venous thrombosis prophylaxis. With coordination with the anesthesia team, the surgical assistant and surgeon turn the patient onto the nonoperative side. A well-padded axillary roll should be placed under the nonoperative axilla. Similarly, the bean bag itself can serve as an adequate axillary roll provided it is positioned and compressed proximal to the axilla. Both knees should be bent, and foam padding should be placed on bony prominences to prevent pressure injuries. The lateral aspect of the downed knee should also be padded to prevent pressure injuries to the common peroneal nerve. Once the patient is properly positioned, a safety strap is placed around the patient and the vacuum suction is turned on for the beanbag to maintain deflation and position.

Traction Setup

After the operative arm is sterilely prepped and draped, the operative arm is placed in sterile stockinette and wrapped in a self-adherent wrap such as Coban (3M Healthcare, St. Paul, MN). The operative arm is then firmly placed into the arm-holding shoulder device, such as the STaR sleeve with the lateral decubitus shoulder traction device (Arthrex, Naples, FL), or the Spider (Smith and Nephew, Andover, MA). Approximately 15 degrees of forward flexion and 45 degrees of abduction will provide good visibility with 10-15lbs of traction. Regardless of the traction device, surgeons should utilize minimum traction necessary to minimize the risk of traction injuries to the neurovascular structures. Forward flexion lessens the threat of traction injury to the upper trunk of the plexus.

Portal Placement

In the lateral decubitus position, the posterior portal is usually established slightly more lateral than your typical posterior portal in beach chair position. In beach chair, the classic teaching on posterior portal's location is to be placed 2 cm inferior and 1 cm medial to the posterolateral corner of the acromion, but in lateral decubitus, the portal will be typically in line with the posterolateral border of the acromion. One can also establish the posterior portal by identifying a soft spot that is parallel to the glenoid in the midportion of the glenohumeral joint. This can be accomplished by taking one hand and stabilize the acromion and using the other hand to translate the patient's humeral head anteriorly and posteriorly relative to the acromion. Once the joint is identified, an incision is made and the arthroscopy trocar can be inserted, aiming towards the coracoid process.

Discussion

Shoulder arthroscopy can be performed with the patient in either the beach chair position or the lateral decubitus position. There are advantages and disadvantages for each patient positioning. The purpose of this review was to give a general overview of lateral decubitus position. One of the major advantages of the lateral decubitus position is the increased

visualization of the glenohumeral joint. With the operative shoulder in traction, it provides especially good visualization of the posterior and posteroinferior glenoid, decreasing the need to create additional portals that can disrupt the rotator cuff[1]. Procedures such as posterior instability and capsular releases are greatly facilitated in the lateral position. In addition, rotator cuff repair may be facilitated in the lateral position as the continual downward traction on the arm may facilitate humeral head coverage. Also, compared to the beach chair position, there is less likelihood of cerebral desaturation[2]. This is especially true when the patient is under general anesthesia; The main disadvantage is the increased risk of neuropraxia due to the traction device[3]. However, forward flexion and judicious use of traction over 10lbs will mitigate this risk.

Patient positioning can play a crucial role in the outcomes of particular shoulder pathologies. In anterior shoulder instability patients, shoulder arthroscopy performed in the lateral decubitus position has shown lower recurrence rates than arthroscopy performed in the beach chair position[4]. A meta-analysis of sixty-four anterior shoulder stabilization studies has shown that the average overall recurrent instability rates were 14.65% in the beach chair group while the rates were 8.5% in the lateral decubitus position group. Other factors like patient selection, adequate capsular tensioning, and sutures anchor placements are important, but patient positioning can also be critical for the success of an arthroscopic stabilization procedure.

Ergonomics in the operating room is also an important factor to consider. Lateral decubitus position has been suggested to allow surgeons to operate with their arms at the sides, rather than in an abducted position, which potentially can increase comfort and decrease fatigue[5]. However, there can be an increase in neck and shoulder strain when the surgeon reaches across the patient's shoulder while using the anterior portal. One can reduce this by moving the operating table obliquely to the anesthesiologist so that it will afford easier access anteriorly. As occupational injuries and work-related musculoskeletal symptoms in orthopaedic surgery are common[6,7], surgeons should take note of their own ergonomics in the operating room and adjust factors like operating room table height, monitor position, length of arthroscopic equipment, and working distance from surgical field to minimize strain and decrease the risk of work-related injuries.

Overall, regardless of which shoulder arthroscopy positioning used, surgeons should be familiar with the setup, the major advantages and disadvantages of each positioning, and select the appropriate positioning for the improved patient outcomes as improper setup can create additional technical difficulties and complexity in shoulder arthroscopy.

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Hand

U·P·O·J

Management of Nailbed Laceration Repair in the Emergency Department: Attending-specific Preference and Tips for Residents

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Introduction

The fingertip is a vital element of the distal finger anatomy, serving several crucial functions including protecting the fingertip, regulating peripheral circulation, and providing sensory and tactile feedback. It is composed of complex anatomy that consists of the nail bed, nail plate, perionychyium (the tissue surrounding the nail). The nail matrix can be compromised due to multiple conditions, including lacerations and

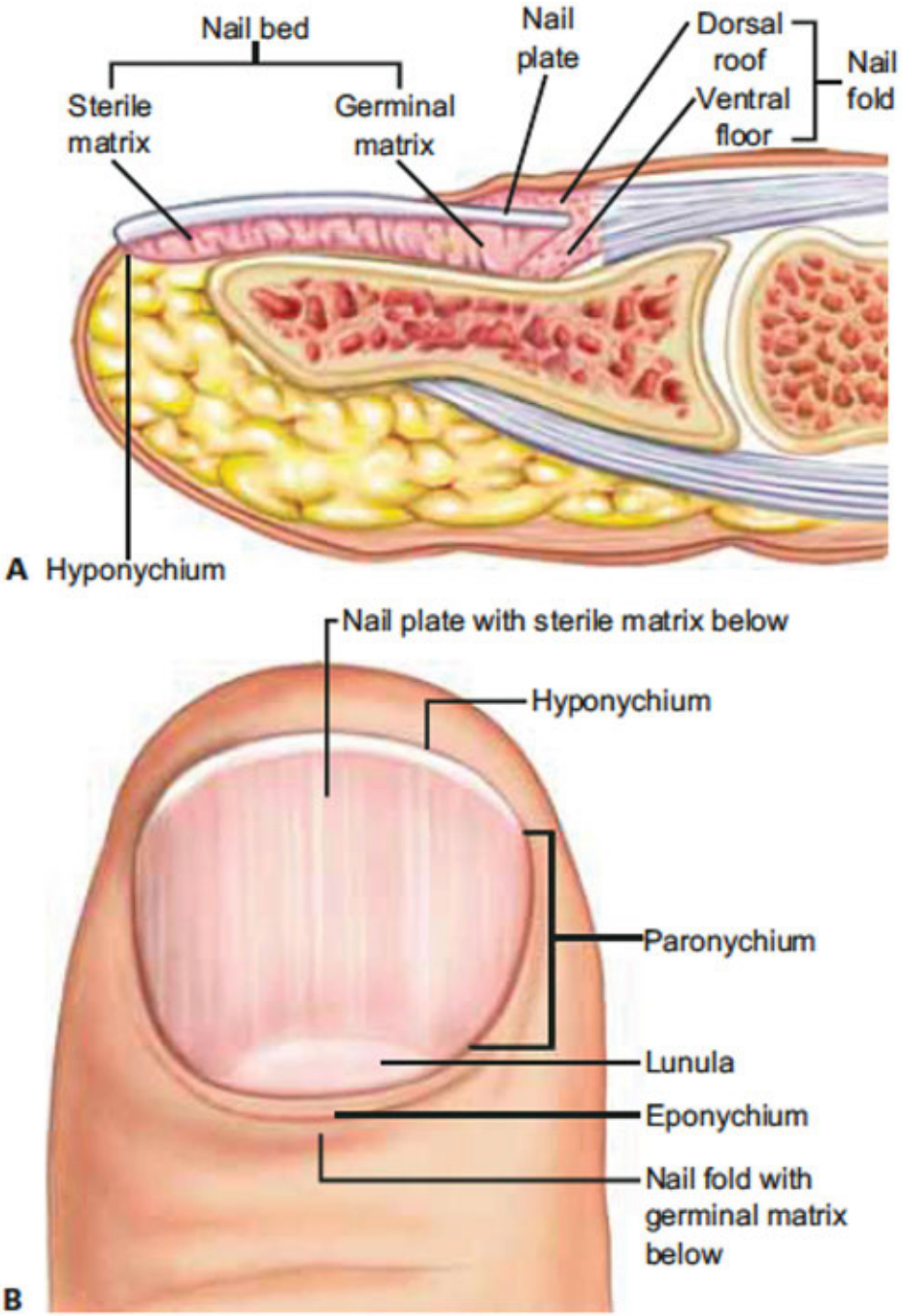

Figure 1. Anatomy of the Perionychium and its associated structures (obtained from Wiesel 2016).

trauma, crush injuries, tumors, and infections. Injuries to the nailbed and surrounding tissue can lead to functional and cosmetic complications, possibly necessitating intervention in the acute period to ensure function and a normal-appearing nail. Several methods exist for management of fingertip trauma. Here we describe the anatomy of the fingertip, procedures for repair of fingertip injuries, and the results of a survey of orthopaedic- and plastic surgery-trained faculty at the University of Pennsylvania regarding their preferred approach to treating such injuries.

Anatomy and Treatment Review

Anatomy

The distal fingertip is comprised of the nail bed, the nail plate, and the surrounding perionychium (Figure 1). The nail bed, which is comprised of the sterile matrix (distally) and the germinal matrix (proximally), is covered by the overlying nail plate. Nail growth originates from the germinal matrix at the proximal end of the nail bed. The proximal end of the nail plate is covered by the nail fold (eponychial fold) and the

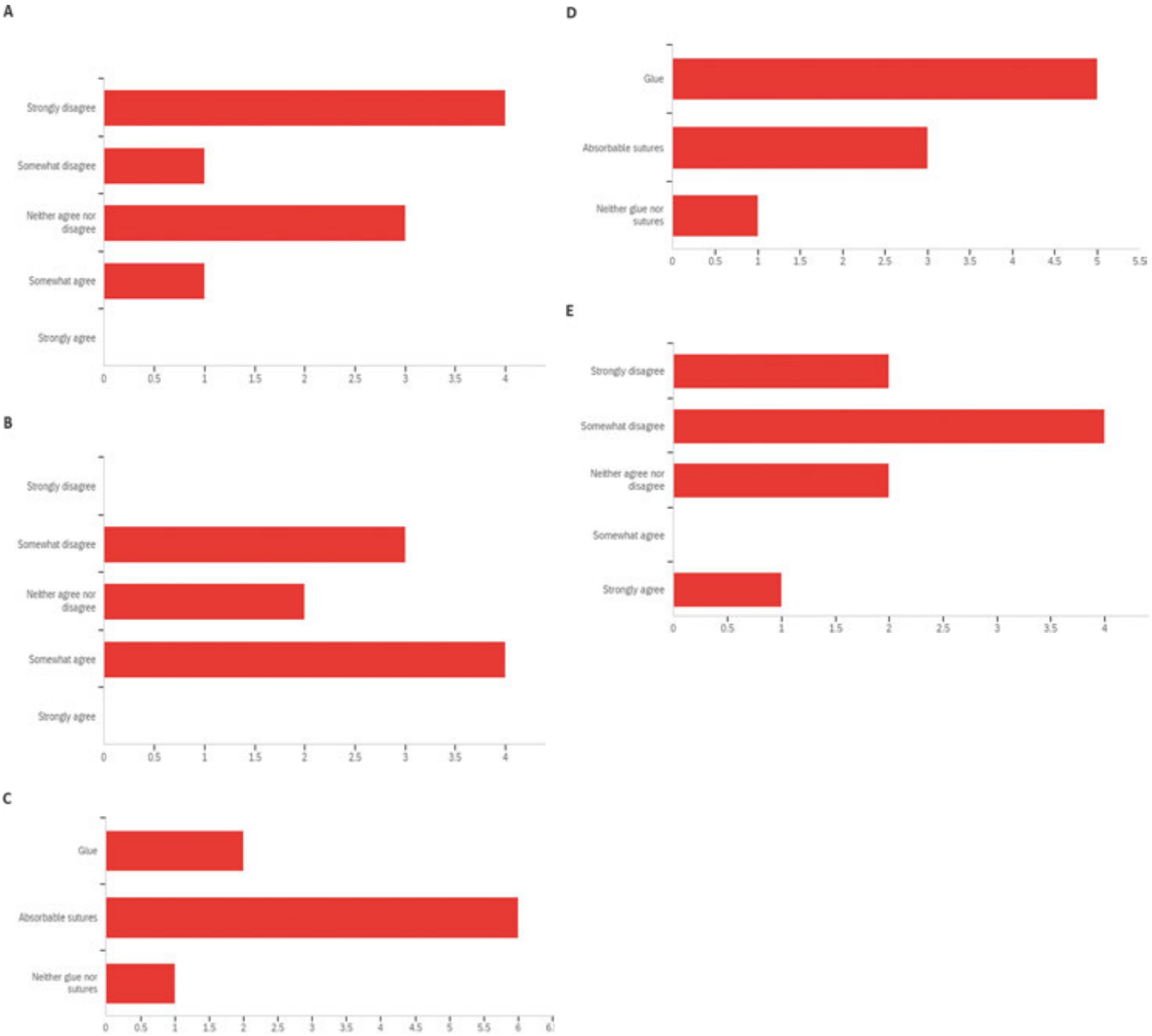

Figure 2. Survey questionnaire and results regarding nailbed injuries. **(A)** Subungual hematomas without evidence of fracture on X-ray require nail removal as part of the treatment. **(B)** Subungual hematomas with evidence of fracture on x-Ray require nail removal as part of the treatment. **(C)** Once the nail plate is removed. A linear laceration without markedly exposed bone is present in the sterile matrix only. This laceration should be treated with glue, absorbable sutures, or neither. **(D)** If a stellate laceration was encountered without markedly exposed bone, this should be treated with glue, absorbable sutures, or neither. **(E)** After removal of the nail plate and laceration repair, stenting open the proximal eponychial fold is necessary.

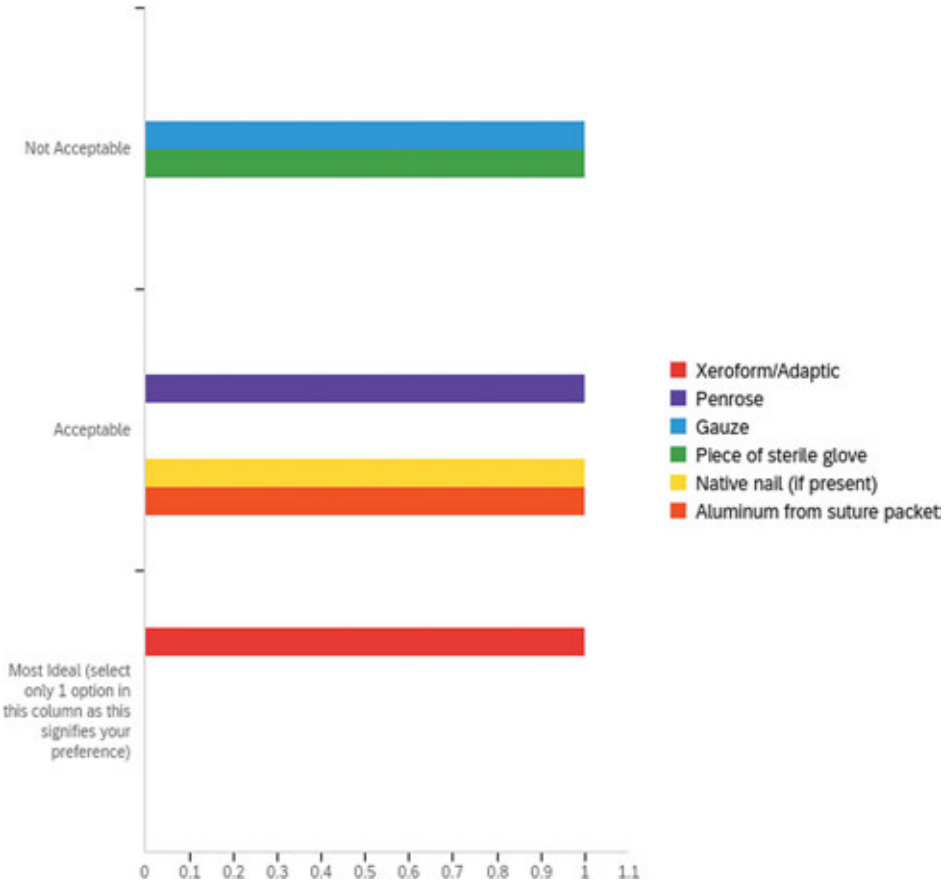

Figure 3. Option for Stenting the proximal eponychial fold in the setting of a laceration (linear or stellate) isolated to the sterile matrix when the nail plate is no longer present.

bordering tissues around the nail are the paronychial folds. The eponychium is the thin layer of tissue that extends onto the nail plate from the nail fold[1].

Procedure

In the setting of fingertip injuries such as subungual hematoma when intervention is indicated and simple trephination is not ideal, a digital block is performed—often with 1% lidocaine without epinephrine. The affected digit is then exsanguinated with a digital tourniquet, then prepared and draped. The nail is then removed with gentle blunt dissection, often with a Freer elevator, deep to the plate and then superficial to the plate proximal to the eponychial fold. Attachments to the paronychial folds are dissected and the nail plate is removed. Traditionally, repair of the sterile matrix consists of approximation of the lacerated with absorbable sutures (e.g., 5-0 chromic gut). Once the repair is performed, the nail fold may be stented open. This can be accomplished with the native nail plate if in good condition and not contaminated, a thin aluminum sheet such as from a suture package, gauze impregnated with petroleum jelly, or a piece of sterile glove. However, O'Shaughnessy, et al.2 reported no difference in outcomes whether the nail plate was replaced or left off after repair. Furthermore, Strauss, et al.3 found no difference in outcomes when the lacerations are repaired with sutures or Dermabond. Despite the current literature, there remains a difference in management based on surgeon preference. This variability creates confusion for consult residents and possibly affects patient outcomes.

Results

Attendings Preference Survey

Nine board-eligible or board-certified hand surgeons from the Orthopaedic or Plastic and Reconstructive surgery departments at the University of Pennsylvania were surveyed regarding their preferred treatment practice of acute fingertip injuries (Figure 2). In the setting of subungual hematoma, with no evidence of fracture on imaging, 44% strongly disagreed with removal of the nail plate as part of the treatment (11% somewhat agreed), while those numbers changed to 44% somewhat agreeing to removing the nail plate in the setting of acute fracture on present on X-ray. Regarding the laceration repair, a minority (22%) favored surgical glue, while the majority preferred primary treatment with absorbable sutures (66.7%) when the laceration was linear. When the laceration was stellate, 55.6% of surgeons preferred the use of glue. Regarding stenting the eponychial fold after laceration repair in the sterile matrix, the majority believed it was not necessary to replace the nail plate (66%), while only one surgeon felt it was necessary to stent it open. Given the option to keep the eponychial fold open, that surgeon preferred aluminum from the suture packet to be used for a stent but noted that the native nail, a penrose, or xeroform/adaptic were acceptable. Dry gauze or a piece of sterile glove were not acceptable options.

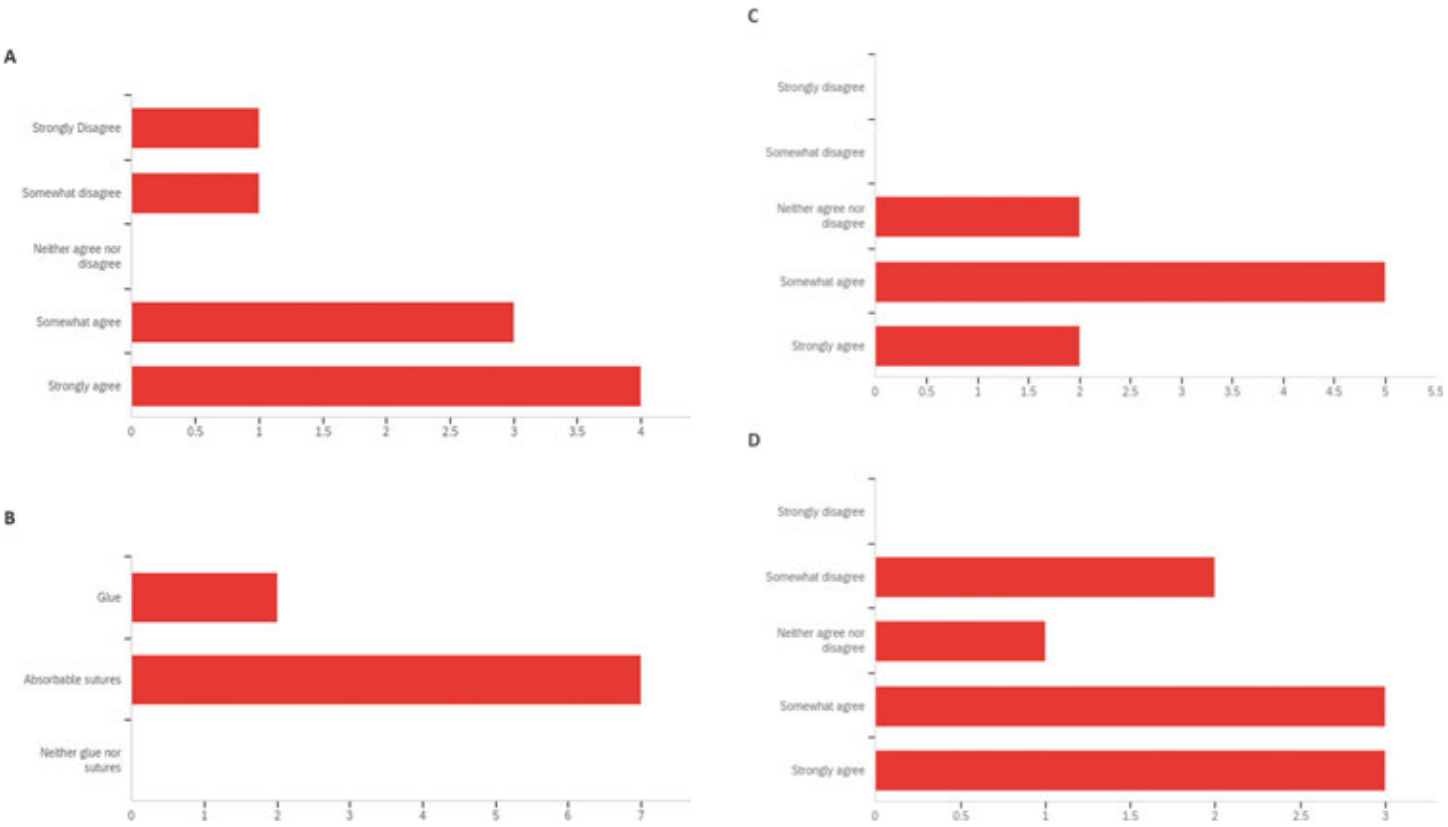

Figure 4. Survey questionnaire and results regarding injuries to the germinal matrix. (A) Lacerations through the proximal eponychial fold and into the region of the germinal matrix require nail plate removal. (B) After removing the nail from underneath the proximal eponychial fold or the nail has already been removed by the trauma. A jagged laceration without exposed bone with slight gapping of the tissue is present that extends through the proximal eponychial fold. This laceration should be treated with. (C) Visual evaluation of the germinal matrix is mandatory in the emergency department to assess injury during initial evaluation of a laceration that extends through the proximal eponychial fold. (D) After repair or non-intervention of a laceration that extends through the proximal eponychial fold when the nail plate is no longer present, stenting open the proximal eponychial fold is necessary.

When the germinal matrix was involved in the laceration, 77.8% of surgeons preferred removal of the nail plate, 77.8% of surgeons preferred sutures for repair of the germinal matrix laceration, and 66.7% of surgeons preferred stenting of the proximal eponychial fold. The native nail was most favored as the object with which the fold was stented (3 of 5), but all other options were acceptable to except for dry gauze (Figure 3). In cases where lacerations involved the proximal eponychial fold and extended into the region of the germinal matrix the majority (44% strongly agreed, 33% somewhat agreed) to the removal of the nail plate. In such cases where there's a lacercation through the proximal eponychial fold, visual evaluation of the germinal matrix should be performed to assess the injury (55% somewhat agree, and 22% strongly agree). Majority also agreed to stent the nailbed open in these injuries (Figure 4).

Conclusion for Residents

There was no clear consensus among the faculty as to the optimal approach to nail bed injuries encountered in the Emergency Department. However, there are valuable learning tips for residents from this survey. Not all injuries absolutely require nail plate removal and clinical judgment should be utilized in each situation. If there is a laceration present, most surgeons favored the use of an absorbable suture. Finally, stenting the eponychial fold open is not mandatory in some situations.

Each injury encountered in the ED is unique and thus should have a tailored treatment approach, which is guided by a discussion between the resident and attending on call.

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U·P·O·J

Traumatic Articular Lesions of the Lunate Fossa Without Corresponding Changes on MRI

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Abstract

We describe a series of patients with the unusual arthroscopic finding of post-traumatic articular cartilage lesions of the lunate fossa. This is a retrospective observational study of five adult patients with a history of trauma, all of whom underwent diagnostic wrist arthroscopy for chronic wrist pain, who were found to have cartilage lesions in the lunate fossa. All patients appeared to have normal radiocarpal joints on magnetic resonance imaging (MRI). No patient sustained a distal radius fracture. Pre-operative wrist radiographs were assessed for scapholunate (SL) angle, SL gap, lunate-capitate (LC) angle, midcarpal arthritis, and ulnar variance. Arthroscopic photos were compared to pre-operative MRIs. In addition to the cartilage lesions, 4/5 patients were found to have scapholunate ligament injuries. These findings suggest that some patients with poorly-characterized chronic post-traumatic wrist pain may have symptomatic articular cartilage lesions involving the lunate fossa despite normal MRIs. These lesions may be associated with scapholunate injuries.

Introduction

In 1984, Watson and Ballet proposed the concept of scapholunate advanced collapse (SLAC) wrist after reviewing over 4,000 wrist radiographs.[1] In this classic paper, the authors associated scapholunate ligament (SL) injuries with radioscaphoid arthritis that developed in a progressive three-stage sequence: Degenerative changes initially emerge between the tip of the radial styloid and the scaphoid (SLAC I). Changes then continue proximally to affect the entire radioscaphoid joint (SLAC II), followed by involvement of the capitolunate joint (SLAC III).

Notably, the radiolunate articulation is spared in this model, thought to be secondary to the spherical nature of the lunate's articulation in the lunate fossa.[2] Due to this unique shape, the radiolunate joint remains congruent regardless of the position or rotation of the lunate. Thus loads are thought to be equally distributed across the joint and the cartilage surface is preserved.[2,3] The scaphoid fossa, however, is more elliptical. Therefore rotatory or translational instability following SL injury disrupts articular congruence at the radioscaphoid articulation, leading to increased contact pressures and subsequent degenerative changes as seen in the SLAC pattern. [2]

Although this SLAC pattern continues to serve as the basis for the surgical treatment of radiocarpal arthritis [4–6], other patterns are beginning to emerge. These include isolated luno-capitate arthritis [7] as well as radiolunate arthritis associated with SL injuries in the absence of radioscaphoid arthritis. [8] Both of these patterns stand contrary to the classic description of Watson and Ballet.

Over the last several years, we have discovered a cohort of patients with lunate fossa articular cartilage lesions found while undergoing diagnostic wrist arthroscopy for chronic, post-traumatic wrist pain. No patient demonstrated the SLAC pattern, the lesions were not visible on MRI, nor had any patient sustained a distal radius fracture, which are known to be associated with radiolunate arthritis.

The primary purpose of this report is to describe our arthroscopic findings of articular cartilage lesions involving the lunate fossa in patients with chronic, post-traumatic wrist pain with normal imaging studies. A secondary aim to is to discuss potential mechanisms leading to this injury pattern, including a possible association with scapholunate ligament injuries.

Materials and Methods

We performed a retrospective observational study on five adult patients with chronic, post-traumatic wrist pain who underwent diagnostic wrist arthroscopy between 2017-2018 and were found to have articular cartilage lesions involving the lunate fossa. No patient had sustained a distal radius fracture. MRIs were obtained prior to surgical intervention, although these were non-diagnostic. All patients elected to undergo wrist arthroscopy for diagnostic evaluation and possible treatment of persistent symptoms that had failed to respond to conservative measures.

Wrist arthroscopy was performed by the senior author at a large academic medical center. Charts were reviewed for data including sex, age, mechanism of injury, and prior treatments. Radiographs including postero-anterior and

lateral views of the wrist were assessed by a fellowship trained upper extremity surgeon using Sectra IDS7 (Sectra Group, Linköping, Sweden) for scapholunate (SL) angle, SL gap, lunate-capitate (LC) angle, and midcarpal arthritis. Ulnar variance was measured using the central reference point as described by Medoff.[9] Pre-operative MRIs and operative reports were reviewed and compared to arthroscopic images, with particular attention to the integrity of lunate fossa and SL ligament.

Wrist arthroscopy was performed using a 2.7 mm 30-degree arthroscope via the standard portals, with 12 pounds of distraction applied across the wrist. The first joint assessed during diagnostic arthroscopy was the radioscaphoid joint. Cartilage lesions were assessed under direct visualization. SL injuries were scored according to the Geissler grading system.[10] In all cases, chondral lesions of the lunate fossa were debrided back to stable borders. SL injuries, when present, were debrided or, for Geissler I injuries, underwent shrinkage with a radiofrequency probe.

Post-operatively, symptoms were assessed via qualitative data from patient-reported outcomes obtained from the electronic medical record. All patients had at least two post-operative appointments, with an average duration of follow-up was 11.5 months (range: 2 to 31 months).

The study was approved by the institutional review board at our institution.

Results

Among the patients in this study, two were female and three were male, with an average age of 41 (range: 35–58) at the time of surgery (Table 1). Median time from injury to surgical intervention was 3 years (range: 0.5–15 years). All patients suffered from chronic, post-traumatic radial and/or mid-dorsal wrist pain secondary to falls on outstretched hands (n = 2), motor vehicle accidents (n = 2), or motorcycle accidents (n = 1). Non-operative treatments included activity modification (n = 5), bracing (n = 4), thumb spica casting (n = 1), and steroid injection into the wrist joint (n = 1). Watson's test was negative for 4/5 patients in the study.

One patient had sustained a scaphoid waist fracture during their initial trauma several years prior to evaluation in our clinic (Patient 1), although radiographs and MRI at the time of our evaluation showed complete healing. No other patient sustained a fracture. MRIs for 5/5 patients were non-diagnostic, though an incidental finding of possible triangular fibrocartilage complex (TFCC) tear was suspected in 2 patients. Otherwise, no specific pathology was described that correlated with the patients' location of pain.

Pre-operative radiographs demonstrated SL angles within normal limits (30-60 degrees) for 3/5 patients (Table 2). 0/5 patients had SL gap $>$ 3 mm on static radiographs. LC angle was within normal limits (0-15 degrees) for 4/5 patients. No patient showed evidence of midcarpal arthritis. 3/5 patients were found to have ulnar positive variance and 2/5 with ulnar negative variance.

Radiographs and MRIs were grossly unremarkable at the radiocarpal joint (Figures 1 & 2). During wrist arthroscopy all patients were found to have radiocarpal synovitis along with an isolated articular lesion in the lunate fossa.The degree of cartilage damage ranged from partial thickness defects

Table 1. Demographics

Subject	Age(yrs)	Sex	Mechanism of Injury	Treatments
Patient 1	35	F	Fall off Motorcycle/Vespa	- Thumb spica cast - Activity modification
Patient 2	39	M	Motor-vehicle collision	- Activity modification - Bracing
Patient 3	36	F	Motor-vehicle collision	- Steroid injection (wrist) - Activity modification - Bracing
Patient 4	58	M	Fall on outstretched hand	- Activity modification - Bracing
Patient 5	38	M	Fall on outstretched hand	- Activity modification - Bracing

Table 2. Radiographic Parameters & Geissler Grades

Subject	SL Angle	SL Gap >3 mm?	LC Angle	Midcarpal Arthritis?	Ulnar Variance	SL Tear
Patient 1	62*	No	10	No	+2.0 mm	Geissler 1
Patient 2	46	No	24*	No	+2.4 mm	Geissler 2
Patient 3	52	No	13	No	+2.6 mm	-
Patient 4	63*	No	2	No	−1.4 mm	Geisler 2
Patient 5	52	No	13	No	−1.0 mm	Geissler 1

*Indicates value is outside normal limits

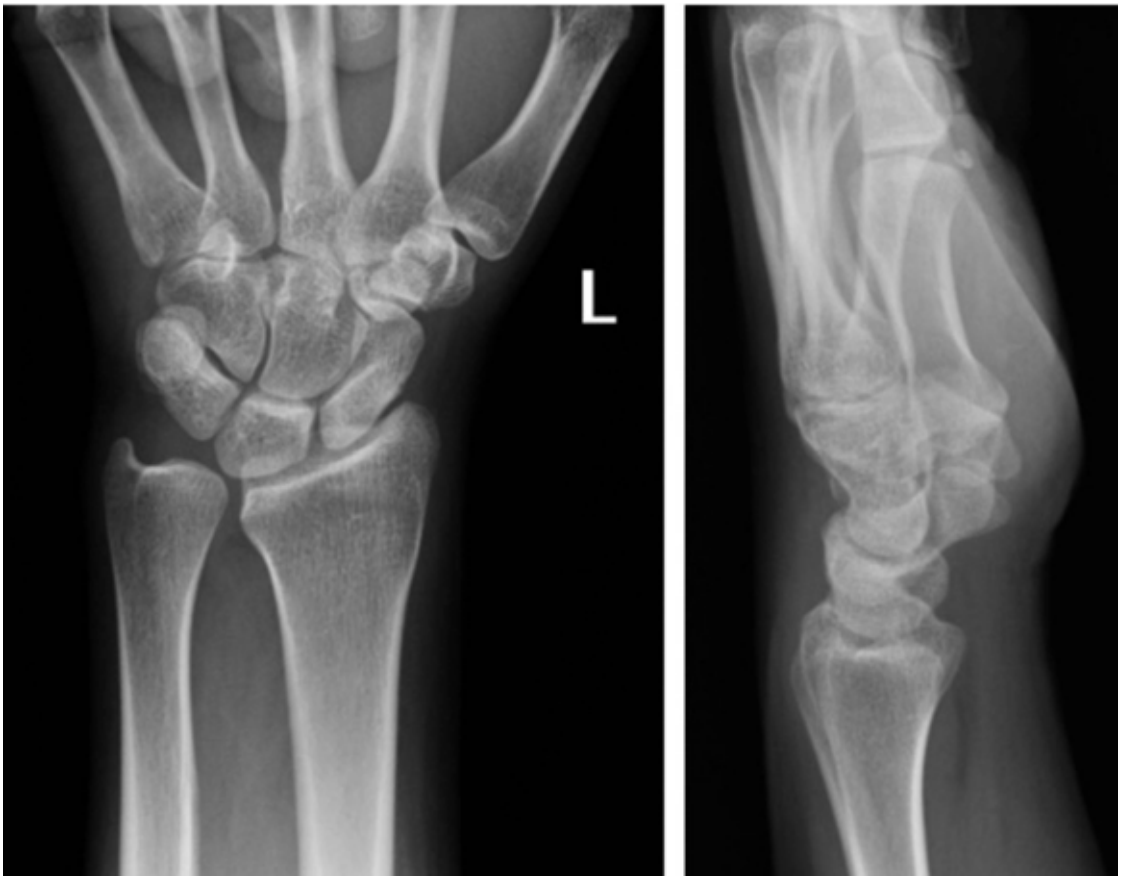

Figure 1. Postero-Anterior and Lateral radiographs of the left wrist of Patient 3, with no evidence of SL laxity or radiocarpal arthritis. Ulnar positive variance is present.

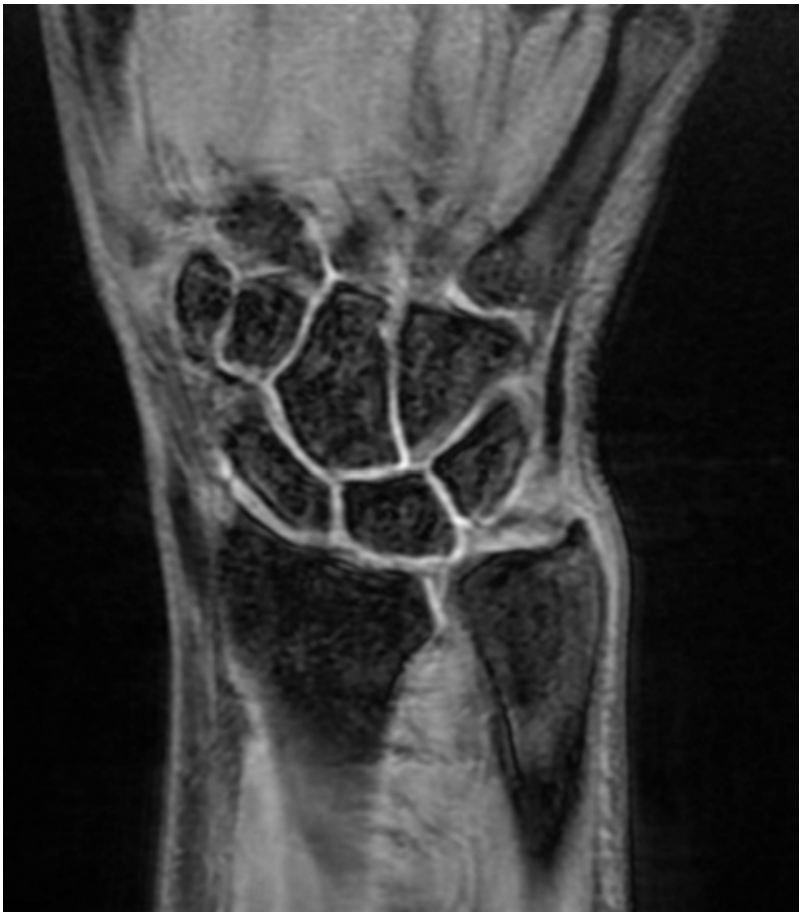

Figure 2. Representative coronal (3D fast gradient echo) MRI image of the left wrist of Patient 3, with normal appearance of the radiocarpal joint. There is no evidence of a cartilage lesion involving the lunate fossa.

in three patients (Figure 3) to full-thickness injuries in two patients (Figure 4). These full-thickness injuries were not immediately apparent, as the cartilage initially appeared to have irregularities or undulations. However, simple manipulation revealed these to be unstable lesions with delamination or lack of adherence to the underlying subchondral bone. All lesions were transverse in orientation (i.e. perpendicular to the orientation of the camera), and associated with delamination and fissuring (Figure 5). 4/5 patients were also found to have scapholunate ligament injuries, two of which were Geissler I with the remainder being scored as Geissler II. 2/5 patients had central TFCC tears.

5/5 patients noted symptomatic and functional improvement following arthroscopic debridement.

Discussion

This case series suggests that a subset of patients with chronic, post-traumatic wrist pain with no corresponding radiographic or MRI findings may have a symptomatic lesion involving the lunate fossa. The transverse orientation of the lesion in association with delamination, fissuring, and radiocarpal synovitis is further suggestive of a chronic injury (Figure 5). In our cohort, the lesion frequently appears to be associated with SL injuries. While cartilage damage can often be expected in patients with a history of intra-articular distal radius fracture, we could not find descriptions of isolated pre-arthritic lunate fossa lesions in our review of the literature.

We propose that a possible mechanism leading to this injury pattern revolves around the integrity of the SL

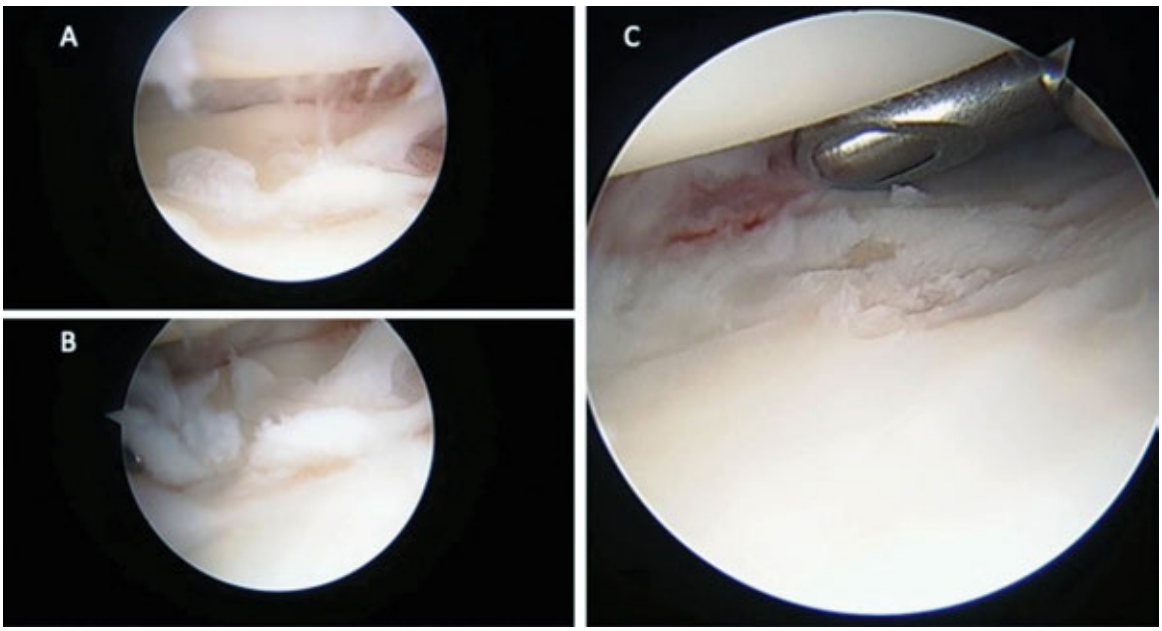

Figure 3. Arthroscopic images of the lunate fossa from Patient 3 from the 3, 4 portal**. (A)** Appearance of the lunate fossa upon insertion of the arthroscope; **(B)** Cartilage manipulation with probe, showing delamination of the unstable cartilage; **(C)** During debridement with shaver, ultimately resulting in a partial thickness lesion with stable borders.

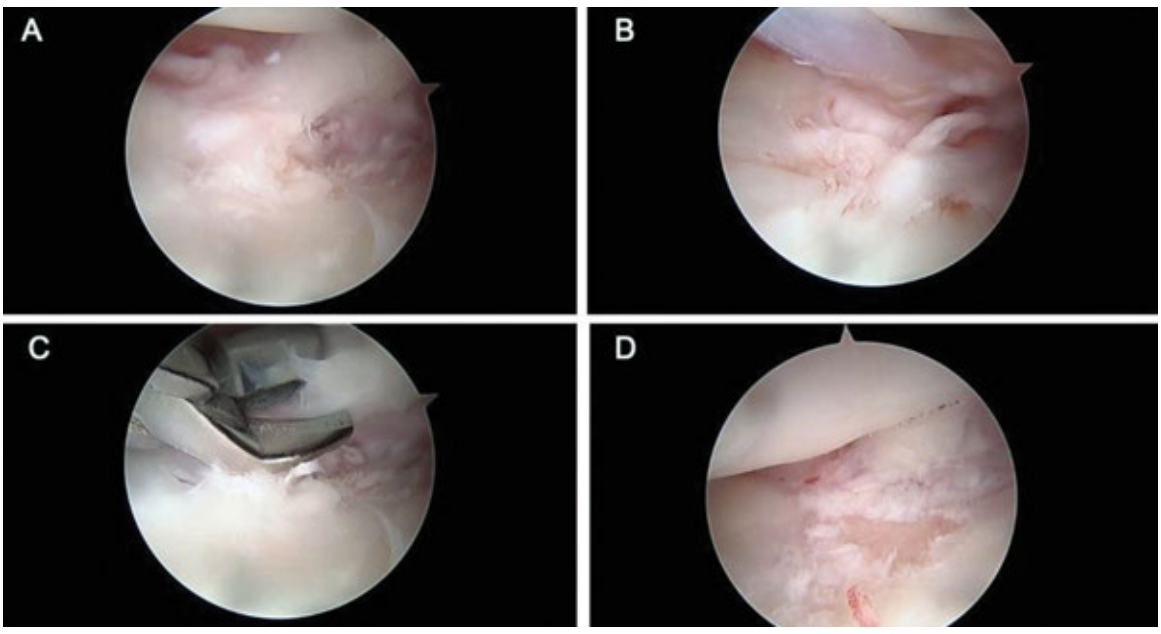

Figure 4 Arthroscopic images of the lunate fossa from Patient 1 obtained from the 3, 4 portal. **(A)** Appearance of the lunate fossa upon insertion of the arthroscope; (**B)** Following debridement with a shaver alone, the full-thickness depth of lesion is not yet appreciated; **(C)** Manual debridement of the abnormal cartilage, demonstrating its lack of adherence to underlying subchondral bone. **(D)** Lunate fossa at completion of debridement, revealing a full-thickness lesion.

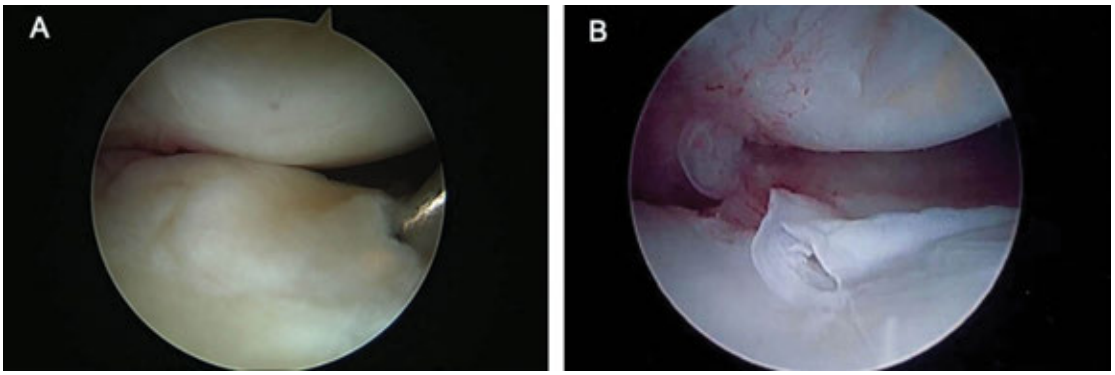

Figure 5. Arthroscopic images of the lunate fossa obtained from the 3, 4 portal upon initial arthroscope insertion in two different patients. **(A)** Patient 4: Undulating cartilage about the volar half of the lunate fossa, with probe lifting up the loose edge due to loss of adherence of articular cartilage to underlying bone. **(B)** Patient 5: Delamination and fissuring of the cartilage about the volar aspect of the lunate fossa. The lesion is transverse in orientation, nearly perpendicular to the arthroscope

ligament. Given that 80% of our patients were found to have SL ligament injuries on arthroscopy, we propose that they are either directly or indirectly associated with the lunate fossa lesions. Under the pretense of a direct association, we hypothesize that the force from the blunt trauma that caused the initial SL ligament injury simultaneously drove the lunate into the lunate fossa, causing a shearing injury to the articular cartilage. Alternatively, it is possible that the force from the initial traumatic event injured the SL ligament in isolation, and over time the lax SL ligament indirectly allowed for repetitive micro shearing of the lunate on the lunate fossa.

On a biochemical level, *in vitro* studies have demonstrated that application of a shearing force to articular cartilage can increase the production of reactive oxygen species, promoting chondrocyte death secondary to oxidative damage.[11] Regardless of the direct or indirect hypothesis, we propose that injury to the SL ligament allows the lunate to apply an abnormal shear force on the lunate fossa, leading to focal articular cartilage lesions.

Classically it is thought that there is a spectrum of SL injury severity, ranging from occult (with no radiographic findings on static radiographs) to SLAC arthritis.[12] A dynamic phase exists between these two ends of the spectrum, characterized by SL angle $>$ 60 with SL gapping $>$ 3 mm on stress radiographs.[12] In the context of the patients in this series, it is interesting to note that only 2/5 patients with SL injuries had SL angles $>$ 60 and 0/5 patients demonstrated SL gapping $>$ 3mm. Unfortunately stress radiographs were not available for these patients, though it is possible these may have shown some degree of dynamic instability given the arthroscopic findings.

Although the classic SLAC pattern of radiocarpal arthritis with sparing of the radiolunate joint remains widely accepted today [13], it is important to note that additional patterns have emerged that stand contrary to this dogma. Most pertinent to our report is a study by Lane et al. that evaluated 21 wrists in patients with radiolunate arthritis without radioscaphoid arthritis. Although the majority of patients in that study demonstrated SL gapping $>$ 3 mm on static XRs, the authors identified a subgroup of $\pm$ patients "that demonstrated radiolunate arthritis in isolation—that is RL joint space narrowing with no RS narrowing and no SL widening".[8] Notably 5/6 of the patients in this subgroup had wrists with SL Angle $>$ 60, consistent with SL laxity.

While it could be inferred that the patients in our case series represent a unique subset of patients who could go on to develop isolated radiolunate arthritis as described by Lane et al., there are two major differences between our studies. First, none of the patients with radiolunate arthritis were "particularly symptomatic," meaning that their symptoms were controlled with conservative measures alone. Second, no patient with radiolunate arthritis presented to clinic following an episode of acute trauma. These two characteristics differ from the patients in our series, all of whom underwent surgical treatment for pain refractory to conservative measures for symptoms that developed from a known traumatic event. Despite these differences, both studies shed light on a unique subset of patients with SL instability and pathology localized to the radiolunate joint—the articulation thought to be spared in the SLAC pattern as described by Watson and Ballet.

Although we only focused on limited post-operative results, such as patient-reported pain levels and functional improvement, our goal was not to describe definitive treatment for this problem. Rather, the primary purpose of this paper was to bring attention to a potential cause of post-traumatic wrist pain in the setting of normal MRI findings and no history of distal radius fracture. Nevertheless, all patients experienced significant pain relief. It is unknown whether this was due to chondral debridement or SL shrinkage, though others have shown improved functional outcomes and pain resolution following electrothermal shrinkage of SL ligament injuries.[14,15]

Moving forward, it is critical for hand surgeons to consider articular lesions of the lunate fossa as a potential cause of chronic dorsal and/or radial-sided wrist pain in patients with a remote history of trauma. The atypical presentation of patients in this series, including the absence of diagnostic findings on physical exam or advanced imaging helps to explain the lengthy delay from injury to diagnostic arthroscopy. Having failed to respond to conservative management, diagnostic arthroscopy was utilized as a treatment of last resort.

This study has several limitations, the first of which is small sample size. We felt it important to publish these early results given their potential significance, as this lesion has yet to receive attention in the literature. Another limitation is the presence of concomitant intra-articular wrist pathology beyond SL ligament injury, including 40% with TFCC tears and 1 prior scaphoid fracture. While some of this pathology

may have contributed to the patients' symptoms, the TFCC tears, for example, would not explain the predominantly radial or middorsal pain endorsed by our patients. Similarly, while the scaphoid fracture may have caused radial-sided wrist pain following the acute episode of trauma years prior to presentation in our clinic, this patient's MRI demonstrated complete healing of the fracture. Moreover, the scaphoid fracture in itself would not explain a cartilage lesion in the lunate fossa given that the scaphoid does not articulate with the lunate fossa.

Conclusion

In conclusion, patients with chronic radial and/or middorsal wrist pain after trauma with no corresponding lesion on MRI may have a symptomatic articular lesion involving the lunate fossa.These lesions appear to be associated with scapholunate ligament injuries without producing the typical SLAC pattern of wrist pathology.We believe the mechanism may be through either a direct shearing force that occurred at the time of injury, or repetitive microtrauma from scapholunate laxity.

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Shoulder and Elbow

Shoulder & Elbow Tips & Tricks: Arthroscopic-Assisted AC Joint Reconstruction

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Background

Acromioclavicular (AC) joint injuries are a common injury seen in the young athlete[1]. It has been proposed that successful reconstruction of the AC joint requires restoration of normal anatomy. There are many surgical techniques available for the treatment of AC joint injuries including fixation with either a plate, wire or screw, coracoacromial ligament transfer, and reconstruction with a free tendon graft[2]. The decision for surgical technique is often predicated on surgeon preference but also relies heavily on the acuity of the injury. Use of tension band devices with suture buttons are often reserved for more acute injuries that are addressed within 4 to ± weeks of injury. As these injuries become more subacute or chronic, the use of tendon reconstruction of the coracoclavicular (CC) ligaments is often recommended.

Reconstruction with free tendon graft provides an advantage over alternative techniques in that it has a load to failure equivalent to that of an intact CCligament[3]. Traditionally, this procedure is performed via an open approach, which requires a large incision and involves detaching the origin of the deltoid from the clavicle. An arthroscopic-assisted approach eliminates these pitfalls while also allowing for clear visualization of the coracoid base, which is essential for graft passage[2].

Case Example

This is the case of a 29-year-old male who presents to clinic with right shoulder pain after a dirt bike crash sustained approximately 10 weeks prior. The mechanism of injury is described as landing directly on the right shoulder after the dirt bike slipped out from underneath him. There were no other injuries. He has no history of previous injury to his right arm.

X-rays obtained in the ER initially showed no evidence of bony or ligamentous injury (FIgure 1). A CT also obtained at the time of his visit to the ED were unremarkable. He was seen in the clinic of a nonoperative orthopaedic provider several weeks after the injury, at which time x-rays demonstrated interval AC joint displacement consistent with a Rockwood type III AC joint injury (Figure 2). A follow-up MRI obtained of his shoulder demonstrated superior subluxation of the distal clavicle at the AC joint, partial tearing of the inferior AC ligament and sprain of the CC ligament (Figure 3), consistent

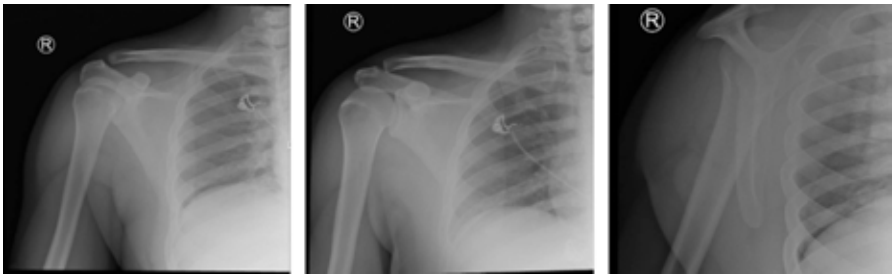

Figure 1. Initial radiographs obtained upon initial presentation to the emergency department the day of injury demonstrate no obvious bony or ligamentous injury.

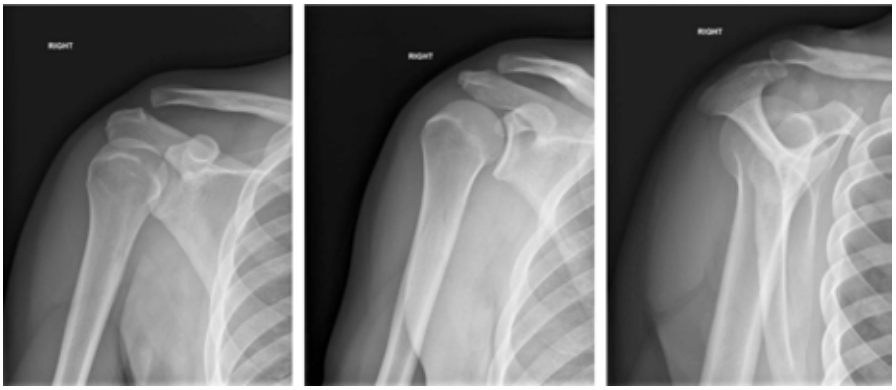

Figure 2. Follow-up radiographs obtained approximately two and a half weeks after the injury demonstrate interval widening of the acromioclavicular joint with almost 100% displacement of the coracoclavicular distance, consistent with a Rockwood Type III AC joint injury.

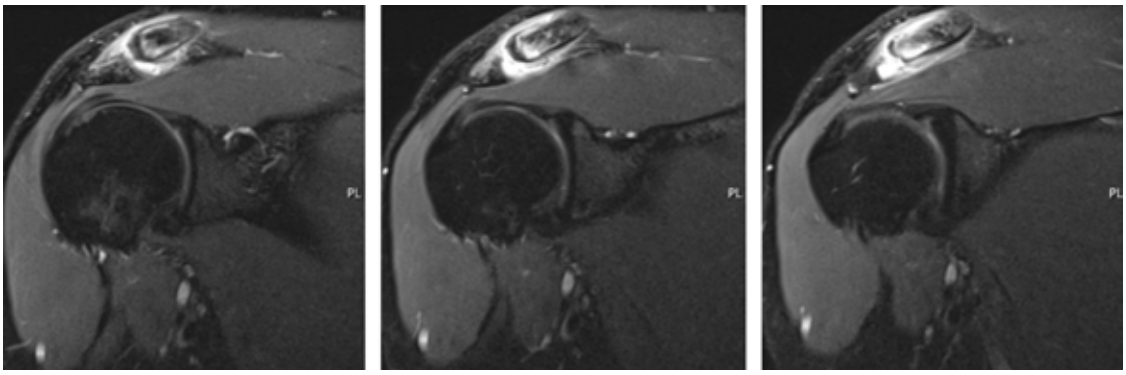

Figure 3. MRI of the right shoulder without contrast demonstrating partial tearing of the inferior AC ligament as well as a sprain of the CC ligaments with likely partial tearing of the trapezoidal ligament.

with radiographic findings. He was seen by a Sports surgeon 11 weeks after his injury at which time x-rays of bilateral AC joints demonstrated a Type III AC joint injury (Figure 4). He was subsequently referred to our clinic.

Upon presentation physical exam was notable for a prominence over the AC joint with superior displacement of the distal clavicle relative to the acromion. There was no appreciable skin tenting present. The patient endorsed significant tenderness to palpation overlying the AC joint. The AC joint was mobile and reducible. Range of motion was notable for external rotation to 70° with the arm at his side and 130° of forward elevation. He had 5/5 strength and a negative lag sign. Pain and an audible click were present within the AC joint with cross-body adduction.

Having failed conservative management in conjunction with having continued pain and instability, the discussion about surgical management was had with the patient. He was consented for an arthroscopic-assisted open reconstruction of the AC joint using semitendinosus allograft.

Author's Preferred Technique

The patient is seen and marked in the preoperative holding area. The patient is brought to the operating room and transferred from the stretcher to the table. After induction of general endotracheal anesthesia, the patient is placed in the beach chair position. The affected upper extremity is prepped and draped in the usual, sterile fashion. After surgical time out, a C-arm is brought in from the ipsilateral side to fluoroscopically visualize the AC joint. A reduction maneuver is performed under fluoroscopy to confirm that the AC joint is reducible (Figure 5).

Attention is turned to the shoulder for a diagnostic arthroscopy through a standard posterior portal. A systematic evaluation is performed of the glenohumeral joint surfaces, subscapularis tendon, biceps tendon, labrum, glenohumeral recesses and rotator cuff to identify concomitant intra-articular pathologies. An anterior portal is then created through the rotator interval, through which a shaver can be introduced to prepare the undersurface of the coracoid. A secondary anterior inferior portal is then established through which the arthroscopic shaver can be introduced to allow for complete preparation of the undersurface of the coracoid. Both of these anterior portals are created above the superior border of the subscapularis to avoid injury. The use of the 70º scope helps to obtain a better view of the undersurface of the coracoid which is cleared of any soft tissue before placement of the drill guide.

After sufficient intra-articular preparation of the coracoid, the open approach to the AC joint is performed. Attention is turned to the superior aspect of the AC joint where a 2 to 4 centimeter incision is made over the distal clavicle. The incision is carried down through skin and subcutaneous tissue to the level of the deltotrapezial fascia, which is then incised along its fibers along the midportion of the clavicle. The periosteum is elevated off the bone with a key elevator. A modified ACL guide is then placed over the top of the clavicle

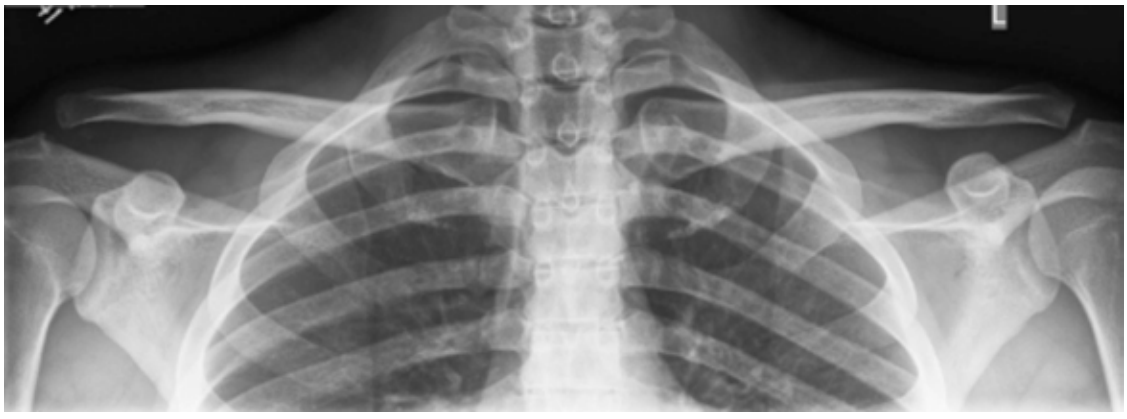

Figure 4. AP radiograph of the bilateral AC joints demonstrating just under 100% displacement of the right AC joint compared to the left.

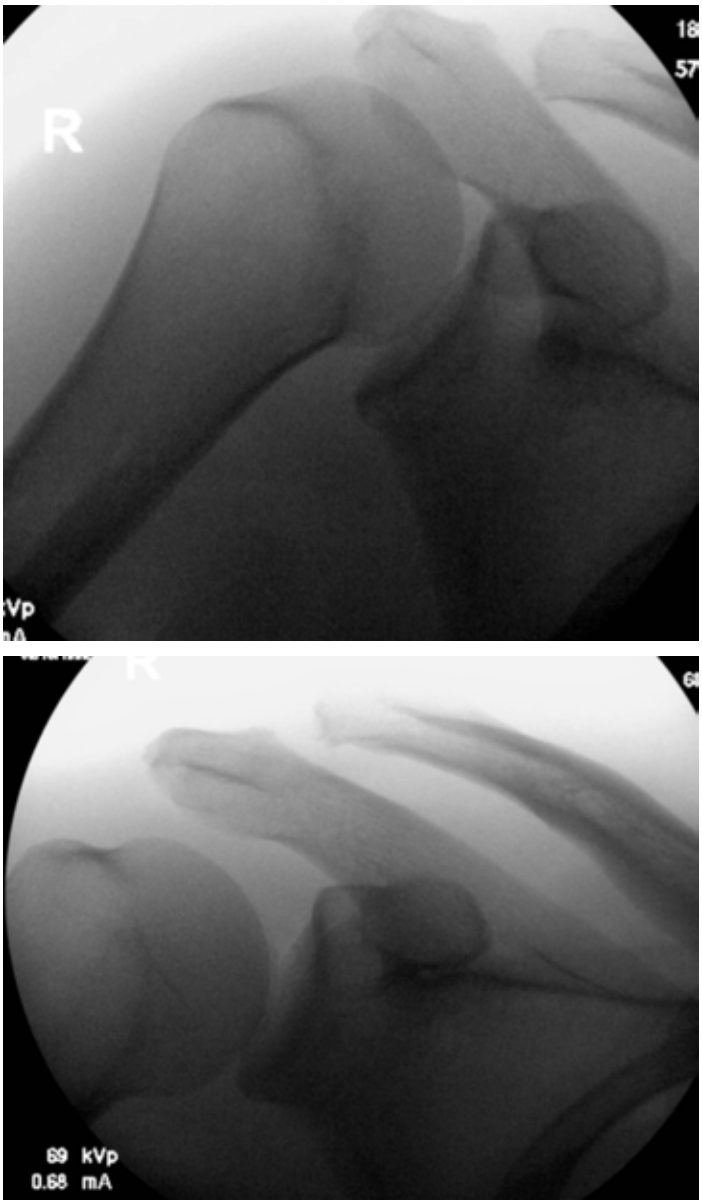

Figure 5. Intraoperative fluoroscopy demonstrating reducibility of the AC joint.

and through the anterosuperior portal to the undersurface of the coracoid under direct arthroscopic visualization.

Next, a cannulated 3 mm drill bit is utilized to drill through the four cortices of the distal clavicle and coracoid. A nitinol wire is passed through the cannulated drill bit. Then, 2 Fiber Tapes placed into a suture button are loaded and shuttled from the anteroinferior portal through the drill holes utilizing the nitinol wire. The sutures are tagged and attention is then turned towards preparation of the allograft reconstruction.

Under direct arthroscopic visualization a switching stick is placed in a position posterior to the clavicle and medial to the coracoid (Figure 6). A dilator is placed over the switching stick to allow for passage of the allograft. A second pathway is created in a similar fashion with use of a switching stick in a position just anterior to the clavicle. These dilated soft tissue pathways are used to best recreate the position of the individual coracoclavicular ligaments without having to drill

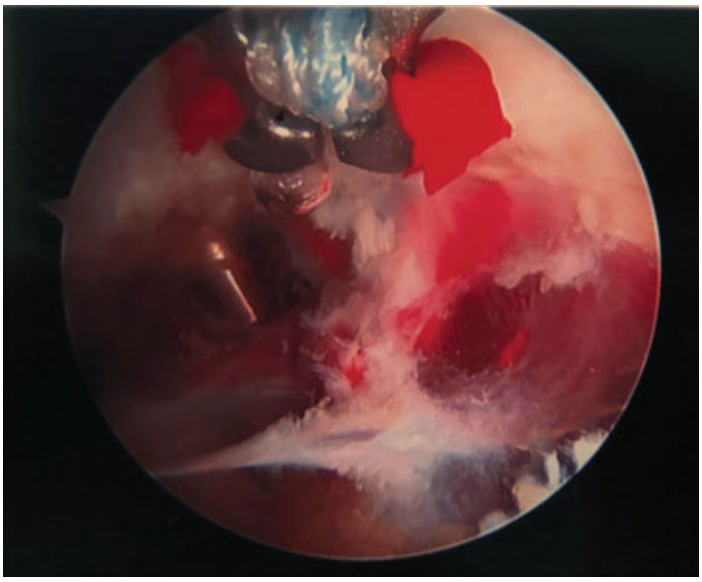

Figure 6. Intra-operative arthroscopic image demonstrating the suture button in place under the coracoid. There is a switching stick present posterior to the clavicle to make a passage for the graft posterior to the clavicle and medial to the coracoid.

their positions through the distal clavicle. Shuttle sutures are placed through both portals and brought out through the anterior portal.

On the back table a semitendinosis allograft is prepared. After allowing the graft sufficient time to defrost, FiberLoop sutures are placed through both ends of the graft in a baseball stitch configuration. Then, with use of the shuttling sutures, the graft is shuttled from the posterior aspect of the clavicle around the medial aspect of the coracoid, laterally around the coracoid and through the anterior aspect of the clavicle. The proper position of the graft is then confirmed arthroscopically, with the graft seated over the coracoid button and against the undersurface of the coracoid.

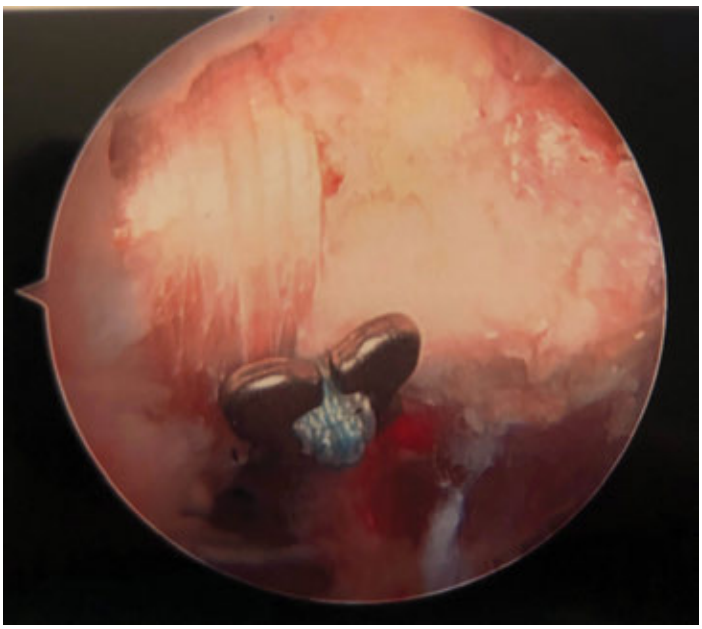

Figure 7. Intra-operative arthroscopic image demonstrating the final position of the graft and suture button under the coracoid.

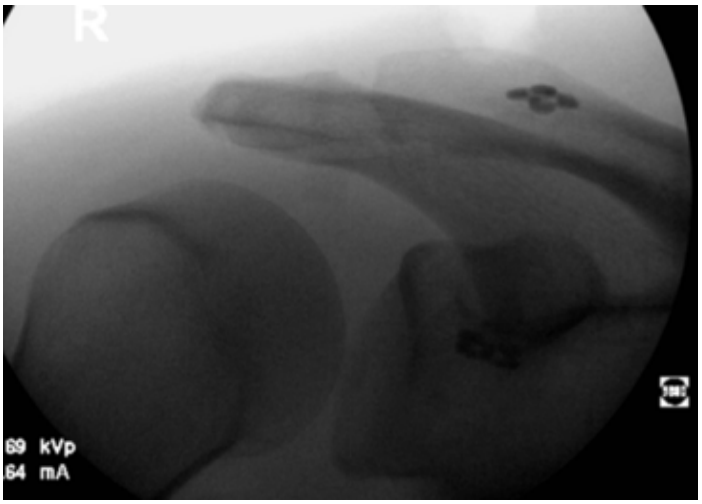

Figure 8. Intraoperative fluoroscopy demonstrating maintained reduction of the AC joint and CC distance after reconstruction with semitendinosus allograft. Suture buttons visualized on the superior and inferior aspects of the distal clavicle and coracoid respectively.

Next, a reduction maneuver is performed to return the AC joint to its anatomic position. The humerus is pushed proximally while the clavicle is pushed down. The Fiber Tape sutures are then tied down sequentially over a button over the superior aspect of the clavicle to reduce the distance of the coracoclavicular joint. The semitendinosis allograft is then tied in a half hitch andsutured in a side-to-side fashion using #2 FiberWire sutures (Figure 7).

C-arm is brought in to fluoroscopically confirm appropriate reduction of the AC joint (Figure 8). The wounds are then irrigated and closed in a standard layered fashion. The wounds are dressed and the arm is placed into a sling.

Post-operatively, the patient is kept non-weight bearing in the sling for the first six weeks after surgery to prevent attenuation of the reconstruction. This is then followed by initiation of formal physical therapy focused on shoulder range of motion and strength.

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Why Total Shoulder Arthroplasty Patients Cancel on the Day of Surgery

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Introduction

Cancellation of elective total shoulder arthroplasty (TSA) is an expected occurrence. The typical cost of canceled elective surgeries is estimated to be $3000 per patient[1] and can lead to hospitals losing nearly $1 million per year[2].The purpose of this study is to identify the frequency and causes of same-day cancellations in total shoulder arthroplasty and determine which treatment path those patients take following their cancellation.

Methods

A consecutive series of 1,189 patients undergoing TSA (anatomic or reverse) at a single institution from 2010 to 2020 was reviewed. All patients who scheduled and subsequently canceled on day of surgery (DOS) or prior to DOS were identified.The etiology of cancellation, time to rescheduling, and subsequent work-up were recorded. Descriptive statistics of the canceled patient cohorts were analyzed. Univariate analysis, chi-square test, and analysis of variance were used to compare each patient cohort.

Results

Of the 1,189 patients, 964 underwent TSA for glenohumeral osteoarthritis. 98 (10.2%) primary TSA experienced cancellations, of which 48 (49.0%) were on the DOS. The most common causes of same-day cancellations were medical reasons (45.8%) and anesthesia-related complication (27.1%). Infection (40.9%) was the most frequently encountered medical reason for cancellation. When compared with patient-requested cancellations, those canceled for medical reasons canceled closer to the scheduled surgery date (0.86 vs. 4.33 days). Ten of the 13 cancellations performed for anesthesia-related reasons were due to cardiopulmonary concerns, and 70% of those patients underwent additional intervention after cancellation.

Discussion and Conclusion

Elective primary TSA were most frequently canceled for medical reasons. Prior literature has suggested that many Medicare patients undergo unnecessary testing prior to non-cardiac surgeries[6], and only a minority of patients cancelled for medical reasons undergo further interventions[5]. The results of this study deviate from that of previous studies. Our results suggest that despite preoperative optimization, day-of-surgery cancellations still occur, and certain patient risk factors and conditions need further workup prior to surgery. In our cohort infection was found to be the most common medical reason for cancellation of a TSA on the day of surgery.

Previous studies have attributed medical-related cancellations to inadequate medical clearance[4,5]. All patients who were canceled for anesthesia-related reasons were medically cleared by their primary care provider prior to surgery. The majority of those patients required additional pre-operative intervention. In conclusion, same-day total shoulder arthroplasty cancellations are unavoidable, but there are modifiable factors that can minimize the risk of cancellation.

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Results of Anatomic Total Shoulder Arthroplasty with Modern Metal-Backed Glenoid

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Introduction

Total shoulder arthroplasty is an effective treatment option for certain patients with glenohumeral arthritis that fail non-operative treatments. Glenoid component failure is a known sequela of shoulder arthroplasty and is one of the most common prosthesis-specific causes for revision.[1] Metal-backed designs were developed to address the limitations of the all-polyethylene glenoid component. By allowing for tissue ingrowth on the porous trabecular surface of the component, it was believed that metal-backed implants could address the problems with loosening seen with cemented all-polyethylene glenoid components.[7]

Initially the experience with metal-backed glenoid components was not favourable, with high rates of loosening requiring revision or conversion procedures.[2] Much of the initial experience could be explained by variations in technique, the technical learning curve of the procedure and limitations to the implant design. More recent literature has suggested that the modern metal-backed glenoid has lower rates of radiolucency, loosening and revision surgery compared to conventional designs.[3,7]

The purpose of this study is to demonstrate that a modern-design metal-backed implant can achieve similar survivorship to historical controls. We hypothesise that there is a learning curve to mastering the technique and that after mastery is achieved, equivalent outcomes can be achieved with a metal-backed design.

Methods

Patient Population:

A retrospective chart review was performed of all patients who underwent total shoulder arthroplasty by a single surgeon between January 1, 2014 and December 31, 2019. Charts were queried based on the CPT code 23472, which represents "total arthroplasty of glenohumeral joint with glenoid and proximal humeral replacement".

Patients that underwent an anatomic total shoulder arthroplasty with a metal-backed glenoid component and had minimum six months of follow-up were included in the analysis. Patients who underwent hemiarthroplasty or reverse total shoulder arthroplasty, revision shoulder arthroplasty, had less than six months of follow-up or underwent an anatomic total shoulder arthroplasty with an all-polyethylene glenoid component were excluded from the analysis.

Demographic information including age, gender, race, ethnicity, BMI, smoking status, and preexisting health conditions was recorded. For each patient implant data was collected as well including size of the glenoid component (small, standard or large), as well as size (mm) and eccentricity (mm) of the humeral head.

Patient charts were evaluated for complications and revision procedures. For complications, the type of complication was recorded. For revision procedures, the time from the index procedure, reason for revision and type of revision was recorded.

Patients were separated into the first forty (Cohort A) and second forty (Cohort B) patients. Patients were separated in this fashion to evaluate for differences in complication and revision rates based on the technical learning curve of the procedure.

Descriptive statistics of the patient cohorts were analysed and reported. Univariate analysis, chi-square test, and multivariate logistic regression were used to compare each patient cohort. Statistical significance was set at $P < .05$, and statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

Results

A total of eighty patients met criteria for the study. Except for differences in rates of connective tissue diseases (eg. SLE, rheumatoid arthritis) and gender, there were no significant differences in demographics between groups. There were 24 (60%) and 15 (37.5%) males in Cohorts A and B respectively ($p = 0.0441$). The average age within the two cohorts was 58.8 and 59.6 years respectively. Average BMI within the two groups was 31 and 33 respectively (Table 1).

There was a significant difference in the revision rate ($p = 0.0052$) between the two cohorts (Table 2). For Cohort A there were 13

Table 1. Demographic Data

	Cohort A	Cohort B	P-value
Age (y)	58.8	59.6	0.6421
Female, No. (%)	24 (40%)	15 (37.5%)	0.0441
BMI	31	33	0.5297
Smoker, No. (%)	7 (17.5%)	8 (20%)	0.5923
Myocardial Infarction, No. (%)	2 (5%)	3 (7.5%)	0.6293
Congestive Heart Failure, No. (%)	3 (7.5%)	4 (10%)	0.6923
Peripheral Vascular Disease, No. (%)	6 (15%	2 (5%)	0.0769
Cerebrovascular Accident, No. (%)	2 (5%)	3 (7.5%)	0.6293
Dementia, No. (%)	0 (0%)	0 (0%)	
COPD, No. (%)	8 (20%)	5 (12.5)	0.1521
Connective Tissue Disease, No. (%)	8 (20%)	0 (0%)	0.0029
Peptic Ulcer Disease, No. (%)	3 (7.5%)	0 (0%)	0.0775
Liver Disease, No. (%)	5 (12.5)	4 (10%)	0.7235
Diabetes, No. (%)	4 (10%)	10 (25%)	0.0775
Leukemia/Lymphoma, No. (%)	0 (0%)	0 (0%)	
HIV/AIDS, No. (%)	0 (0%)	3 (7.5%)	0.0775
Chronic Kidney Disease (Mod - Severe), No. (%)	6 (15%	2 (5%)	0.136

Table 2. Revision Rates of Cohorts A & B

	Cohort A	Cohort B	P-value
Revision Rate No. (%)	13 (16.25)	3 (3.75)	0.0052
Months to Revision from index procedure Mean (Range)	17.8 (1-43)	12.7 (8-19)	

revisions that took place at an average 17 months (range: 1 to 43 months) from the index procedure. The causes for revisions included rotator cuff tearing (n = 4), shoulder instability (n = 3), shoulder pain and/or dysfunction (n = 3), subscapularis tear (n = 2) and stiffness (n = 1). Eleven patients underwent revision total shoulder arthroplasty, while one patient underwent subscapularis repair and another underwent revision of the humeral component. The patient that underwent revision of the humeral component went on to undergo conversion to reverse total shoulder arthroplasty five months later.

For Cohort B there were 3 revisions that took place at an average 12.7 months (range: 8 to 19 months) from the index procedure. The causes for revision included rotator cuff tear (n = 1), adhesive capsulitis (n = 1), and posterior shoulder instability (n = 1). All patients underwent conversion to a reverse total shoulder arthroplasty.

There was no significant difference in complication rates (p = 0.2371) between groups. Within Cohort A there were 16 subjects who experienced complications, whereas in Cohort B there were 11 subjects who experienced complications. Within Cohort A complications included rotator cuff tears or insufficiency (n = 5), adhesive capsulitis (n = 4), and subscapularis tears (n = 2). There were ± patients who underwent procedures post-operatively including arthroscopic lysis of adhesions and/or capsular release (n = 3), manipulation under anesthesia (n = 1), and arthroscopic debridement (n = 2). Within Cohort B complications included rotator cuff tears (n = 3), adhesive capsulitis (n = 2). There was one death and one patient who developed a C. acnes prosthetic joint infection that was treated with arthroscopic debridement six months post-operatively.

There was no significant difference in component sizes between groups (Tables 3 & 4). Specifically, there was no difference in humeral head size (p-value .2601), humeral head eccentricity (p-value 0.3871), or glenoid size (p-value 0.7918). There were no significant differences in component sizes between those patients that required revision and those that did not (p-values 0.7914, 0.9842, and 0.6954 for humeral head size, humeral head eccentricity and glenoid size respectively) (Tables 5 & 6).

Discussion

The most notable finding of this study was that the revision rate for the first 40 patients was more than four times greater than that of the second 40 patients (p = 0.0052). A previous study by Kempton et al. observed a learning curve of 40 cases

Table 3. Glenoid Component Sizes of Groups A & B

	Cohort A	Cohort B	P-value
			0.7918
Large No. (%)	7 (8.75)	9 (11.25)	
Standard No. (%)	20 (25.00)	20 (25.00)	
Small No. (%)	13 (16.25)	11 (13.75)	

Table 4: Humeral Component Size of Cohorts A & B

	Cohort A	Cohort B	P-value
Humeral Head Size (mm)	47.65	47.9	0.6552
Humeral Head Eccentricity (mm)	3.175	2.6	0.4932

Table 5. Glenoid Component Sizes of Revision and Non-Revision Groups

	Revision Surgery number (%)	No Revision Surgery number (%)	P-value
			0.6954
Large, No. (%)	2 (12.50)	14 (21.87)	
Standard, No. (%)	9 (56.25)	31 (48.43)	
Small, No. (%)	5 (31.25)	19 (29.68)	

Table 6: Humeral Component Size of Revision and Non-Revision Groups

	Revision	Non-Revision	P-value
Humeral Head Size (mm)	47.75	47.78	0.7914
Humeral Head Eccentricity (mm)	2.79	2.89	0.9842

for surgeons performing reverse total shoulder arthroplasty.[6] The results of this study would suggest that there is a learning curve to performing anatomic TSA with a metal-backed implant and that the threshold for obtaining more predictable results with the implant occurs after the first 40 surgeries.

Historical studies have demonstrated worse outcomes amongst cohorts of patients undergoing anatomic total shoulder arthroplasty with metal-backed glenoid implants. Boileau et al. demonstrated inferior results of metal-backed implants compared to all-cement polyethylene components at a minimum of three years in their prospective, randomised trial, with a 20% incidence of loosening and 20% incidence of revision surgery amongst 20 patients randomised to a metal-backed implant.[2] A more recent systematic review performed by Papadonikolakis and Matsen demonstrated revision rates for anatomic TSA with metal-backed glenoid components three times that of all-polyethylene components. (Papadonikolakis et al., 2014) In their study 77% of revisions for all-polyethylene components were performed for loosening while 62% of revisions in the metal-backed group were performed for other reasons such as rotator cuff tear, component fracture, screw breakage, or component dissociation.

More recently, a systematic review comparing modern metal-backed glenoid designs with conventional designs observed significantly lower revision rates with modern designs. (Kim et al., 2020) One of the modern designs described in the Kim et al. study was that designed by LimaCorporate, a design utilised by the senior author for the patients included in this study. Features of the prosthesis that may make it superior to traditional metal back glenoids include its stiff, thick metal back designed to minimise wear, hydroxyapatite coating on the central peg and stable fixation through 2 screws and a central peg.

To the best of our knowledge there are no studies that have assessed revision and cation rates based on size of glenoid and humeral components for anatomic total shoulder arthroplasty. It has been suggested that because the metal-backed glenoid tends to be thicker, the articular surface may be lateralized, which could potentially increase the risk of rotator cuff or subscapularis failure (Katz et al., 2013). In our study there was no difference in revision rates based on component size nor was there any difference in component size between the two cohorts.

One of the most common modes of failure observed amongst patients in this study was rotator cuff tearing or insufficiency, making up 31.25% of all reasons for revision. In a systematic review by Papadonikolakis and Matsen, cuff failure was the reason for revision in only 4% of 200 subjects who underwent TSA with a metal-backed glenoid.[9] The results of this study were closer to that of the systematic review of Kim et al., wherein rotator cuff failure was the reason for revision in 21.4% of patients that required revision after TSA with a modern design metal-backed glenoid.[7]

There are several limitations of this study related to its retrospective nature, the lack of long-term follow-up data, and the small patient numbers. Future studies would include radiographic data on implant loosening and patient outcomes scores. This study adds to the current body of literature by confirming that lower revision rates can be achieved with a modern-design metal-backed glenoid implant after completing enough cases to achieve mastery.

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To APE or not to APE? Case Series and Novel Technique of Arthroscopic Polyethylene Exchange for Metal-Backed Glenoids in Total Shoulder Arthroplasty

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Introduction

Anatomic TSA is a very good solution for active patients with end-stage glenohumeral arthritis[1,2]. Despite excellent results for pain relief and functional improvement, glenoid loosening has continued to be a common cause of failure in anatomic TSA[3–8]. Loosening is typically caused by poor glenoid implant placement or rotator cuff failure[9].

Glenoid implant placement can be a particularly challenging issue in patients with glenoid deformity. Several studies have shown an increased complication rate in patients with biconcave glenoids, or in those with excessive retroversion[10,11]. Corrective reaming has classically been used to address posterior erosion; however, this has been shown to only be effective to about 15 degrees[12]. The attempt at correcting more retroversion can potentially lead to joint line medialization and peg perforation through the glenoid vault[13]. Other techniques to address glenoid deformity include bone grafting, augmented glenoid components, and metal-backed glenoid implants[14].

Metal-backed glenoids were initially introduced as a solution to the problem of loosening of polyethylene glenoid implants. Modular implants were developed to offer the benefit of secure fixation to the glenoid, along with ease of revision to reverse shoulder arthroplasty, as the metal portion of the glenoid component does not need to be removed[15]. Concern began to arise as several studies showed a greatly increased revision rate in metal-backed implants compared to their all-polyethylene counterparts[16–20].

Due to these reports of increased failure, more caution has been employed with their use, and several design modifications have been made with more modern implants. Recent studies have shown promise with these modern designs[21,22]. At our institution, metal-backed implants are implemented with very narrow indications, typically in younger patients with severe glenoid deformity. This is a population in which polyethylene glenoids tend to fail more frequently[10,11]. Due to the patients' age, there is a high likelihood of revision surgery during their lifetime. To minimize the morbidity of multiple open surgeries, we created a novel, arthroscopic technique for polyethylene exchange.

Materials and Methods

Surgical Technique:

We perform this procedure in the beach chair position; however, the lateral decubitus position can also be used. After induction of anesthesia, a standard posterior viewing portal is developed. The camera is introduced into the shoulder and a diagnostic arthroscopy is performed. Next, an anterior working portal is created. If a deltopectoral approach was used for the primary surgery, the portal can be made in line with the previous incision. If needed, debridement can be performed with an arthroscopic shaver. A small Cobb elevator is inserted through the anterior portal and used to lever the polyethylene off the metal baseplate (Figure 1).

The anterior incision is then extended approximately 2 centimeters to allow for space for the implant. A radiofrequency ablation device can also be used to open the rotator interval to allow for ease of removal. An arthroscopic grasper is then used to remove the polyethylene from the shoulder. The new polyethylene implant is then inserted through the extended anterior portal (Figure 2). An arthroscopic probe is used to rotate the implant to the appropriate orientation (Figure 3). A Cobb elevator is then reintroduced through the anterior portal and medial pressure is applied to click the polyethylene into the metal baseplate. The elevator can then be used to gently try to elevate the polyethylene to ensure it is fully docked. The camera can also be moved to the anterior portal to visually confirm complete seating. Arthroscopic fluid can then be evacuated from the shoulder, and the portals closed.

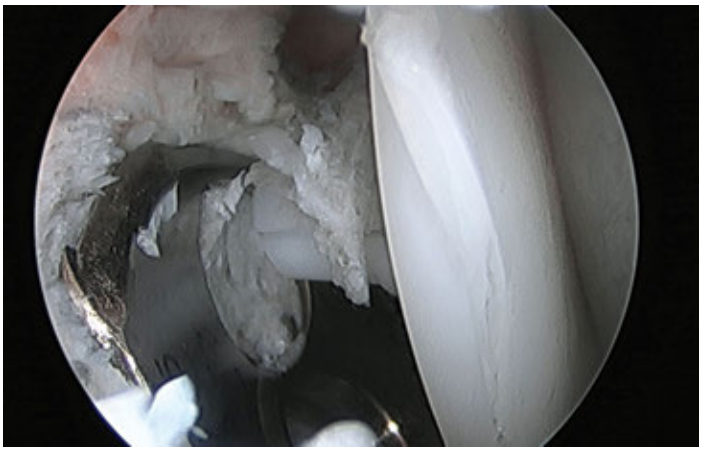

Figure 1. The polyethylene is disengaged from the metal baseplate using a Freer elevator or Cobb elevator and removed through the anterior portal.

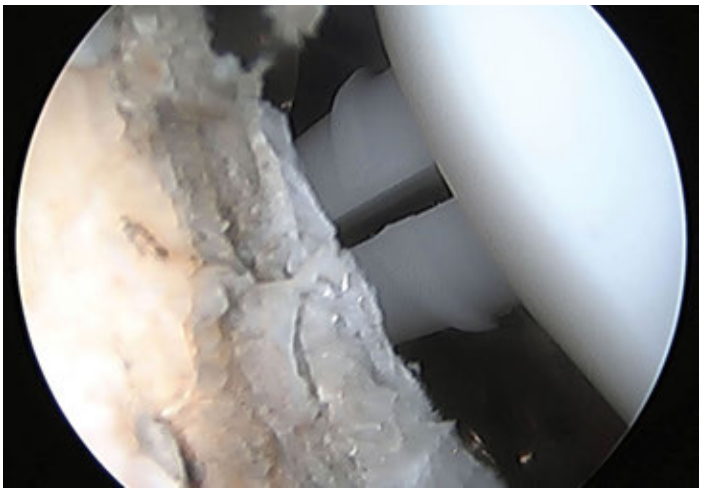

Figure 2. The new polyethylene liner is inserted through the anterior portal, rotated to the correct orientation, and snapped into place using a Cobb elevator.

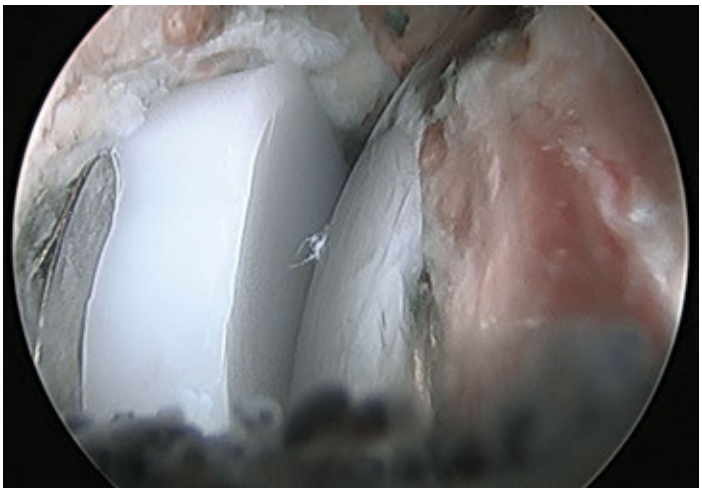

Figure 3. The scope can be used from the posterior and anterior portals to confirm complete seating of the liner.

Results

Patient 1

A 39-year-old male heavy equipment operator presented to clinic with complaints of left shoulder pain. He had a history of multiple left shoulder dislocations that was treated many years prior at an outside facility with an open capsular shift. MRI showed severe glenohumeral arthritis with 38 degrees of glenoid retroversion (Figures 4 and 5). After failing extensive conservative management, the patient elected to undergo a total shoulder arthroplasty. The procedure was performed

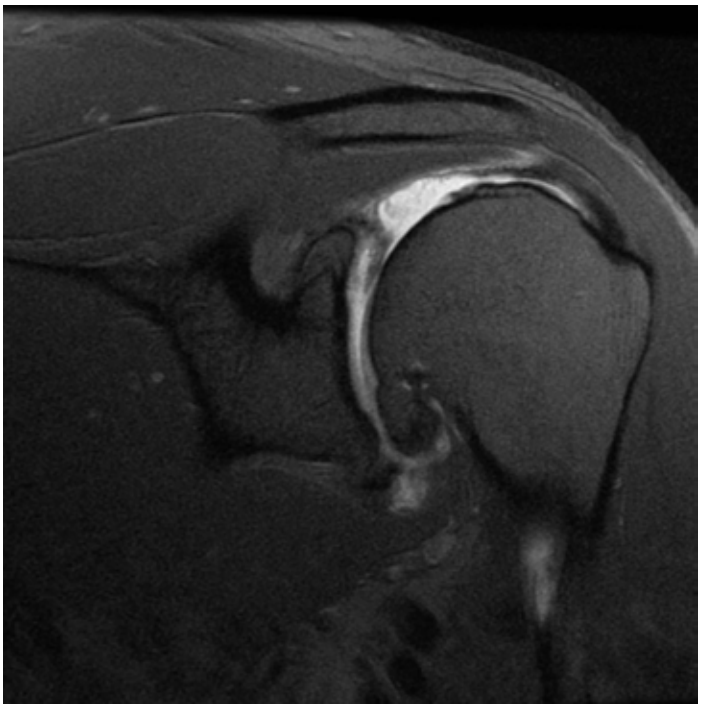

Figure 4. Coronal MRI demonstrating glenohumeral arthritis with a large inferior osteophyte.

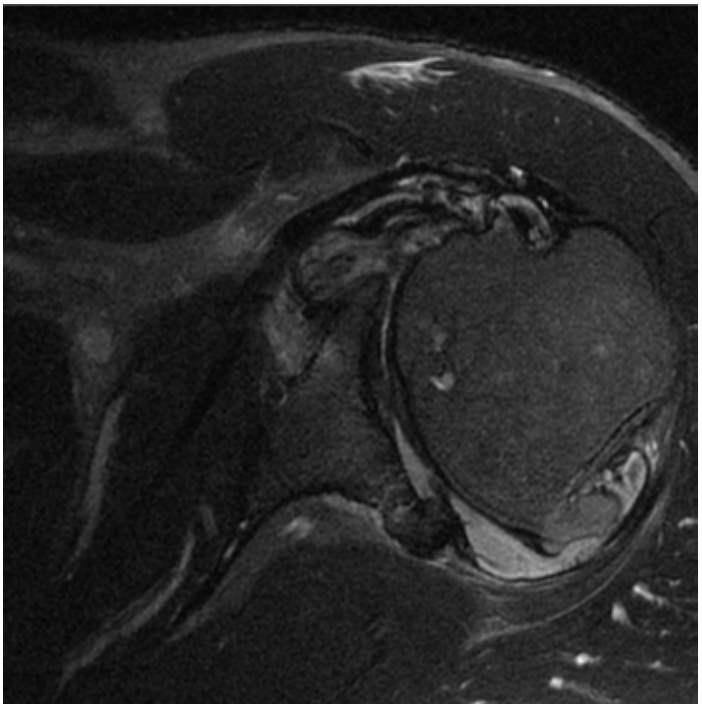

Figure 5. Axial MRI showing severe glenoid retroversion. This was likely due to overtightening of anterior structures after multiple previous surgeries for instability.

using a modular, metal-backed glenoid implant (SMR System, Lima Corporate, Villanova, Italy).

Patient did very well with his arthroplasty, with no pain and full range of motion at 1.5 years after surgery. Patient subsequently was lost to follow up until 5 years postoperatively, when he presented to clinic with complaints of left shoulder pain. Repeat radiographs showed evidence of asymmetric polyethylene wear, with some erosion of the metal baseplate (Figures 5 and 6). The patient underwent arthroscopic debridement and polyethylene exchange. At 9-month follow-up, he has no pain. He has active forward elevation to 170 degrees and external rotation to 40 degrees. Radiographs show appropriate position of the humeral component in relation to the glenoid (Figures 7 and 8). He is very satisfied, with a Subjective Shoulder Value of 90, American Shoulder and Elbow Surgeons score of 100, and a Penn Shoulder Score of 97.

Patient 2

A 46-year-old male attorney presented to clinic with complaints of chronic right shoulder pain. He had a history of traumatic posterior shoulder dislocation and instability that was treated with multiple arthroscopic procedures and an open posterior glenoid bone block augmentation at an outside facility. CT showed the prior bone block augmentation with two screws and washers and significant glenoid wear with humeral head flattening, consistent with post-traumatic glenohumeral osteoarthritis (Figure ± and 7). After failing extensive conservative management, the patient elected to undergo a total shoulder arthroplasty and removal of prior hardware. The procedure was performed using a modular, metal-backed glenoid implant (SMR System, Lima Corporate, Villanova, Italy).

At the 3-month follow-up, patient progressed well with his arthroplasty with active forwarded elevation to 150 degrees and no pain with external rotation to 45 degrees. At the 9-month follow-up, patient had some discomfort and impingement signs at extreme range of motions but was

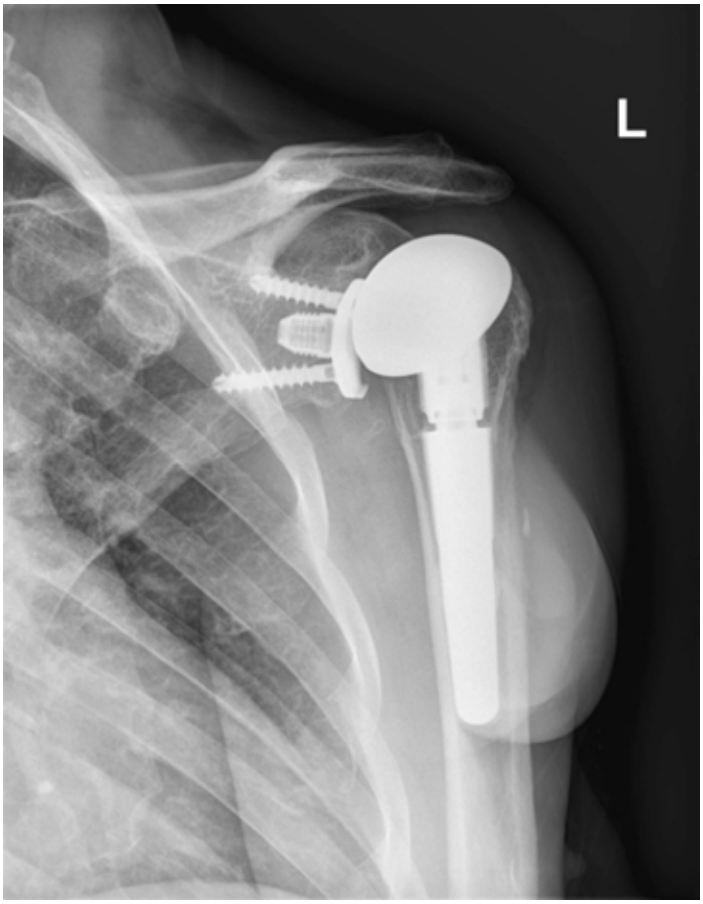

Figure 6. Grashey radiograph demonstrating narrowing of space between humeral and glenoid components, indicating excessive polyethylene wear.

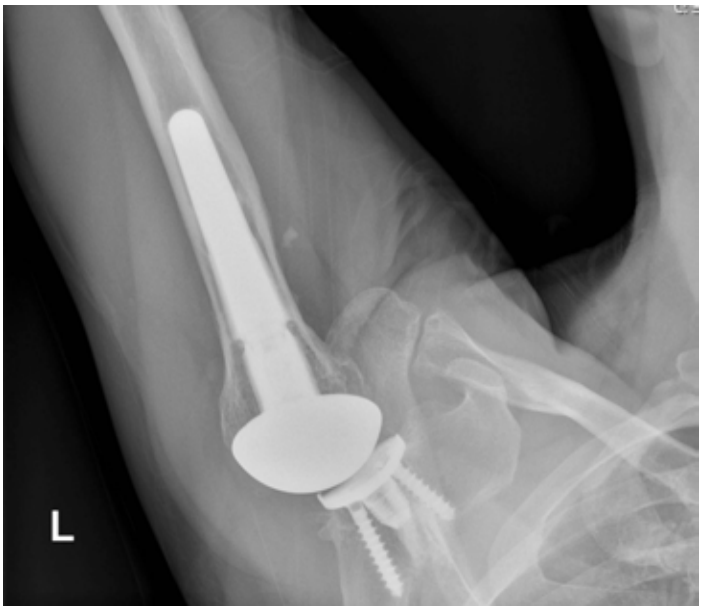

Figure 7. Axillary radiograph indicating polyethylene wear.

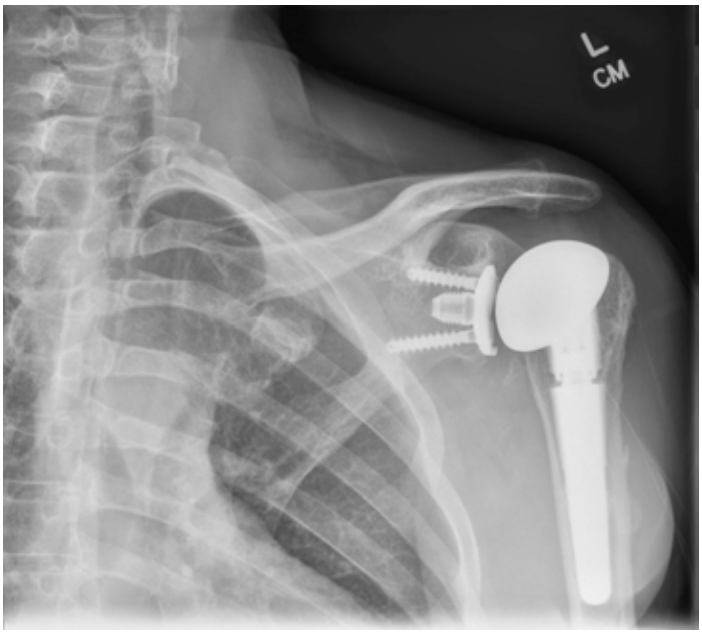

Figure 8. Grashey radiograph after APE procedure performed, demonstrating restoration of appropriate space between humeral and glenoid components.

able to perform his daily activities of living. At 1.5 years, patient had increasing right shoulder pain, but good range of motion. Repeat radiographs showed evidence of asymmetric polyethylene wear, and it appeared that the humeral head was beginning to subluxate posteriorly, potentially indicating rotator cuff imbalance (Figures 9 and 10). The patient underwent arthroscopic assessment, which showed that the subscapularis muscle was intact, but mildly attenuated. There also was a very small undersurface partial tear of the supraspinatus muscle. A debridement and APE was performed. At the 1-year follow-up since the liner exchange, patient continued to have shoulder pain with forward elevation to 90 degrees and external rotation to 40 degrees. He continued to have pain, and was converted to a reverse total shoulder arthroplasty at 3.5 years after the initial shoulder arthroplasty (Figure 11).

Discussion

Revision shoulder arthroplasty can be a very morbid procedure, especially in a younger patient. With revision of a traditional, cemented, all-polyethylene glenoid implant, component removal can compromise bone stock, as well as soft tissue quality, which can make each subsequent surgery progressively more difficult, and potentially necessitate revision to a reverse total shoulder arthroplasty (RTSA).

Sheth, et al. reported on revision of failed anatomic TSA to another anatomic TSA. Revisions were performed for a variety

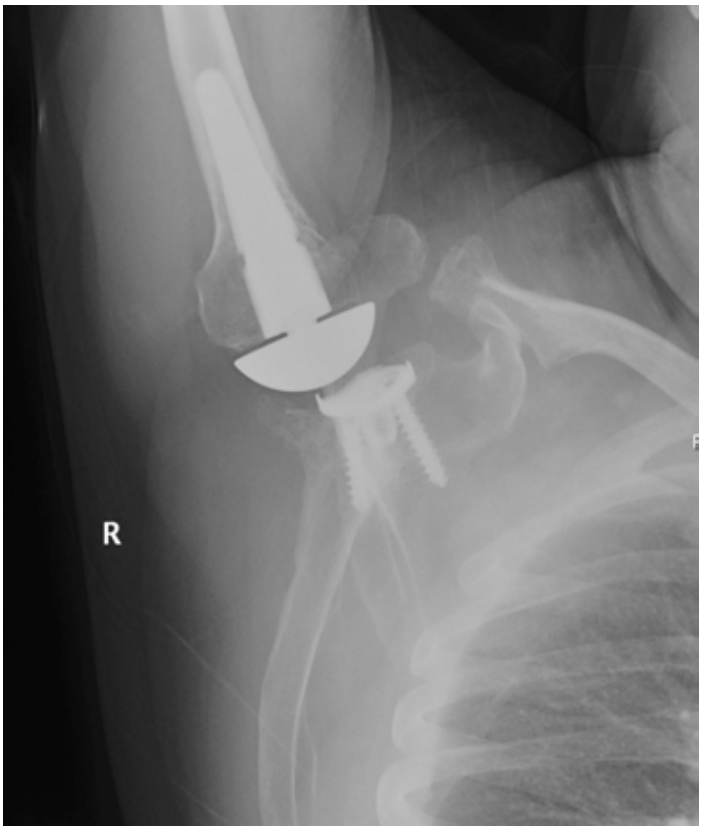

Figure 10. Axillary radiograph showing posterior subluxation of the humeral head. Likely due to soft tissue attenuation due to multiple previous procedures for posterior instability.

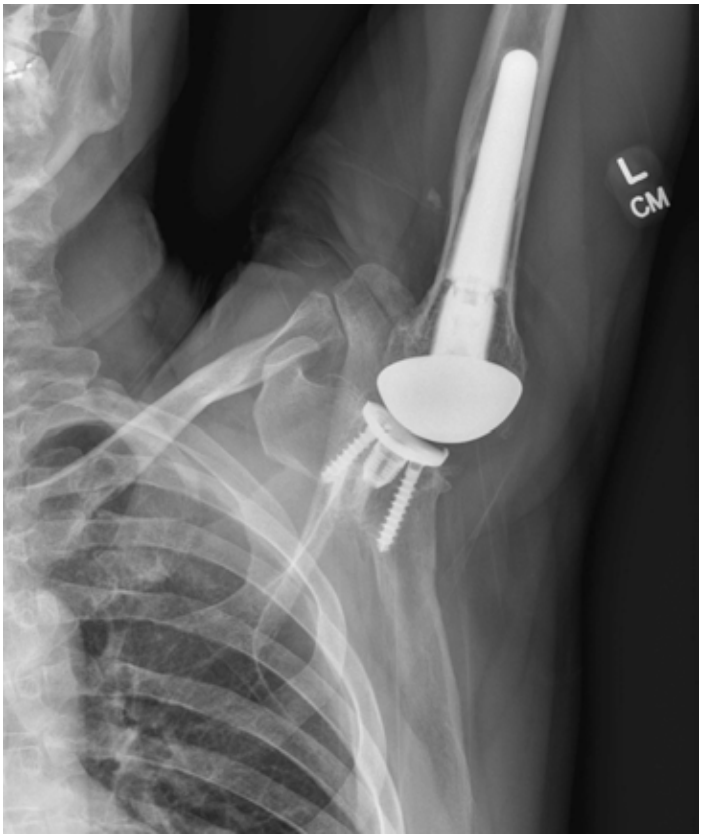

Figure 9. Axillary radiograph showing restoration of joint space, as well as appropriate rotator cuff balance, with the humeral head well-centered in the glenoid.

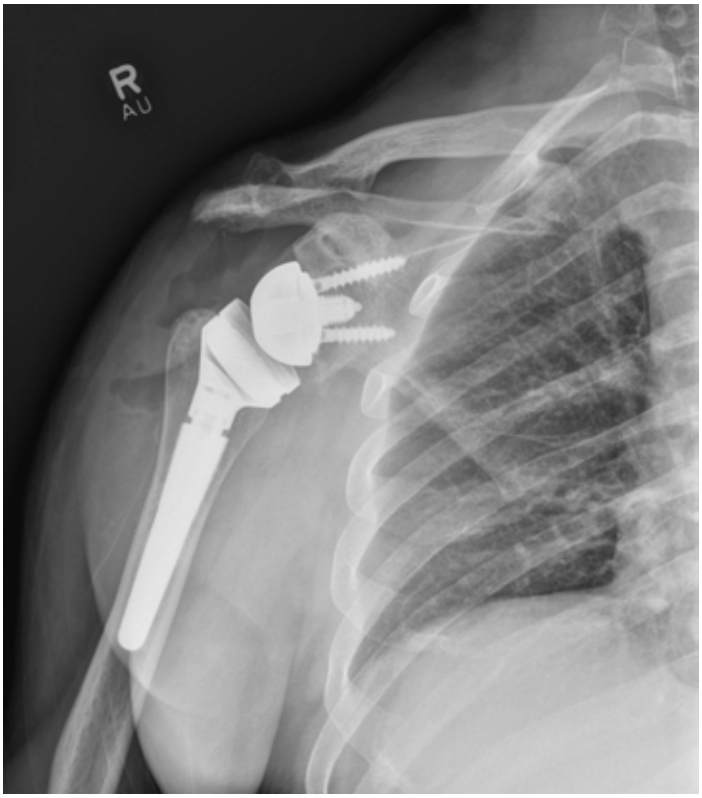

Figure 11. The patient was converted to a reverse shoulder arthroplasty after failing the APE procedure. This was likely due to rotator cuff imbalance causing persistent shoulder dysfunction.

of reasons. Outcome scores and range of motion values were inconsistent, and there was a survival rate of only 60% at 4 years.

Black and colleagues performed a retrospective review of patients aged 65 and younger of patients who underwent RTSA as a salvage for failed primary arthroplasty[23]. They found that these patients did well in terms of pain and functional improvement, but had lower subjective outcome scores compared to patients who underwent primary RTSA. They noted that the relatively high complication rate for revision surgery, and recommended setting appropriate expectations with patients before surgery.

Gauci, et al. reviewed revision shoulder arthroplasty performed over a 20-year period at two tertiary centers[24]. They found that 21% of their cohort required multiple reinterventions, mostly due to soft tissue insufficiency or infection. The final implant, regardless of number of procedures was a RTSA in 48% of cases.

Young, active patients with severe glenohumeral arthritis and glenoid deformity offer a significant challenge to the shoulder surgeon. These patients have a very high risk of revision during their lifetime, regardless of the type of implants used[25,26]. While modular metal-backed glenoid implants have the potential for accelerated polyethylene wear, they do offer the advantages of solid glenoid fixation and easy polyethylene exchange. It is our practice to closely monitor these patients, and to scrutinize radiographs for signs of polyethylene wear. With our novel APE technique, polyethylene implant exchange can be performed relatively quickly, with very little insult to the patient's soft tissue, and with very good results, as seen in our first patient. Patient selection is pivotal for this procedure. As demonstrated in our second patient, rotator cuff imbalance can predispose the shoulder to failure, and other revision options should be pursued in these cases.

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Adult Reconstruction

Adult Reconstruction Tips & Tricks: Systematic Approach to THA Templating

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Introduction

Hip arthroplasty has consistently been shown to relieve pain and improve function[1,10]. Advancements in implant design, surgical technique, and anesthesia have increased the reliability of the hip prosthesis and decreased risk of complications. However, hip arthroplasty procedures at times fail[4,8]. These failures can be secondary to excessive wear at certain locations from component position, dislocation, and fixation failure. Mechanical failure is also multi-factorial and dependent on materials, design, position, bone quality, as well as biologic response to wear debris[1,7]. Many of these factors leading to arthroplasty failure are not under the control of the surgeon. Fortunately, thorough preoperative planning may mitigate the likelihood of factors leading to failure.

Total hip arthroplasty templating processors anticipate the size and position of implants prior to surgery. Meticulous planning allows surgeons to anticipate potential difficulties, to reproduce hip biomechanics, to minimize leg length inequalities, and to achieve reproducible results[3,5,9].

The above can be achieved by following a step-by-step approach that encompasses first analyzing the appropriate radiographs, establishing appropriate radiographic and anatomical landmarks, identifying and correcting limb length discrepancy, and lastly templating the acetabulum and the femoral components.

Radiographic Analysis

First and foremost, total hip arthroplasty templating requires standard sets of radiographs. The first image obtained should be a low AP pelvic radiograph with the x-ray beam centered on the pubis. Low AP pelvic films allow the surgeon to visualize the proximal third of the femur and are in approximately the same horizontal plane as the x-ray source. The AP views are obtained with the patient lying supine on the table with the hips internally rotated about 10 to 15° which accounts for normal anteversion of the femoral neck while the neck is parallel to the film. An adequate AP Pelvis XR demonstrates the following findings: the coccyx is roughly 3cm directly superior to the pubic symphysis, the obturator foramina, teardrops, and prominence of the lesser trochanters are symmetric, and the spinous processes are midline.

Figure 1 reveals a helpful demonstration as to the anatomical landmarks that are helpful to define preoperatively to help assist with templating[1]. Important landmarks for the femoral side include the medullary canal, greater and lesser trochanter, as well as the saddle point which is determined by drawing a line that connects the superior portion of the femoral neck with the medial portion of the greater trochanter.

If the radiographs are obtained with the hips overly rotated internally or externally, the true femoral offset and length will be underestimated. Femoral offset is defined as the distance from the femoral head center of rotation to a line bisecting the long axis of the femur. A good method to determine an acceptable amount of internal rotation is to analyze the amount of lesser trochanter shown on imaging. From the medial aspect of the femur, less than 5mm of the lesser trochanter should be visualized.

The surgeon must also know the magnification of the radiograph obtained. The standard magnification is 20%. This can be accomplished when the x-ray tube is 1 m from the tabletop and the film is placed in a tray 5 cm below the table. Magnification markers can also improve precision in templating. Magnification markers consist of a plexiglass tube with two lead spheres embedded at an exact distance of 100 mm.

Placement of the magnification marker can be at two separate locations. First, the marker can be placed at the level of the greater trochanter against the patient's skin. While the second way involves placing the object close to the pubis symphysis between the patient's legs and in the plane of the greater trochanter. However, this location may not be received well by patients and radiology technicians. Notably, placing the marker closer to the pubic symphysis induces less projection errors and thus leads to less magnification errors in clinical practice (2). Increasing the distance between the x ray source and the patient as well as decreasing the distance between the patient and the film will both serve to decrease magnification factor.

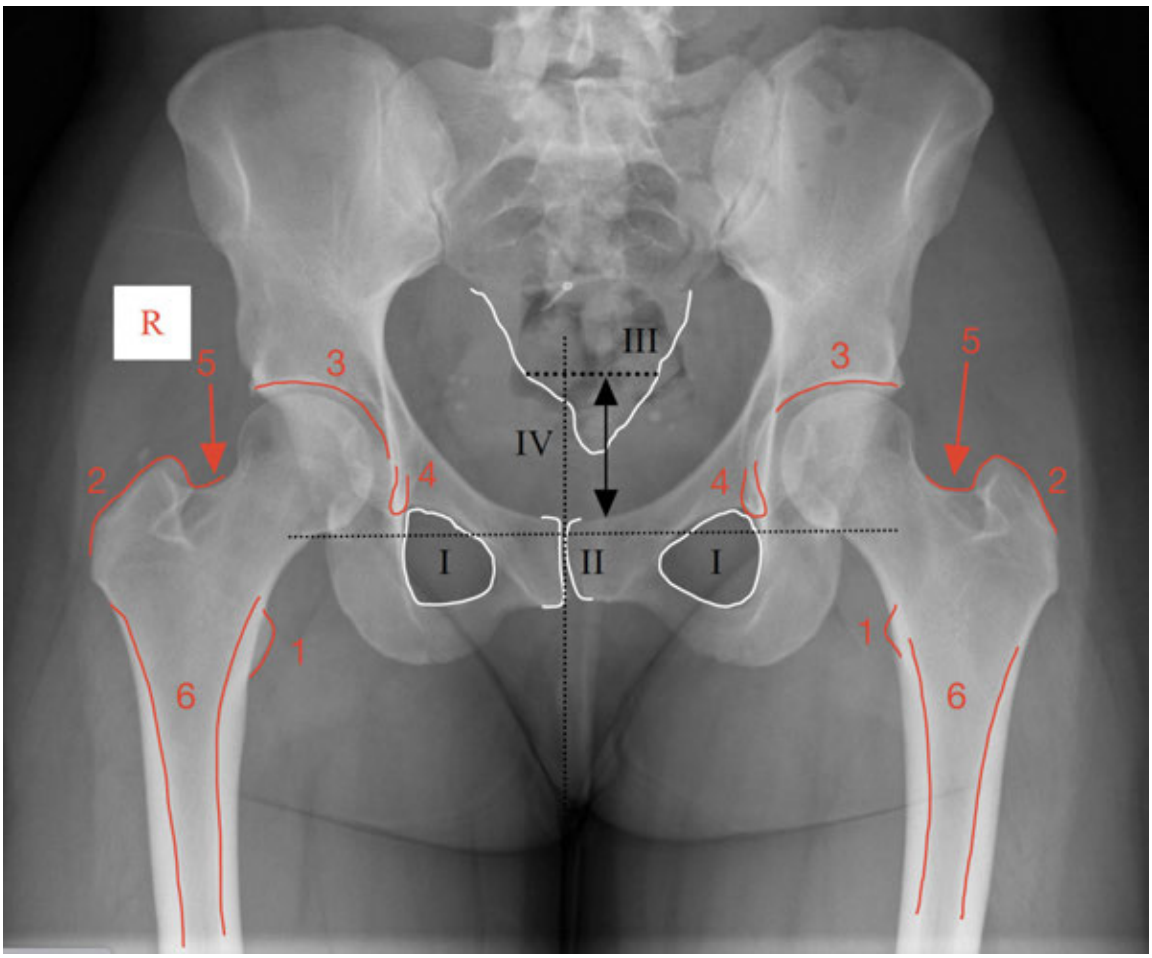

Figure 1. Standing anterior posterior pelvic radiograph for templating the hip. **(A)** Anatomical landmarks: 1. Lesser trochanter; 2. Greater trochanter; 3. Acetabular roof; 4. "Teardrop"; 5. "Saddle"; 6. Femoral shaft. **(B)** Landmarks for assessing radiographic quality: I. Obturator foramen; II. Pubic symphysis; III. Sacrum; IV. Distance between pubic symphysis and sacrococcygeal joint.

THA Templating

Historical perspective

Before computer models for templating for THA became standardized, templating previously occurred with the use of pre-made drawings. In order to perform this, radiographs were printed out with landmarks drawn in by hand. Templates of the acetabular components and femoral components were then physically overlaid beneath the radiographs. Multiple templates of varying sizes could then be used in order to estimate the most appropriate fit. Disadvantages to this method include the amount of time required to template as well as difficulties evaluating the image magnification factor.

General overview

Templating should follow the steps of surgery: acetabular side first, followed by the femoral side. The measured distances and implant sizes should be recorded following a pre-established order so that the surgical team understands and follows the plan throughout the surgery. The first step in templating is to draw a horizontal reference line through the base of both teardrops. These radiographic landmarks are the superposition of the most distal medial wall of the acetabulum and the anterior and posterior horns of the acetabulum[1,6].

The teardrops are the most accurate anatomic landmarks in relation to the bony acetabulum because they are located close to the center of rotation of the hip joints[2,6]. Alternative horizontal reference lines can be drawn through the most distal aspect of the sacroiliac joints and through the most distal aspect of the ischial tuberosities. However, the farther away from the center of the hip joint that anatomic structures lie, the more potential error is introduced by pelvic rotation. Several key radiographic landmarks, which can be visualized during acetabular exposure, should be marked before cup templating: the base of the teardrop, the ilioischial line, and the superolateral margin of the acetabulum[2,6]. The acetabular roof, which bears a significant portion of the body's weight, should also be drawn.

There are a variety of different methods to calculate the limb-length discrepancy both anatomically and radiographically. The actual limb-length discrepancy is determined by measuring the distance between the anterior superior iliac spine and the medial malleolus. The functional limb-length discrepancy is what the patient perceives while in a standing position; it can be determined by placing blocks under the affected side until the patient feels the limbs' length to be "equal"[3].

Another radiographic method on an AP pelvis is to draw a horizontal line that connects the ischial tuberosities taking note to bisect the bilateral medial femoral cortices.

Then, draw a second horizontal line that connects the lesser trochanters at their most proximal aspects. Finally, measure the distance between the lesser intertrochanteric line and the intertuberosity lines. Alternatively, a line connecting the base of the bilateral teardrops can be used instead of the intertuberosity line.

Acetabular Templating

In order to template the acetabulum, first draw a horizontal reference line through the base of the teardrops and identify three anatomic landmarks as stated earlier: the base of the tear drop, the ilioischial line, and the superolateral margin of the acetabulum. Next, an appropriately sized cup is placed in 40 degrees (+/− 10 degrees) of abduction in the frontal plane. The medial portion of the cup should lie near the ilioischial line, and the inferior border of the cup should lie in close proximity to the distal end of the teardrop. Once the template is in an adequate position, mark the acetabular component center of rotation (COR). Next, compare the templated COR to the contralateral center to determine whether they area at the same vertical and horizontal difference from the reference line. The difference may be recorded to compensate for limb-length discrepancies[2].

Furthermore, there are multiple conditions that should be evaluated when templating and the appropriate adjustments should be made pre- and/or intraoperatively. These include but are not limited to the following: 1) In cemented cups, templating should allow for a uniform cement mantle of 2 to 3 mm. If lateral coverage of the cup is incomplete, the uncovered area should be measured and reproduced during surgery. 2) In patients with protrusio acetabuli, care should be taken when reaming to not extend to the full depth of the protruded medial wall and to consider bone graft to fill the defect. Proper placement of the cup improves soft-tissue tension and decreases the possibility of impingement. 3) Patients with a lateralized acetabulum secondary to medial osteophytes will also require attentive reaming to ensure that the acetabulum is reamed until the ligamentum teres, pulvinar, cotyloid notch and transverse acetabular ligament are visualized. Failure to remove the medial osteophyte can lead to a lateralized cup resulting in suboptimal fixation and insufficient coverage.

Femoral Templating

In order to template the femur, choose a femoral implant that approximates the size of the medullary canal. Take note of the potential use of cement for the femoral component as this may impact the size of the stem. Also note the potential insertion depth of the femoral component to address any potential leg length discrepancies. Pre-operatively mark the femoral intended femoral neck resection level as well as the femoral head center of rotation.

Relative superior/inferior placement of the COR between the acetabulum and the femur can impact the limb lengths. If the acetabular COR is superior to the femoral COR, the limb will be shortened. Conversely, if the acetabular COR is inferior to the femoral COR, the limb will be lengthened.

Relative medial/lateral placement of the center of rotation (COR) between the acetabulum and the femur can impact the offset. If the acetabular COR is medial to the femoral COR, the offset will be decreased. If the acetabular COR is lateral to the femoral COR, the offset will be increased. Offset can also be modified by altering the length of the femoral neck, selecting stems with varying neck shaft angles, as well as choosing a stem with more or less offset.

Conclusion

Preoperative planning is essential to total hip arthroplasty. Templating allows assessing the relation of the different anatomical and radiographic landmarks to anticipate difficulties prior to surgery. However, it might be difficult if not done in a systematic approach. Consistently performing THA templating and reproducing the situation combined with the appropriate surgical implantation and techniques should help the surgeon reduce the number of potential complications and help perform the procedure expediently.

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U·P·O·J

Acetabular Revision in Total Hip Arthroplasty: Using Tantalum Uncemented Porous Metal Cups and Augments

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Introduction

Total hip arthroplasty (THA) is one of the most successful surgical procedures in medicine.[1] As a result of their reproducible success, THAs are reportedly within the top five fastest growing procedures in the United States (US).[2] However, as THAs are performed in younger, more active populations with greater life expectancies, orthopaedic surgeons will increasingly encounter patients indicated for revision surgery as the population of patients living with a prosthetic hip continues to rise.[3,4] Approximately 50,220 revision THAs (rTHA) were performed in 2014, and Schwartz et al. predicted rTHA rates to increase by 43-70% by 2030.[5] In general, rTHAs are associated with longer lengths of inpatient hospital stays, more peri-operative complications, higher costs, and constitute a group of more technically demanding procedures.[6–8]

Revision THA encompasses reoperation of either the acetabular component, femoral component, or both. Acetabular revision is most commonly performed for the following etiologies: instability (33%), mechanical loosening (24.2%), implant failure (10.8%), periprosthetic osteolysis (8.1%), bearing surface wear (8.0%), peri-prosthetic infection (4.7%), and peri-prosthetic fracture (1.8%).[9,10] One of the most challenging problems facing orthopaedic surgeons at the time of revision is acetabular bone loss. The focus of this article is on the indications and techniques for the use of uncemented tantalum/porous metal cups and modular porous metal augments in the setting of acetabular bone loss.

Preoperative Evaluation

History, Physical Exam, Labs, and appropriate imaging should be obtained during evaluation for potential revision surgery. Hip pain should be defined based on its character, temporal course, exacerbating and alleviating factors, and any prior attempted treatments.[11] Groin pain with weightbearing should raise suspicion for an intra-articular pathology. Start-up pain is typically indicative of loosening of either one or both components.[12]

Gait examination provides insight into the status of the abductors, as well as overall patient mobility. The skin should be inspected for healed sinuses, superficial infections, and overall soft-tissue sleeve integrity. Prior incisions should be noted, as they may dictate the surgical approach employed for rTHA.

Leg-length discrepancies should be recorded as they may suggest hip center migration or other pathologies such as peri-prosthetic fracture or femoral component subsidence.[13] A thorough neurovascular exam should be performed to rule out confounding sources of pain. Provocative maneuvers may assist in identifying and localizing pain generators. A positive Stinchfield test (groin or deep gluteal pain that increases with a resisted straight leg raise), is associated with acetabular component or intracapsular pathology.[14,15]

All rTHA patients should have a serum erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) prior to surgery. Elevated inflammatory markers should prompt aspiration of the hip joint, with fluid sent for cell count with differential and culture. Current Musculoskeletal Infection Society (MSIS) criteria should be applied to determine the likelihood of infection.[16,17]

Standard weightbearing anteroposterior (AP) radiographs of the pelvis and hip, and cross-table lateral (L) of the hip should be obtained pre-operatively. Proper visualization of landmarks such as the anterosuperior column, teardrop, superior acetabular dome, and ischium or posteroinferior column are paramount to proper evaluation of acetabular bone loss. The increased resolution of CT scans detects acetabular bone loss with greater sensitivity than X-rays.[18,19] Metal artifact reduction sequence (MARS) MRI should be considered in the setting of failed metal-on-metal hip replacements to identify the presence of a pseudotumor.

Acetabular Bone Loss Classification

Surgeons must appropriately characterize the degree of bone loss in patients undergoing rTHA procedures before attempting to address acetabular defects. Paprosky et. al introduced a

classification system in 1994 favored by the authors of this chapter, as we believe it guides treatment of acetabular bone loss.[22] This classification utilizes four radiographic features to quantify and localize bone loss involving hip center position, the superior acetabular dome, the medial wall, and the posterior column.[11]

The bone loss pattern must then be classified in order to guide treatment. Type I defects exhibit minimal bone loss with no hip center migration, no ischial lysis, no teardrop osteolysis, and an intact Köhler's line. Type II defects exhibit hip center migration $<$ 3cm, in one of three directions, and thus are further subcategorized as type A, B and C. Type IIA defects demonstrate anterosuperior migration without ischial or teardrop osteolysis, and don't violate Köhler's line. Type IIB defects demonstrate superolateral migration with minimal ischial osteolysis, and without teardrop destruction or violation of Köhler's line. Type IIC defects demonstrate medial hip center migration with mild ischial osteolysis, mild teardrop destruction, and disruption of Köhler's line.

Type III defects are subdivided into Type A and B defects. Type IIIA defects ("up and out") exhibit $>$ 3cm of superolateral hip center migration, moderate ischial and teardrop lysis, and an intact Köhler's line. (Figure 1.) Type IIIB defects ("up and in") exhibit superomedial hip center migration, severe ischial and teardrop osteolysis, and a disrupted Köhler's line. (Figure 2.) Type IIC, IIIA and IIIB defects may be associated with chronic pelvic discontinuities, with the highest incidences seen with type IIIB defects.[11] The classification system is advantageous not only due to its descriptive and quantitative nature, but because it has demonstrated validity in correlating with intraoperative bone loss while having good reliability among observers.[23,24]

Intra-operative Bone Loss Assessment

In the case of rTHA, surgeons should select a surgical exposure that affords optimal visualization of the posterior ilium and posteroinferior column. The authors recommend a posterior approach to the hip, as this permits excellent access to the posterior acetabulum and is extensile.

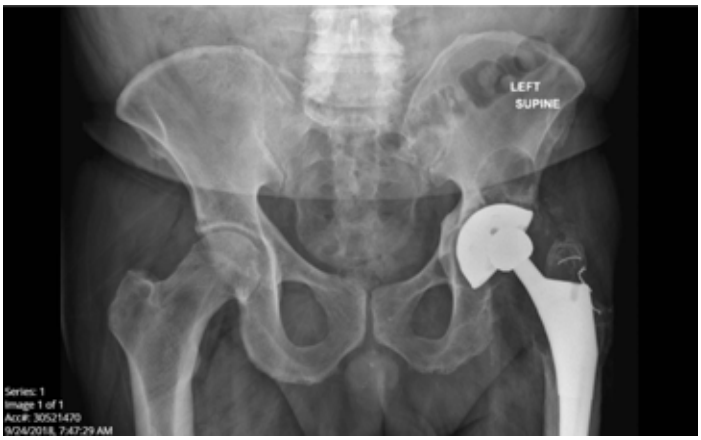

Figure 1. AP Pelvis x-ray of a patient with eccentric polyethylene wear and osteolysis. Following cup removal, the "up and out" defect would be classified as a Paprosky IIIA defect.

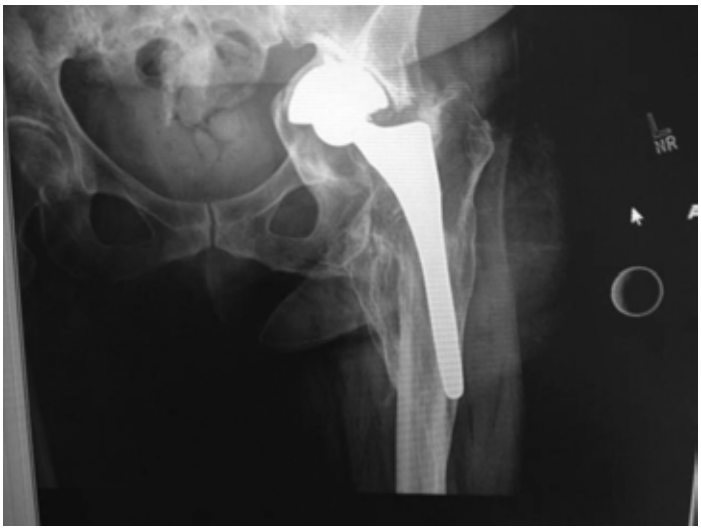

Figure 2. AP Pelvis x-ray of a patient with an "up and in" Paprosky IIIB defect without a chronic pelvic discontinuity. The stem is also malpositioned and will require revision.

Following adequate exposure, implant removal should be executed in a manner which minimizes iatrogenic bone loss. At this stage in the procedure, the surgeon can determine whether an isolated acetabular revision is indicated. The proceeding discussion will focus specifically on isolated acetabular revisions with porous tantalum shells and modular porous metal augments for severe acetabular bone loss.

Intra-operative assessment of acetabular bone loss begins with debriding the acetabular fossa. In cases of massive bone loss (such as Paprosky Type IIIA and IIIB defects), surgeons must orient themselves by identifying the true hip center using the location of the transverse acetabular ligament.[25] In cases when the TAL is difficult to identify, the inferior margin of the acetabulum can be located with the use of intra-operative fluoroscopy. For the purpose of this paper, we assume a chronic pelvic discontinuity is not present intra-operatively. However, this must be ruled out in all cases of acetabular revision when bone loss is encountered.

Type I and most Type II defects seldom require the use of modular porous metal augments, and can be treated successfully with a hemispheric component alone. However, Type IIIA and IIIB defects typically require additional structural support. Type IIIA defects are often reconstructed with uncemented, porous hemispheric implants combined with a modular, porous metal augments or a structural allograft. Type IIIB defects lack both anterosuperior and posteroinferior column support. An uncemented acetabular device must be used in some capacity with either a reconstruction cage, modular porous metal augments, or structural allograft.[10,11,26]

What is the function of your augment?

Revision acetabular reconstruction is executed with four key principles: (1) establishing intimate contact between the implant and host bone; (2) creating a stable construct with minimal micromotion; (3) implanting a construct that adequately distributes physiologic load to the remaining host

acetabular bone stock; and (4) achieving biologic fixation of the construct.[25]

Importantly, modular porous metal augments must serve a specific function. *Sheth et al.* described the use of augments to fall into two broad categories based on their function: primary stability vs supplemental fixation. The authors explain that an augment provides primary stability when used to address intracavitary defects, and provides supplemental fixation for extracavitary defects.[27] Intracavitary defects are those which directly involve the anterosuperior and/or posterorinferior columns of the acetabulum.

Extracavitary defects involve the posterosuperior wall or dome. (Figure 3.) The function of the augment will determine whether the augment should be placed prior to or following cup insertion. All augments should be unitized to the cup with cement.

Acetabular Revision for a Paprosky IIIA Defect using Tantalum/Porous Metal Cups and Augments.

The surgeon should initiate the reconstruction with sequential hemispheric reaming on reverse in the anatomic location of the native hip center. Reaming is performed until interference fit of the reamer is achieved between the anterosuperior and posteroinferior columns. If there is adequate support, a tantalum acetabular revision shell can be opened and implanted in the appropriate version and inclination. Adjuvant screw fixation with 4-5 screws with good purchase is required, and 1-2 screws should be placed in the ischium and/or superior pubic ramus to avoid abduction failure of the construct.

Attention should then be turned to the location of the defect where an augment is appropriate. In the case of an "up and out" Paprosky IIIA defect, the defect is superolateral, and the augment here will provide supplemental fixation. (Figure 4) Once a satisfactory fit between both the augment and the acetabulum has been achieved, the augment should be secured with screws and unitized to the cup with polymethylmethacrylate (PMMA) cement.[25]

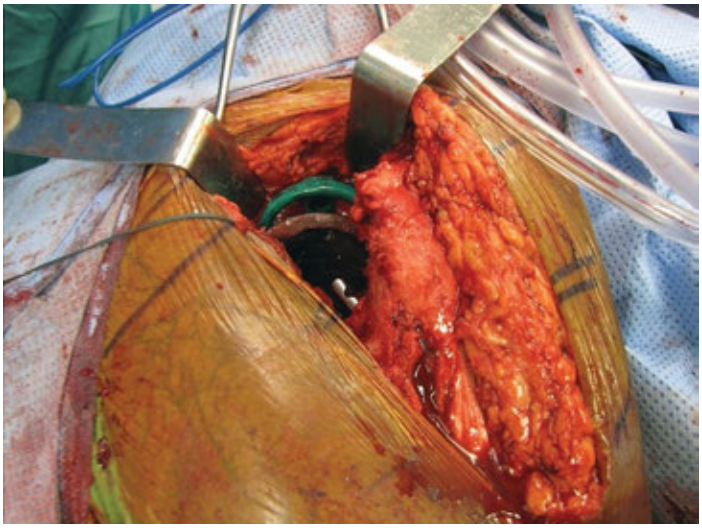

Figure 3. Intra-operative image demonstrating a posterosuperior trial augment in place. The real augment will provide supplemental fixation to the overall construct, is placed after the cup is inserted, and is unitized to the cup with cement.

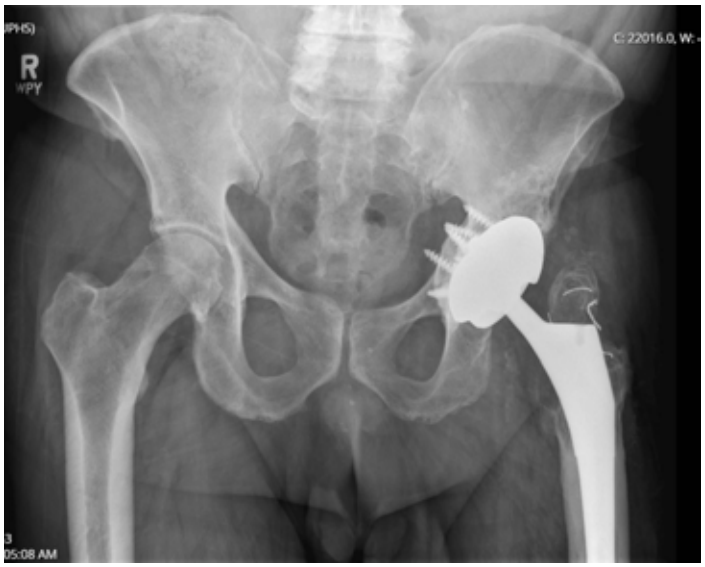

Figure 4: AP Pelvis x-ray of the patient in Figure 1 at 24 months following reconstruction of the Paprosky IIIA defect. The defect was reconstructed with a porous tantalum shell with a modular porous metal augment posterosuperiorly.

Acetabular Revision for a Paprosky IIIB Defect using Tantalum/Porous Metal Cups and Augments

Paprosky IIIB defects represent the most severe acetabular bone loss patterns. These defects are commonly referred to as "up and in" defects exhibiting >60% loss of acetabular bone stock. Following acetabular exposure, and ruling out a chronic pelvic discontinuity, the reconstruction begins with reverse reaming at the anatomic location of the acetabulum. Due to the degree of anterosuperior column bone loss, an augment is typically needed to reconstruct the anterosuperior column. In the setting where the cup being implanted is larger than 66 mm, an augment can be placed anterosuperiorly for intracavitary reduction which decreases the acetabular size by 1 cm and brings the hip center inferior and lateral—closer to the native hip center.[25,27] In cases with massive defects, two augments may be placed into the defect prior to cup insertion; this is known as the Dome technique.[28]

Augments provide primary stability to the overall construct when placed for the purpose of reconstructing the anterosuperior column. (Figure 5.) The augment is secured with screws, and a reamer is used to ream on reverse between the augment and the host posteroinferior column. Once interference fit is achieved between the reconstructed anterosuperior column and the native posteroinferior column, the reamer disengages from the reamer handle and can be used as a surrogate cup.

Once the cup size has been chosen, cement should be placed on the augment interface where it will contact the cup. Following cup insertion in the appropriate position, adjuvant screw fixation with 4-5 screws and at least 1-2 inferiorly placed screws (i.e., "kickstand" screws) should be performed, with the latter serving to prevent abduction failure of the cup.

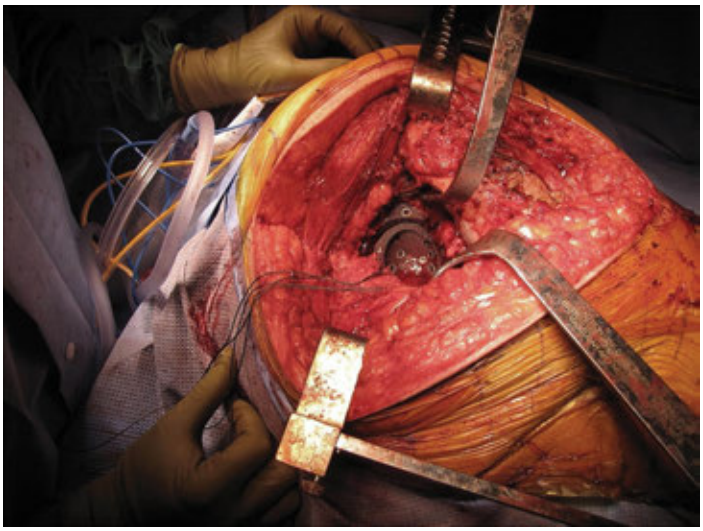

Figure 5. Intra-operative image demonstrating an augment used to reconstruct the anterosuperior column. The augment will provide primary stability to the overall construct, is placed prior to cup insertion, and is unitized to the cup with cement.

Appropriate sites for kickstand screw insertion include the ischium and superior pubic ramus. At this time, a decision is made whether a posterosuperior augment is needed for supplemental fixation. If adjuvant screw fixation is inadequate due to the amount or integrity of the residual bone stock, an augment for supplemental fixation should be used. (Figure 6)

For supplemental fixation, an "orange slice" augment is placed posterosuperiorly against host bone. The augment is secured with screws placed across the dome of the acetabulum. PMMA cement should be interposed between the augment and the hemispheric cup interface. For both Paprosky Type IIIA and Type IIIB defects, a liner is cemented into position. In both cases, cementation will create a locked construct less prone to failure.

Post-Operative Management

Patients should receive appropriate perioperative antibiotics at the time of surgery. We recommend obtaining tissue cultures at the time of revision. Patients are kept touchdown weightbearing for ± weeks and then advanced to 50% weightbearing for an additional ± weeks. At 12 weeks, patients are typically advanced to weightbearing as tolerated if they have demonstrated no interval change in component position on serial, post-operative radiographs.

Summary of Clinical Outcomes

Outcomes for rTHA for Paprosky IIIA and IIIB defects with uncemented porous cups and augments have been encouraging. The majority of studies over the past decade report excellent survivorship with short to mid-term follow up.[29-35] The results with this technique, when accounting for all causes (infections, recurrent dislocations, periprosthetic fractures etc.), demonstrate a low failure rate (< 10%). When looking at failure rates specifically for aseptic loosening, survivorship has been reported as high as 100% at the short to mid-term follow-up.[30-35]

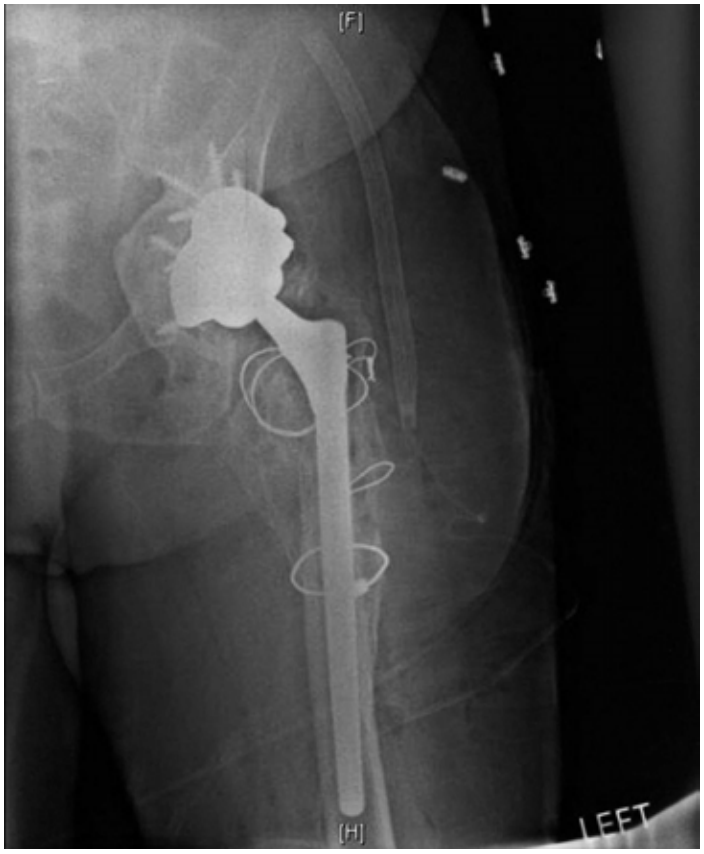

Figure 6. AP hip x-ray of the patient in Figure 5 immediately following reconstruction of the Paprosky IIIB acetabular defect and femoral stem revision. The reconstruction was performed with a tantalum revision shell and a posterosuperior modular porous metal augment for supplemental fixation.

Similar clinical success was also observed in studies with mid to long-term follow-up. Most recently, *Lochel* et al. presented their findings in 31 patients with 10 year follow-up and reported 92.5% survivorship of the acetabular component.[36] The rate of revision for aseptic loosening in this cohort was 5.6%, with failures attributed to poor screw fixation. Two of these failures required acetabular revision for a chronic pelvic discontinuity.

Jenkins et al. also published similar results in 2017 after following 28 and 22 Paprosky Type IIIA and IIIB acetabular defects, respectively.[38] They reported 100% survivorship at 5 year follow-up, and 97% at 10 years with aseptic loosening as the primary endpoint. It should be noted that of the two failures, one did not utilize the described technique with multiple screws and PMMA cement between the augment and the acetabular shell– this may suggest further support for the technique we describe in this chapter. The authors reported decreased survivorship at 7 years in hips with an associated chronic pelvic discontinuity.

The study with the greatest number of combined Paprosky IIIA and IIIB defects was performed by *Grappiolo* et al. They reported on 42 Type IIIA and 13 Type IIIB defects and demonstrated 96.4% and 92.8% survivorship at 2 and 5 years, respectively. Of the four acetabular revisions, three were due to aseptic loosening and 1 one was due recurrent instability.

Table 1. Reported outcomes for the use of uncemented porous cups and augments for Paprosky III (A&B) acetabular bone loss

Author	Year	N	Defect Type	Mean Follow up	Outcome
Lochel J.[36]	2019	53	22 IIIA 9 IIIB	10 years	92.5% survivorship at 1 years. 3 aseptic loosenings believed to be from in adequate screw fixation
O'Neill, C.J.[29]	2018	38	29 IIIA 9 IIIB	36 months	3 revisions: 1 for deep infection. 2 for aseptic loosening. Four of the IIIB defects exhibited pelvic discontinuity.
Eachempati, K.K.[30]	2018	41	36 IIIA 5 IIIB	39.4 months	100% survivorship. In one patient, augments were used to provide both primary stability and supplemental fixation.
Jenkins, D.R.[38]	2017	58	28 IIIA 22 IIIB	5 year minimum	2 revisions (3%): 1 of which had pelvic discontinuity
Flecher X. [39]	2017	51	7 IIIA 5 IIIB	6.8 years	16 of the 51 hip constructs used augments. 1 patient required revision for septic loosening. 100% survival for aseptic loosening at 64 months. Global survivorship was 92.3% at 64 months.
Grappiolo, G.[37]	2015	55	42 IIIA 13 IIIB	53.7 months	Survival rate at 2 and 5 years was 96.4% and 92.8%. Four (7.3%) of 55 hips underwent acetabular components revision: three cases of loosening (5.4%), and one of recurrent instability (1.8%) were reported
Meneghini, R.M.[31]	2015	8	7 IIIA 8 IIIB	16.5 months	No failures reported
Butayong E.D.[32]	2014	24	19 IIIA 3 IIIB 2 PD*	37 months	2 failures due to septic loosening. 92% still demonstrated osteointegration.
Molicnik, A.[33]	2014	25	6 IIIA 3 IIIB 1 PD*	20.5 months	100% survivorship with respect to aseptic loosening
Abolghasemian, M.[40]	2013	34	18 minor column defect 14 major column defect 2 PD*	64.5 months	3 cases of aseptic loosening, 2 of which had PD at time of revision
Gehrke, T.[41]	2013	46	18 IIIA 28 IIB	46 months	2 of these hips demonstrated aseptic loosening, both of which were IIIA defects.
Del Gaizo D.J.[42]	2012	37	37 IIIA	60 months	One patient underwent revision for aseptic loosening. 7 were revised for periprosthetic femur fracture; 3 for infection; 2 for recurrent dislocation
Davies, J.H.[43]	2011	46	21 IIIA 11 IIIB 4 PD	50 months	100% Survivorship with respect to aseptic loosening
Flecher, X.[44]	2010	72	23 IIIA 8IIIB	4 years	100% Survivorship with respect to aseptic loosening
Van Kleunen, J.P.[34]	2009	97	19 IIIA 16 IIIB	45 months	100% Survivorship with respect to aseptic loosening
Weeden S.H.[35]	2007	43	33 IIIA 10 IIIB	2.8 years	26 constructs had augments, 10 of which had pelvic discontinuity. 1 failure due to loosening due to sepsis (98% survivorship).

Even in the face of such positive results, the majority of these studies fail to distinguish isolated Type IIIA and IIIB defects from defects with an associated chronic pelvic discontinuity. This is an important distinction which may dictate the use of an alternative technique for acetabular reconstruction rather than those described in this chapter. In 2018, *Eachempati* et al. studied isolated IIIA and IIIB defects without an associated chronic pelvic discontinuity in 41 patients.[30] They reported 100% survivorship at mean 39.4 months follow -up. This study reinforces the concept of considering isolated Paprosky IIIA and IIIB defects and those with an associated chronic pelvic discontinuity as separate entities. It also illustrates the effectiveness of the techniques described in this chapter, assuming patients have been properly indicated.

Summary

In this this chapter, we detailed key principles of evaluating and surgically managing acetabular bone loss. We identify two severe acetabular defect patterns, Paprosky IIIA and IIIB without pelvic discontinuity, as indications for the use of tantalum/porous hemispheric cups and augments. While these augments come in various shapes and sizes, the ultimate use of these augments depend on their function. When appropriately employed, uncemented porous metal cups and augments may serve as powerful tools for improving revision THA outcomes. Although longer term clinical studies are needed, available data on the use of this technique in the setting of severe acetabular bone loss is very promising.

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Foot and Ankle

Foot & Ankle Tips & Tricks: Posterior Ankle Pain After Ankle Sprain: Bony and Soft Tissue Impingement

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Introduction

Ankle sprains are one of the most common musculoskeletal injuries in participants of a wide range of activity types and sports. Likely due to their high prevalence and favorable prognosis, ankle sprains are often regarded as benign injuries. However, these injuries can lead to persistent pain and functional compromise. The incidence of residual symptoms after an acute ankle sprain is variable but has been reported with rates of between 40% and 50% leading to decreased performance, absence from competition in sports, occupational absence and difficulties with activities of daily living.[1,2] Posterior ankle pain after ankle sprains has been less highlighted in the literature. Persistent posterior ankle pain can develop by overuse, repetitive plantar flexion, or a traumatic event, often combined with certain anatomic features, that can lead to impingement symptoms.

Pathoanatomy

Pathoanatomic features developing posterior ankle impingement can be divided into two categories: Bony structures and soft tissue structures. The bony structures responsible for posterior ankle impingement include os trigonum or Stieda's process, also known as trigonal process, of the talus. The incidence of os trigonum of talus has been reported between 5% and 11% but Peace et al reported a prevalence rate of 30% in ballet dancers.[3,4] This structure is usually asymptomatic, but it can become symptomatic after an injury, especially in individuals participating in sports requiring repeated ankle plantar flexion. A Stieda's (trigonal) process of the talus is an abnormal elongation of the lateral tubercle of the talus and may cause symptoms similar to os trigonum.

The soft tissue structures related to posterior impingement include tendon problems such as flexor hallucis longus (FHL) tenosynovitis, posterior ankle joint capsule injury, and posterior ligament injury. FHL tendon is a secondary stabilizer of the ankle when the ankle is in full plantar flexion. It traverses the fibro-osseus groove between the lateral and medial posterior talar tubercle. It then coursed under sustantaculum tali of the calcaneus. Because of this anatomic relation, repetitive plantar flexion places constant pressure on the FHL tendon leading to tenosynovitis. In the setting of FHL tenosynovitis, various symptoms including pain and the ankle instability may stimulate posterior ankle impingement. Posterior capsular or ligament injuries can occur from repetitive hyperplantar flexion of the ankle. This repetitive microtrauma promotes fibrosis and thickening of these soft structures.[5]

Furthermore, soft tissue posterior impingement can be divided according to the location of the impingement. Posteromedial impingement most commonly arises from repetitive inversion injury with the ankle plantar-flexed. In this setting, the hypertrophic fibers of the posterior tibiotalar ligament are entrapped in the posteromedial ankle gutter. An eversion injury including a tear of the posterior tibiotalar ligament is a less common mechanism of posteromedial impingement. Koulouris et al demonstrated that the hypertrophied ligament can come in contact with the flexor tendons and partially encase the tibialis posterior (40% of cases), the FHL (16%), or the flexor digitorum longus (8%). Accessory muscles can also be associated with posterior ankle pain but much less frequently. Peroneous quartus muscle is the most common of these muscles with a reported prevalence of 7% to 22%. Additionally, an accessory flexor digitorum longus and a low FHL muscle belly can also be sources.[6–8]

Diagnosis

The diagnosis of posterior impingement is based primarily on clinical history and physical examination. Typically, patients complain of chronic or recurrent posterior ankle pain that is associated with forced plantar flexion or push-off activities. For dancers, the pain usually develops when they are in a relevé position, whether full-pointe or demi-pointe. For kicking sports, such as soccer, pain occurs while kicking the ball that requires the ankle in a hyperplantar flexed position. Any history of injury or overuse of the

ankle joint must be considered. On physical examination, pain is usually deep and there is tenderness at the posteromedial or posterolateral aspect of the ankle. Posterior ankle pain that is reproduced with passive maximal planar flexion indicates posterior ankle impingement. This is known as a positive "plantar flexion test." If passive hallux dorsiflexion motion with the ankle held in full dorsiflexion reproduces pain, then FHL tendon abnormality such as tenosynovitis may also exist. Os trigonum or Stieda's (trigonal) process pain is more often posterolateral, whereas FHL tendon problems are more posteromedial.Athletes affected by posterior ankle pain tend to have inversion motion of the foot to compensate for the loss of plantar flexion. This may increase the risk of ankle sprains, calf strain, and toe curling.

Weight-bearing plain radiographs of the foot, anteroposterior, lateral, and oblique views should be obtained. A lateral radiograph is essential to detect the presence of an os trigonum and an acute or chronic fracture of Stieda's (trigonal) process. In addition to standard radiographs, a weight-bearing lateral radiograph with the ankle in maximum plantar flexion will be helpful in investigating the likelihood of posterior impingement. However, the presence or absence of os trigonum or Stieda's (trigonal) process on a plain radiograph may not necessarily suggest clinical symptoms.

Magnetic resonance image (MRI) may reveal bone marrow edema in the os trigonum or Stieda's (trigonal) process and signal changes of posterior ankle representing inflammation and scarring of the adjacent soft tissue. Other findings such as FHL tenosynovitis or chondral injury of the posterior talus can be detected on MRI. It also provides information to determine the origin of posterior ankle pain between bony and soft tissue impingement.[9,10] Dynamic ultrasound can be useful to further evaluate posterior ankle pain. It may provide valuable information about soft tissue versus bony impingement related to posterior ankle pain through its dynamic evaluation. FHL tenosynovitis with intrasheath fluid can be detected. In addition to finding pathoanatomic structures, a local anesthetic injection can be performed under the guidance of ultrasound, which may also have diagnostic value. Computed tomography is helpful to evaluate osseous structures causing posterior impingement and to identify the presence of nondisplaced or minimally displaced fractures. Zwiers et al reported a prevalence of 30.3% in patients without posterior impingement complaints with computed tomography imaging, which is more common than previously reported (Figure 1). [11]

Treatment

The initial treatment of posterior ankle pain after ankle sprain is nonoperative and have been shown to be effective. Nonsurgical treatment includes rest, ice, medication such as nonsteroidal anti-inflammatory drugs, and avoidance of activity requiring ankle plantar flexion. Corticosteroid and anesthetic injections are also options for symptomatic relief. Mouhsine et al reported that these injections provided pain relief in 84% of cases in their study.[12] Hedrick and McBryde demonstrated that such nonoperative treatment had a success rate of 60% for posterior ankle impingement in their over 10-year follow-up study.[13] They utilized ice, rest, anti-inflammatory medications and avoidance of forced plantar flexion and local steroid

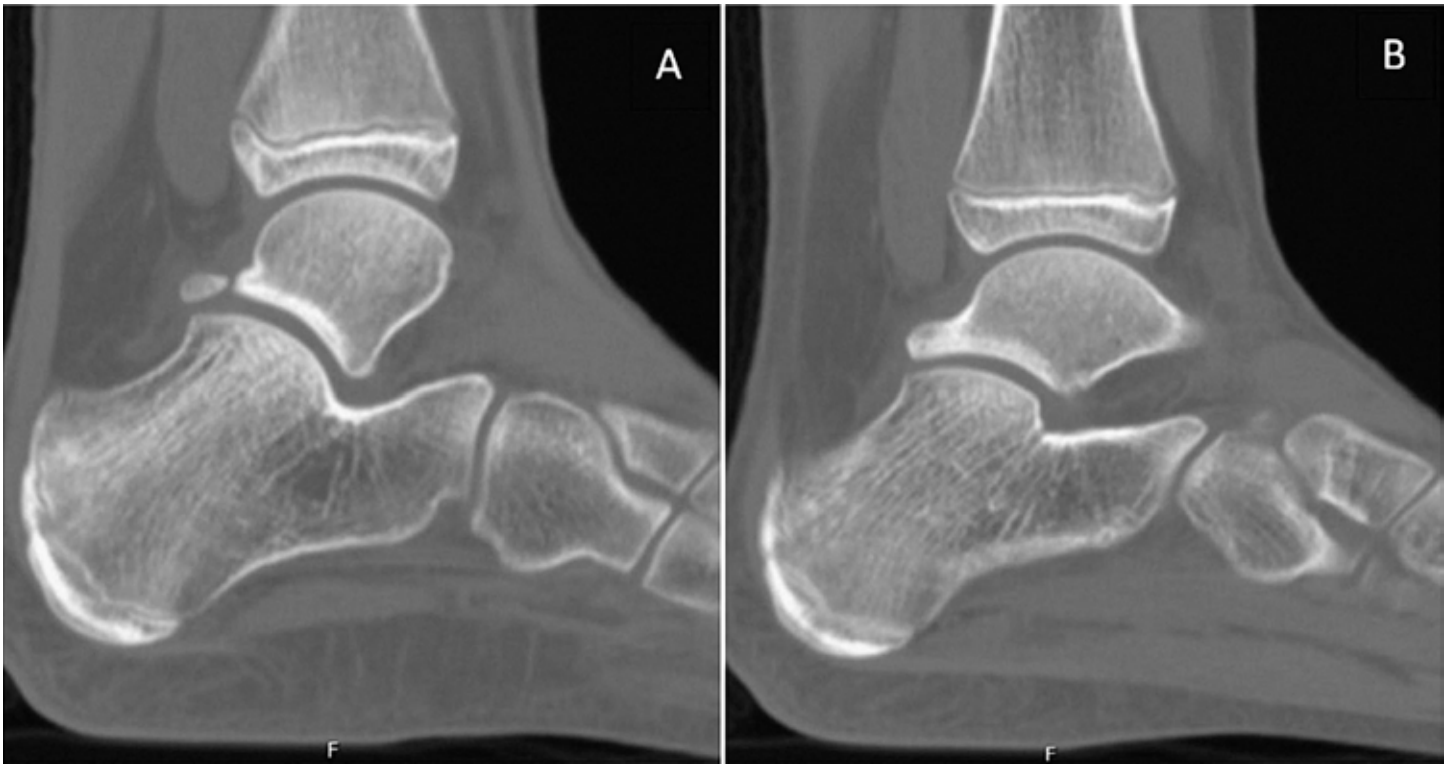

Figure 1. CT findings for posterior impingement. (A) Os trigonum of the talus; (B) Posterior process (also known as trigonal process) of the talus.

injection or temporary immobilization in a short leg walking cast in some individual cases. Albisetti et al described a nonsurgical treatment regimen for managing posterior ankle impingement in ballet dancers.[14] They restricted demi-pointe and en pointe work until the pain subsided and prescribing anti-inflammatory medication. Proprioception exercises can also strengthen and stretch the deep lower leg muscles. Nine out of 12 dancers returned to normal dancing and 3 underwent operative intervention. However, the authors indicated that it was not easy for professional athletes or dancers to take time off for conservative management. Coetzee et al suggested a treatment strategy for these professional athletes.[3]co A controlled ankle motion boot can help to treat the posterior ankle impingement if it is possible for the athlete to rest for a few weeks. Nonsteroidal anti-inflammatory drugs can be used at the same time. A dance rehabilitation program can start once the patient is able to walk pain free. They recommended a fluoroscopically guided cortisone injection if the flare-up occurs during performance season when taking time off is not possible.

Operative intervention can be considered if pain persists despite nonsurgical treatment, particularly in the athletes or dancers who want to continue training and performing. In addition, a study has shown that once there is a symptomatic osseous impingement, it seldom resolves completely without operative management. Open excision of an os trigonum is traditional and can be performed using a posteromedial or posterolateral approach. Hedrick and McBryde reported that open excision of a symptomatic os trigonum provided good to excellent results in 88% of patients in their case series.[13]

An open posteromedial approach can be used to manage posterior ankle pathology, including excision of os trigonum or Stieda's (trigonal) process. FHL tendon can be easily accessed with this approach, as many patients with posterior ankle impingement are dancers. For this approach, the patient is positioned supine with a bump under the opposite hip to externally rotate the involved leg. Most dancers have more external rotation than internal rotation in their hips, making positioning more difficult for a posterolateral approach. This is one of the advantages of using an open posteromedial approach in dancers. A thigh tourniquet is used. An incision is made centered at the os trigonum along the posteromedial ankle. The interval between flexor digitorum longus (FDL) tendon and the neurovascular bundle is used. The laciniate ligament is carefully incised. The neurovascular bundle is retracted posteriorly, and FHL tendon is identified. The sheath for the FHL tendon is routinely released to ensure that there is no stenosing tenosynovitis or impingement. If there is tenosynovitis or tear along the FHL tendon, tenosynovectomy is performed and tear of FHL is repaired. The FHL tendon is then retracted posteriorly to expose the os trigonum or Stieda's (trigonal) process. It is mobilized using a freer elevator and dissecting scissors from the surrounding tissue. The os trigonum is then removed. The Stieda's (trigonal) process of the talus is then excised using a narrow osteotome if needed. The ankle is then placed into full plantar flexion to confirm that there is no further evidence of impingement.

Some surgeons prefer the posterolateral approach as this approach is safer and easier than the posteromedial approach. The patient is in the supine position with a bump placed under the affected leg to provide adequate access to the lateral ankle. A thigh tourniquet is used. Incision is made behind the lateral malleolus. The sural nerve and its branches are carefully identified and pro- tected. An interval between the Achilles tendon and peroneal tendon is used. The posterior ankle capsule is incised, and os trigonum or Stieda's (trigonal) process are identified. They are resected completely using a freer elevator and osteotome. The FHL tendon needs to be assessed and careful inspection is required. If there is any pathology along the FHL tendon such as a low muscle belly, synovitis or nodules, or tear, then the tendon should be debrided and addressed adequately.

A third option is a posterior arthroscopy to manage posterior ankle pathology including os trigonum. The authors described their arthroscopic procedure with a step by step instruction. The procedure is performed in a prone position with 2 posterior portals: posterolateral and posteromedial. The posterolateral portal is made adjacent to the lateral border of the Achilles tendon at the level of the lateral malleolus; the posteromedial portal is created on the medial border of the Achilles tendon. An arthroscopic shaver is always with the blade facing away from the neurovascular bundle, lateral to FHL tendon. A pituitary rongeur is used to remove the os trigonum. With this arthroscopic approach, periarticular pathology such as calcification or scar tissue and pathology of the posterior ankle/subtalar joint can be diagnosed and treated. Arthroscopic procedure for posterior ankle pathology has demonstrated good results with low complication rates and early return to sports activities. Scholten et al also demonstrated that endoscopic treatment of posterior ankle impingement yielded satisfactory results comparable with the results of open surgery reported in the literature.

Comparison amongst the three procedures remains a challenge as there has not been a shared standardized outcome measurement applied all three techniques. There are only a few open surgery studies using the AOFAS scoring system. Most papers have their own nonvalidated rating system such as poor-fair-good-excellent. In 2010, Gou et al compared clinical outcomes and time to return to activity between open and endoscopic removal of the os trigonum. The posterolateral open approach was used, and the endoscopic technique described by Van Dijk was adopted in their study. They showed no difference between the 2 methods in clinical outcomes. However, patients who underwent endoscopic excision had a shorter time to return to previous sports.

Conclusion

Improper diagnosis and inappropriate treatment of posterior ankle impingement can result in persistent and chronic pain, resulting in reduced mobility and function in daily living activities and returning to sports. Posterior ankle pain is usually developed by an overuse injury or ankle trauma in patients performing repetitive forced plantar flexion

sports, often combined with specific anatomic features at the posterior talus that can cause bony and soft tissue impingement. Understanding clinical history and various causes of posterior ankle impingement is critical for proper diagnosis and proper treatment. Though most patients will improve with nonoperative management, surgeons have multiple approaches available that have shown to be effective if a patient's symptoms are refractory to medical management.

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Development and Validation of a Patient Decision Aid for the Treatment of Ankle Arthritis

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Introduction

Health care is shifting toward a more patient-centered paradigm as patients take a more active role in the medical decision-making process[1]. This paradigm helps promote the patient's values and autonomy. Patient decision aids have begun to play an increasingly valuable role in decision making because of their ability to increase patients' involvement and likelihood of making informed, values-based choices[2]. In the field of orthopaedic surgery, decision aids of various formats, including short online interactive tools, brochures, videos, and booklets[3], have been developed for patients with hip and knee osteoarthritis. These tools result in improved patient knowledge, higher reported shared decision making, and lower decisional conflict[3].

To our knowledge, treatment decision aids are unavailable for patients with ankle arthritis. The decision process for ankle arthritis treatment is more complex than for hip or knee osteoarthritis because it is a 2-step process. For hip or knee arthritis, the decision revolves around whether to pursue surgery, with arthroplasty being the preferred operative treatment. For ankle arthritis, the patient must first decide whether to pursue surgery and then they must decide whether to pursue ankle arthroplasty or ankle arthrodesis. The goals of our study were to develop the Ankle Arthritis Patient Decision Aid[4–6] and to validate the tool in a representative patient population. We hypothesized that the decision aid would improve patient knowledge about ankle arthritis treatment options, and that patients would consider it to be a useful tool for the decision-making process.

Methods

Development of the Decision Aid

In August 2018 and September 2021, we performed a literature review using PubMed, CINHAL, and Embase with the assistance of a medical informationist and found that no patient decision aid had been described for end-stage ankle osteoarthritis. We then created the Ankle Arthritis Patient Decision Aid on the basis of the International Patient Decision Aid Standard and the Dell Medical School's Patient Decision template[7]. The decision aid used plain language and up-to-date scientific information. The tool scored 8.9 on the Flesch-Kincaid readability test[8], meaning that a reader would require higher than an 8th grade reading level (based on the US grade levels of 1–12) to understand the tool.

Survey Methods

Eighty patients of 2 surgeons at a US academic foot and ankle practice were recruited from October 2020 to June 2021 using an electronic medical record messaging system. Participants reviewed the tool and answered survey questions that evaluated its quality and factors affecting treatment choice in a hypothetical patient scenario in which they were asked to imagine they had advanced ankle osteoarthritis. We evaluated the tool decisional conflict scores on the Low Literacy Decisional Conflict Scale questionnaire[9] (maximum, 40 points, with higher scores indicating greater uncertainty), pre- and post-knowledge test scores (maximum, 8 points), and helpfulness scores (maximum, 7 points). We compared pre- and post-test knowledge scores using paired Student t-tests. Alpha = .05. Participants were provided with a free-response space at the end of the survey to provide additional, open-ended feedback on the decision aid.

Results

Knowledge Scores

The mean (± standard deviation) knowledge scores improved from 4.8 ± 1.2 (pre-test) to 6.7 ± 1.3 (post-test). The post-test knowledge scores were significantly higher than the pre-test scores, with a mean improvement of 1.9 ± 1.4 points after participants reviewed the decision aid ($P < .001$) (Table 1).

Decisional Conflict

When presented with a hypothetical patient scenario, 57 participants chose nonoperative treatment, 12 chose ankle arthrodesis, and 11 chose ankle arthroplasty. The mean (± standard deviation) decisional conflict score was

Table 1. Treatment Choices, Decisional Conflict Scores, and Knowledge Scores for the Ankle Arthritis Patient Decision Aid

Parameter	Mean ± SD	P
Decisional conflict score[1]	4.1 ± 5.7	
Knowledge scores[2]		
Pre-test	4.8 ± 1.2	< .001
Post-test	6.7 ± 1.3	

SD, standard deviation.

[1]The decisional conflict score was calculated using the Low Literacy Decisional Conflict Scale, which consists of questions to assess choice difficulty. Higher scores indicate greater difficulty deciding decisively between treatment options (maximum score, 40 points).

[2]The knowledge score was the number of author-designed true/false questions covering the risks, benefits, and outcomes of the treatment options that each participant answered correctly (maximum score, 8 points).

4.1 ± 5.7, indicating minimal uncertainty when deciding (Table 1).

Factors Influencing Decision

The factors most frequently noted by participants as having "great" influence in their treatment choice were, "I would like to maintain a high level of activity" (73%, n = 58), "risk of surgical complications" (44%, n = 35), "recovery time" (41%, n = 33), and "risk of increased rate of arthritis in adjacent joints" (40%, n = 32) (Table 2). Factors that many participants indicated as having no influence on their choice were, "I know someone who has experienced ankle fusion" (79%, n = 63) and "I know someone who has experienced ankle replacement" (78%, n = 62) (Table 2).

Most participants in all age groups (except 75 and older) cited maintaining a high level of physical activity as a factor that greatly influenced their choice. Most participants who were greatly influenced by a desire to maintain a high level of activity chose nonoperative intervention (n = 36, 62%). Of those in this group who chose surgery, 11 (50%) chose ankle arthrodesis and 11 (50%) chose ankle arthroplasty.

Helpfulness

The mean helpfulness score was 5.9 ± 1.2. Most participants somewhat agreed (30%, n = 24) or strongly agreed (58%, n = 46) with the following statement: "The Ankle Arthritis Patient Decision Aid would be helpful if I actually had to decide between treatment options for ankle arthritis".

Decision Aid Quality

Fifty-eight participants (73%) thought the decision aid contained a balanced representation of the treatment options, and 57 (71%) found the amount of information presented to be "just right" (Table 4). Most participants (69%, n = 55) found the tool easy to understand. Twenty-one participants (26%) had medium difficulty understanding the tool. The mean quality rating was greater than 3 for each aspect of the decision aid (treatment option descriptions, advantages and disadvantages for each option, and the direct comparison of each option), suggesting that the tool contained information of good to excellent quality.

Discussion

The Ankle Arthritis Patient Decision Aid was created to support patients with advanced ankle osteoarthritis in choosing among ankle arthroplasty, ankle arthrodesis, and nonoperative treatment. Participants' knowledge of treatment options increased significantly after reviewing the decision aid, and decisional conflict was low. Factors that greatly affected participants' treatment choices included risk of complications, recovery time, risk of increased rate of arthritis in adjacent joints, and desire to maintain a high level of physical activity. Participants considered the decision aid to be helpful, unbiased, understandable, and containing high-quality information. The increase in knowledge scores, low decisional conflict scores, and overall positive evaluations of the Ankle Arthritis Patient Decision Aid support the validity of the tool.

When presented with a hypothetical scenario in which they were asked to imagine that they developed advanced ankle osteoarthritis, most participants chose nonoperative treatment. This finding is expected because nonoperative treatment is

Table 2. Common Considerations and Their Influence on Participant Decision-Making Regarding Nonoperative Treatment, Ankle Arthrodesis, and Ankle Arthroplasty for Treatment of Ankle Osteoarthritis.

Factor	Degree of Influence, N (%)		
	None	Some	Great
Recovery time	10 (13)	37 (46)	33 (41)
Risk of operative complications	8 (10)	37 (46)	35 (44)
I would like to maintain a high level of activity	6 (7.5)	16 (20)	58 (73)
I know someone who has experienced ankle replacement	62 (78)	8 (10)	10 (13)
I know someone who has experienced ankle fusion	63 (79)	10 (13)	7 (8.8)
Risk of wearing out the implant over time	16 (20)	45 (56)	19 (24)
Risk of increased rate of arthritis in adjacent joints	8 (10)	40 (50)	32 (40)

the first-line treatment for osteoarthritis[10]. Among those who chose operative treatment, similar proportions chose ankle arthrodesis and ankle arthroplasty. This similarity may suggest a need for more information regarding operative options or an indifference in opinion between the 2 choices. Of note, the factor most cited as having great influence in treatment choice was the desire to maintain a high level of physical activity. Of participants greatly influenced by a desire to maintain a high level of activity, 62% (n = 36) chose nonoperative intervention, whereas 71% (n = 57) of all participants chose nonoperative intervention. This finding suggests that patients who value physical activity may be more likely than those who live a more sedentary lifestyle to consider operative intervention. It is important for physicians to consider a patient's likelihood of returning to normal activity, as well as their goals, when evaluating treatment options.

Our study has several limitations. First, most participants were white, female, and older than 55 years, all of which may limit the generalizability of our results. However, age may be of little importance because osteoarthritis most commonly affects older individuals. Second, our recruitment of a patient population from orthopedic foot and ankle practices captures responses from individuals who likely have greater insight into and experience with foot and ankle conditions than the general population does. Third, patients who could not access the internet or read in English were excluded from the study. This exclusion also limits the generalizability of our results. Future directions for study include additional surveys targeting clinicians, patients with advanced osteoarthritis of the ankle, and patients who have undergone medical and surgical treatment for the disease. We hope to gain additional feedback regarding the breadth of information provided in the decision aid and to use it to further improve the tool. Additionally, creation of a digital form of the decision aid would improve accessibility.

Conclusions

The Ankle Arthritis Patient Decision Aid significantly improved patient knowledge regarding treatment options for ankle osteoarthritis and was considered by participants to be a helpful, unbiased, comprehensible tool that contained high-quality information. These results support the decision aid as an effective tool for helping patients with ankle osteoarthritis in their treatment decision-making process. Participants cited risk of complications, recovery time, risk of increased rate of arthritis in adjacent joints, and desire to maintain a high level of physical activity as key factors influencing their treatment selection. Providers can support patients and practice patient-centered care by recognizing patients' values and providing tools such as the Ankle Arthritis Patient Decision Aid to better inform patients of their options.

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Oncology

The Role of Imaging in the Evaluation of Suspected Bone Lesions

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Introduction

Cancer is widely recognized as one of the most devastating diagnoses in medicine. Worldwide, there was an estimated incidence of 24.5 million cancer cases, a number that is increasing year by year. (31560378) Society has invested heavily in better understanding and treating cancer, significantly increasing the lifespan of patients with malignancy.[1]

The natural course of many cancers, even with treatment, is to metastasize, and bone is the third most common site.[1] The most common carcinomas to metastasize to bone include lung, breast, prostate, renal, and thyroid; multiple myeloma also commonly affects the skeletal system. In general, metastases indicate advanced disease and are an independent risk factor for early death in cancer patients.[2] The likelihood of developing metastatic disease depends on the histologic grade of the tumor, response to treatment, and patient demographic factors. Osseous metastases can destroy the local architecture of bone, which can eventually lead to loss of cortical integrity. These lesions often result in significant morbidity for the patient and can require operative fixation. A pathologic fracture, a fracture through an osseous metastatic lesion, is associated with high morbidity and potentially loss of the patient's functional independence. Thus, metastatic lesions necessitate early diagnosis and treatment to prevent ambulatory dysfunction and further functional decline.

Primary bone tumors can be either benign or malignant. Benign bone tumors, such as osteoblastomas and non-ossifying fibromas, are a heterogenous group of tumors that can often be mistaken for malignant tumors to the untrained eye. While their true incidence is unknown, it is estimated that they are present in 30-40% of children.[3] Sarcomas, or primary malignancies of the musculoskeletal system, are much less common, with an estimated incidence of 3,910 cases per year in the United States.[4] Even with modern chemotherapy, sarcomas carry a poor prognosis, with 5-year survival ranging from 38.5% to 91.7% with an average 5-year survival of 58.9%.[5] Early diagnosis and complete resection are necessary to mitigate morbidity and mortality.

Role of Imaging in Workup of Osseous Lesions

As in other areas of orthopaedic surgery, imaging is paramount to successful diagnosis, treatment planning, and prognostication. Most primary and metastatic bone tumors can be initially detected on plain radiographs (X-rays). X-rays are diagnostic in many conditions, especially certain benign lesions and metastases in patients with other known osseous disease. Advanced imaging, such as computed tomography (CT) can be used to provide more detail about the bone involvement, particularly in metastatic disease of the pelvis. Magnetic resonance imaging (MRI) is necessary for diagnosis and surgical planning in primary bone tumors.

Plain Radiography

After a history and physical examination, X-ray is the next step in evaluating a bone lesion. In certain bone lesions, the radiographic appearance is pathognomonic, i.e., unique enough to confidently make a diagnosis without additional diagnostic tests. Such entities include unicameral bone cyst, non-ossifying fibroma, and fibrous dysplasia. Furthermore, the interpreting physician can use lesion characteristics, such as the pattern of bone loss, surrounding sclerosis, periosteal reaction, and matrix formation, to determine whether a lesion appears benign or malignant. For example, lytic lesions with a well-defined border and a sclerotic rim are slow-growing and often benign, whereas lytic lesions with a moth-eaten appearance and ill-defined borders are more likely to be malignant. Similarly, periosteal reaction can indicate an aggressive process; malignant lesions often demonstrate a laminated reaction with visible Sharpey's fibers, often also known as a "sunburst" pattern. Bone lesions with an associated soft tissue mass can raise the periosteum and lead to formation of a Codman's triangle. The matrix, or substance within an osseous lesion, can be used for diagnostic purposes. Patterns of stippling or "rings-and-arcs" formations, as seen in chondroid matrix, are common in enchondromas and chondrosarcomas; a dense but fluffy (or "cloud-like" appearance), indicating osteoid matrix, is seen in bone-forming lesions such

as osteosarcomas (see Tables 1 and 2), and a "ground glass" appearance, with absent trabeculae, characterizes fibrous dysplasia.

Computed Tomography

If plain radiographs do not provide sufficient detail of the osseous anatomy, CT scans may be helpful to better evaluate the lesion. CT is the preferred imaging modality for assessing bone defects and cortical integrity, particularly in the scapula, spine, pelvis, ribs, and chest wall. It can help determine the need for intervention (radiation, percutaneous cement injection, or open surgical stabilization) for pelvic metastases by characterizing the available bone stock. It can also be diagnostic for certain lesions, in particular osteoid osteoma, where it can visualize the pathognomonic central, lytic nidus representing a vascular structure surrounded by sclerosis and cortical thickening.

CT is also useful in cancer staging. In a patient presenting with osseous metastases and unknown primary, CT of the chest, abdomen, and pelvis can identify the origin. For a new diagnosis of sarcoma, CT of the chest is indicated to rule out metastases, which most commonly occur in the lungs. Following initial treatment, surveillance CT is often used to monitor for disease progression.

Table 1. Imaging characteristics of benign and malignant lesions of bone by age

Age	Well-defined Lytic Lesion	Ill-defined Lytic Lesion	Sclerotic Lesion
0-10	Eosinophilic granuloma Unicameral bone cyst	Eosinophilic granuloma Ewing's Sarcoma Leukemia Lymphoma	Osteosarcoma
10-20	Non-ossifying fibroma Fibrous Dysplasia Osteofibrous Dysplasia Eosinophilic granuloma Unicameral bone cyst Aneurysmal bone cyst Chrondroblastoma Chondromyxoid fibroma	Ewing's Sarcoma Eosinophilic granuloma Osteosarcoma	Osteosarcoma Fibrous Dysplasia Eosinophilic granuloma Osteoid osteoma Osteoblastoma
20-40	Giant cell tumor Enchondroma Chondrosarcoma Brown Tumor Osteoblastoma	Giant cell tumor Malignany fibrous histiocytoma	Enchondroma Osteoma Bone island Parosteal osteosarcoma Healed prior lytic lesions
40+	Metastases Multiple myeloma Geode	Metastases Multiple myeloma Chondrosarcoma	Metastases Bone island

Table 2. Common Benign versus Malignant Tumors by Site

Site	Benign	Malignant
Diaphysis	Fibrous Dysplasia Enchondroma Osteofibrous dysplasia	Adamantinoma Ewing's Sarcoma Periosteal osteosarcoma Lymphoma
Metaphysis	Non-ossifying fibroma Aneurysmal bone cyst Unicameral bone cyst Enchondroma Osteoid Osteoma Osteoblastoma	Osteosarcoma Malignant fibrous histiocytoma Lymphoma
Epiphysis	Chondroblastoma Giant cell tumor Osteomyelitis	Chondrosarcoma
Multiple	Eosinophilic granuloma Fibrous dysplasia Hemangioendothelioma Enchondroma Osteochondroma Osteochondroma Non-ossifying fibroma Multiple hereditary exostoses Ollier's Syndrome Maffucci's Syndrome Jaffe-Companacci Syndrome Paget's Disease Hyperparathyroidism Bone infarcts	Leukemia Lymphoma Metastatic disease Multiple Myeloma

Magnetic Resonance Imaging

MRI is the diagnostic method of choice when locally staging musculoskeletal tumors due to its high resolution and ability to differentiate between tissue types based on proton density signatures. The high spatial resolution of MRI allows it to best identify soft tissue involvement and the tumor's anatomic relationship to important structures such as nerves and arteries. Different MRI sequences are available to better identify different tumor components. T1 weighted sequences provide the best view of anatomy, with water represented as low intensity, muscle as intermediate intensity, and fat as high intensity. T2 weighted sequences allow for better identification of pathology, including edema surrounding a tumor, with fluid detected as high signal intensity. Since fat is also represented with a high signal intensity on T2 sequences, tumors with a high fatty component (e.g. liposarcomas) or adjacent to areas of high fat density can be visualized using fat suppressed (FS) T2 weighted sequences. It is important to recognize that large areas of edema can be seen in both benign and metastatic lesions. While MRI is particularly useful in the diagnosis of primary bone lesions and operative planning, it is rarely indicated for metastatic lesions; in these situations, X-ray or CT is often all that is required for operative planning.

Cases Demonstrating Judicious Imaging Use

Case 1

A 74-year-old female presented to the orthopaedic oncology clinic as a referral from radiation oncology for evaluating of right thigh pain. Past medical history significant for stage IV non-small cell lung carcinoma status post multiple rounds of radiotherapy and chemotherapy. X-ray demonstrated a well-circumscribed lytic lesion within the anterior cortex of the femoral diaphysis, worrisome for an impending pathologic fracture (Figure 1). No further imaging was needed to determine the diagnosis or treatment plan, and the patient successfully underwent intramedullary nail fixation.

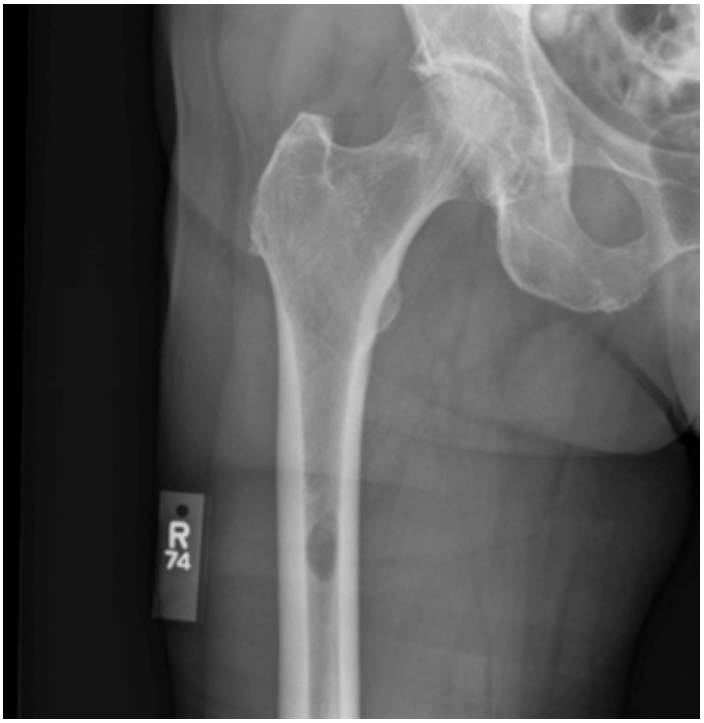

Figure 1. Lytic lesion located in the femoral diaphysis. Not shown is the lateral film indicating the lesion was within the anterior femoral cortex.

Case 2

An 84-year-old male presented to the orthopaedic oncology clinic with hip pain of 3 months duration that started while playing golf. His medical history includes multiple myeloma with osseous involvement, currently on pembrolizumab. X-ray demonstrated a known iliac lytic lesion with new extension into the superior acetabulum. Given the patient's lesion location in the pelvis, a CT scan was obtained to visualize the bone in more detail (Figure 2). This CT demonstrated an intact acetabulum with enough residual bone to attempt percutaneous stabilization with cement injection rather than open pelvic reconstruction.

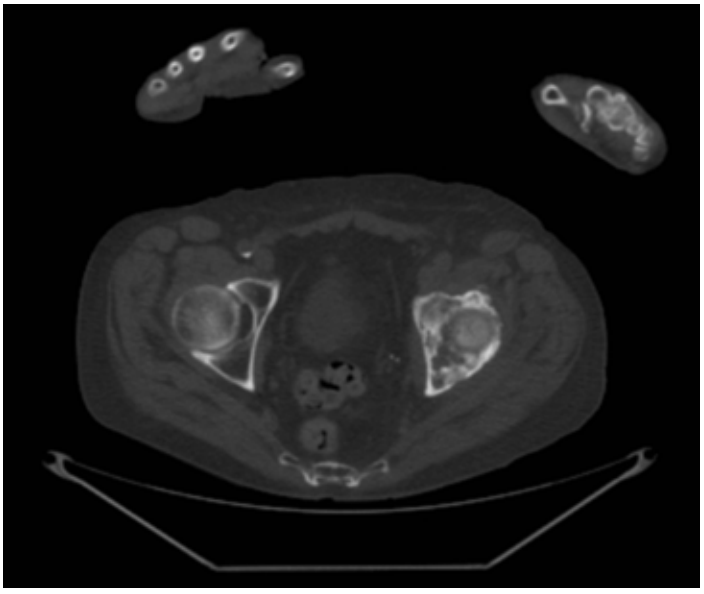

Figure 2. Destructive lesion of the left ilium extending down to the superior aspect of the left acetabulum. CT imaging indicated given the complex anatomy of the pelvis and possible percutaneous palliative treatment options.

Case 3

A 59-year-old male was referred for new diagnosis of a biopsy-proven dedifferentiated bone sarcoma of his right pelvis. MRI was ordered to determine the precise extent and location of the tumor, as well as proximity to critical surrounding structures. Based on the results, the surgical team determined that an internal hemipelvectomy would be necessary to achieve wide resection. (Figure 3).

Conclusion

Primary and metastatic bone lesions represent a significant morbidity and mortality, necessitating expedient and accurate diagnosis while avoiding subjecting the patient to unnecessary

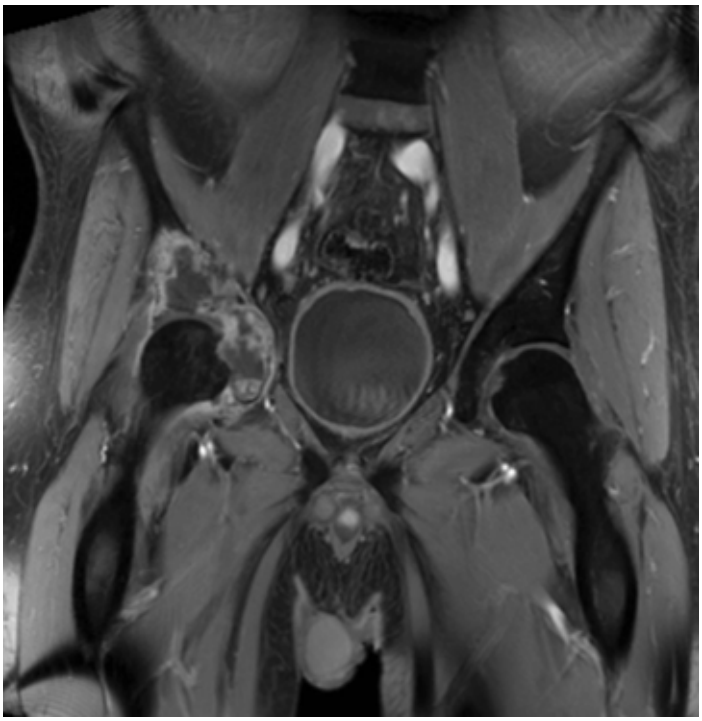

Figure 3. Post contrast fat suppressed T1 MRI with locally aggressive sarcoma within the right pelvis. Note that fluid is dark on a T1 sequence, but contrast shortens tissue relaxation times and thus increases signal, as seen in the edema and vascularity surrounding the right pelvic lesion.

tests. XR is routinely used in initial workup, and CT may be useful to provide further detail of osseous destruction. MRI is typically reserved when necessary for diagnosis and treatment planning of primary bone lesions.

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Orthoplastics

Orthoplastics Tips & Tricks: Free Lateral Arm Flap for Reconstruction of the Hand Following Traumatic Injury: A Case Presentation

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Introduction

Upper extremity injuries are extremely common, with an estimated incidence of over 1,000 per 100,000 persons per year.[1] While many of these injuries can be easily managed, large or complex injuries of the hand and upper extremity may require advanced reconstruction by a subspecialist. Defects following burns, infection, or tumor removal pose similar concerns. Critically important structures such as bone, tendon, blood vessels, and nerves are often exposed, and may benefit from free tissue transfer. While there are many options available for soft tissue coverage, each has unique advantages and disadvantages. When choosing an adequate flap or graft, the surgeon must take into account the size and location of the zone of injury, complexity of the injury, status of the surrounding tissue, exposure of the vital structures, and health status of the patient as well as smoking and nutrition status.[2] Other important factors include operative time, constant vessel anatomy, and donor site morbidity. The goal is to optimize reconstruction of form, function, and aesthetics for the patient.

Free tissue transfer provides the surgeon with vascularized soft tissue coverage as well as the option for bone, nerve, and tendon transfer. There are many free tissue options available for upper extremity defects including the groin flap, anterolateral flap, radial forearm flap, scapular flap, and lateral arm flap.[2,3] Because it tends to be thin and supple, the free lateral arm flap is an attractive choice for soft tissue covering around the hand and distal forearm.

The free lateral arm flap was first described by Song et al. in 1982 as a septocutaneous flap.[4] It was further popularized by Katsaros et al as a highly dependable free flap for small to moderate size tissue defects, known for its versatility with the option to raise the flap on its own, with underlying tendon, with bone, or with fascia only.[5,6] The lateral arm tissue can also be used as a sensate flap given its innervation by the posterior brachial cutaneous nerve.[7]

Here we discuss the case of an 18-year-old patient who required reconstruction and soft tissue augmentation of his first web space after a traumatic injury left him with a contracture that limited the function of his dominant hand. A fasciocutaneous lateral arm free flap was selected to provide a durable and supple surface to his first webspace after contracture release and thereby optimize the functional outcome of his hand reconstruction.

Case Report

An 18-year-old right hand dominant male patient with no significant past medical history was referred to our clinic after sustaining a traumatic injury to the right hand in an ATV accident one year prior. At the time of injury, he suffered a Bennett's fracture of the right thumb, open transverse fractures of the index, long, ring, and small finger metacarpals and concomitant partial degloving of the hand (Figure 1). Prior to presentation to our clinic the patient had undergone multiple procedures on his right hand, including pinning of the metacarpal fractures with Kirscher wires (**Figure 2)**, hand fasciotomies, and skin grafting to the volar hand.

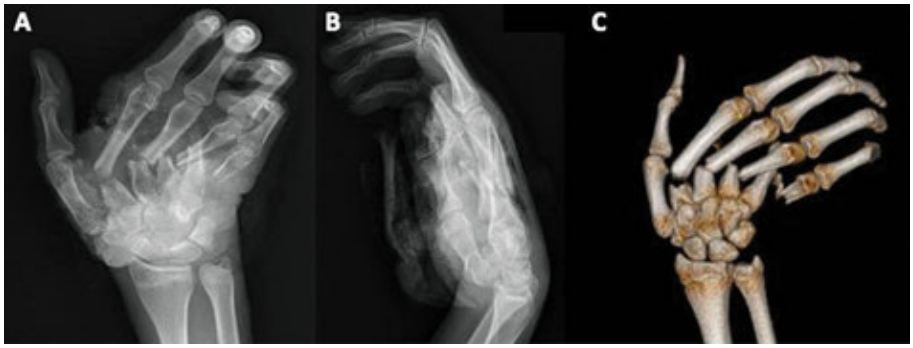

Figure 1. Imaging at time of injury. **(A)** AP and **(B)** lateral radiographs of the right hand at time of injury. **(C)** Three-dimensional reconstruction of a CT scan of the right hand.

One year after his initial injury, the patient had residual deformity of the right hand, with limited function, primarily due to loss of the fist web space due to scar contracture with associated fixed internal rotation of the thumb. He had swan neck deformities of the index through small fingers with ulnar deviation of all digits (Figure 3). His sensibility was intact throughout the hand except for hypoesthesia over the dorsal, radial aspect of the index finger. He had significant atrophy of the thenar musculature. A strong triphasic doppler signal was present over the dorsal branch of the radial artery. Imaging demonstrated malunion of the metacarpal shafts with a windswept appearance of the hand (Figure 4). The distal radius, ulna, and carpal bones appeared atraumatic and well aligned. The patient's chief complaint was impaired function of his dominant hand due to pain and position of his thumb. To address this complaint the patient and our team opted to pursue fusion of the thumb carpometacarpal (CMC) joint, first webspace contracture release and first webspace widening and deepening using lateral arm flap.

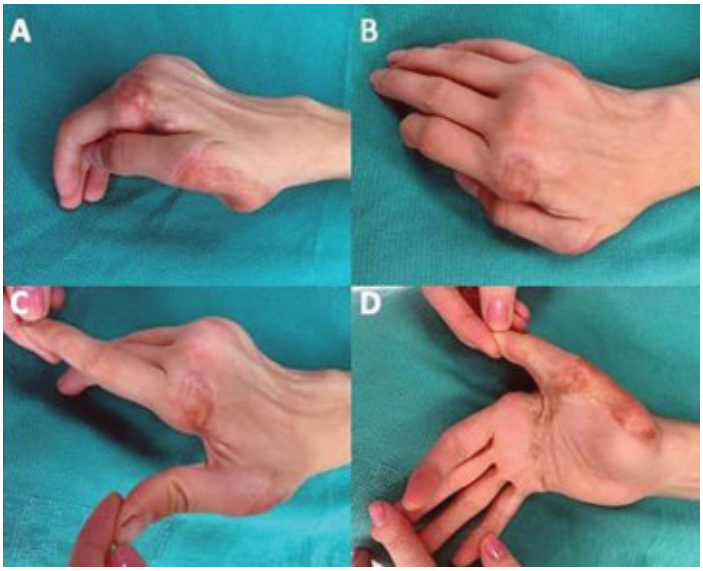

Figure 3. (A-D) Pre-operative images demonstration residual deformity of the hand with first web space contracture.

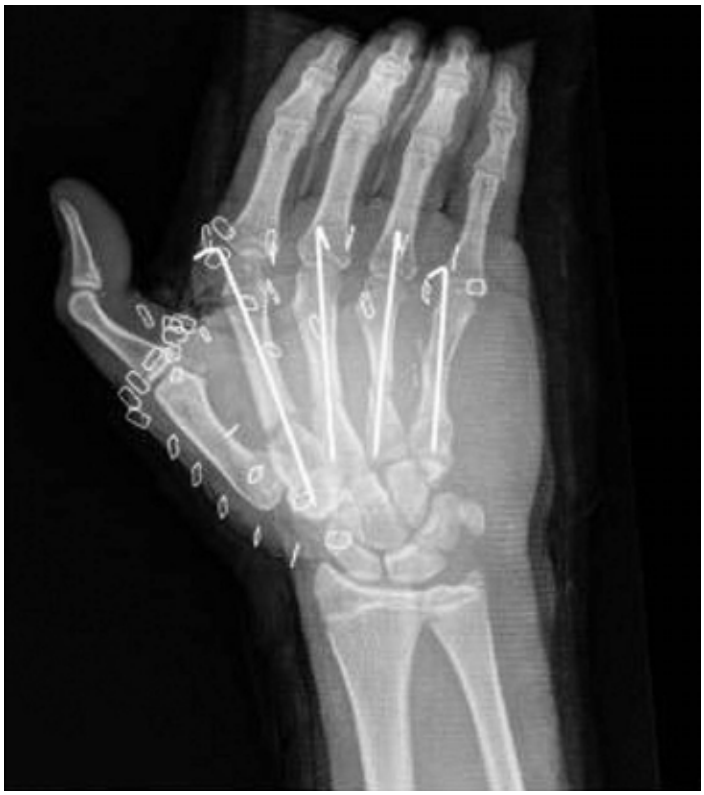

Figure 2. Initial post-operative AP radiograph of the right hand from surgical procedure prior to presentation.

At the time of surgery, tourniquet was placed and inflated to 250mmHg. A zig-zag incision was made over the dorsal aspect of the first web space. An adductor tenotomy was the performed and the thumb was freed from the scar tissue in the first web space and palm. Next, dissection was carried down to the level of the thumb CMC joint. An arthrotomy was performed, and the base of the metacarpal was found to have collapsed and without healthy cartilage from previous trauma. An osteotomy of the metacarpal base was performed to optimize position the thumb for opposition and pronation. What little articular cartilage remained on the trapezium was removed and fusion with Kirschner wires and tension band was performed. The web space was further opened to the degree possible by taking down scar tissue and a template was created for the cutaneous portion of the free flap.

The template was placed and traced at the distal aspect of the ipsilateral upper arm. The anterior border was incised initially, and dissection was performed to the level of the biceps and brachioradialis muscles. A fasciocutaneous flap was raised from anterior to posterior visualizing and including the septocutaneous perforators arising from the posterior radial collateral pedicle. The posterior incision was made and

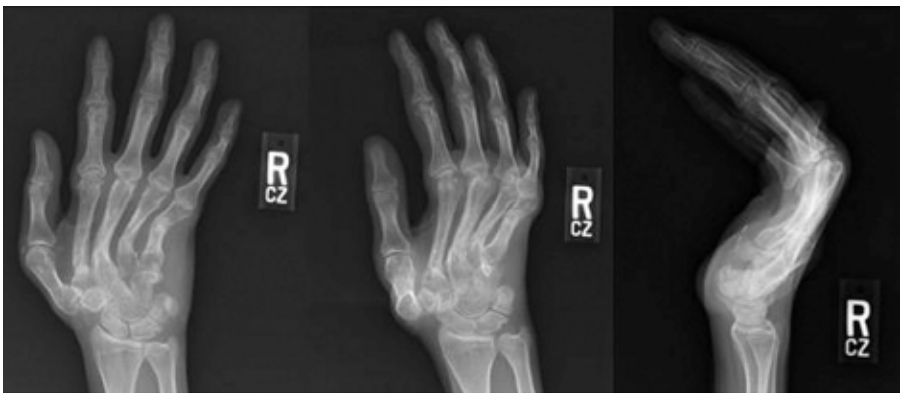

Figure 4. Imaging at time of presentation. **(A)** AP, **(B)** oblique, and **(C)** lateral radiographs of the right hand at time of presentation, demonstrating residual bony deformities of the metacarpals.

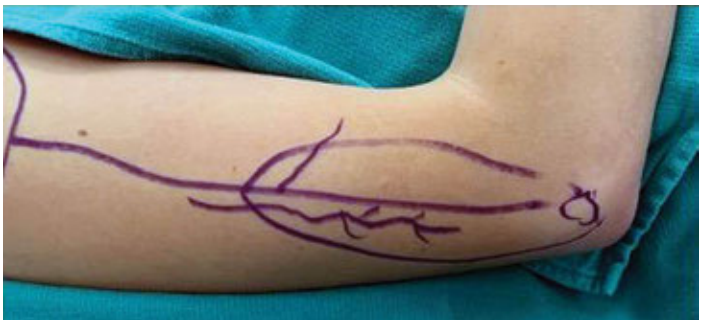

Figure 5. Right arm at time of surgery demonstrating template for lateral arm flap.

the fasciocutaneous flap was again raised to the pedicle. The pedicle was clipped distally and raised from distal to proximal taking a small amount of periosteum from the humerus at the distalmost aspect where the pedicle was so closely adhered to the bone. Tourniquet was deflated and removed. The posterior radial collateral artery was dissected and traced behind the lateral head of the triceps where it branches off the brachial artery. During the proximal dissection the radial nerve was visualized and protected. The posterior cutaneous branch of the forearm as it came into the flap was dissected and included. The pedicle was divided, and the flap was brought down to the hand (Figure 6). The donor site was closed in layers over 15Fr round blake drain.

At the hand, an end-to-end anastomosis was made between the pedicle and the dorsal branch of the radial artery over the thumb. Two concomitant veins were coapted using a 2mm sized venous couplers. A superficial branch of the radial nerve was coapted to the posterior cutaneous nerve branch on the flap. The flap was inset without tension and closed with nylon sutures (Figure 7). Radiographs were obtained post-operatively (Figure 8). The patient was placed in a soft dressing with a plan for a flap debulking procedure after eight weeks (Figure 9). He will continue occupational therapy for range of motion exercises to optimize his functional outcome.

Anatomy

The blood supply to the lateral arm flap is reliable and consistent. The flap is supplied by the radial collateral artery which originates from the brachial artery and wraps

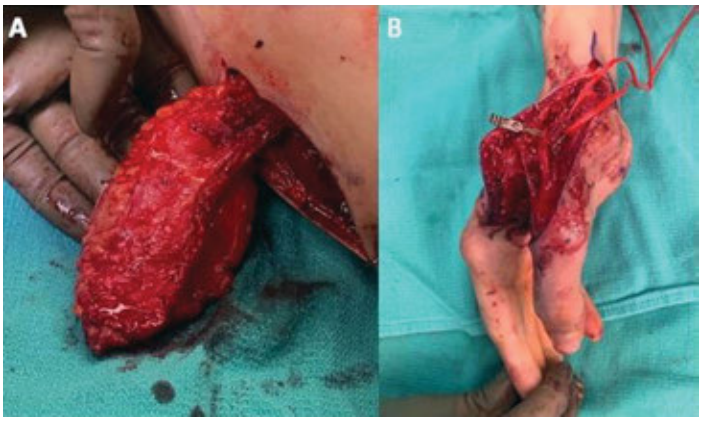

Figure 6. Intra-operative donor and recipient flap sites. **(A)** Dissected lateral arm flap with visible posterior radial collateral pedicle. **(B)** First web space after contracture release with exposed dorsal branch of the radial artery.

posteriorly around the humerus. As it descends, midway between the acromion and the lateral epicondyle, the artery enters the lateral intermuscular septum between the deltoid insertion anteriorly and the triceps posteriorly. Here it divides into the anterior and posterior radial collateral arteries. The posterior radial collateral artery runs between the triceps brachii and brachial muscles distally along the humerus. It is the posterior branch which supplies the lateral arm and lateral forearm flaps. Three to five septocutaneous perforator

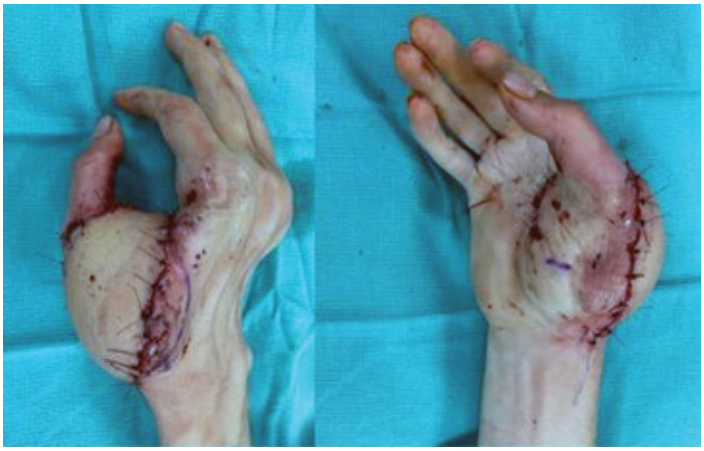

Figure 7. Immediate post-operative images with well-perfused lateral arm flap within the first web space.

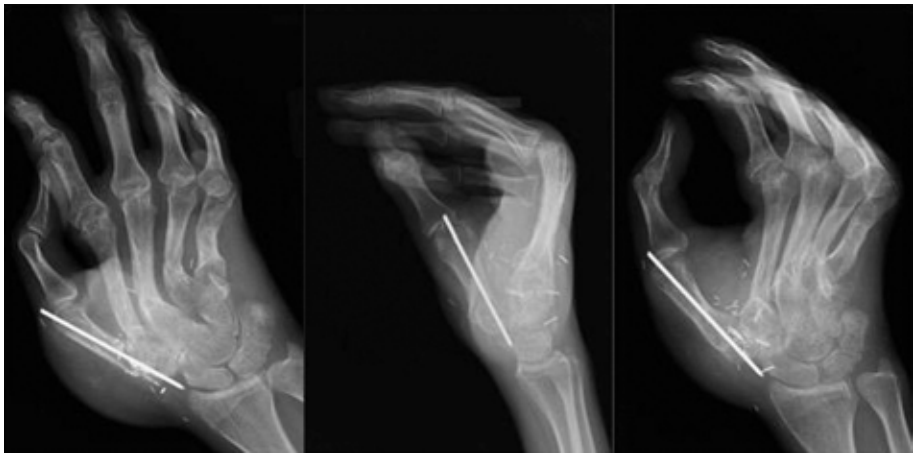

Figure 8. Immediate post operative radiographs of the right hand.

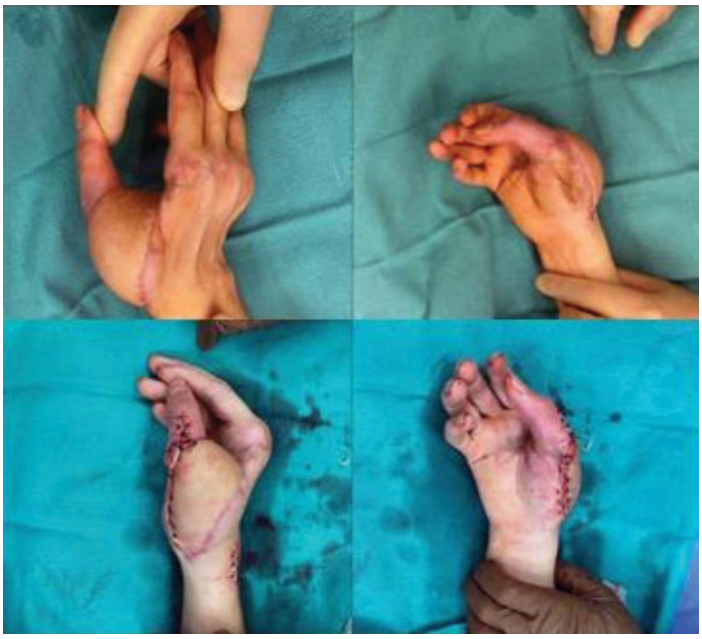

Figure 9. Pre and post operative clinical images at eight week post operative procedure for flap debulking demonstrating healthy flap with functional position of the thumb.

arteries in the lateral intermuscular septum of the upper arm provide the blood supply to the fasciocutaneous flap. It ultimately anastomoses with the interosseous recurrent artery around the level of the lateral epicondyle.[2,5,8,9] The posterior cutaneous nerve of the arm arises from the radial nerve in the spiral groove and accompanies the posterior radial collateral artery, innervating the skin of the lateral upper arm.[5]

The vascular pedicle not particularly long and runs underneath the flap itself. When traced back to the takeoff of the brachial artery a vascular pedicle of 7 – 8 cm can be possible with an arterial diameter of 1.5 – 2.0 mm.[5] There is generally a paired venae comitantes with a dominant vein typically a similar diameter to the artery. Fascia up to 12 x 9 cm may be used with good axial perfusion.[9] Other variations include taking a cutaneous portion of the flap extending distal to the elbow in a "hockey stick" shape. If needed a piece of vascularized bone on a cuff of periosteum from the humerus can be raised with the flap measuring 1.5cm wide.

Discussion

The upper extremity and the hand specifically are regions that often require complex reconstruction in the setting of trauma or large soft tissue defects. Reconstruction of the hand is technically demanding given the close proximity and heterogeneity of very functional structures within the hand and forearm.[8] This is further made challenging due to the requirement of reconstructing surfaces with a low coefficient of friction which permit smooth gliding of structures—in particular tendons—with movement. The lateral arm can yield a variety of tissue for free transfer, including skin, fascia, muscle, tendon, and bone. The use of fascial tissue from this region allows for versatile soft tissue coverage. Creating a gliding surface for tendons clinically decreases the prevalence of adhesions and allows for maximal tendon excursion. The lateral arm flap has the added advantage of limiting preparation, draping, and surgical dissection to a single extremity as compared to free tissue transfer from the commonly used anterolateral thigh flap. While free fascia can also be harvested from additional sites the posterior calf, dorsal thoracic region, and temporoparietal region, the lateral arm is optimal for defects of the hand given the ease of access during surgery and the excellent tissue quality making three dimensional defect coverage easier.[9] The lateral arm flap can be harvested in the supine, lateral, or prone position.[9] Graft harvest from the lateral arm and donor site preparation in the ipsilateral extremity can be performed under the same tourniquet without the need for repositioning. Utilizing other common grafts often requires prepping and draping other areas of the body, which can lead to logistical difficulties in the operating room. This is also advantageous in that the flap can be harvested entirely under axillary block in ipsilateral upper extremity defects, eliminating the need for general anesthesia in patients who are higher risk utilizing a regional block.[6,10] The selection of a lateral arm flap with regional anesthesia coordination can also facilitate a decrease in post-operative pain if the surgical team requests use of an indwelling pain catheter.

Conclusion

The lateral arm free flap is a versatile, reliable flap that allows for soft tissue coverage of complex wounds in the hand and upper extremity. It is particularly useful given its ability to create a gliding surface for tendons and other structures to reduce adhesion formation. We believe that our patient will regain meaningful use of his hand following the reconstruction of his first web space utilizing a free lateral arm flap. The choice of a lateral arm flap assisting with patient comfort and minimized morbidity to other extremities, facilitating increased functionality of his dominant arm.

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Pediatrics

U·P·O·J

Pediatrics Tips and Tricks: Initial Management of Pediatric Both Bone Forearm Fractures

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Introduction

Both-bone forearm fractures are among the most frequently encountered types of fractures in children.[1] Due to the unique properties of immature skeleton, guidelines generally dictate a slightly higher acceptable angulation with respect to fixation in developed bone.[2] There is general consensus in opting for closed reduction and casting as opposed to surgical fixation when possible, though current literature has not established the optimal fixation method for forearm fractures.[3] Here, we aim to review the management of pediatric both bone forearm fractures.

Clinical Presentation

Fractures of the radial and ulnar shaft in the pediatric population are most commonly as a result of a fall onto an outstretched arm. Patients will often present with immediate pain and obvious deformity to the forearm, especially if the fracture necessitates reduction. A careful examination of the pediatric patient should include an assessment for any evidence of an open fracture, neurovascular deficits, soft tissue/compartment swelling, and ipsilateral injuries in the upper extremity.[4]

Radiographs

Initial evaluation of both bone forearm fractures should include the usual anteroposterior (AP) and lateral radiographs, including the entirety of the radius and ulna. Dedicated radiographs of the ipsilateral elbow and wrist may often be necessary to fully evaluate the injury.

Generally accepted values for residual deformity varies by age. In patients 10 years or younger, acceptable alignment includes $<$ 15 degrees of angulation, $<$ 45 degrees of malrotation and $<$ 1cm of bayonet apposition or shortening. In patients older than 10 years, acceptable alignment includes $<$ 10 degrees of angulation, $<$ 30 degrees of malrotation and no bayonet apposition or shortening (Table 1). Angulation is typically measured on a radiograph orthogonal to the plane of maximal deformity. Rotation of the radius can be assessed with the location of the bicipital tuberosity and radial styloid, which should be 180 degrees in orientation apart from each other on an AP radiograph. In addition, the ulnar styloid and the coronoid process of the ulna should also be 180 degrees apart from each other on the lateral view (Figure 1).

As these pediatric patients approach skeletal maturity (within 1-2 years of skeletal maturity), it is important to remember that the tolerances of residual deformity become more inflexible as their ability to remodel significantly decreases.[5,6]

Treatment

Non-operative Management

Non-operative treatment for radial and ulnar shaft fractures with closed reduction and casting remains the standard of care.[7] With closed reduction and immobilization, it is important to ensure the restoration of angulation, rotation and length of the fracture within acceptable limits (Table 1). To perform a successful closed reduction of a both bone forearm fracture, adequate analgesia is required; which, in the pediatric population often requires anesthesia or sedation. After closed manipulation of the fracture, it is imperative to apply adequate casting or splinting to maintain the reduction. Principals of casting the forearm include adequate cast padding to protect the skin and bony prominences, adequate molding of the cast to maintain reduction even after swelling resolves, sufficient interosseous mold, straight ulnar sided border and a cast index of $<$ 0.81

Table 1. Satisfactory Residual Deformity of Diaphyseal Forearm Fractures

Age	Angulation	Malrotation	Shortening
0-10 years	<15	<45	<1cm
>10 years	<10	<30	None
Approaching skeletal maturity	0	0	None

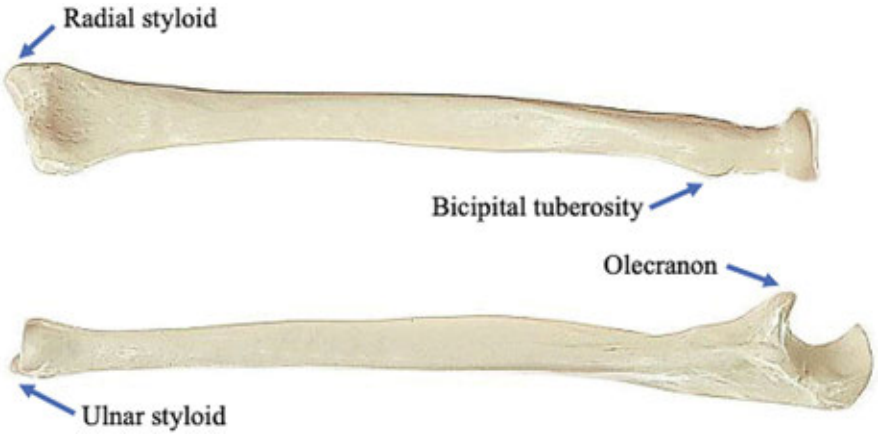

Figure 1. The radius shown from an AP view, illustrating the radial styloid and bicipital tuberosity oriented 180 degrees apart. The ulnar shown from a lateral view, also illustrating the olecranon and ulnar styloid oriented 180 degrees apart.

(the ratio of sagittal to coronal width of the cast at the inner edges of the cast at the fracture site).[8]

The goal with non-operative management of both bone forearm fractures is to achieve acceptable functional outcomes of the upper extremity, with restoration of range of motion of the elbow and wrist and minimal loss, if any, of forearm pronation and supination.[9]

Operative Management

As previously mentioned, the gold standard of care for most forearm fractures in children is non-operative treatment. However, indications for surgical fixation in children and adolescents include open fractures and the inability to maintain an acceptable closed reduction in a cast. As children approach skeletal maturity, acceptable criteria for radiographic displacement becomes comparable to that of adults. Two main options exist in the operative treatment of pediatric forearm fractures: elastic intramedullary nailing and open reduction internal fixation with standard plating technique. Each approach offers its own set of advantages and disadvantages that are at the discretion of performing surgeon to consider in each clinical scenario. Flexible intramedullary nailing has been popularized because it can offer a percutaneous fracture fixation option with less surgical dissection and lower biologic cost. Disadvantages of flexible nails include skin irritation at the tip of the nail, and the need for a second procedure for hardware removal. In contrast, operative fixation with plates requires more extensive surgical dissection at the fracture site but can offer direct anatomic reduction. Despite their differences, intramedullary nailing and plating offer similar outcomes[10] and their use is ultimately, in most situations, based on the surgeon's discretion.

Considerations

There are various relatively common complications that occur with pediatric both bone forearm fractures and its treatment modalities. With closed management, there is a risk of loss of reduction, refracture, loss of range of motion, and cast issues. McQuinn et al. report that that initial displacement of the fracture $>$ 50% and inability to achieve anatomic reduction with closed manipulation as risk factors for re-displacement.[11] They also highlight the importance of an adequate cast mold, with the cast index being the most useful measure of the cast mold.[8,11]

Another complication known to radial and ulnar shaft fractures is the risk of re-fracture, with rates between 1.4-4.9%.[12,13] Residual malalignment of the radius or ulna after reduction can lead to loss of range of motion, particularly in pronosupination. Loss of range of motion could also result from contracture of the interosseous membrane.[14] Providers should be vigilant of developing compartment syndrome which tends to be more common in open fractures, those with ipsilateral distal humerus fractures, and fractures with difficult reductions or surgical treatment.[4,14,15]

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The Epidemiology of Pediatric Basketball Injuries Presenting to US Emergency Departments: 2011-2020

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Introduction

Basketball is one of the most popular sports in the United States and accounts for 26% of all pediatric sports injuries, or roughly 260,000 injuries each year[1-2]. Previous epidemiologic studies have evaluated trends of pediatric and adolescent basketball injuries in the early 2000's[2–4]. Several studies have described injuries in basketball by focusing on middle school[5], high school[3,6–8], or college athletes[8]. While these earlier studies have established trends, such as common injury locations and gender specific injury rates[6-9], there is a paucity of literature examining trends in injury epidemiology since the advent of the COVID-19 pandemic. This study updates the national epidemiology of basketball-related injuries in children and adolescents, offers insight into the trends of these injuries during the decade of the 2010's, and describes the effect of the COVID-19 pandemic on injury patterns.

Methods

Data Source

The US Consumer Product Safety Commission operates a statistically valid injury reporting system called the National Electronic Injury Surveillance System (NEISS). NEISS data represent cases of sport or product-related injury presenting to a representative sample of 100 US EDs.[11,12] NEISS data include detailed patient and injury information. Cases of injury in patients less than 20-years-old associated with the product code 1205 (basketball and related equipment) between January 1st, 2011 and December 31st, 2020 were included in the analysis. No cases were excluded.

The NEISS database contains a variable characterizing injury diagnosis which was grouped for purposes of analysis. Diagnoses were categorized as laceration (lacerations, punctures, amputations, and nonbone avulsions), soft tissue injury (contusions and/or abrasions and hematomas), fracture, strain or sprain, concussion (including nerve injury), dislocations, and other (dental injury, foreign body, hemorrhage, internal organ injury, tympanic membrane rupture).

Statistical Analysis

An interrupted time series analysis was performed with pre- and post- linear trend estimation using March 1, 2020 as the

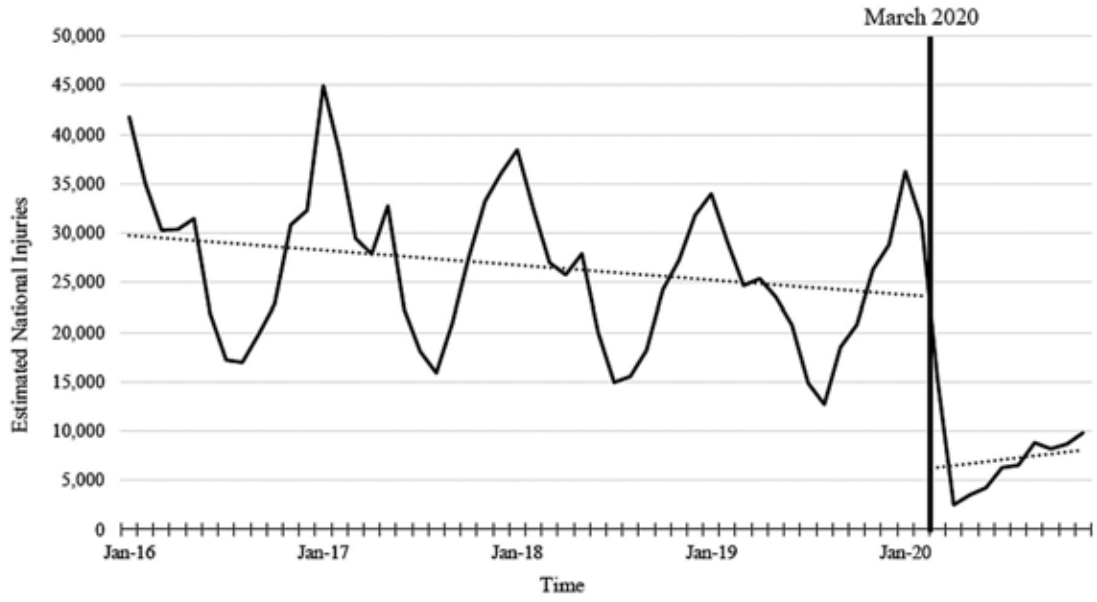

Figure 1. Effect of COVID-19 on Trends of National Basketball-Related Injuries: 2016-2020. Dotted lines demonstrate the national trend of injuries before and after the start of the COVID-19 pandemic in March 2020.

Table 1. National Estimates and Characteristics of Pediatric Basketball Injuries: 2011-2020

Characteristic	Cases, n	Estimates	%	95% CI	
				Lower	Upper
Total	104046	3210953	100.0%	2655812	3766094
Sex					
Male	80245	2445248	76.2%	1993552	2896944
Female	23801	765705	23.8%	648690	882721
Age Group					
under 5	739	17315	0.5%	13217	21414
5 to 9	7687	206621	6.4%	162101	251141
10 to 14	47498	1389462	43.3%	1143051	1635872
15 to 19	48122	1597555	49.8%	1323101	1872010
Injury Type					
Laceration	7846	253462	7.9%	209642	297283
Soft Tissue	12058	373248	11.6%	301932	444564
Fracture	18655	524426	16.3%	433398	615455
Strain/Spain	36915	1221958	38.1%	1014269	1429647
Concussion	4960	124801	3.9%	98327	151274
Dislocation	2996	94841	3.0%	79176	110505
Other	20616	618218	19.3%	444064	792371
Body Part					
Shoulder	3558	113244	3.5%	95011	131477
Elbow	5520	152644	4.8%	123925	181362
Hand	24467	767704	23.9%	628936	906472
Knee	12828	377790	11.8%	305414	450167
Foot	26292	863252	26.9%	711714	1014790
Head	13021	378862	11.8%	308688	449036
Face	10451	319400	9.9%	264391	374409
Trunk	7111	211992	6.6%	167453	256530
Other	798	26066	0.8%	16916	35216
Disposition					
Released	102158	3169934	98.7%	2622574	3717293
Hospitalized	1879	40854	1.3%	29610	52099
Fatalities	3	68	0.0%	-28	164
Unknown	6	97	0.0%	-36	231
COVID-19					
Before March 2020	101275	3137284	97.7%	2595651	3678917
After March 2020	2771	73670	2.3%	54019	93320

interrupting timepoint. The pre-COVID-19 trend was used as a baseline predictor to estimate the total difference in injuries attributable to the COVID-19 pandemic from March to December 2020. US census data for each corresponding year was used to calculate the rate of injury.This study was exempt from institutional review.

Results

During the 10-year study period there were 3,210,953 (95% CI = 2,655,812 − 3,788,094) basketball-related injuries nationwide in persons < 20 years-old corresponding to an incidence of 391 per 100,000 population. Overall estimates and injury characteristics are shown in Table 1. The mean age of injury was 14.4 years (95% CI 14.3-14.5). Over 93% of

injuries occurred in children > 10 years old with over half of all basketball-related injuries occurring in 15–19 year-olds. Basketball-related injuries followed an expected seasonal pattern with 43% of injuries presenting between December and March—the period coinciding with national middle- and high school basketball seasons. August had the fewest number of basketball-related injuries. Males accounted for 76.2% of the injuries, while females accounted for 23.8% of injuries. The ratio of male-to-female injury was similar across all age groups.

Strain or sprain was the most common injury type (38.1% of injuries) followed by fractures (16.3% of injuries) and soft tissue injuries (11.6% of injuries). Half of all injures were to the hands or feet (23.9% and 26.9% of injuries, respectively). The head and the knee were injured at the same rate (11.8%). Concussions and dislocations each made up 3% of total injuries during the study period. The majority injuries did not result in hospitalization (98.7%).

Effect of COVID-19

There was a decrease in injuries coinciding with the COVID-19 pandemic shutdowns in March and April 2020. From March-December 2020, during the COVID-19 pandemic, 155,638 fewer basketball-related injuries occurred than would have been expected based on pre-COVID-19 trends ($p < 0.001$, Figure 1). From January 2011 to March 2020, basketball related injuries had been declining at a rate of 77 injuries/month (924 per year). The post-COVID-19 trend indicates that basketball-related injuries increased at a rate of 196 injuries/month as the country slowly reopened during the remainder of 2020. There were no significant changes in the type of basketball injuries presenting during the COVID-19 pandemic ($p > 0.5$ for all age groups).

Discussion

To our knowledge, this is the first study using national data to classify basketball related injuries in the latter half of the 2010 decade. While there was a general trend of decreased injuries in total, there was not a notable shift in proportions of injury type and location as compared to similar studies using data before this study period. Most injuries were seen in males and in individuals ages 10 to 19 years old. Overall, the most common injuries seen were strain/sprains or fractures of the foot or hand. These kinds of injuries have consistently been shown to be the most common in basketball.[3,8].

The COVID-19 pandemic has had a profound impact on all aspects of daily life for children, including participation in recreational and organized sports. This study's estimated reduction in basketball injuries during the COVID-19 pandemic matches the trend seen in single center and multicenter studies evaluating all pediatric sports injuries during COVID-19[10]. Such studies have postulated that despite the decrease in the overall number of injuries, basketball was one of the sports that continued to cause injuries during the pandemic as it could be played at home or outside in groups. This was noted by an increase in the proportion of injuries occurring in or around the home as a result from low or high-energy falls.[10]

Strengths & Limitations

This study has several limitations related to the use of the NEISS database. The data only represent injuries presenting to United States Emergency Departments and are therefore unable to account for subclinical injuries. Because of this, our analysis likely underestimates the true incidence of basketball-related injury. Strengths of this study include its nationally representative nature, and its 10-year timeframe.

Conclusion

The COVID-19 pandemic caused a significant decrease in the number of basketball injuries in 2020, but there was no significant shift in the injury pattern or characteristics on a national level.

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Does Patient Race, Ethnicity, or Socioeconomic Status Impact Surgical Decision Making? Analysis of a Common Pediatric Orthopaedic Surgical Procedure

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Introduction

Racial and ethnic minority patients continue to experience disparities in orthopedics. Several studies have indicated that minority and low-income patients experience higher rates of nonoperative treatment and delayed surgery for a variety of orthopedic conditions[1-5]. One study surprisingly found higher rates of percutaneous pinning of supracondylar humerus (SCH) fractures among Black and Hispanic patients[6]. This study was conducted over 15 years ago and was limited to an inpatient database. Furthermore, there is a lack of current literature evaluating racial and ethnic disparities in outpatient surgical decision making for common pediatric fractures that can be variably treated with non-operative or operative management. The aim of this study was to examine whether patient race, ethnicity, or insurance status was associated with differences in operative rate for type II SCH fractures.

Methods

This retrospective cohort study at a single tertiary pediatric hospital evaluated patients between the ages of 2-12 years old who were initially evaluated at an outpatient orthopedic clinic visit for a type II SCH fracture between 2013-2021. Patients with type I or III SCH fracture patterns, open injuries, polytrauma, vascular injuries, or underlying skeletal dysplasia were excluded. Inpatient encounters were excluded given that the surgeon often may have provided surgical decision making without face-to-face interaction with the patient. Diagnosis was confirmed based on radiographic reports, operative notes, and ICD9/10 codes. Demographic, injury, and treatment characteristics were collected for each patient. Operative versus nonoperative intervention was confirmed based on a data query combined with corresponding CPT codes. Surgical treatment, as defined by closed reduction with percutaneous pinning or open reduction with internal fixation, was grouped as a single cohort and compared with the cohort of fractures that were treated nonoperatively. Fisher exact and $\chi 2$ tests were performed to evaluate the difference in operative rate by race, ethnicity, and insurance status.

Results

A total of 1539 patients with type II SCH fractures were available for study with a mean age of 5.8 +/− 2.6 years. 155 patients (10%) were treated with operative intervention, whereas 1384 patients (90%) were treated nonoperatively. There were 866 patients (56%) who were initially stabilized at an outside facility prior to surgical evaluation at one of the institution's outpatient orthopedic clinics (Table 1). There was no difference operative rate between patients who were first stabilized at an outside facility compared to those first evaluated at an outpatient orthopedic clinic (11% versus 9%, $p = 0.13$). There was no difference in the proportion of patients who underwent operative intervention for treatment of their type II SCH based on the patient's race, ethnicity, or insurance status (Table 2). Non-white surgeons had a higher operative rate than white surgeons (14% versus 8%, $p = 0.001$), however, when controlling for surgeon race there was no difference in the operative rate based on patient race, ethnicity, or insurance status (Table 3).

Discussion

Multiple studies have demonstrated racial and ethnic disparities of surgical outcomes[7-9], however there is a lack of current literature evaluating disparities in outpatient surgical indications for pediatric fractures[10,11]. A prior study demonstrated that Black and Hispanic patients were more likely to undergo closed reduction with percutaneous pinning of SCH fractures compared to White patients[6]. However, this study was conducted over 15 years ago and was limited to an inpatient database. Given that outpatient visits may represent a significant number SCH fractures, our results are necessary to elucidate the decision making in this area to be more representative of the entire population of patients with these injuries. It is important

Table 1. Demographics of Pediatric Type II Supracondylar Humerus Fracture

Variable		Total Population (n=1539)
Age at Injury (y)		5.76 +/− 2.56
Age at Injury (y)		
	<5	784
	6 to 9	603
	10 to 12	152
Sex		
	Male	763 (49%)
	Female	776 (51%)
Race		
	White	908 (59%)
	Black	174 (11%)
	Asian	99 (6%)
	South Asian	27 (2%)
	American Indian/Native Alaskan/Hawaiian	7 (0.5%)
	Multiracial	42 (3%)
	Other	264 (17%)
	Refused	18 (1.5%)
Ethnicity		
	Non-Hispanic	1380 (90%)
	Hispanic	136 (9%)
	Refused	23 (1%)
Payor		
	Commercial	1092 (71%)
	Medicaid	391 (25%)
	Self-Pay	19 (1.5%)
	Government (Tricare)	10 (1%)
	Other	27 (1.5%)
Mechanism of Injury		
	Low energy fall	590 (39%)
	High energy fall	214 (14%)
	Sport	50 (3%)
	Passenger in Body Powered Vehicle	35 (2%)
	Passenger in Motorized Vehicle	12 (1%)
	Direct Blow	15 (1%)
	Not Reported	623 (40%)
Treating Surgeon Race		
	White	1103 (72%)
	Non-White	436 (28%)

Data are given as mean +/− standard deviation or n (%)

Table 2. Demographic Differences in Treatment Type for Type II Supracondylar Humerus Fractures

Variable		Nonoperative Intervention (n=1384)	Operative Intervention (n=155)	P value
Race				0.865
	White	812 (89.4%)	96 (10.6%)	
	Black	157 (90.2%)	17 (9.8%)	
	Asian	92 (92.9%)	7 (7.1%)	
	South Asian	26 (96.3%)	1 (3.7%)	
	American Indian/Native Alaskan	6 (86%)	1 (14%)	
	Multiracial	39 (92.9%)	3 (7.1%)	
	Other	235 (89%)	29 (11%)	
	Refused	17 (94.4%)	1 (5.6%)	
Ethnicity				0.53
	Non-Hispanic	1242 (90%)	138 (10%)	
	Hispanic	120 (88%)	16 (12%)	
	Refused	22 (96%)	1 (4%)	
Payor Status				0.906
	Commercial	980 (90%)	112 (10%)	
	Medicaid	352 (90%)	39 (10%)	
	Self-Pay	18 (95%)	1 (5%)	
	Government (Tricare)	10 (100%)	0 (0%)	
	Other	24 (89%)	3 (11%)	

Data are given as adjusted percentage receiving procedure and significance level from Pearson Chi Square Test

to understand that our study only included type II SCH fractures, while Slover et al. included all operatively managed SCH fractures (types II-IV). Current treatment guidelines recommended treating type III and IV fractures with surgery, whereas type II fractures could be treated with either casting or surgical intervention[12]. Given that surgeons could treat type II fractures either operatively or nonoperatively, there was a greater opportunity for bias in decision making relative to the other fracture types. It is unclear if our results are due to changes in treatment over time or due to different decision making for patients in the outpatient setting.

There have also been disparities in pediatric orthopedic care based on insurance status including longer time to initial evaluation and surgery[13-16], and higher risk of being lost to follow up[17,18]. However, few studies have readdressed surgical decision making for pediatric fractures based on insurance status[10]. Our study revealed there was no difference in the proportion of patients who received operative treatment based on insurance status. However, one must be aware that there may be unrecognized differences in surgical decision making based on hospital type and region.

This study has several limitations. Our study's operative rate differs from the literature surrounding operative treatment of type II SCH fractures. Epidemiologic studies have reported an operative rate ranging from 5-48%[19,20]. Over the past few years there has been a shift to treating type II SCH fractures with operative intervention[12]. Our study likely underestimates the overall operative rate as we only included patients who were initially seen in the outpatient setting. Since the majority of type II SCH fractures are first evaluated in the Emergency Department there are likely many patients who received operative intervention that were not included in this study. There is also potential for co-treatment and selection bias since over half of our cohort was initially stabilized at an outside facility. Our results are unlikely to have been skewed by this occurrence as the operative rate for patients who were initially stabilized at an outside facility did not differ from those who were first seen in an orthopedic clinic.There is also potential for reporting bias via misclassification of race and ethnicity as this data is self-reported. Future geographically diverse multicenter studies are needed to explore this issue on a national level.

Conclusion

Outpatient clinical decision making for type II SCH fractures is not disproportionately influenced by patient race, ethnicity, or insurance status. It is paramount to continue efforts to elucidate and eliminate disparities in fracture care based on race and socioeconomic status in order to optimize care for all populations.

Table 3. Demographic Differences in Treatment Type for Type II Supracondylar Humerus Fractures by Surgeon Race

3A – Operative rates for Non-White Surgeons

Variable	Nonoperative Intervention(n=374)	Operative Intervention (n=62)	P value
Race			0.404
White	222 (87%)	34 (13%)	
Black	44 (86%)	7 (14%)	
Asian	20 (91%)	2 (9%)	
South Asian	6 (86%)	1 (14%)	
American Indian/Native Alaskan	1 (50%)	1 (50%)	
Multiracial	10 (77%)	3 (23%)	
Other	68 (84%)	13 (16%)	
Refused	3 (75%)	1 (25%)	
Ethnicity			0.929
Non-Hispanic	335 (86%)	55 (14%)	
Hispanic	35 (85%)	6 (15%)	
Refused	4 (80%)	1 (20%)	
Payor Status			0.843
Commercial	262 (85%)	45 (15%)	
Medicaid	94 (85%)	16 (15%)	
Self-Pay	6 (86%)	1 (14%)	
Government (Tricare)	4 (100%)	0 (0%)	
Other	8 (100%)	0 (0%)	

3B – Operative Rates for White Surgeons

Variable	Nonoperative Intervention (n=1010)	Operative Intervention (n=93)	P value
Race			0.364
White	590 (90%)	62 (10%)	
Black	113 (92%)	10 (8%)	
Asian	72 (93%)	5 (7%)	
South Asian	20 (100%)	0 (0%)	
American Indian/Native Alaskan	5 (100%)	0 (0%)	
Multiracial	29 (100%)	0 (0%)	
Other	167 (91%)	16 (9%)	
Refused	14 (100%)	0 (0%)	
Ethnicity			0.333
Non-Hispanic	907 (92%)	83 (8%)	
Hispanic	85 (90%)	10 (10%)	
Refused	18 (100%)	0 (0%)	
Payor Status			0.711
Commercial	718 (91%)	67 (9%)	
Medicaid	258 (92%)	23 (8%)	
Self-Pay	12 (100%)	0 (0%)	
Government (Tricare)	6 (100%)	0 (0%)	
Other	16 (84%)	3 (16%)	

Data are given as adjusted percentage receiving procedure and significance level from Pearson Chi Square Test

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An Analysis of Femoral Nerve Block Use for Pediatric ACL Reconstruction

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Introduction

Femoral nerve blocks (FNBs) are the most common form of regional anesthesia used for pediatric anterior cruciate ligament (ACL) reconstruction (ACLR). The use of these blocks has increased in recent years.[1-3] While some studies suggest that FNBs slow the return to sports and have implications on quadriceps and hamstrings strength,[4] others demonstrate benefits, such as improving postoperative pain control.[5] FNBs can be used as a single-shot injection or a catheter that provides continued infusion.

In this study we aim to (1) determine the rates of use for single-shot versus continuous-catheter FNBs and compare rates between ambulatory surgery centers (ASC) and the main hospital, (2) assess time needed for anesthesia administration by block technique to determine efficiency, and (3) analyze differences in postoperative pain control. We established two *a priori* hypotheses: (1) that on average the time used for single-shot FNBs would be less than the time for continuous-catheter FNBs, and (2) that there would not be a difference in postoperative pain, as measured by the self-reported 10-point pain scale at the patient's 1-week postoperative clinic visit.

Methods

This retrospective study was approved by the Institutional Review Board at Children's Hospital of Philadelphia (IRB #15-012614). Our patient cohort was identified from a tertiary referral center and affiliated ambulatory surgery centers and consists of pediatric patients ($\leq$18 years of age) who underwent primary ACLR (CPT code 29888) and received a FNB in 2018 or 2019. Patients undergoing revision ACL reconstruction (n = 7) as well as those requiring multiligamentous reconstruction were excluded (n = 48). To achieve 80% power for our study, we calculated a needed sample size of 171.

The type of nerve block (single-shot vs. continuous-catheter) was recorded for each patient along with the location of surgery (Main vs. ASC), time required for anesthesia administration and pain scores at the first postoperative visit.

To compare the two cohorts, we used univariate statistics (t-tests and Mann-Whitney U for continuous variables; Chi-squared and Fisher Exact tests for categorical variables). A p-value of 0.05 was considered statistically significant. The analysis was completed using Stata 16.0 (Stata Corp, College Station, TX).

Results

In total, 256 ACLRs were reviewed. Patients received a single-shot FNB in 159 of these surgeries (62.1%) and a continuous-catheter in 97 surgeries (37.9%). One patient had a preoperative catheter FNB and a postoperative single-shot FNB and was excluded from further analysis. There was no difference in age or gender by nerve block technique (Table 1). Individuals who had surgery at Main were significantly more likely to have a continuous-catheter than those at an ASC. The time spent administering anesthesia was significantly longer among patients who received a continuous-catheter as compared to a single-shot (Figure 1). While Main had longer anesthesia times on average, continuous-catheter administration was still significantly longer than single-shot at both Main and ASCs individually. Pain scores were not significantly different between the FNB cohorts or between Main and ASCs.

Discussion

This study demonstrated that there was no difference in 1-week postoperative pain between patients receiving a continuous-catheter versus or single-shot FNB, but that increased time was spent administering the former. The rate of FNB use in ACLR has been increasing.[1-2] and we believe that it is important to understand the rates of each FNB technique at our institution. Overall, single-shot FNBs were used for 159 surgeries (62.1%) and continuous-catheters were used in 94 surgeries (37.9%). Patients undergoing surgery at the main hospital were significantly more likely to have a continuous-catheter. The rates of use by age and sex did not differ.

Our study found no difference in 1-week postoperative pain between FNB types. While continuous-catheters have been associated with

Table 1. Patient and Procedure Characteristics for by Type of Femoral Nerve Block

Patient Demographics	Single-shot n (%)	Continuous-catheter n (%)	P-value
	159 (62.1%)	97 (37.9%)	
Age †	15 (13-17)	15 (14-17)	0.227
Sex			0.778
Male	84 (61.3%)	53 (38.7%)	
Female	75 (63.0%)	44 (37.0%)	
Location			< 0.001*
Main	14 (13.2%)	92 (86.8%)	
Ambulatory	145 (96.7%)	5 (3.3%)	
Anesthesia Start to Anesthesia Ready (in min) †	23 (20-29)	46 (42-56)	< 0.001*
Pain Level †	1 (0-3)	1 (0-4)	0.414

*P-value < 0.05

†Median and Interquartile Range reported for continuous variables

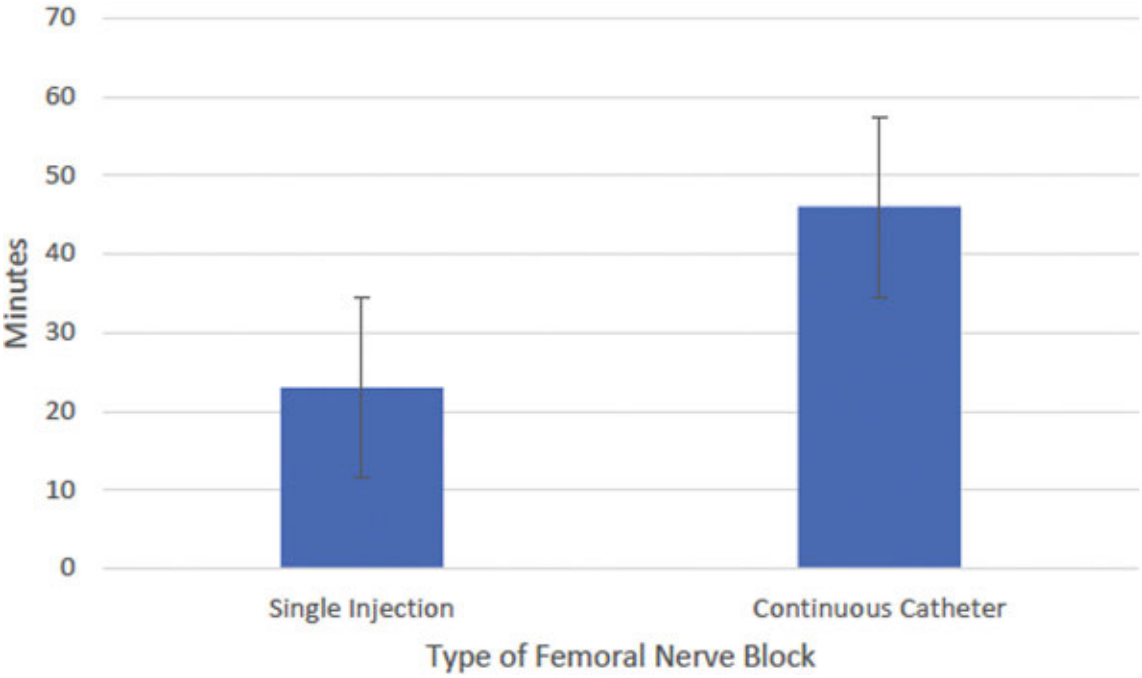

Figure 1. Average Time for Anesthesia Administration by Type of Femoral Nerve Block

decreased pain for other procedures, there is limited research in the pediatric ACLR population and both FNB techniques are considered highly effective for postoperative analgesia.[8] Okoroha et al found that immediately postoperatively, a single-shot FNB decreased pain as compared to local liposomal bupivacaine.[8] There is also some data to suggest that single-shot FNBs may improve long term functional outcomes, but the data is mixed.[9-11] We have found in prior studies quality outcomes and efficiency in the outpatient setting using single-shot nerve block for patients with isolated ACL injury.[12-13] These quality outcomes, as well as the time and cost efficiency of single-shot relative to catheter FNBs noted in the current study may provide surgeons with optimism regarding single-shot block use as a supplement to general anesthesia.

Notably, the time spent administering a single-shot FNB was significantly shorter than the time spent for a continuous-catheter FNB. Previous research has shown that the use of continuous regional anesthesia increases the cost to the patient and the hospital.[12] The use of single-shot FNB in the case of isolated ACL reconstruction in pediatric patients may decrease hospital costs by decreasing time in the operating room, while providing quality analgesia for patients.

Strengths & Limitations

Our study is limited due to its retrospective nature, which limited the available outcomes data. We recognize that catheters are responsible for early pain control and while we did not include pain scores for the first 24 hours, there

was no return to the facility for pain in either group. We also could not definitively determine the cause of time differences. It is possible that the difference in time spent administering anesthesia in the tertiary referral center and the ambulatory surgery center may be due to the presence of trainees in the tertiary referral center. However, this is unlikely to be the only contributing factor.

Conclusion

Patients were more likely to undergo continuous-catheter FNB at Main compared to the ASC. While overall anesthesia time took longer at the Main hospital, at both the ASC and Main locations, single-shot FNB took significantly less time than placement of a continuous-catheter FNB, and the 1-week postoperative pain scores did not differ. Further studies should compare a more comprehensive postoperative pain course between these techniques and providers should consider the costs as well as risks and other benefits to the patient when choosing either a continuous-catheter or single-shot FNB.

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Are Height and Weight Associated with Mechanism of Injury for a Toddler's Fracture? A Retrospective Evaluation of Playground Related Toddler's Fractures

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Introduction

The toddler's fracture, a non-displaced spiral fracture of the tibial shaft, is one of the most common lower extremity injuries in children ages 1-3 years old[1,2]. This fracture pattern is thought to be due to a twisting force to the lower leg which can occur after a child falls or gets their foot caught on a playground slide[3,4,5]. Playground slide injuries are one of the most common causes of toddler's fractures[6,7].

Although the association between playground slides injuries and lower extremity fractures has been explored, studies specifically evaluating toddler's fractures and slide related injuries are limited[6,8,9]. Given the increasing incidence of playground related injuries[6,10], there is a need for an updated understanding of the factors that place patients at risk for toddler's fractures in order to provide adequate guidance to parents and federal regulations.

The purpose of this study is to evaluate if there are demographic differences between patients who sustained a toddler's fracture on a slide versus a non-slide injury and those riding in the lap of an adult versus alone.

Materials and Methods

We performed a retrospective cohort study evaluating all patients, ages 5 months to 11 years, who were diagnosed with a nondisplaced spiral shaft fracture of the tibia at a single tertiary pediatric hospital between 2015-2021. Patients who had a displaced spiral tibial shaft fracture, non-spiral tibial shaft fracture, or concomitant fibula fracture were excluded from the study. Authors collected demographic, injury, and treatment data for all patients who met inclusion criteria.

Standard descriptive statistics were used to report demographic variables and bivariate analyses were conducted to identify demographic differences between patients with slide versus non-slide injuries and those riding alone versus riding in the lap of an adult.

Results

Of the 652 pediatric injuries, 230 (35%) were displaced tibial shaft fractures, non-spiral tibial shaft fractures, or had concomitant fibula fractures, and 15 (4%) were missing mechanism of injury, leaving 407 available for analysis. Demographic, injury, and treatment details are presented in Table 1.

Over 90% of slide injuries occurred in patients who were 0 to 3 years old, while only 67% of non-slide injuries occurred in the same age group ($p < 0.001$). Patients injured going down slides were significantly shorter ($p<0.001$) and lighter weight ($p<0.001$) than those who experienced non-slide injuries (Table 2). When controlling for age, including only patients 0-3 years old, patients injured on a slide were still significantly shorter and weighed less than those who experienced non-slide injuries (32.9 +/− 2.49 inches versus 33.78 +/− 2.70 inches, $p = 0.046$;12.38 +/− 1.86 kg versus 13.00 +/− 2.49 kg, $p = 0.01$). There were proportionally fewer slide related toddler's fractures for children above 30 inches and 20 kilograms (Figure 1).

The majority of slide injuries occurred when riding in the lap of an adult (68%). However, there were no significant demographic differences between those who were injured while riding alone versus riding in the lap of an adult (Table 2).

Discussion

Our retrospective cohort study demonstrated that patients who developed a toddler's fracture from a slide related injury were significantly younger than those who were injured via other mechanisms. Patients injured on a slide were also significantly shorter and weighted less, even when controlling for age, and there were proportionally fewer slide related fractures for children above 30 inches and 20 kilograms. We were unable to identify a subgroup of patients based on demographic characteristics that

Table 1. Population Demographics for Toddler's Fractures

Characteristics	Variable		Total Population (n= 407)
Demographic Characteristics	**Age at Injury (years)**		2.05 (1.5 to 3)
		0-3 years	305 (75%)
		3-6 years	73 (18%)
		6-9 years	23 (6%)
		9 and older	6 (1%)
	Height (inches)		35.98 (32.8 to 43.8)
	Weight (kg)		13 (11.34 to 15.2)
	Sex		
		Male	253 (62%)
		Female	154 (38%)
	Race		
		Caucasian	291 (72%)
		African American	48 (12%)
		Asian	13 (3%)
		Other	49 (12%)
		Refused	6 (1%)
	Ethnicity		
		Non-Hispanic	399 (98%)
		Hispanic	8 (2%)
		Laterality	
		Right	220 (54%)
		Left	187 (46%)
Injury Characteristics	**Mechanism of Injury**		
		Fall	198 (49%)
		Playground Injury (Slide)	131 (32%)
		Playground Injury (Other)	22 (5%)
		Sports	9 (2%)
		MVC	1 (1%)
		Other (Collision or unwitnessed)	46 (11%)
	Initial Treatment		
		Long Leg Cast	272 (67%)
		Short Leg Cast	57 (14%)
		Splint	57 (14%)
		CAM Boot	20 (5%)
Treatment Characteristics	**Complications**		
		Skin breakdown from cast	7 (2%)
		Reinjury after cast removal	5 (1%)
		Compartment Syndrome or Neurovascular Injury	0 (0%)
	Length of Follow Up (days)		29 (23 to 42)

Data is presented as n(%), mean +/− SD, or median (IQR)

Table 2. Evaluating Demographic Differences for Toddler's Fractures

Slide versus Non-Slide Injuries

Parameter		Slide Injuries (n=131)	Non-Slide Injuries (n=276)	Chi Square	P value
Age at Injury (years)		1.85 +/− 0.683	3.02 +/− 2.07		**<0.001[a]**
Age at Injury (years)					
	0-3 years	121 (92%)	184 (67%)	33.026	**<0.001[b]**
	3-6 years	10 (8%)	63 (23%)		
	6-9 years	0 (0%)	23 (8%)		
	9 and older	0 (0%)	6 (2%)		
Height (inches)		33.37 +/− 2.90	38.33 +/− 6.93		**,0.001[a]**
Weight (kg)		12.44 +/− 1.98	15.86 +/−- 7.79		**,0.001[a]**
Sex				0.609	0.435[b]
	Male	85 (65%)	168 (61%)		
	Female	46 (35%)	108 (39%)		
Laterality				0.149	0.75[b]
	Right	69 (53%)	151 (58%)		
	Left	62 (47%)	125 (42%)		

Sliding Alone vs Sliding in lap of an Adult

Parameter		Sliding Alone (n=42)	Sliding in lap of Adult (n=89)	Chi Square	P value
Age at Injury (years)		2.07 +/− 0.80	1.75 +/− 0.60		**0.057a**
Age at Injury (months)				6.892	0.142[b]
	0-11 months	1 (2%)	2 (2%)		
	12-23 months	20 (48%)	63 (70%)		
	24-35 months	16 (38%)	19 (21%)		
	36 - 47 months	4 (10%)	4 (4%)		
	48 -59 months	1 (2%)	1 (1%)		
	60-72 months	0 (0%)	0 (0%)		
Height (inches)		34.21 +/− 2.99	32.95 +/− 2.79		0.071[a]
Weight (kg)		12.87 +/− 2.1	12.23 +/− 1.91		0.094[a]
Sex				0.47	0.493[b]
	Male	29 (69%)	56 (63%)		
	Female	13 (31%)	33 (37%)		
Laterality				4.857	**0.028[b]**
	Right	28 (67%)	41 (46%)		
	Left	14 (33%)	48 (54%)		

Data is presented as n(%), mean +−- SD, or median (IQR). a- Independent T tests, b- Pearson Chi square test. P values listed in bold indicate significance less than 0.05

would be more likely to be injured when riding down a slide in the lap of an adult versus riding alone.

Our study mirrors earlier epidemiologic studies demonstrating that toddler's fractures are a common pediatric lower extremity injury that primarily occur after falls and playground injuries[2, 6,8,11]. Given the increasing incidence of playground related injuries in recent years[6,10] in conjunction with our finding that over one third of toddler's fractures result from playground slide injuries, there is a need for an updated understanding of the factors that place patients at risk for these injuries in order to provide adequate information for federal interventions such as the US Consumer Product Safety Commission (CPSC). The CPSC has recommendations on age-appropriate playground equipment, however there are

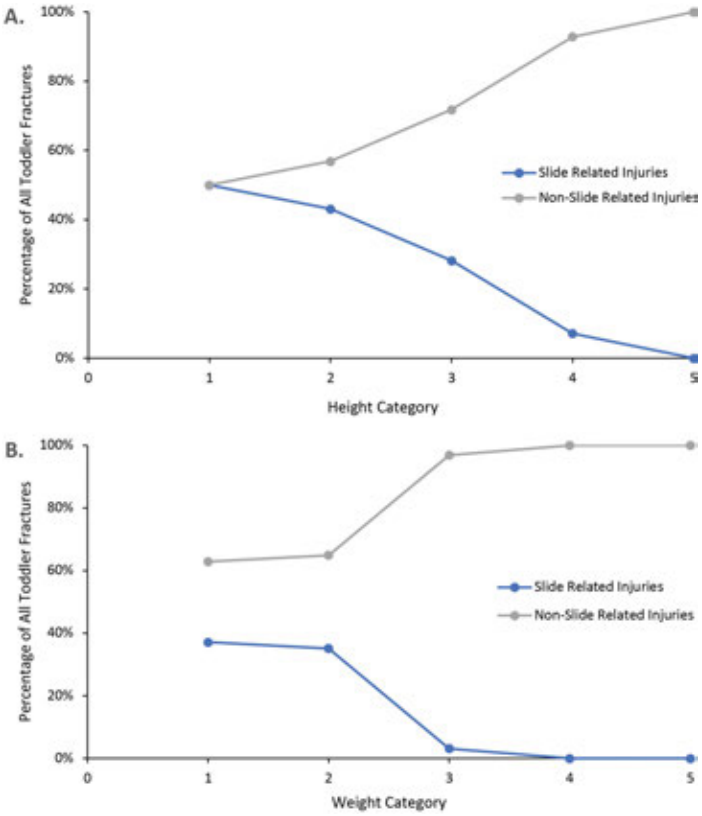

Figure 1. Percent of all Toddlers Fractures as a function of height and weight. Panel a) The height categories are as follows: 1: 25-30 inches, 2: 30-35 inches, 3:35-40 inches, 4:40-45 inches, 5:45+ inches. Panel b) The weight categories are as follows: 1: 0-10kg, 2:10-20kg, 3:20-30 kg, 4: 30-40 kg, 5: 40+ kg.

no current height, or weight restrictions regarding playground slide use[12]. Based on the average height and weight of children in the US, our findings suggest that children up to age 4-5 years old may be at an elevated risk of a slide related injury[13].

Riding on the lap of an adult on a slide also poses serious risk for a child. Recent literature suggests that children less than 3 years old were over 12 times more likely to be identified as being on a lap at the time of injury as compared to older children[6]. While our study demonstrated that the highest proportion of slide injuries occur in children younger than 3, we did not find a difference in the age between those who rode the slide alone and those who rode in the lap of an adult. One possible reason for this difference is that the prior study included all lower extremity injuries while our study solely evaluated toddler's fractures. However, given that the highest proportion of slide related injuries occurred in children 0-3 years old, our recommendation is that parents exhibit extreme caution when allowing children less than 3 years old to go down slides either alone or accompanied by an adult.

This study is limited by the retrospective design and the geographic location of this single center study.This study was also not designed to assess whether quarantine restrictions during the COVID-19 pandemic influenced the demographics or common mechanism of injury. Previous research has demonstrated there was an overall decrease in playground related injuries during the first months of the COVID-19 pandemic[14]. Finally, given that many toddler's fractures are occult it is unclear if there are demographic differences between patients included in the study and those that were not evaluated for injury.

Conclusion

Height and weight are associated with mechanism of injury for toddler's fracture, and parents must use extreme caution when a child under 30 inches or 20 kg rides a slide.

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Bone and Development

The Addition of Cerclage Wiring Does Not Improve Fixation of Mid-Diaphyseal Periprosthetic Humerus Fractures

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Introduction

The increased use of total shoulder arthroplasty (TSA) to treat osteoarthritis has led to an increase in periprosthetic fractures, especially in the elderly population. Reconstruction of humeral periprosthetic fractures continues to be a difficult task, with an overall complication rate ranging between 20% to 40%, and a nonunion rate up to 13%. Open reduction internal fixation with plates and screws is often used to address mid-diaphyseal fractures, but this poses a technical challenge because the stem of the TSA implant prevents bicortical screw purchase. Cerclage techniques (wrapping thin Kirchner wires around the plate and bone) have been used to provide additional support to a lateralized locking plate. Recently, the introduction of polyaxial locking screws has provided surgeons with the ability to gain improved screw purchase around the stem of the TSA implant without sacrificing rigidity of the screw-plate interface. It is currently unclear if this design feature eliminates the need for cerclage wiring to provide additional support. The purpose of this study was to determine the fixation strength of mid-diaphyseal periprosthetic fracture reconstructions using polyaxial locking plates with and without cerclage wires. We hypothesized that, although cerclage wiring provides limited support to the reconstruction in isolation, it is not a significant contributor to overall construct stability.

Methods

Eighteen synthetic (4th generation Sawbones) left humeri were implanted with a TSA implant by a fellowship-trained orthopaedic surgeon. Periprosthetic fractures were modeled by creating a ± mm osteotomy 10 mm distal to the tip of the humeral stem. Fractures were reconstructed with three separate techniques (n = 6): cerclage only (C), screws only (S) and cerclage with screws (CS) (Figure 1A). Specimens underwent dynamic axial compression and torsional test protocols. Compression tests modeled loaded motions, such as rising from a chair, which have transient centers of pressure on the humeral head. A custom jig that uses the humeral head as a fulcrum in a see-saw mechanism was designed for this study (Figure 1B). Controlled displacements were applied to the left side of the see-saw with a universal test frame and the opposite side was balanced by a spring. This setup resulted in humeral head contact forces between ~150-350 N. Because the crosshead of the test frame does not directly contact the humeral head, a thin film pressure sensor (Tekscan) was used to measure loads and 3D motion capture was employed to measure interfragmentary motions. Samples were cycled for 1000 cycles. For torsional tests, a custom mold was used to apply controlled moments of 2 Nm for 10 cycles, followed by a ramp to 10 degrees of valgus rotation relative to the shaft at 1 deg/s (Fig 1C). For both test modes, a bilinear fitting algorithm was used to determine stiffness in the toe and elastic regions of the stiffness curves. Differences between groups were determined by performing one-way ANOVAs with pairwise comparisons, with significance set to $p < 0.05$.

Results

Compression testing revealed no significant differences in stiffness between the C, S, and CS groups immediately after reconstruction (10 cycles) and after cyclic loading (1000 cycles) (Figure 2). Although stiffness values during compression were similar between groups, non-destructive torsional testing revealed significantly lower stiffnesses in the C group when compared to the other groups (Figure 3A&B). After 10 cycles the C group had a toe region stiffness of 0.816 ± 0.3 Nm/deg, while the S group (1.436 ± 0.3 Nm/deg, $p = 0.0039$) and CS group (1.268 ± 0.5 Nm/deg, $p = 0.076$) were substantially higher. For rotational stiffness in the elastic region, the C group demonstrated a decrease in stiffness (0.373 ± 0.1 Nm/deg) while the S and CS groups showed significantly higher elastic stiffnesses of 0.880 ± 0.1 Nm/deg and 1.069 ± 0.3 Nm/deg ($p < 0.001$ for both comparisons). Destructive torsional testing revealed differences in toe stiffness between the C group (0.607 ± 0.1 Nm/deg) and the S group (0.959 ± 0.2 Nm/deg, $p = 0.0113$), with similar findings compared to the CS group (0.928 ± 0.3 Nm/deg, $p = 0.0415$). Significant changes in

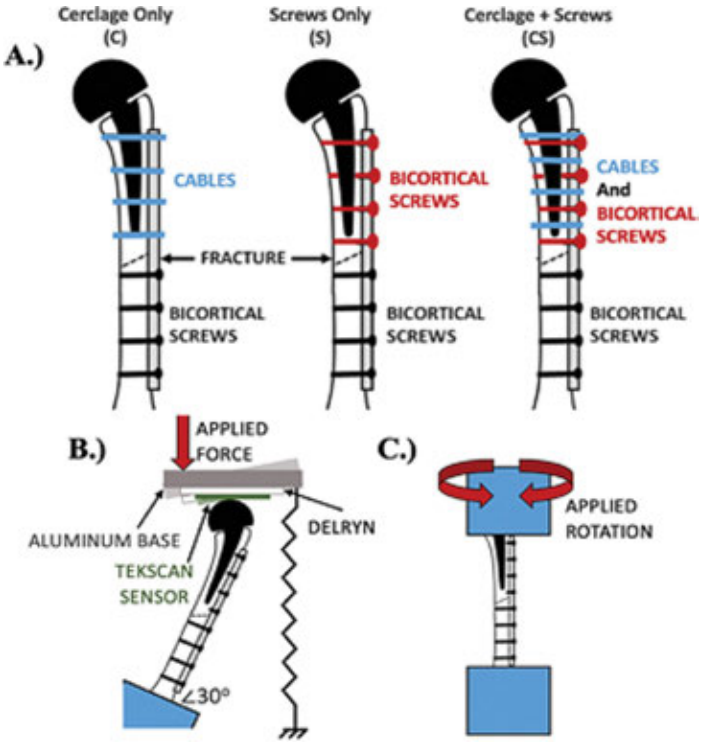

Figure 1. (A) Visualization of specimens in the C, S, and CS groups after fixation; **(B)** Axial see-saw test setup; **(C)** The torsional tests performed.

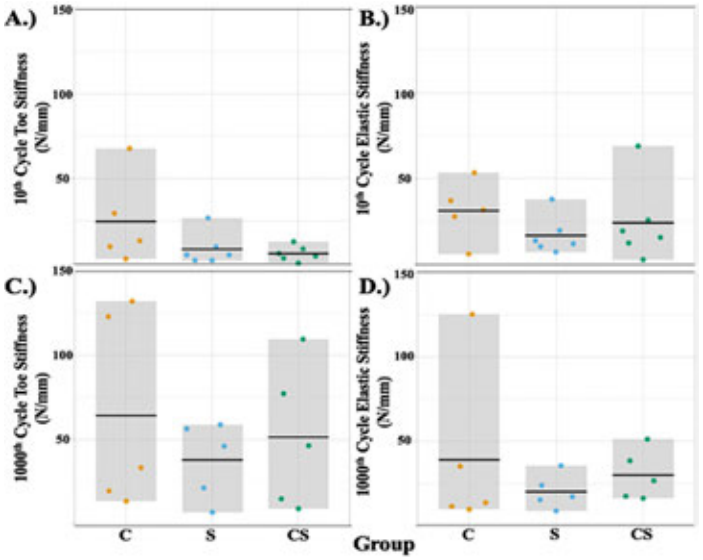

Figure 2. (A) Toe stiffness after 10 cycles; **(B)** Elastic Stiffness after 10 cycles; **(C)** Toe stiffness after 1000 cycles; (D) Elastic stiffness after 1000 cycles.

rotational stiffness were not present in the elastic region of the curve. Finally, there were significant differences in the maximum torque achieved. Group C showed a maximum torque of 6.331 ± 0.8 Nm, and specimens in group S (8.057 ± 0.5 Nm) and CS (7.527 ± 1.0 Nm) were significantly higher than C, but not compared to each other.

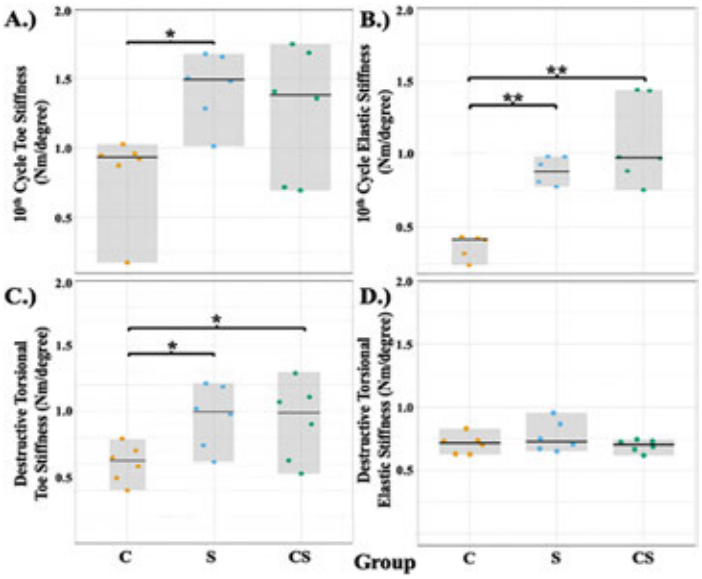

Figure 3. (A) Toe stiffness after 10 cycles of non-destructive torsion; **(B)** Elastic Stiffness after 10 cycles non-destructive torsion; **(C)** Toe stiffness during destructive torsion; **(D)** Elastic stiffness during destructive torsion. (*) represents a statistical difference of $p<0.05$ and (**) represents a statistical difference of $p<0.001$.

Discussion

Results from this study indicate that the addition of cerclage wiring does not improve initial fixation of polyaxial locking plates in humeral periprosthetic fracture reconstruction. Interestingly, the isolated use of cerclage wiring provided remarkably strong fixation during compression tests. However, qualitative assessments during experimentation indicated that this group experienced settling as specimens were loaded into the jig. Similarly, torsional ramp to failure testing indicates significant differences in toe stiffness, but not in the elastic region. This may be explained by some toggling of the cerclage-supported proximal fragment at low torques followed by stiff behavior as the bone engages with the wire support. This study was limited to the analysis of synthetic bones and further testing should be conducted with a cadaveric model.

Significance/Clinical Relevance

Fixation of periprosthetic humerus fractures continue to be challenging. Although it may be tempting to believe that initial fixation strength can be improved with the addition of cerclage wires, this technique provides no biomechanical advantage.

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U·P·O·J

Mechano-active Therapeutic Release to Preserve Subchondral Bone After Nanofracture in a Large Animal

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Introduction

During microfracture, the subchondral bone is perforated to enable the upward migration of marrow cells. While beneficial for repair tissue formation, these subchondral perforations can lead to bony cysts and resorption, compromising the foundation on which the neocartilage forms. To extend the lifetime of cartilage repair and minimize bone damage, smaller diameter, deeper marrow stimulation holes (nanofracture – Nfx) can limit bone resorption[1]. In this study, we aimed to further preserve the subchondral bone after Nfx by locally delivering osteogenic therapeutics to the cartilage-to-bone interface. To do so, we designed mechanically activated microcapsules (MAMCs) applied at the osteochondral interface, and locally release small bioactive agents—triiodothyronine (T3) and ß-glycerophosphate upon mechanical loading. We hypothesized that the delivery of therapeutic MAMCs would reduce bone resorption and stimulate local bone formation at the osteochondral interface, as assessed 1 and 2 weeks post-Nfx.

Methods

Osteogenic assessment

Mesenchymal stromal cell (MSC) pellets (200,000 cells/pellet) were precultured in chondrogenic media with TGF-ß3 (10 ng/mL), administered a single dose of T3 (10 nM) and ß-glycerophosphate (10 mM) (or not for the controls), and further cultured for 2 weeks in chemically defined media, as previously described by Mueller et al[2]. An alkaline phosphatase (AP) assay was performed on collected culture media at the terminal time point.

MAMC fabrication

MAMCs were fabricated as previously described, and osmotically annealed[3]. Sinking behavior was assessed in saline. The mechano-release profiles of the MAMCs were tested in direct compression using an Instron.

Surgical model

Six adult male Yucatan minipigs underwent a unilateral cartilage defect repair procedure. Six 5 mm diameter chondral defects were created in the trochlear groove. The treatment groups included: Nfx alone (n = 2/animal), Nfx + control MAMCs (n = 2/animal), and Nfx + therapeutic MAMCs (n = 2/animal). Therapeutic MAMCs delivered 1.3 ng T3 and 432 µg ß-glycerophosphate to the respective defects. Nanofracture was performed with a 1.2 mm diameter SmartShot® device (2 holes/defect). At the time of surgery, all animals received an intravenous injection of xylenol orange1. The animals were euthanized 1 (N = 3) and 2 (N = 3) weeks post-surgery.

Post-mortem analyses

Osteochondral units were prepared for microcomputed tomography (µCT) scanning. The samples were then cryosectioned to the midplane of each defect, and serially stained (mineral label, tartrate resistant acid phosphatase (TRAP), AP, Toluidine Blue)[4]. The remaining samples were further embedded in paraffin wax, sectioned, and stained.

Statistics

Figure 1A: t-test, Figure 1D, 2C, 2E: ANOVA, Bonferroni corrections. Data shown: mean ± standard deviation.

Results

A single dose of T3 and ß-glycerophosphate increased AP activity of MSC pellets (Figure 1A). These therapeutic agents were selected for encapsulation in MAMCs. Control MAMCs were slightly larger in diameter than the therapeutic MAMCs (Figure 1B). However, the shell thickness to diameter (t/d) ratio of each batch was similar (control: 0.08, therapeutic: 0.06). The MAMCs settled to the bottom surface of a glass vial (2.5 cm depth of saline) within 15 seconds (Figure 1C), and both batches had similar mechano-release profiles (Figure 1D). Post-surgery, all animals were weight-bearing within 2 hours (Figure 2A). All defects were utilized for each outcome (Figure 2B). The therapeutic MAMCs significantly reduced volumetric bone resorption in comparison to Nfx alone (Figure 2C). Interestingly, mineral labeling appeared similar after 1 week, but differences were marked at 2 weeks (Figure 2D). There were significant decreases in label coverage in both

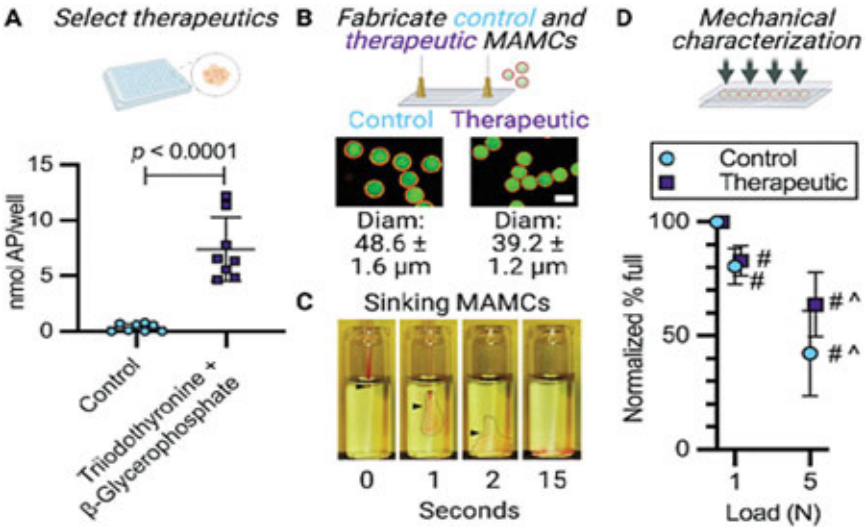

Figure 1. Development of mechanically activated microcapsules (MAMCs) containing osteogenic therapeutics—triiodothyronine and ß-glycerophosphate. **(A)** Alkaline phosphatase (AP) activity 2 weeks after a single dose of osteogenic agents to MSC pellets. **(B)** Fabricated MAMCs with and without osteogenic agents. Scale bar = 50 μm. **(C)** Sinking timeline in saline. **(D)** Mechanical characterization of MAMCs. #, ^ $p < 0.05$ compared to unloaded MAMCs, or MAMCs loaded to 1N, respectively (within the same condition).

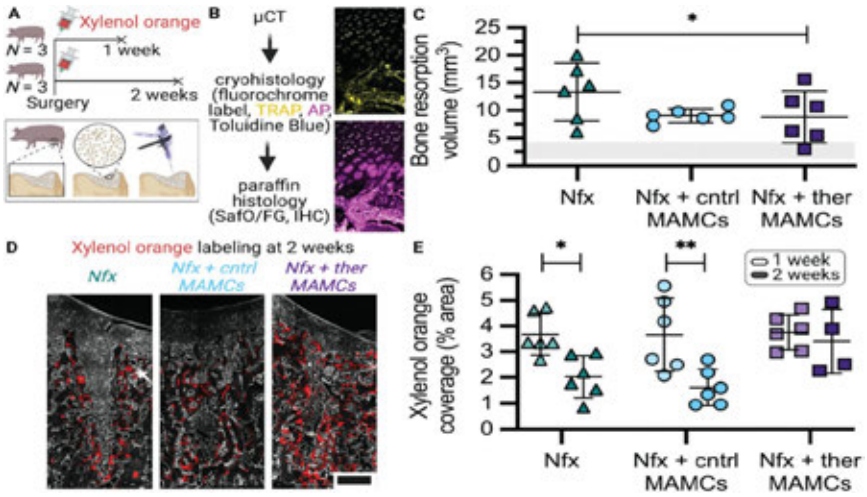

Figure 2. In vivo assessment of MAMCs containing osteogenic therapeutics to preserve bone structure after nanofracture. **(A)** Study and surgical outlines, respectively. **(B)** Outcome measures. TRAP: tartrate resistant acid phosphatase (yellow), AP: alkaline phosphatase (magenta). **(C)** Volumetric bone resorption after 2 weeks as assessed by μCT. Shaded region depicts range of values at 1 week. n = ± defects/condition. * $p < 0.05$. **(D)** Representative mineral labeling after 2 weeks. Scale bar = 1 mm. (E) Xylenol orange coverage near nanofracture hole at 1 week and 2 weeks post-labeling. n = 4-6 defects/condition per time. * $p < 0.05$, ** $p < 0.01$.

control groups, while label intensity was maintained with therapeutic MAMCs at this time (Figure 2E).

Discussion

Because mineral label incorporation is expected to occur over a 48 hr period post-injection, labeling coverage should be similar at later time points, unless label resorption is occurring. In our study, we observed a decrease in xylenol orange coverage in the Nfx alone, and NFx + control MAMCs group from the 1 to 2-week time point. However, the therapeutic MAMCs protected against this loss in label coverage. The intra-group variability observed for the therapeutic MAMC group may be attributed to the retention of the MAMCs within the defects. MAMCs were delivered within a saline solution and could have theoretically left the defect space after Nfx. We were unable to assess MAMC retention in this model, because of the overlying repair tissue. Future studies will ensure MAMC localization by incorporating these drug carriers within a scaffold or crosslinked hydrogel carrier material.

Significance

These data support the use of MAMCs for therapeutic delivery in load bearing environments, and the implementation of bone fluorochrome labeling to elucidate dynamic bony changes in large animals. This is the first assessment of therapeutic MAMCs in a large animal model.

Acknowledgements

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U·P·O·J

Proteomic Screening Identifies Novel Biomarkers of Synovial Joint Disease in Mucopolysaccharidosis I Dogs

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Introduction

The mucopolysaccharidoses (MPS) are a family of inherited lysosomal storage diseases characterized by deficient activity of enzymes that degrade glycosaminoglycans (GAGs) due to mutations in associated genes[1]. MPS I is characterized by deficient α-L-iduronidase (IDUA) activity, leading to progressive accumulation of poorly degraded heparan and dermatan sulfate GAGs in cells and tissues[2]. Synovial joint (e.g. hip, knee, hands and shoulder) abnormalities in MPS are prevalent, and patients experience significantly decreased quality of life due to pain and mobility impairment[2]. Studies suggest that progressive joint disease can be traced to a combination of developmental abnormalities and chronic inflammation, which accelerates soft tissue degeneration[3,4].There is a clinical need for specific biomarkers for assessment of joint disease progression and response to therapy. The naturally-occurring canine model of MPS I exhibits progressive synovial joint abnormalities similar to human patients, making it a clinically-relevant platform for biomarker discovery. The objectives of this study were to undertake an unbiased proteomic screen to identify molecular biomarkers upregulated in the synovial fluid (SF) of MPS I dogs and identify circulating (serum) biomarker candidates that may serve as strong predictors of synovial joint disease.

Methods

Animals and Sample Collection

With IACUC approval, serum and SF was collected from ± x MPS I affected and 5 x heterozygous control dogs at 12 months-of-age. Blood was collected from the cephalic vein, allowed to clot, then centrifuged and serum collected. Animals were then euthanized, stifle (knee) joints opened, and SF collected (~200µl) using an 18-gauge needle.

Mass Spectrometry

Total protein concentration was assessed using the bicinchoninic acid assay. SF was pretreated with hyaluronidase, and proteins in both SF and serum were denatured, reduced, alkylated, and digested into peptides. Peptide separation and mass spectrometric analyses were carried out using a Thermo Scientific UltiMate 3000 UPLC coupled to a Q Exactive HF Orbitrap LC-MS/MS System.

Bioinformatics and Statistical Analysis

Peptides were identified using Spectronaut software and Perseus was used to establish statistically-significant fold changes in protein abundance in MPS I vs control samples. Spearman's rank-order tests were used to examine correlations between serum and synovial fluid ($p<0.05$).

Results

In SF and serum samples, mass spectrometry identified 812 and 415 unique proteins, respectively. Principal component analyses (Figures 1A and B) demonstrated clustering of control and MPS I samples for both SF and serum, confirming significant effects of disease state on relative protein abundance. Examining SF, there were 151 proteins that exhibited significantly different abundance in MPS I vs control (Figure 1C), and of these, 104 exhibited a log2 fold change > 1. For serum, there were 154 proteins that exhibited significantly different abundance in MPS I vs control (Figure 1D), and of these, 64 exhibited a log2 fold change > 1. There were 50 proteins for which abundance was significantly different for both SF and serum, and of those, 32 exhibited a significant correlation in abundance between SF and serum across all 11 samples. To identify a shortlist of 10 biomarker candidates predictive of joint disease, these proteins were ranked according to their relative elevation in SF (MPS I vs control, Figure 2). Spearman correlation coefficients (SF vs serum) ranged from 0.64 to 0.90 for these 10 proteins (Figure 3).

Discussion

In this study, we identified novel candidate biomarkers of synovial joint disease in MPS I using the clinically-relevant canine model. Importantly, there were strong correlations between the abundance of these biomarkers in SF and serum, suggesting that they may serve as circulating biomarkers that specifically reflect

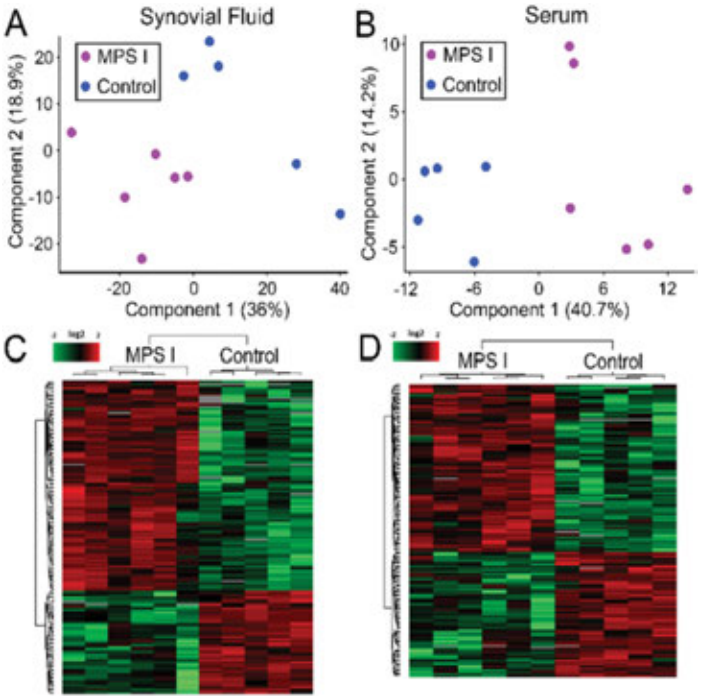

Figure 1. Principal component analysis plots showing clustering of samples as a function of disease slate for both **(A)** Synovial fluid and **(B)** Serum. Heat maps showing differences in protein abundance between MPS I and heterozygous control samplcs for **(C)** Synovial fluid and **(D)** Serun.

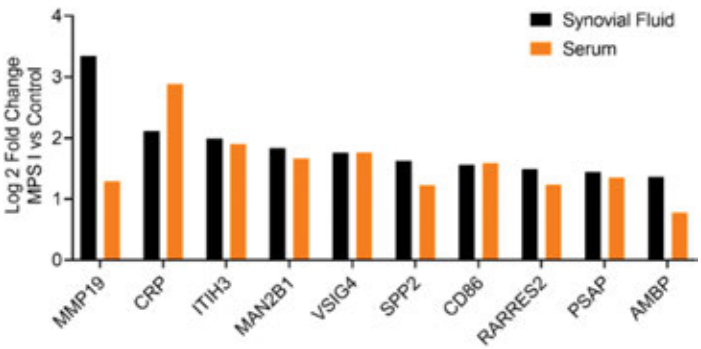

Figure 2. Candidate protein biomarkers that exhibit significantly elevated abundance in both synovial fluid and serum from MPS I dogs comparcd to heterozygous controls (all $p<0.05$).

joint disease severity and enhancing their clinical utility. These markers also provide novel insights into mechanisms of joint disease. For example, MMP19 (matrix metalloproteinase-19) cleaves aggrecan, a major component of healthy articular cartilage5. ITIH3 (inter-α-trypsin inhibitor heavy chain 3), while known to play a role in several neurological diseases, is also important for matrix stabilization[6], suggesting it may also play a role in joint health. RARRES2 (retinoic acid receptor responder 2 or chemerin) is an adipokine and inflammatory mediator that is elevated in both osteoarthritis and rheumatoid arthritis[7,8]. Finally, MAN2B1 (alpha-mannosidase) is a lysosomal hydrolyze, and its elevated abundance likely reflects broader lysosomal dysfunction secondary to IDUA deficiency. Ongoing work will further validate these biomarkers by undertaking correlations with structural and biomechanical changes in MPS I joints from both dogs and human patients.

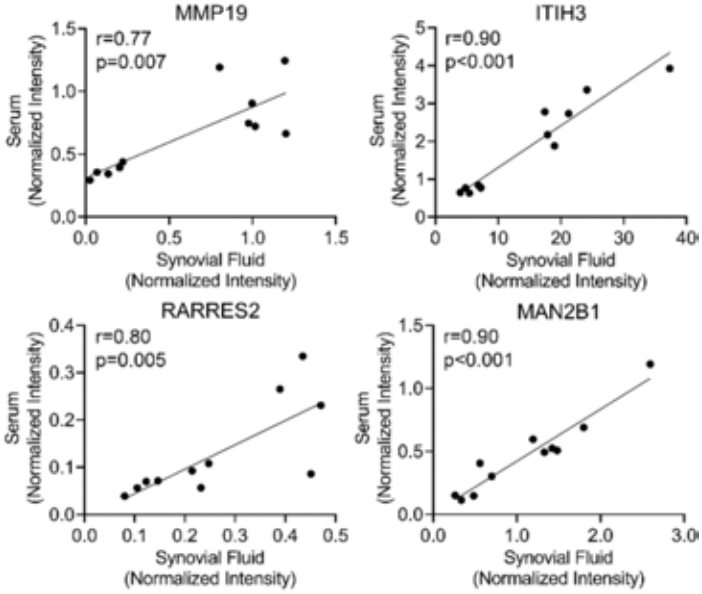

Figure 3. Plots for candidate biomarkers showing strong correlations between protein abundance in synovial fluid and serum. r = Spearman correlation coefficient.

Significance

Patients with MPS I exhibit debilitating synovial joint disease that negatively impacts quality of life. In this study we identify novel biomarker candidates that may permit minimally invasive monitoring of joint disease progression and response to therapy.

Acknowledgments

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U·P·O·J

Strut Thickness But Not Unit Cell Length Alters Mechanical Properties of 3D Printed Rib Implants: A Preliminary Study

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Introduction

Chest flail injuries, where two or more ribs are fractured, are painful injuries which can lead to long-term disability and even mortality[1]. Open reduction internal fixation with titanium plates and screws is commonly used to reduce these fractures but this technique has undesirable clinical outcomes, with up to 15% of patients requiring revision surgery[2]. Changing the mechanical properties of implants with additive manufacturing techniques may allow us to address patient-specific needs, which ultimately improves clinical outcomes. In large additively manufactured parts, it is known that changing strut thickness and unit cell length of a lattice (Figure 1) can effectively change mechanical properties[3,4,5,6]. However, little is known about how lattice architecture of rib implants influences mechanical properties of the implant—primarily because they are only 1.5 mm thick. The purpose of this study was to investigate how discrete changes to strut thickness and unit cell length change mechanical properties of titanium rib implants in bending (Figure 1). We hypothesized that altering the strut thickness and unit cell length of the lattice would lead to significant changes in bending stiffness and yield load.

Methods

24 test coupons that were similar width and thickness of existing rib fracture fixation plates (100 x 10 x 1.5 mm) were printed with a medical grade titanium alloy (Ti-6Al-4V Grade 23) powder. 20 coupons had 5 different lattice structures (n = 4) and solid coupons were used as the control (n = 4) (Figure 1). Test coupons had a shell thickness of 0.25 mm, and a 1 mm thick internal lattice section. For the lattice structures, unit cell length ranged from 1-3 mm, and strut thickness ranged from 0.225-0.425mm, which resulted in porosities ranging from 36-86%. External surfaces of the plates were designed with 13 holes (1 mm diameter) to allow powder drainage after manufacturing. All specimens were subjected to stress relief via heat treatment prior to testing. The geometric qualities and surface characteristics were evaluated via scanning electron microscopy (SEM). 4-point bending tests were performed to evaluate mechanical properties of each design. Tests were performed at 1.3 mm/min in a universal test frame with 25 mm spans between support and compression anvils. Bending stiffness, yield load, bending strength, toughness, post-yield energy, and maximum load were calculated[7]. Results were tested for normality followed by one-way ANOVAs and pairwise comparisons to determine statistical significance ($p < 0.05$).

Results

Changes in strut thickness and unit cell length led to significant changes in bending stiffness (Figure 2A), max load, and toughness, but no significant changes to yield load (Figure 2B) or bending strength were found. The most porous group (S225L3) exhibited a bending stiffness of 32.8 ± 1.4 N/mm, whereas the least porous group (S425L1) had a value of 38.4 ± 0.4 N/mm ($p < 0.001$) (Figure 2A). The bending stiffness for control specimens was in the middle of this range (34.8 ± 1.5 N/mm). Similarly, maximum load increased from 286.2 ± 3.3 N in the most porous group to 339.1 ± 6.2 N in the least porous group ($p = 0.002$), while the control group had a value of 322.0 ± 12.1 N. S225L1

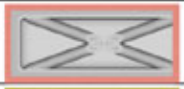
Group Names	Lattice Cross Section	Strut Thickness (mm)	X-direction unit cell length (mm)	Porosity (%)
S225 L3		0.225	3	86
S225 L2		0.225	2	84
S225 L1		0.225	1	78
S325 L1		0.325	1	58
S425 L1		0.425	1	36
Control		N/A	N/A	0

Figure 1. Cartoon diagram of the 5 different lattice cross sections used in this study. Strut thickness ranged from 0.225 to 0.425 mm and unit cell length ranged from 1 to 3 mm.

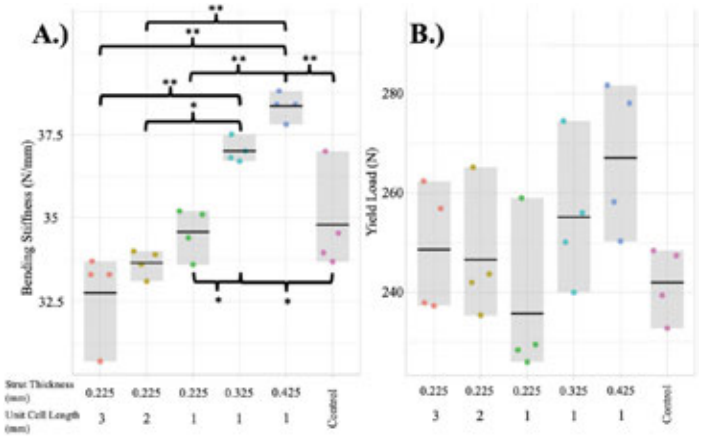


Figure 2. Bending Stiffness and Yield Load results for the 5 heat-treated lattice cross section designs and control specimen groups. (*) and (**) denotes a statically significant difference between two groups ($p < 0.05$ and $p < 0.001$, respectively).

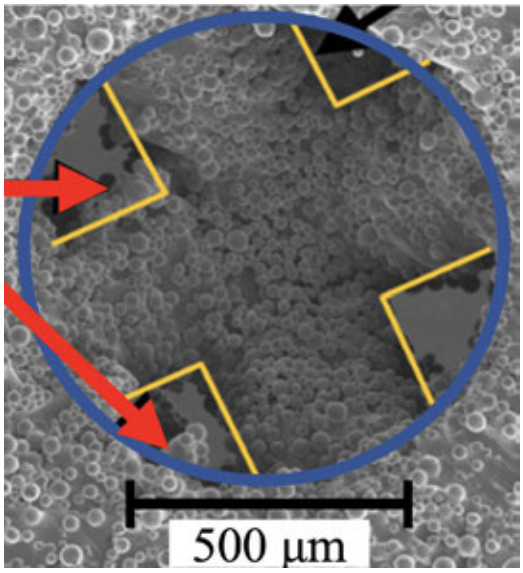


Figure 3. Representative SEM image of drainage hole (blue circle) with struts joining at node (yellow lines), and small powder agglomerations (red arrows.)

exhibited the lowest toughness (5.0 ± 0.4 J/mm^3), while S425L1 had the highest toughness (9.7 ± 2 J/mm^3, $p < 0.001$), while the control was 9.2 ± 0.3 J/mm^3. Measures of yield load (between 235.7 ± 15.6 N and 267.1 ± 15.2 N) and bending strength (between 2946.6 ± 194.8 and 3338.5 ± 190.4 Nmm) indicated no significant differences between groups. Finally, SEM images revealed successful formation of a lattice structure around each drainage hole, with some small agglomerations of powder clusters around the rim (Figure 3).

Discussion

Results of this study rejected our hypothesis, that changing both strut thickness and unit cell length would have a significant impact on mechanical properties. Our findings suggest that changing the lattice structure of a thin plate does not elicit the same changes in mechanical properties as cubic structures tested in previous experiments[4,6]. These preliminary results suggest that alterations to lattice structure can effectively modulate bending stiffness of a rib implant to be greater than or less than a solid control. At the same time, changes to lattice architecture does not significantly impact yield load. When taken together, this means that porous implants may bend more easily but resist permanent deformation at similar loads as their stiffer counterparts. Further testing is needed for refined, full-sized implant designs that include holes for screw placement. Future designs will also incorporate internal gradient-based lattice designs that seamlessly alter mechanical properties along the length of the implant.

Significance/Clinical Relevance

This study provides insight into our ability to fundamentally alter rib fracture implant performance by changing the internal lattices of additively manufactured parts. Future implant designs can leverage this approach to improve congruency between implants and native bone, which may reduce incidence of revision surgery and improve overall clinical outcomes.

Acknowledgements

DePuy Synthes provided materials and technical support for this study.

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Engineered Hierarchical Surface Roughness Regulates Mesenchymal Stem Cell Spreading, Proliferation, and Differentiation on Titanium Implants

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Introduction

Titanium has been widely used for orthopedic implants given its excellent biocompatibility and high strength and durability[1]. Multiple surface modification techniques have been introduced to enhance cell interaction and differentiation, including promotion of osteogenesis and bone formation[2]. All cell types, including progenitor cells [e.g., mesenchymal stem cells (MSCs)], are responsive to biophysical cues they experience within their microenvironment. These cues can include material stiffness, organization, deformation, and surface topography[3]. Such cues elicit reorganization of the internal cyto-architecture and mechanical signaling of cells and can be leveraged to direct lineage specification. Our team recently developed a method to enhance the topology of titanium implant surfaces using an Electron Beam Melting (EBM), and here, we explored how this manufacturing process impacted initial MSC interactions, spreading, proliferation, expansion, and osteogenic differentiation.

Methods

Human mesenchymal stem cells were purchased (hMSC, Lonza, male 23 years), and passage two cells ($5 \times 10^{\wedge 4}$ cells) were seeded onto one of 3 surfaces: 1) Smooth Titanium (Smooth), and two proprietar 3D-printed (P3D) titanium surfaces [Electron Beam Melting (EBM)], which consist of a hierarchical surface roughness that spans from the macro to nano-scale having lesser 2) P3D1 or greater 3) P3D2 surface roughness. Surface characterization was performed using scanning electron microscopy and surface profiles were determined via image analysis (ImageJ) of brightfield micrographs, where average roughness values (R_a) were determined according to ASME B46.1. Cell seeded titanium surfaces (diameter 20 mm) were cultured in a serum containing basal growth media (BM) or in an osteogenic media (OM). Throughout a 21-day culture period, cell morphology was assessed by staining for filamentous actin (phalloidin), and cell area and aspect ratio (> 25 cells from n = 3 surfaces) was calculated using Image J. In addition, cell proliferation was assessed using the Alamar Blue assay (n = 6 samples/group) and osteogenic differentiation was evaluated by RT-PCR of Type-I Collagen (COL-I) and Osteocalcin (OCN) (n = 6 samples/group). Statistics were performed using ANOVA with Tukey's post hoc testing with 95% confidence interval.

Results

SEM images showed evidence of a hierarchical surface roughness spanning from the macro to the nanoscale [average roughness (R_a): P3D1: 50 ± 4 μm, P3D2: 65 ± 6 μm] (Figure 1A, B), and initial MSC adhesion showed marked differences between smooth and rough surfaces (Figure 1A). This was confirmed via Phalloidin staining and quantification shown in Figure 2. On smooth surfaces (Smooth), MSCs adopted a large spread area with abundant stress fibers on Day 1, while on the rougher surfaces (P3D1 and P3D2), MSCs had a smaller spread area (Figure 2A-C) with fewer and smaller focal adhesions (not shown). Both cell area and aspect ratio were significantly lower (by >25%) on the P3D1 and P3D2 surfaces, compared to cells on smooth titanium ($p<0.05$) (Figure 2A-C). With respect to proliferation, throughout the 21 days of culture, hMSCs expanded rapidly on both smooth and rough surfaces, with no significant differences in the either BM or OM culture condition (Figure 3A). RT-PCR analysis of BM conditions

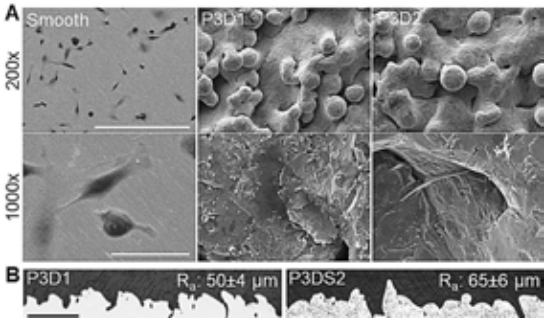

Figure 1. (A) Representative SEM images of MSC seeded titanium surfaces: Smooth, P3D1, or P3D2 [Scale bars = 300 μm (top) and 50 μm (bottom). **(B)** Representative micrographs of P3D1 and P3D2 and average roughness values (Ra) (Scale bar = 500 μm).

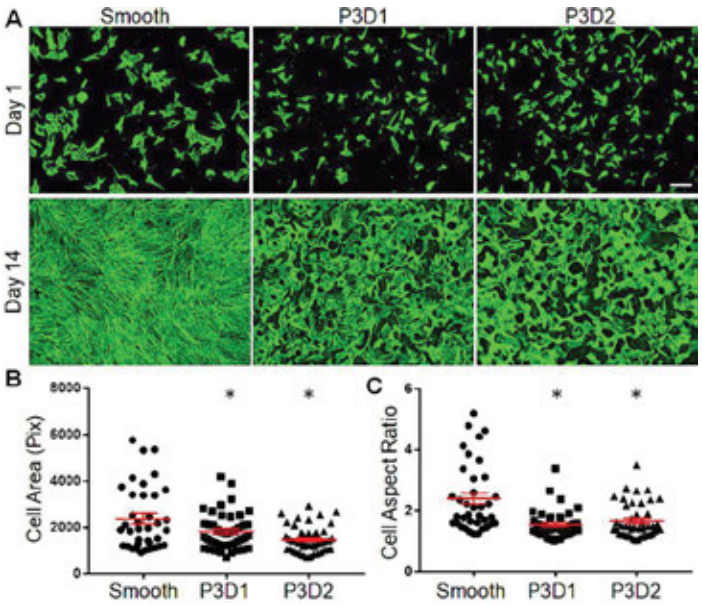

Figure 2. (A) Representative actin staining of MSC seeded titanium surfaces: Smooth, P3D1, or P3D2, Scale bar = 100 μm. **(B)** Quantification of cell area and aspect ratio on Day 1 (n > 30, mean ± SEM, *: p<0.05 vs. Smooth).

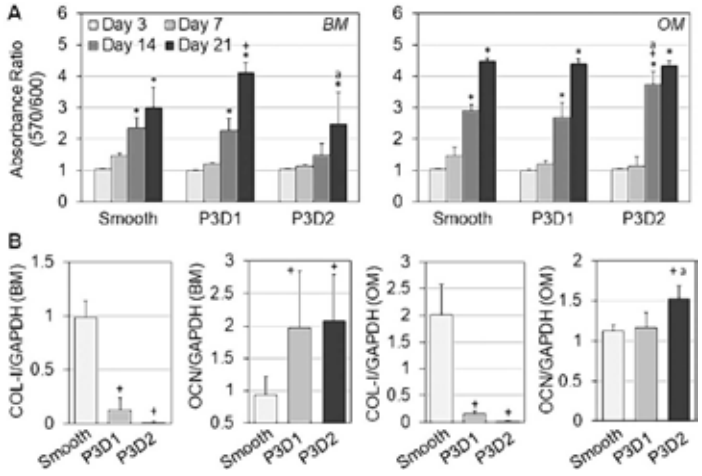

Figure 3. (A) Cell proliferation assessed by the Alamar blue assay. **(B)** Osteogenic gene expression determined by RT-PCR on Day 14 in hMSC cultured in basal growth media (BM) or osteogenic differentiation media (OM). (n = 6, *: p < 0.05 vs. Day 3, +: p < 0.05 vs. Smooth, a: p < 0.05 vs. P3D1).

showed that COL-I was more highly expressed on smooth surfaces than on rough surfaces, while OCN expression was higher on the rough surfaces (Figure 3A). In OM conditions, COL-I expression remained considerably higher on the smooth surface compared to the rough surfaces, while OCN expression was higher on the P3D2 surface (Figure 3B).These data indicate that the smooth surfaces may lead to fibrogenic differentiation of hMSCs, while surfaces with enhanced roughness may promote osteogenic differentiation.

Discussion

Our findings indicate that MSCs rapidly adopt a spread morphology on stiff, smooth titanium surfaces. Conversely, materials produced with a proprietary EBM build theme promoted less initial spreading but greater osteogenic differentiation over time when compared to smooth Ti. Taken together, these findings demonstrate that proprietary 3D printed titanium implants can be produced with surface features that regulate adhesion, spreading, and differentiation of bone marrow derived MSCs. Improvements engendered by rough surfaces may result in greater boney tissue formation when such surfaces are used for spinal fusion procedures. Future work will explore the mechanism by which this 3D printed surface roughness improves osteogenesis and its impact on mineral deposition and bone formation *in vivo*. Our data show that controlling the surface roughness on titanium implants regulates hMSC morphology and osteogenic differentiation propensity, which may enhance bone formation in clinical scenarios where rapid osseointegration and fusion are required.

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Cartilage, Meniscus and Disc

Effects of Organ Culture and Mesenchymal Stem Cell Delivery on the Cellular Composition of the Nucleus Pulposus

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Introduction

Intervertebral disc degeneration is a major cause of low back pain, the leading cause of disability worldwide.[1] Emerging cell-based therapies targeting the disc nucleus pulposus (NP), including those employing adult mesenchymal stem cells (MSCs), have shown promise in preclinical studies. However, consistent demonstration of efficacy and clinical translation is impeded by a poor understanding of the mechanisms of action. MSC-mediated mechanisms of action may include immunomodulation of endogenous cells, or direct reconstitution of native NP tissue.[2] Whole disc organ culture is a powerful preclinical tool for investigating such mechanisms under controlled conditions that closely recapitulate the *in situ* biochemical and biophysical microenvironments.[3,4] The objective of this study was to apply single cell RNA sequencing (scRNA-Seq) to investigate the effects of MSC delivery on the cellular composition of the NP using a whole disc organ culture model.

Methods

Lumbar spines were obtained postmortem from three male large frame goats, and discs were isolated and allocated to 3 experimental conditions: 1) NP cells freshly isolated from discs postmortem (i.e. no organ culture); 2) NP cells isolated after 7 days of whole disc organ culture; and 3) NP cells and MSCs isolated after 7 days of whole disc organ culture. For this final group, allogeneic adult goat bone marrow-derived MSCs (0.2×10^6 in 200µl saline) were injected into the NPs of discs on day 0. For all conditions, cells were isolated from the NP using a central 5mm biopsy punch followed by collagenase digestion. For organ culture, bony end plates were removed and discs were cultured with intact cartilaginous end plates in basal media (DMEM + 10% FBS) under limited swelling conditions [3]. For each condition, isolated cells from 5 discs were pooled, assessed for viability using trypan blue staining, and analyzed using scRNA-Seq. Libraries were generated using the Chromium controller (10X Genomics) and sequencing was performed using the Illumina HiSeq platform. Unsupervised clustering was conducted using Seurat and KEGG pathway analyses performed. Finally, one disc from each organ culture condition was assessed for cell viability using *in situ* live/dead staining.

Results

A total of 28,898 cells were sequenced (median 1284 genes/cell and 4904 UMIs/cell): 13,697 freshly isolated NP cells (94% viability), 7,637 NP cells after organ culture (86% viability), and 7,566 NP cells and MSCs after organ culture (74% viability). Lower viability for both organ culture conditions was confirmed by *in situ* live/dead staining (Figure 1). UMAP plots generated for each condition using identical analysis parameters identified ± unique cell clusters (Figure 2), with the percentage of cells present within each cluster differing between conditions. The number of cells in cluster 1 remained relatively consistent between conditions. In contrast, the percentage of cells in cluster 2 in both organ culture conditions was greatly diminished (< 7% of total cells). Cluster 5, largely absent in freshly isolated NP cells and NP cells alone after organ culture, comprised 28.15% of total cells for combined NP cells and MSCs after organ culture. In contrast, cluster 6, largely absent for freshly isolated NP cells, and combined NP cells and MSCs after organ culture, comprised 4.32% of total cells for NP cells alone after organ culture. Cluster-specific gene expression analyses performed for pooled cells across all 3 conditions (Figure 3) revealed that expression of NP-specific extracellular matrix (ECM) genes (ACAN, COL2A1 and COL6A3) was highest in cluster 2, and lowest in cluster 6. Expression of inflammatory/cell stress genes, including JUN, NFKBIA and PTGS2, was elevated in cluster ± vs other clusters. Pathway analysis also revealed down regulation of ECM-related and PI3K-Akt signaling pathways in both clusters 5 and ± compared to cluster 1, while there was upregulation of TNF-α signaling in cluster ± vs cluster 5.

A

Experimental Condition	% Viability after Isolation
Freshly Isolated NP Cells	94%
NP Cells after Organ Culture	86%
NP Cells and MSCs after Organ Culture	74%

B

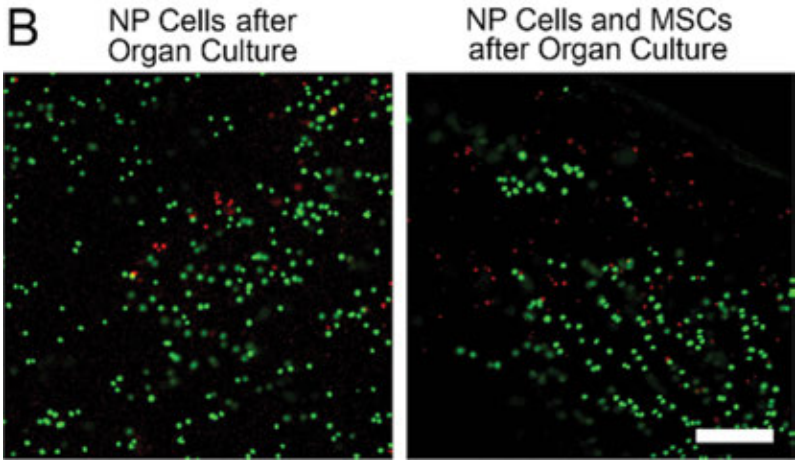

Figure 1. (A) Percent viability of isolated cells from each condition prior to scRNA-Seq. **(B)** Representative in situ live (green) and dead (red) staining of cells for organ culture groups (scale = 100μm).

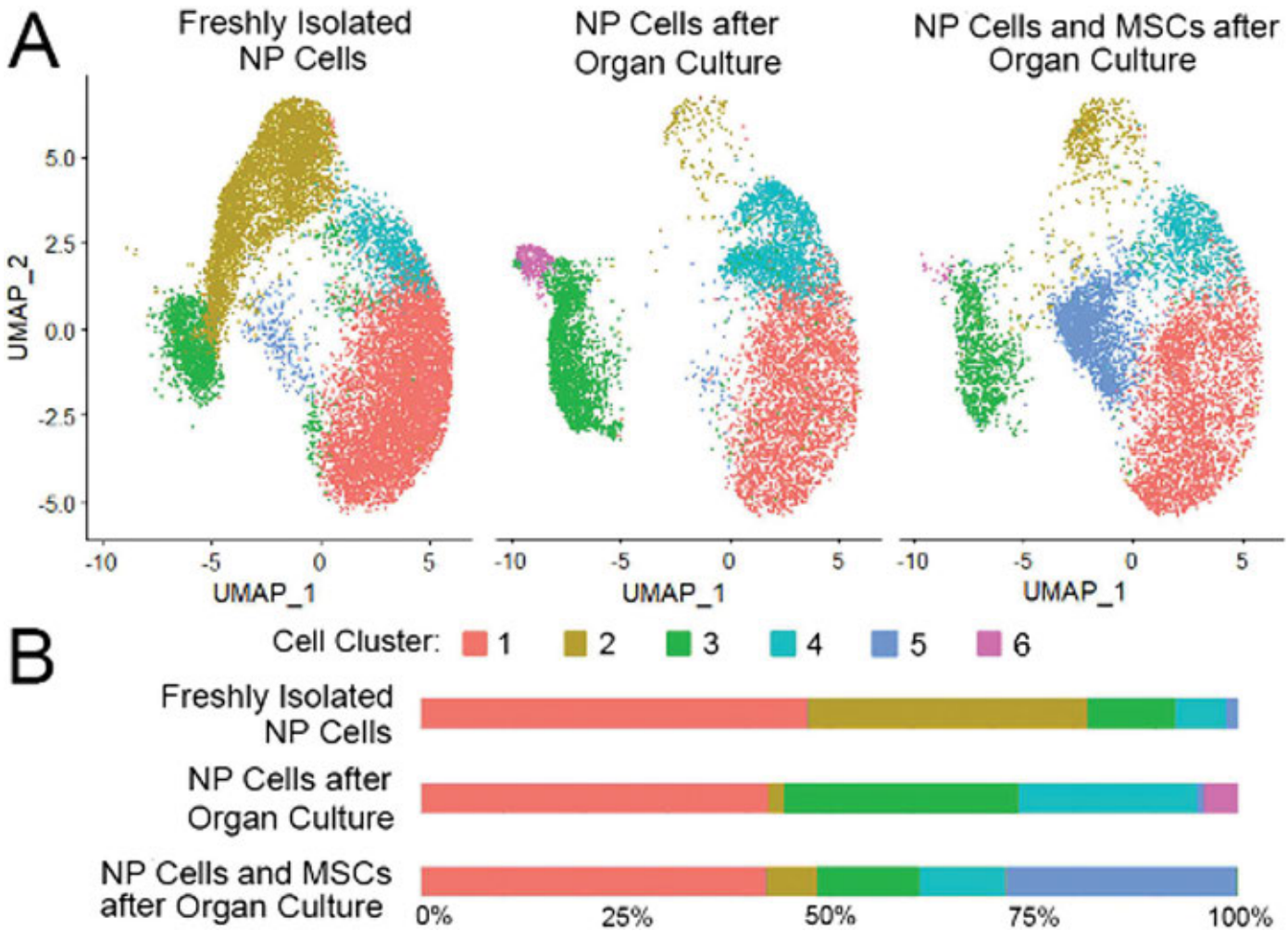

Figure 2. (A) UMAP plots showing the presence of six distinct cell clusters for each of the three experimental conditions. **(B)** Graph showing how the percentage of cells in each cluster varied between experimental conditions.

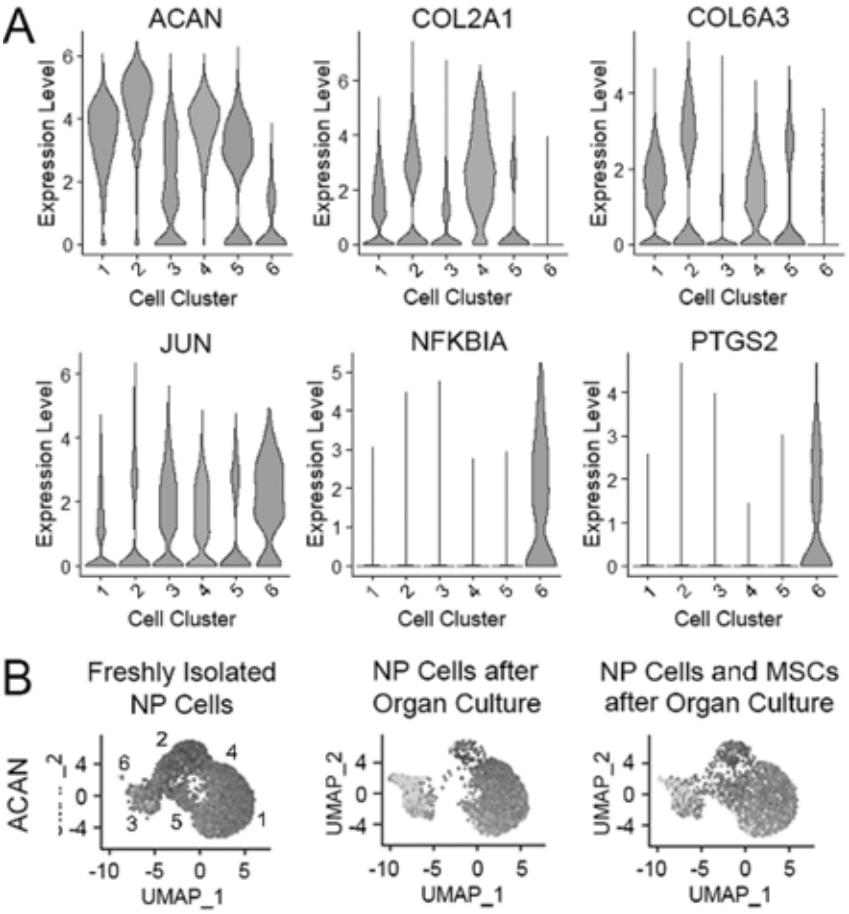

Figure 3. (A) Violin plots showing relative expression of ECM and inflarmnatory/cell stress genes in each cluster. **(B)** UMAP plots showing relative expression of ECM genes in each cluster.

Discussion

The goat is an established model for studying lumbar disc degeneration and cell-based therapies.[5] In this study we provide evidence of cell heterogeneity with the NPs of adult goat intervertebral discs, including distinct subpopulations characterized by unique gene expression profiles, a result that is consistent with recent scRNA-Seq studies of both bovine and human discs showing similar heterogeneity.[6,7] Organ culture models are used extensively as preclinical tools to study disc degeneration and therapeutic intervention.[3,4] Here we show that while organ culture did preserve some phenotypic properties of NP cells, there was an overall decrease in expression of key ECM genes after 7 days, potentially due to cell stress and/or de-differentiation. While discs were maintained under limited swelling conditions in this study, it is possible that bioreactors that apply physiological loading during culture[4] may be able to better maintain native cell characteristics. Delivery of MSCs resulted in suppression of pro-inflammatory signaling, supporting a potential immunomodulatory role for these cells.

Significance

Stem cell-based regeneration of the intervertebral disc is a promising treatment strategy for low back pain patients. In this study we provide insights into the cellular composition of the disc NP and potential mechanisms underlying MSC-based NP regeneration.

Acknowledgments

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U·P·O·J

Surgical Reattachment of the Anterior Horn Slows OA Progression in a Large Animal Injury Model

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Introduction

The meniscus is a critical tissue for the mechanical function of the knee. Meniscal injuries are common, and when injured, the ability of the meniscus to distribute loads is impaired, leading to aberrant forces on the knee cartilage and progression to OA[1]. Our previous work developed an arthroscopic model of DMM, where the anterior horn of the meniscus was resected[2] This model resulted in deleterious changes in the knee cartilage, however many of these changes appeared to be transient, as the anterior horn attachment scarred back in place and began bearing load[2]. The aim of this study was thus two-fold: 1) to increase the severity of the initial DMM injury to induce a more degenerative cartilage pathology, and 2) to evaluate whether surgical repair via acute reattachment could prevent progression to an OA phenotype.

Methods

Eight skeletally mature (12-month-old) Yucatan minipigs underwent mini-arthrotomy of the right stifle. In all animals, the anterior attachment of the medial meniscus was transected. This attachment was either immediately repaired using a vertical mattress suture and suture anchor (Repair) or a 5mm section of the attachment was resected *en bloc* (Injury). Animals were sacrificed at ± weeks post-op, and intact contralateral limbs were used as controls. All animal procedures were performed with IACUC approval. After euthanasia, stifle joints were dissected, synovium tissue was identified and isolated, and the tibial plateaus were assessed for cartilage wear using India ink. Osteochondral segments of the medial tibial plateau were removed. These were potted using a low-melting temperature bismuth alloy with the cartilage surface exposed, submerged in a PBS solution containing protease inhibitors, and indented with a 2mm diameter spherical indenter at four locations—two each on cartilage regions previously covered by the meniscus or on more central uncovered regions. Fifteen-minute duration creep tests at a 0.1N load were fitted to a model of Hertzian biphasic creep[3], and values for compressive modulus, tensile modulus, and permeability were determined. Values for the covered and uncovered regions were averaged. Next, osteochondral tissues were scanned via uCT at 70kVp, 85μA, with a voxel size of 10.3μm. Trabecular thickness and bone volume fraction were calculated for 3mm diameter cylindrical regions of interest superficial (0-1mm) and deep (2-4mm) to areas previously covered or uncovered by the meniscus.These osteochondral units were then decalcified, paraffin processed, embedded, sectioned, and stained with Safranin O/Fast Green. Synovium sections were stained with Hematoxylin/Eosin. All quantitative data were compared with one-way ANOVA followed by Tukey's post hoc tests, with significance set at $p < 0.05$.

Results

Injured joints showed more macroscopic signs of degeneration than intact controls, with a significantly greater proportion of the medial tibial plateau positive for India ink staining. Qualitatively, repair joints showed less wear than injured joints and were not significantly different from the Intact group (Figure 1**).** While tensile and compressive modulus were not significantly different between groups in covered and uncovered regions of the cartilage, the uncovered permeability trended higher

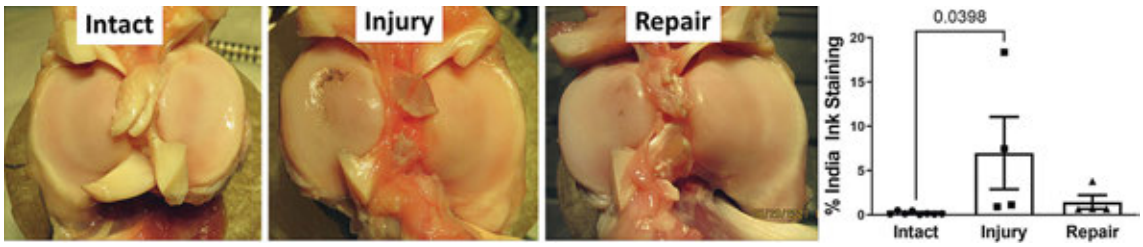

Figure 1. Group median images of tibial plateau with India ink staining and quantification of medial tibial plateau cartilage damage (% area positive, mean ± SD).

(p = 0.084) in the Injury vs. Intact groups (Figure 2). The bone volume fraction in the covered, superficial zone of the Injury group was significantly higher than that of the Intact group, and trended higher than that of the Repair group (p = 0.054). Intact and Repair were not significantly different. The trabecular thickness in the covered deep zone was significantly higher in the Repair group compared to Intact. Histologically, the Injury group showed more degeneration and greater proteoglycan loss compared to the Intact or Repair groups, and the synovium in the Injury group showed the greatest signs of inflammation.

Discussion

This study evaluated osteoarthritic changes in the porcine knee in a model of meniscus injury and repair. Macroscopic as well as histological evidence suggests that the repair of the transected anterior root of the medial meniscus was chondro-protective and slowed joint degeneration. This is further supported by analysis of the subchondral bone, which showed sclerotic changes immediately below the cartilage in the Injury group that were attenuated in the Repair group. Changes in deep zone trabecular thickness on the medial (covered) side of the joint may indicate bony remodeling in response to the suture anchor. Increases in cartilage permeability are an early indicator of OA[4], and permeability trended higher in the Injury group compared to Intact. These data are consistent with clinical evidence of the therapeutic impact of meniscal root repair[5]. However, this pilot study was limited in sample size; while showing promising trends, most mechanical indicators of cartilage health did not reach the level of statistical significance. Despite these limitations, this study indicated that anterior root repair in this large animal model of meniscus injury slowed the progression of OA. Ongoing work is evaluating changes to the femoral condyle, and the inflammatory profile of the synovial fluid, and future

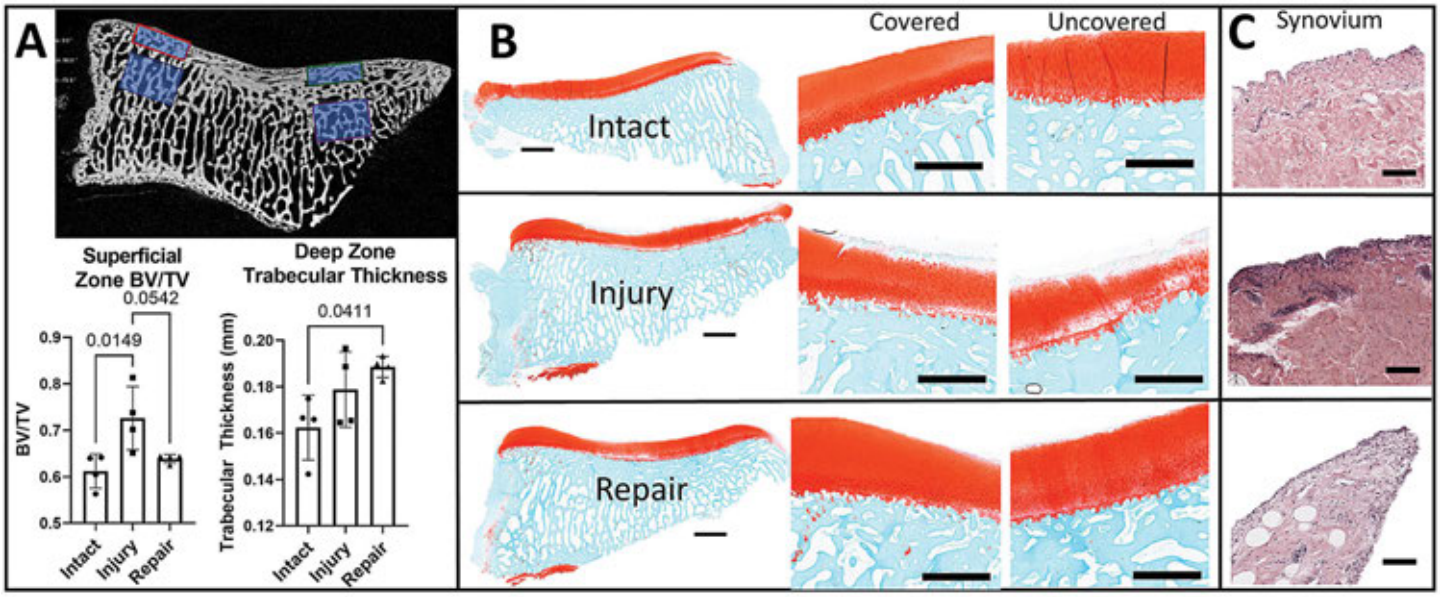

Figure 2. Compressive and tensile moduli and permeability of uncovered tibial plateau cartilage (mean ± SD).

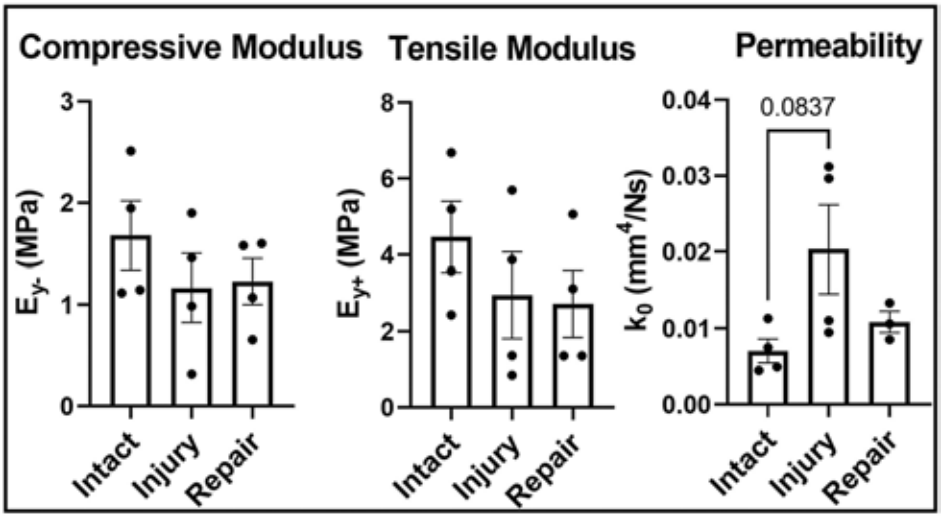

Figure 3. (A) Subchondral bone analysis showing ROIs within medial tibial plateau. Superficial zone BV/TV and deep zone trabecular thickness in covered region (mean ± SD); **(B)** Representative Safranin O /Fast green stained medial tibial plateaus. Scale = 2mm, 1mm insets; **(C)** Hematoxylin/Eosin-stained synovium from each group. Scale = 0.1mm.

studies will address limitations in sample size and extend the post-surgical time point to assess the durability of repair.

Significance/Clinical Relevance

This study demonstrated that meniscal root repair slows the progression of OA in large animal DMM model. Not only is this data relevant from a clinical perspective but establishes a test bed for the evaluation of therapies for OA.

Acknowledgement

This work was supported by the NIH and the Department of Veterans Affairs.

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A Large Animal Model of Motion Segment Degeneration for Evaluation of Engineered Disc Replacements

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Introduction

Back and neck pain have become ubiquitous in modern society, and while the causes of spinal pain can be multifactorial, degeneration of the musculoskeletal components of the spine is a primary contributor. Although the intervertebral discs are the most commonly studied region of the motion segment with respect to degeneration and repair, it is becoming increasingly evident that degeneration of adjacent structures, such as the facet joints, vertebral endplates and paraspinal muscles, occurs concomitant with disc degeneration.[1] However, crosstalk between these adjacent components of the spinal motion segment during degeneration and following repair remains understudied, particularly in pre-clinical animal models. As a novel treatment strategy for end-stage disc and vertebral endplate degeneration, our group developed a composite, tissue engineered endplate and disc replacement (eDAPS).[2] We previously evaluated the eDAPS following *in vivo* implantation in a healthy goat cervical spine, however, the performance of the eDAPS in a degenerative spine, where pathology may be present in multiple spinal structures (as would be in human patients), remains unexplored. The purpose of the current study was to establish a model of spinal motion segment degeneration in the goat cervical spine via minimally invasive chemonucleolysis, quantifying alterations to disc and facet cartilage structure and mechanics, vertebral bone remodeling and trans-endplate small molecule diffusion.

Methods

With IACUC approval, four goats underwent a procedure to induce degeneration of the C2-C3 and C4-C5 intervertebral discs. Animals were anesthetized, and fluoroscopic guidance was utilized to identify the spinal levels of interest and place a 22G spinal needle within the central nucleus pulposus (NP). Discs were injected with either 200μL of 2U (n = 4 levels) or 5U (n = 4 levels) chondroitinase-ABC (ChABC), with doses based on our previous work in the lumbar spine (REF). The C3-C4 disc was utilized as a healthy control level. At 12 weeks post-ChABC delivery, animals underwent *in vivo* magnetic resonance imaging (MRI) at 3T to obtain T2 and T1 maps before and 30 minutes following intravenous administration of 0.1 mmols/kg of the non-ionic MRI contrast agent gadodiamide, to quantify diffusive transport into the disc.[3] Following euthanasia, vertebral body-disc-vertebral body motion segments and the accompanying facet joints were isolated. Motion segments were subjected to a biomechanical testing protocol consisting of 20 cycles of compression (0 to −100N) at 0.5 Hz, followed by 1 hour of creep loading at −100N. Mechanical properties (toe and linear region modulus, transition and maximum strain) were calculated from the 20th cycle of compression, and normalized to disc height and area, measured from the MR, as previously described.[4] Each facet articular surface was subjected to indentation testing using a 1mm indenter applying 15 minutes of creep loading at −0.1N. Mechanical properties including permeability (k_0), strain dependent permeability constant (M), tensile modulus, and compressive modulus were calculated from fits of the displacement-time curves using a Hertzian biphasic creep model.[5] For NP T2 values and disc mechanical properties, statistical differences ($p < 0.05$) were assessed via ANOVA with Tukey's post-hoc. Differences in pre- and post-contrast NP T1 relaxation times were assessed via paired t-tests. Differences in facet cartilage mechanics were determined via two-tailed Student's t-test.

Results

T2-weighted MRIs (Figure 1A), illustrated the spectrum of disc degeneration achieved by varying ChABC dosage, with 5U ChABC resulting in complete loss of signal from the NP at 12 weeks post-injection. This corresponded with a significant reduction in NP T2 relaxation times, indicative of reduced water and proteoglycan content (Figure 1B).[6] *In vivo* T1 mapping demonstrated a reduction in T1 relaxation times in the spinal tissues following contrast agent administration (Figure 1C). The reduction in NP T1 relaxation time from pre- to post- contrast injection was significant in the control and 2U discs, but was not in the 5U discs, suggesting that small molecule, trans-endplate diffusion

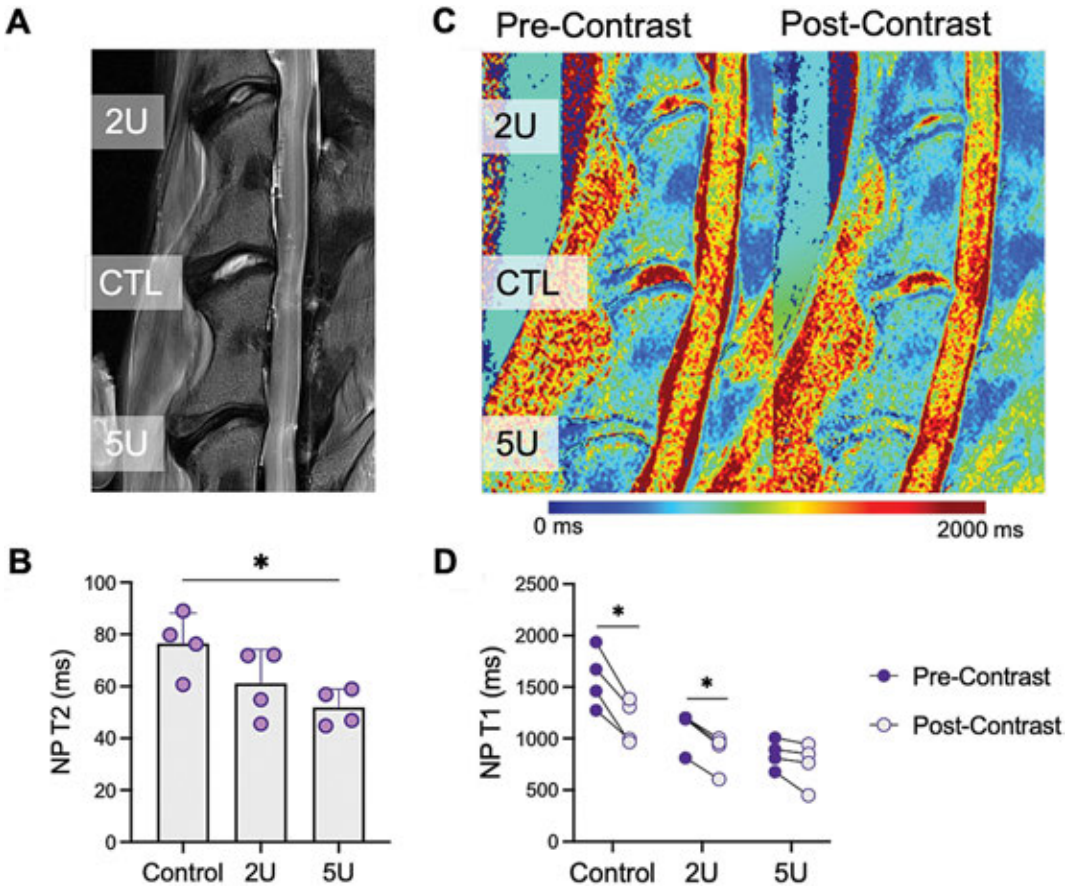

Figure 1. (A) Representative T2-weighted MRI of the goat cervical spine. **(B)** Quantification of T2 relaxation times in the nucleus pulposus. **(C)** In vivo T1 maps before and after gadodiamide administration from which (D) NP T1 relaxation times were calculated as a metric of contrast agent diffusion into the disc. (*=$p<0.05$).

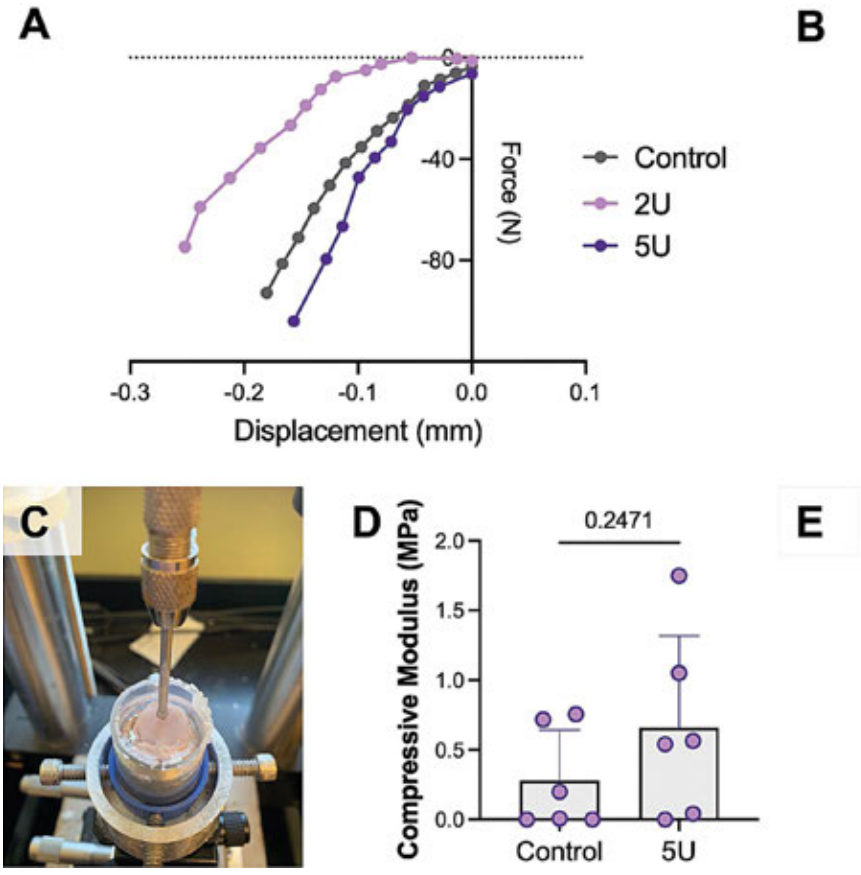

Figure 2. (A) Representative force-displacement curves from disc compressive mechanical testing, and **(B)** creep strain by group. **(C)** Facet cartilage creep indentation testing setup from which cartilage **(D)** compressive modulus and **(E)** the strain-dependent permeability constant, M, were determined.

was reduced in these severely degenerative discs (Figure 1D).[3] Motion segment force-displacement curves (Figure 2A) suggested a loss of compressive mechanical properties in the 2U discs, followed by stiffening in the 5U group. There was a trend towards increased creep strain in the 5U group compared to healthy controls (Figure 2B). Creep indentation testing of the facet articular cartilage adjacent to disc in the 5U ChABC group revealed trends towards altered cartilage mechanical properties, suggestive of degeneration, particularly an increase in compressive modulus and a reduction in the constant M, which dictates strain-dependent permeability (Figure 2C-E). No significant differences were detected in k_0 (Ctl: 0.0019 $mm^4/Ns \pm 0.001$; 5U: 0.0022 $mm^4/Ns \pm 0.001$) or tensile modulus (Ctl: 4.3 MPa ± 3.0; 5U: 2.6 MPa ± 1.0 MPa).

Discussion

In this study we established a large animal model where degeneration manifests across multiple components of the three-joint complex. Higher doses of ChABC resulted in more severe disc degeneration, as characterized via quantitative *in vivo* MRI. *In vivo* scanning also permitted quantification of small molecule diffusion into the disc; this was reduced in the 5U discs 12 weeks following ChABC injection. This may be due to remodeling of the vertebral bone and vasculature, as we have observed in a rabbit disc puncture model.[3] Mechanical properties of the disc, particularly creep strain, were altered substantially with degeneration, consistent with previous work.[4] These altered disc mechanics likely resulted in aberrant mechanical loading of the facet joints *in vivo*,[7] precipitating the articular cartilage degeneration suggested by altered cartilage indentation mechanical properties. The primary limitation of this study is its small sample size, making statistical differences in disc and facet cartilage mechanical properties difficult to detect given the heterogeneity in these measures. Ongoing work is focused on increasing this sample size and performing correlations across quantitative measures of disc and facet degeneration over longer durations to assess the progression motion segment degeneration.

Discussion

This large animal model provides a platform for studying the crosstalk between the discs and facet joints during degeneration at human length scales. Future work will utilize this model for the pre-clinical evaluation of a whole, tissue engineered disc replacement in a physiologically relevant degenerative scenario, in addition to other novel regenerative medicine approaches for the treatment of degenerative disc disease.

Acknowledges

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Fabrication of Extracellular Matrix-Based Hydrogel System for Meniscus Repair: Donor Age-Dependent Effects on Meniscal Fibrochondrocytes

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Introduction

The meniscus serves an important role in load-bearing and distribution in the knee.[1] Injuries to this tissue can greatly influence joint motion and daily living.[2] Meniscus injuries occur frequently,[3] and their insufficient repair frequently lead to potential osteoarthritis. Since the meniscus tissue unfortunately has limited vascularity and deficient healing capacity, new therapeutic strategies are required for treating meniscal injuries.[4] Recently, various biomaterials have been introduced to develop tissue engineered scaffolds for meniscal repair and replacement. In particular, decellularized meniscus extracellular matrix (Me-DEM), a bio-ink material capable of 3D cell printing, has been introduced as a promising bioactive material for meniscus regeneration given its bioactive properties.[5] In addition, it is known that the ECM components change with tissue development impacting cellular phenotypes and functionalities.[6] However, it is still unclear how changes in ECM components with the meniscus development impacts meniscus cell behaviors and their regenerative capacities. Thus, in this study, we fabricated age-dependent DEM [extracted from fetal meniscus dECM (FDEM) or adult meniscus dECM (ADEM)]-based hydrogel systems, and further we evaluated how the age-dependent DEM regulates gene expression, proliferation, and matrix productions differently in juvenile bovine meniscal fibrochondrocytes.

Methods

Fetal (3rd trimester) and adult (< 30 months) bovine menisci were collected and decellularized in 0.3% SDS/PBS (w/v), 3% Triton-X100/PBS (v/v), and 7.5U/ml Deoxyribonuclease/PBS. FDEM and ADEM pre-gels were prepared by digesting in 0.5M acetic acid solution (Figure 1A).[5,7] Hematoxylin and eosin (H&E) staining was carried out to evaluate the decellularization and

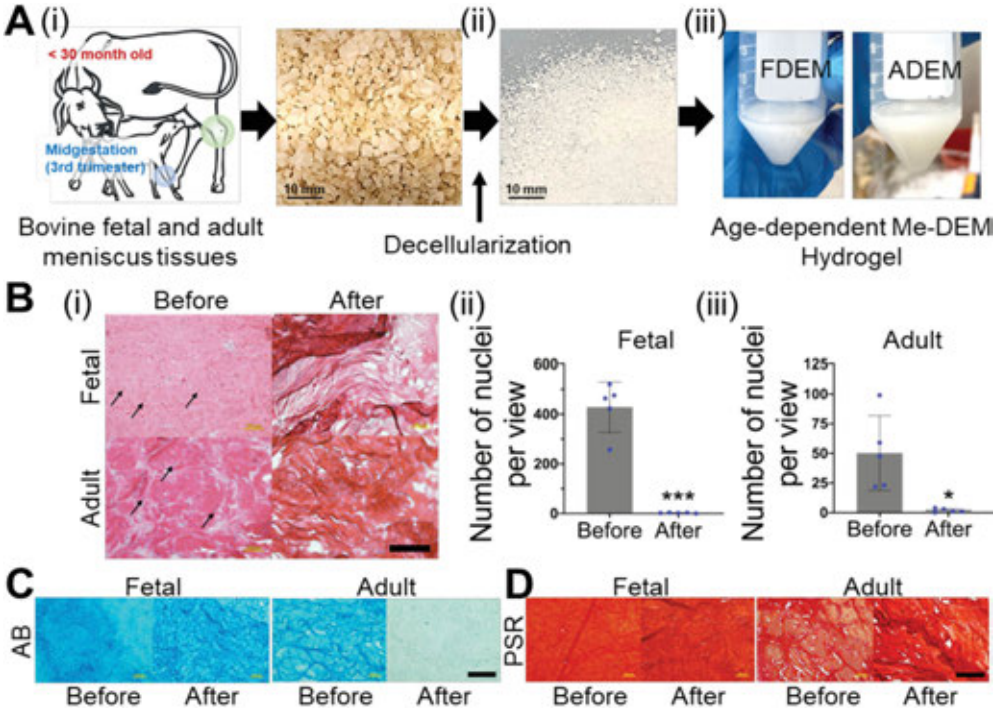

Figure 1. (A) Schematics showing the preparation of age-dependent Me-DEM hydrogels: (i) chopped bovine meniscus tissues, (ii) decellularized meniscus powders, (iii) fabricated FDEM and ADEM hydrogels. **(B)** Representative images of H&E (arrows: nuclei, scale bar: 200 um), quantifications of the number of nuclei in FDEM (ii), or in ADEM (iii) (*$p < 0.05$, ***$p < 0.001$). Representative images of AB **(C)**, and PSR **(D)** (scale bar: 200 um).

meniscus extracellular matrix preservation. The number of nuclei present on the H&E images was counted. Alcian Blue (AB) and Picrocirius red (PSR) staining were performed to confirm the glycosaminoglycan and collagen preservation respectively. The FDEM and ADEM were cross-linked under 37°C for 30 minutes. To prepare the conditioned media, 3.3% DEM [FDEM, ADEM, or FDEM+FEDM (50:50) dissolved in fresh chemically defined (CM) media (v/v)] was incubated under 37°C for 5 days.[8] Juvenile bovine meniscal fibrochondrocytes (MFC, P2) were seeded and cultured on tissue culture plates in basal growth media for 24 hours and the media were replaced with CM media (Ctrl), chondrogenic media CM containing TGF-β3, or the donor age-dependent (FDEM or ADEM) conditioned media (Figure 2A). Cells stained by Phalloidin were imaged at day 3, and the cell areas were quantified by ImageJ. Super-resolution STORM imaging (using ONI) and analysis of histone-H2B (H2B) organization were carried out to determine nano-scale chromatin organization at day 1.[8] Gene expression level of Collagen type-I (Col-I), Aggrecan (ACAN), and ADMST in the MFCs at day 5 were determined using RT-PCR. A short-term MTT assay was performed at day 5 to assess cell proliferation. In addition, at day 5, the PSR staining and 5-(4,6-dichlorotriazinyl) aminofluorescein (DTAF) staining were performed to determine protein expression from the cells.

Results

The loss of nuclei in the FDEM or ADEM tissues after the decellularization was confirmed by H&E staining (Figure 1B). While no change in GAG contents in the FDEM after the decellularization was observed, the process decreased the GAG contents in the ADEM (Figure 1C). PSR confirmed that collagen was preserved in both groups (Figure 1D) after the decellularization. When the MFCs were cultured in the conditioned media (FDEM or ADEM), increases in cell areas were observed in all DEM-based conditioned media conditions (Figure 2B). Interestingly, changes in the nano-scale chromatin condensation status and gene expression in MFCs were dependent on the media conditions. Compared to the Ctrl media condition, the treatment of TGF-β3 (10.9%), or FDEM (2.3%) increased the chromatin condensation status, while the treatment of ADEM significantly decreased chromatin condensation (by 7.7%) in MFCs (Figure 2C). In addition, the treatments of DEM enhanced the Col-1 expression in MFCs with a significant increase in the FDEM condition, while the media condition decreased the ACAN expression (Figure 2D). Interestingly, the changes in gene expression with the TGF-β3 treatment significantly opposite to those with the DEM treatments (Figure 2E). The expression level of ADMST (which is a marker of ECM remodeling) in the FDEM group was higher than that in the ADEM or the FADEM group (Figure 2E). Finally, the cell proliferation levels were significantly lower in all DEM

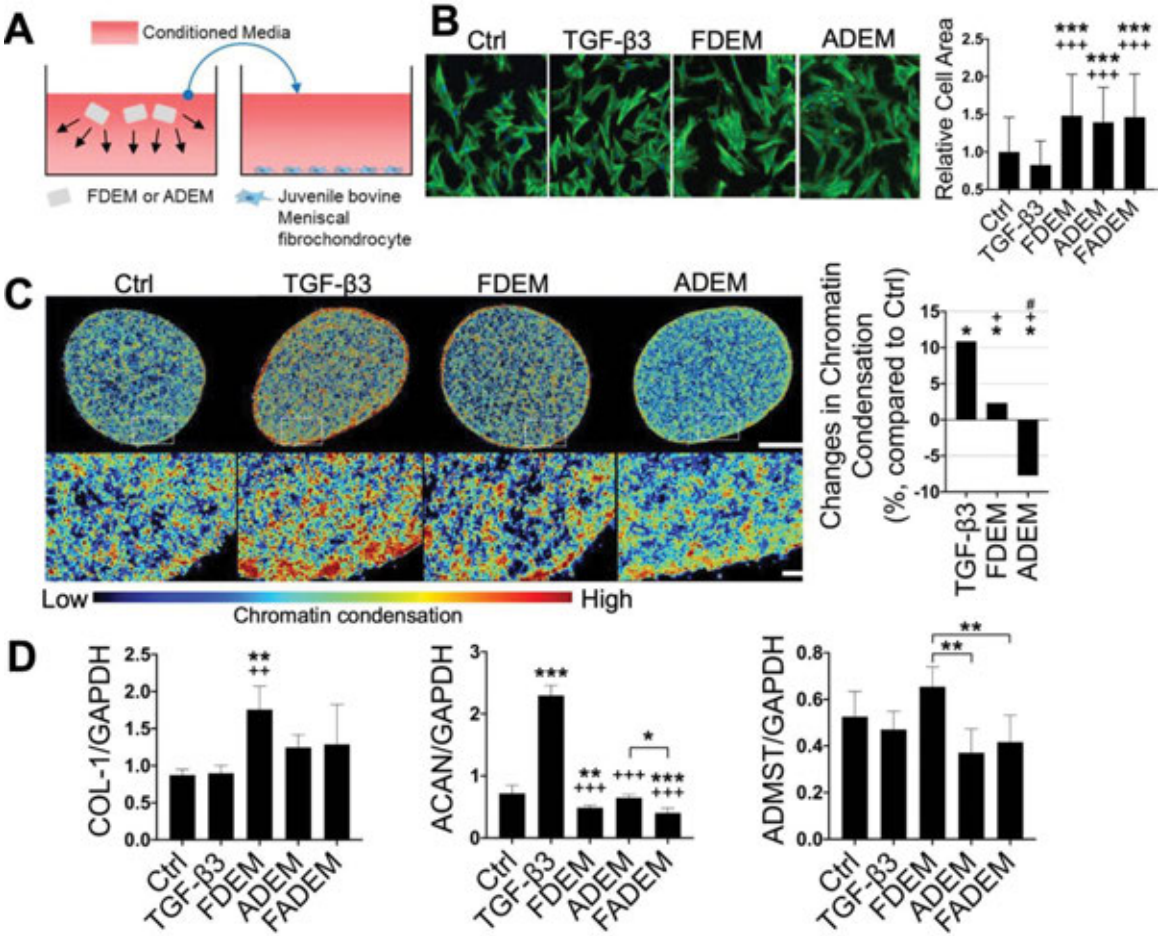

Figure 2. (A) Schematic of in-vitro cell culture in conditioned media. **(B)** Representative F-actin images and relative cell area of MFC cultured for 3 days in conditioned media (FEDM: fetal ECM, ADEM: adult ECM, FADEM: fetal + adult ECM (50:50) (n = 50), **(C)** H2B STORM analysis and quantification of chromatin condensation in MFCs [Scale bar: 1 μm (top) and 500 nm (bottom)], **(D)** Gene expression of COL-1, ACAN, and ADMST at 5 days (n = 5, *: $p < 0.05$ vs. Ctrl, **: $p < 0.01$ vs. Ctrl, ***: $p < 0.001$ vs. Ctrl, +: $p < 0.05$ vs. TGF-β3, ++: $p < 0.01$ vs. TGF-β3, +++: $p < 0.001$ vs. TGF-β3, #: $p < 0.05$ vs. FDEM, ##: $p < 0.01$ vs. FDEM, ###: $p < 0.001$ vs. FDEM).

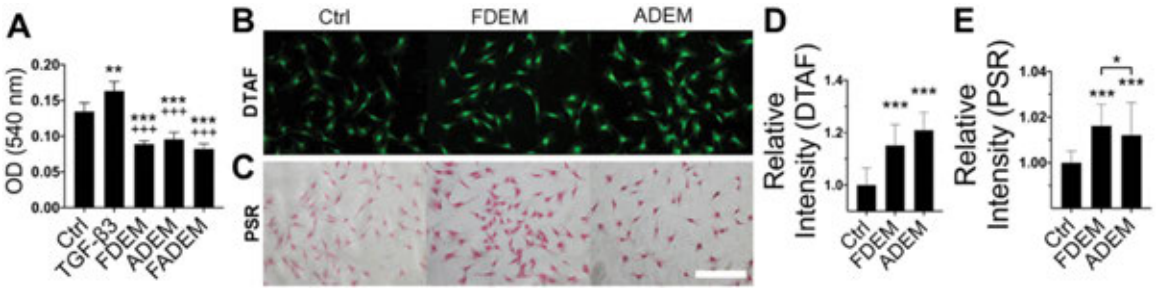

Figure 3. (A) MTT assay result (n=5). Representative images of DTAF **(B)** or PSR staining **(C)**, Scale bar: 200 μm. Quantifications of the relative intensity of the DTAF **(D**, n = 25**)** or PSR staining in MFCs **(E**, n = 25**)** (*: $p < 0.05$ vs. Ctrl, **: $p < 0.01$ vs. Ctrl, ***: $p < 0.001$ vs. Ctrl, +: $p < 0.05$ vs. TGF-β3, ++: $p < 0.01$ vs. TGF-β3, +++: $p < 0.001$ vs. TGF-β3).

groups than in other groups (Figure 3A). However, through DTAF and PSR staining, we found that MFCs in the FDEM and ADEM groups produced more ECM and collagen than MFCs in the Ctrl group (Figs. 3B-E).

Discussion

In this study, we have shown that the treatments of DEM regulate nano-scale chromatin organization, gene expression, proliferation, and matrix production in MFCs. Interestingly, the DEM effects on MFCs are donor age-dependent, and are significantly different from the TGF-β3 treatment. Ongoing studies are focused on elucidating the molecular mechanisms of the donor age-dependent effects of DEM on MFCs using mass spectrometry (to investigate changes in ECM components with the meniscus development) and RNA-seq (to examine how age-dependent ECM impacts transcriptome profiling in MFCs) for their therapeutic potential.

Acknowledgements

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Intervertebral Disc and Facet Cross-talk in a Rabbit Puncture Model of Spine Degeneration

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Introduction

28.5% of adult Americans suffer from lower back pain[1], which is frequently associated with intervertebral disc degeneration (IVDD). While IVDD has become a fairly well studied condition, there still remains a deficit in our understanding of how facet osteoarthritis (OA) contributes to degeneration of the whole motion segment. Facet osteoarthritis is a significant source of low back pain[2] and likely plays a critical role in the changing articulation of motion segments as they degrade[3]. Our previous work using a rabbit-puncture model of disc degeneration established the use of clinically relevant imaging and multi-scale characterization techniques to evaluate changes in the disc[4]. In this study, we expand on that rabbit model, linking IVDD with changes to facet cartilage to better understand the degeneration of the full motion segment in response to acute trauma.

Methods

Five New Zealand White male rabbits underwent surgery using an established IACUC approved rabbit-puncture model[4], in which 4 levels between L23 and L67 were punctured, two using a 16G needle and two using a 21G needle, leaving one adjacent level as a healthy control. At 10 weeks post-puncture, all animals were intravenously administered the small molecule, non-ionic MRI contrast agent, gadodiamide, 30 minutes prior to euthanasia[5]. Following euthanasia, experimental (n = 20) and control (n = 5) motion segments underwent coronal MRI T1 and T2 mapping to quantify small molecule diffusion across the endplate and disc T2 relaxation times, respectively. Motion segments from two rabbits (n = 8 experimental, n = 2 control) were subject to mechanical testing, consisting of 20 cycles of tension (21 N) and compression (42 N)[4]. Motion segments were subsequently scanned using μCT to quantify bone morphometry and then decalcified and processed for paraffin histology. Samples were sectioned in the sagittal plane and stained with Hematoxylin and Eosin and Alcian Blue/Picrosirius Red. Control discs from this study were pooled with controls levels from our previous work[4]. Corresponding facets (n = 16 experimental, n = 4 control) were dissected away from the motion segments for creep indentation mechanical testing[6] at one point on each articular surface. Facets (n = 9 experimental, n = 8 control) were processed for paraffin histology, sectioned in the sagittal plane at a thickness of 10 μm, and stained with Safranin-O and Fast Green. All disc and facet histology were scored using a 3-scorer consensus system according to the OARSI scoring system for rabbit cartilage[7] and the ORS Spine section intervertebral disc scoring system[8], respectively. All data was analyzed using a two-tailed T-test or a One-Way ANOVA with a Tukey's post-hoc test. Significance was defined as $p < 0.05$.

Results

With increasing severity of disc puncture, markers of disc degeneration became more pronounced at 10 weeks post-puncture. Composite T2 maps revealed a decrease in disc water content, primarily in the nucleus pulposus (NP) (Figure 1A). On histology, a loss of distinction between the nucleus pulposus and annulus fibrosus (AF) regions was observed as well as progressive reduction in NP size, loss of overall disc height, and increase in AF lamellar disorganization, culminating in an instance of NP herniation (Figure 1B-C). These structural changes yielded significant stiffening of the IVD in the 16G puncture discs, compared to controls and 21G puncture discs (Figure 1D). A reduction in small molecule transport into the NP was also measured, particularly in 16G punctured discs (Figure 1E) and was accompanied by increased vertebral endplate bone volume fraction (Figure 1F), primarily driven by trabecular thickening. Corresponding facets showed early signs of cartilage degeneration. Facet cartilage indentation testing suggested an increase in compressive moduli alongside a decrease in cartilage permeability (Figure 2A). Surface fibrillations and irregularities were observed in both experimental groups. Notably, facets corresponding to 21G punctured discs experienced a loss of Safranin-O staining in the superficial zone and a loss of chondrocyte

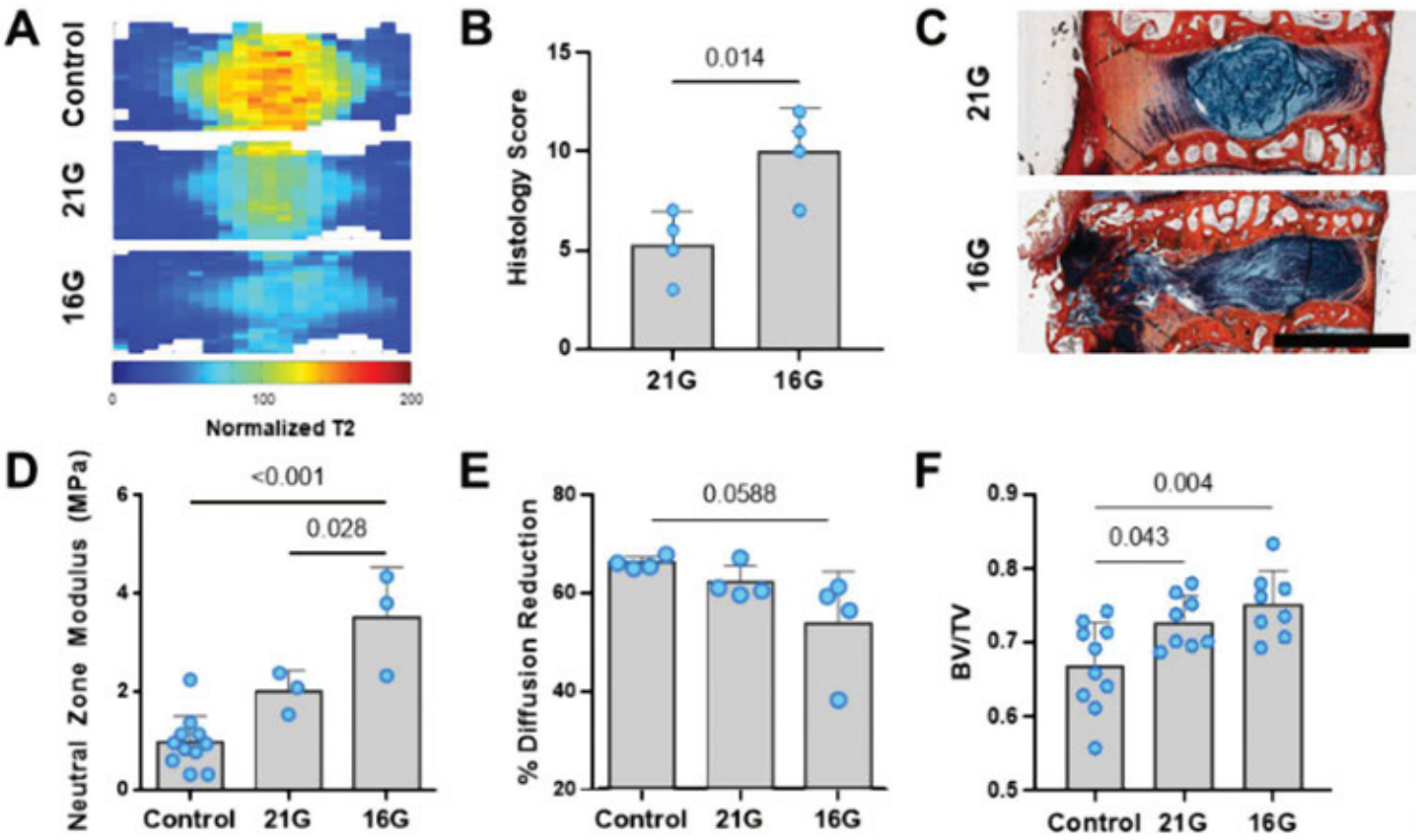

Figure 1. For control and puncture intervertebral discs: **(A)** Average T2 MRI maps, **(B)** consensus ORS Spine histology scores, **(C)** representative Alcian Blue/Picrosirius Red histology (scale bar = 4 mm), **(D)** neutral zone modulus from compression-tension mechanical testing, (E) small molecule diffusion reduction across the endplate, and (F) bone volume fraction as determined by ΔCT.

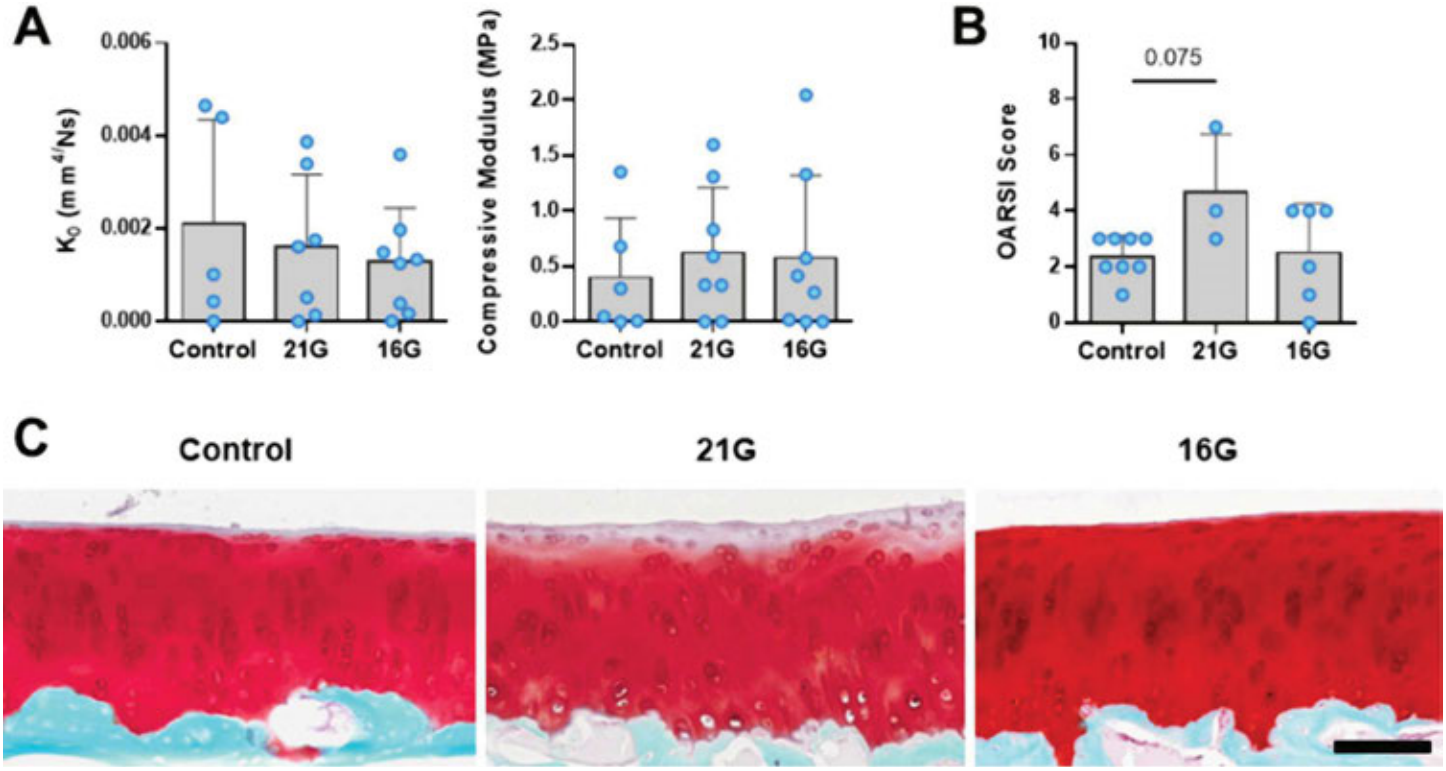

Figure 2. For control facets and facets corresponding to punctured discs: **(A)** Permeability and compressive modulus from creep indentation mechanical testing, **(B)** consensus OARSI scores, and **(C)** representative Safranin-O, Fast Green histology (scale bar = 100 mm).

density and columnar organization when compared to both control facets and 16G puncture facets (Figure 2B-C).

Discussion

After 10 weeks, intervertebral discs followed an increasingly severe path of degeneration with increasing diameter of needle puncture. Disc degeneration was characterized by a progressive loss of water in the NP, which is likely linked to a loss of proteoglycans and an increase in matrix density. Increased endplate bone density adjacent to the punctured discs also led to a decrease in small molecule transport into the disc, which, at later time points, may further exacerbate the degenerative cascade. Overall, the adjacent facets in both groups underwent minimal remodeling in comparison to the discs. However, histologically, while there was an increase in facet OA between the control facets and 21G puncture facets, there was little change in the 16G puncture facet cartilage.This may be linked to the stiffening of the anterior compartment of the motion segment observed in this group. As the disc becomes stiffer, through both the formation of osteophytes anteriorly and the deposition of fibrotic matrix, the facets are progressively offloaded. The significant stiffening of 16G discs compared to 21G discs may be shielding the facets from cumulative, severe loads, minimizing the progression of cartilage osteoarthritis as is seen in offloading studies in the knee[9]. Overall, 10 weeks does not seem to be a sufficient time scale for facets to respond to the changing mechanical and biochemical environments of the corresponding discs. Longer study durations would likely elucidate the progression of facet deterioration and how that progression affects the entire motion segment.

Significance

This work links our knowledge of IVDD with facet osteoarthritis, allowing for a better understanding of the progression of whole motion segment degeneration, which can aid in informing the development and evaluation of novel regenerative strategies for spinal degeneration.

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Single-Cell Transcriptomics Reveals Emergent Nucleus Pulposus Cell Subpopulations in the Postnatal Mouse Disc

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Introduction

Intervertebral disc degeneration is a major cause of low back pain, the leading cause of disability worldwide.[1] Emerging cell-based therapies targeting the disc nucleus pulposus (NP), particularly those employing adult stem cells, have shown promise in preclinical studies;[2] however, efficacy has been limited by the inability of these therapeutic cells to sufficiently mimic the phenotype of native NP cells, including survival in the nutrient poor disc microenvironment and production of a proteoglycan-rich extracellular matrix (ECM). During development, NP cells uniquely arise from the embryonic notochord,[3,4] transitioning from a role focused on tissue patterning through secretion of long-range morphogens, to one more focused on ECM production and maintenance.[5,6] The mechanisms underlying this transition in NP cell function remain poorly understood, and may provide important clues for optimizing adult stem cells for therapeutic, regenerative application. The objective of this study was to use single-cell transcriptomics to investigate emergent NP cell heterogeneity in the postnatal mouse disc. We hypothesized that the postnatal mouse disc contains multiple NP cell subpopulations with unique gene expression profiles that reflect distinct functional roles.

Methods

Single Cell RNA-Sequencing

To obtain notochord-derived NP cells for single cell RNA sequencing (scRNA-Seq), we used a Shh-cre;R26R-tdTomato mouse model, which leverages the fact that all cells of the embryonic notochord express Shh, and produces constitutive expression of tdTomato at the ROSA26 locus in these cells and their progeny (i.e. a fate map), including when Shh is no longer expressed. With IACUC approval, mice were euthanized at 30 days-of-age, and disc cells isolated via mechanical dissociation and brief collagenase digestion. TdTomato+ cells were then purified using FACS. Libraries were generated using the Chromium controller (10X Genomics) and sequencing was performed using the Illumina HiSeq platform. Three replicate sequencing experiments were performed. Unsupervised clustering was conducted using Seurat, and differentiation trajectory analysis was performed using Monocle

Histology

Lumbar spines were isolated from mice aged 0, 7, 14, 30 and 60 days, fixed in formalin, decalcified and processed for paraffin histology. Mid-sagittal sections were stained with Alcian blue and picrosirius red (ABPR) to demonstrate glycosaminoglycan (GAG) and collagen, respectively. Additionally, mid-sagittal, calcified cryosections were obtained from the lumbar spines of both Shh-cre;R26R:tdTomato and wild type mice at these same ages for fluorescent localization of NP cells and immunofluorescent localization of subpopulation-specific cell surface markers, respectively.

Results

Single Cell RNA-Sequencing

The three replicate scRNA-Seq experiments exhibited high reproducibility, and results were therefore pooled prior to further analyses. A total of 1116 notochord-derived NP cells (median 1445 genes/cell and 4854 UMIs/cell) were identified within the total sequenced cell population. UMAP plots revealed the presence of two distinct NP cell clusters exhibiting distinct gene expression profiles (Figure 1A). Differentiation trajectory analysis showed that cells in clusters 1 and 2 aligned along a pseudo-timeline (Figure 1B). Cluster-specific gene expression analyses demonstrated that NP cells in both clusters exhibited high expression of established NP markers including KRT18 and 19, and T, while expression of NP-specific ECM genes ACAN, COL2A1 and COL6A1 was confined to cells in cluster 2 (Figure 2). Based on the differential expression of these ECM genes, cells in clusters 1 and 2 were denoted early and

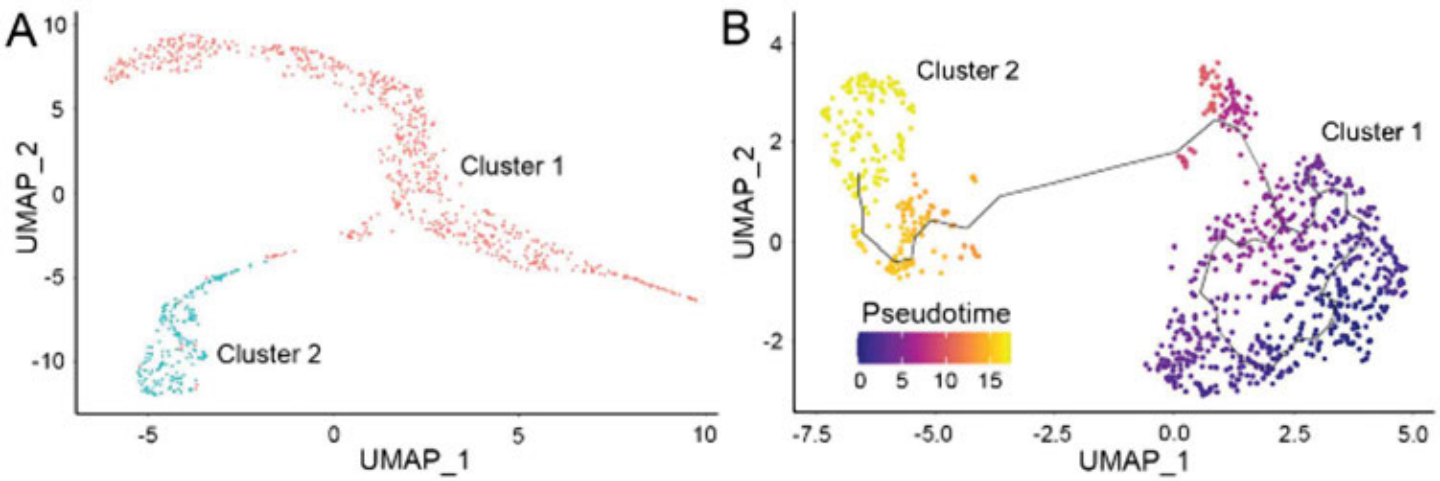

Figure 1. (A) UMAP plot showing clustering of two distinct populations of notochord-derived NP cells. **(B)** Differentiation trajectory analysis showing the pseudo-temporal transition from cluster 1 to 2 cells.

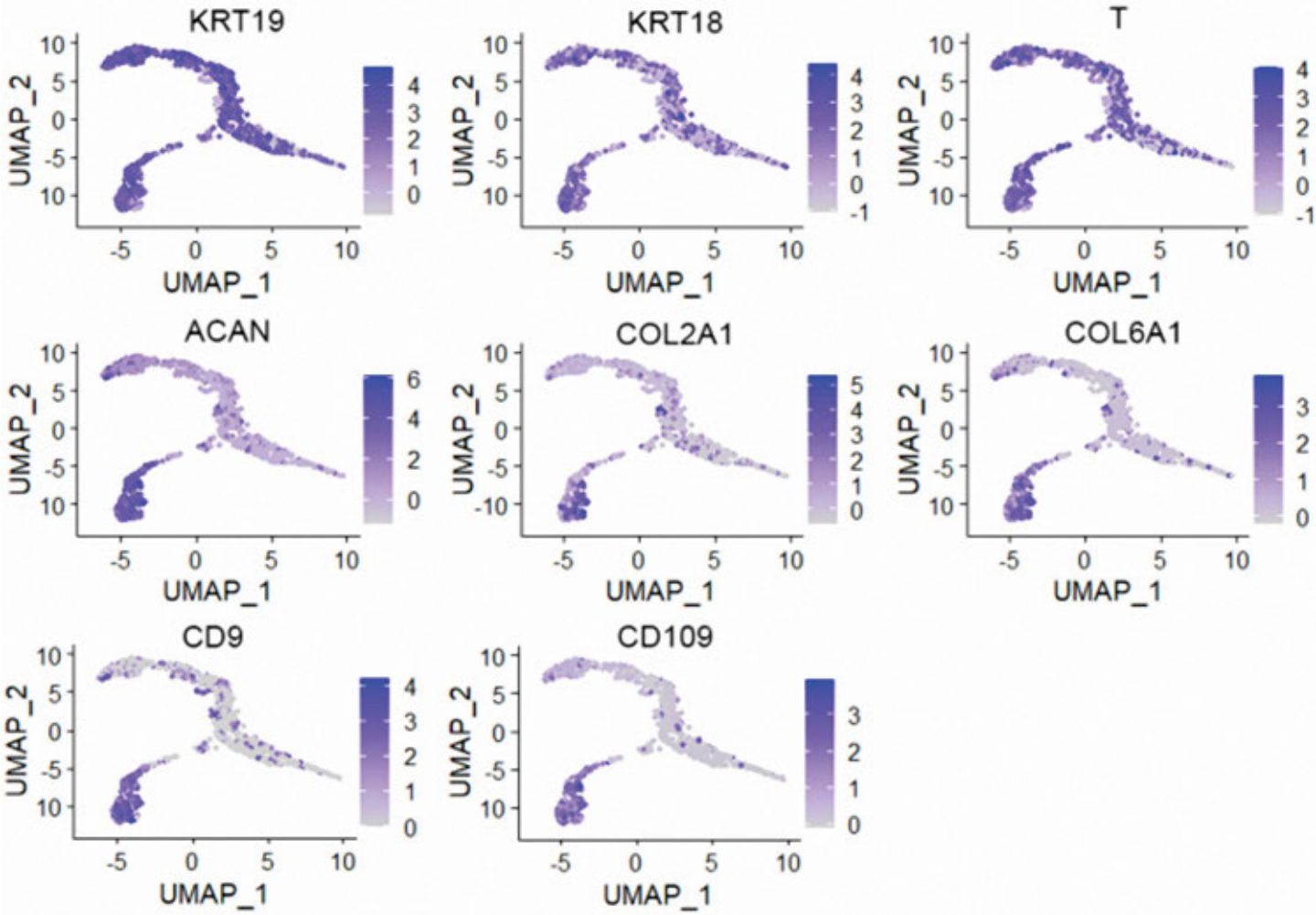

Figure 2. UPAP plots showing relative espression of NP marker, ECM and cell surface marker genes in each cell cluster.

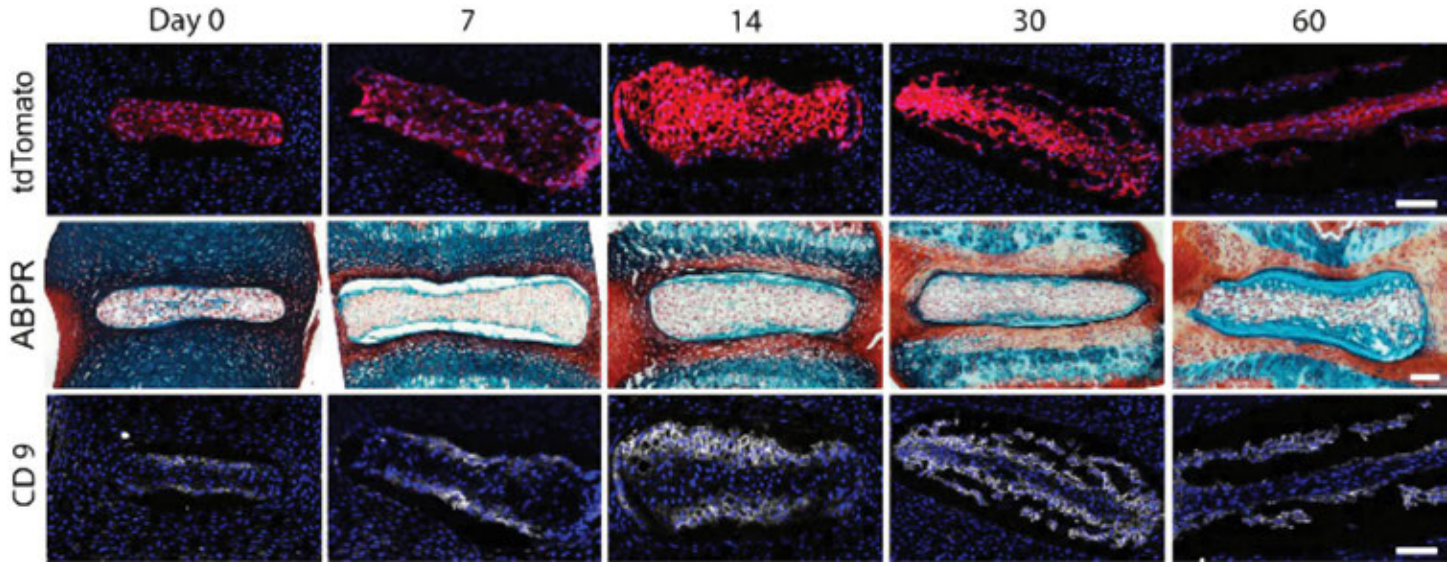

Figure 3. TdTomato+ cells in the NPs of discs from Shh-cre;R26R:tdTomato mice aged 0 to 60 days **(top).** Alcian blue/picrosirius red-stained sections showing progressive accumulation of GAG-rich ECM in the peripheral regions of the NP with increasing age **(middle).** Immunoflorescent staining showing CD9-positive cells confined to the peripheral regions of the NP **(bottom).** Scale = 100μm.

late-stage NP cells, respectively. In addition to high ECM gene expression, late-stage NP-cells uniquely expressed the cell surface markers CD9 and CD109

Histology

Fluorescence imaging revealed tdTomato expression throughout the NP. ABPR staining showed progressive ECM deposition in the NP from day 0 to 90. Notably, an emergent halo of GAG-rich ECM was apparent surrounding a central region of vacuolated cells. Immunofluorescent staining for CD9 demonstrated that late-stage NP cells co-localized with this emerging halo of GAG-rich ECM at all ages examined.

Discussion

In this study we provide the first evidence of emergent heterogeneity amongst NP cells in the postnatal mouse disc. Specifically, we established the existence of early and late-stage NP cells, which exhibit distinct gene expression profiles reflecting unique functional roles. Findings suggest that early-stage NP cells residing at the center of the NP give rise to late-stage NP cells that reside at the periphery, and are responsible for producing the halo of proteoglycan-rich ECM. This ECM is crucial for maintaining disc hydrostatic pressure and resisting axial compressive forces. Importantly, our results also identified candidate surface markers, CD9 and CD109, which are uniquely expressed by late-stage NP cells. Histological findings suggest that the transition from early to late-stage NP cells occurs progressively during postnatal growth.This may explain the eventual depletion of early stage (historically referred to as "notochordal" cells) in other species, including humans. Ongoing work will confirm these findings by examining additional ages in the mouse using scRNA-Seq. Our ultimate goal is to leverage these findings to develop an optimized, cell-based therapy for disc regeneration.

Significance

Stem cell-based therapies for disc degeneration hold significant promise for patients with chronic low back pain. The results of this study expand understanding of the cellular mechanisms underlying postnatal disc formation, and suggest target characteristics for therapeutic stem cells.

Acknowledgements

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Superficial Layer Meniscus Cells Migrate Faster and are Less Mechanosensitive than those in the Meniscus Body

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Introduction

The knee meniscus supports dynamic joint motion and load transmission via its specialized organization and extracellular matrix (ECM) constituents. The meniscus contains an outer vascularized zone, an inner avascular zone, and two horns that anchor the meniscus to the tibia. Covering the entire tissue is a thin, specialized superficial layer. Previous studies have shown differences in superficial layer meniscus cell phenotype, ECM constituents, alignment, density, and mechanical properties compared to the deeper tissue of the meniscus body[1]. Recent work also demonstrated the critical role of progenitor cells localized to the superficial layer in meniscal wound repair[2]. However, it has also been noted that the repair tissue that does form contains altered extracellular matrix structure and composition and this may compromise the mechanical properties of the repair[3]. Therefore, gaps exist in our understanding of the cells that reside within this specialized superficial layer, and how they are mobilized in response to injury. The purpose of this study was to investigate the mechano-response of superficial cells to changes in mechanical environment as well as their migration potential, relative to donor-matched cells from the central region of the meniscus body. An understanding of the difference between the superficial and body zones of the meniscus may help connect pathology with cellular behavior to inform novel therapies.

Methods

Juvenile bovine medial and lateral menisci were dissected from two donors. Biopsy punches (12 mm diameter) were used to generate samples from the meniscus.

Histology and Staining

Samples were processed and embedded in paraffin. Sections (7 m thickness) were stained with toluidine blue to visualize tissue morphology.

In vitro culture

A custom device (Figure 1) was used to isolate samples from the superficial zone (~100 m depth) and deeper (body) zones (1 mm depth). Tissue sections were minced and incubated at 37C in basal media (DMEM with 10% fetal bovine serum and 1% penicillin / streptomycin / fungizone) for two weeks, during which time cells migrated from tissue and onto the tissue culture plastic. Cells from each region were frozen for subsequent assays and used between passage 1 and 3.

Substrate stiffness, Immunofluorescent staining, Imaging, and Analysis

5, 10, and 55 kPa polyacrylamide gels were prepared on glass slides and coated with fibronectin as in [4] prior to seeding with cells from the superficial and body zones. Cells were stained with Hoechst 33342 (nuclear stain), phalloidin (f-actin stain), and goat anti-YAP/TAZ (1:1000 in 1% BSA). Confocal microscopy was used to acquire images for each channel using the same imaging parameters across the samples, followed by quantification of cell area, aspect ratio, and YAP/TAZ nuclear to cytoplasmic ratio (Cell Profiler).

2D Wound Healing Assay

Cells were plated in six-well tissue culture dishes at 4 x cells per well and cultured to confluence. Next, a 200 ml pipette tip was used to scratch the cell monolayer. Images were taken using a

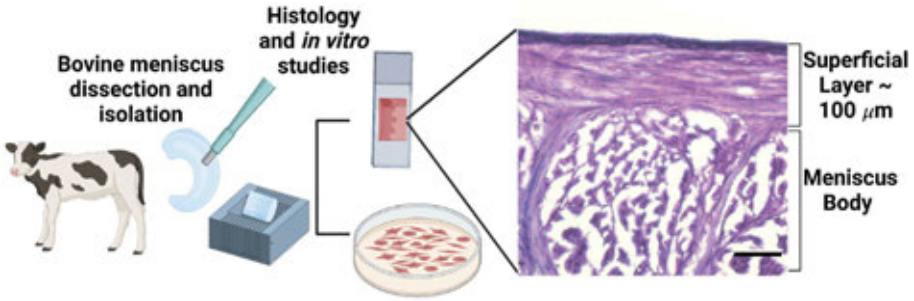

Figure 1. Study design. Juvenile bovine menisci were isolated for histology and in vitro cell culture studies. Images shows toluidine blue staining of superficial and deeper body zones. Scale bar: 100 m.

brightfield inverted microscope every 2 – 4 hours after scratching. Wound closure was computed and analyzed using ImageJ.

Statistics

Figure 2B, 2C: ANOVA. Figure 3B: t-test.

Results

Histological analysis confirmed that the superficial layer was distinct from the deeper meniscus body, as previously reported[5] (Figure 1). When placed on substrates of differing stiffness, superficial layer cells showed differences in mechano-response (Figure 2A). Specifically, superficial meniscus cells were smaller on stiffer substrates (10 and 55 kPa) and had a decreased level of nuclear YAP/TAZ in comparison to body cells. The spread area of superficial cells showed little change with increasing stiffness (Figure 2B), while there was a marked increase in spread area for body meniscus cells with increasing stiffness (Figure 2B). Notably, the superficial and body meniscus cells had similar areas at the smallest stiffness, but a significant difference in spread area at higher stiffnesses (Figure 2B). Similarly, body cells had more nuclear YAP translocation as compared to superficial cells (Figure 2C), indicating that superficial were not as mechanoresponsive as body cells. Superficial cells also migrated faster than body cells (Figure 3A-B). At 36hrs, the scratch wound completely closed for superficial zone cells, whereas the wound remained nearly 50% open for body zone cells. These results indicate that superficial cells have a higher migration potential than body cells on tissue culture plastic.

Discussion

This study shows mechanobiological differences between superficial cells and the rest of the meniscus, specifically in mechanosensation and migration potential. Previous work characterized superficial cells as progenitors for meniscus regeneration [2]. Our findings suggest that the fast migration and decreased response to substrate stiffness could account for their rapid filling of meniscus defects and may impact how they form new repair matrix. Further characterization of meniscus repair matrix is needed to elucidate the role of superficial layer cells in regeneration. Future studies will assess the proliferation rate, cytoskeletal regulation, and matrix formation potential of superficial layer cells.

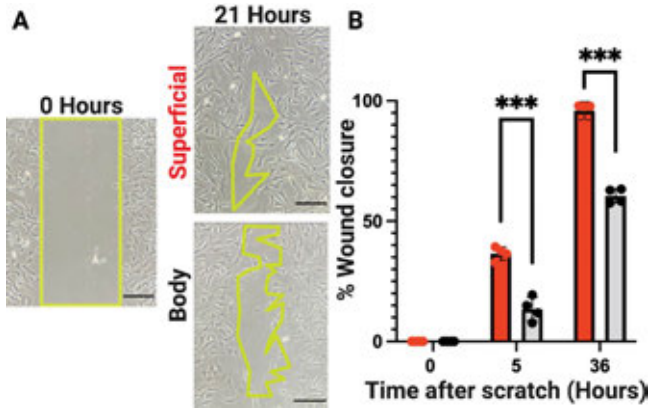

Figure 3. 2D Migration Assay. Superficial cells closed the wound faster than cells from the body of the meniscus. A) Image at left shows wound at time zero. Middle images show wound after 21 hours. B) Quantification of wound closure over 36 hours. Sample number: 5 per group, ***$p < 0.001$. Scale bar: 150 m.

Significance

This work shows key mechanobiological distinctions between the superficial layer cells and the rest of the meniscus. The lower mechanosensitivity of superficial layer cells despite their high migration potential suggests that, albeit their progenitor nature, those cells respond less to micromechanical cues. These results may connect the progenitor nature of superficial layer cells with the poor intrinsic healing potential of this progenitor population in the meniscus.

Acknowledgements

This work was supported by the NIH/NIAMS (R01 AR075418, R01 AR056624, P30 AR069619), the Center for Engineering MechanoBiology (CMMI-1548571), and the HHMI Gilliam Fellowship (GT13516).

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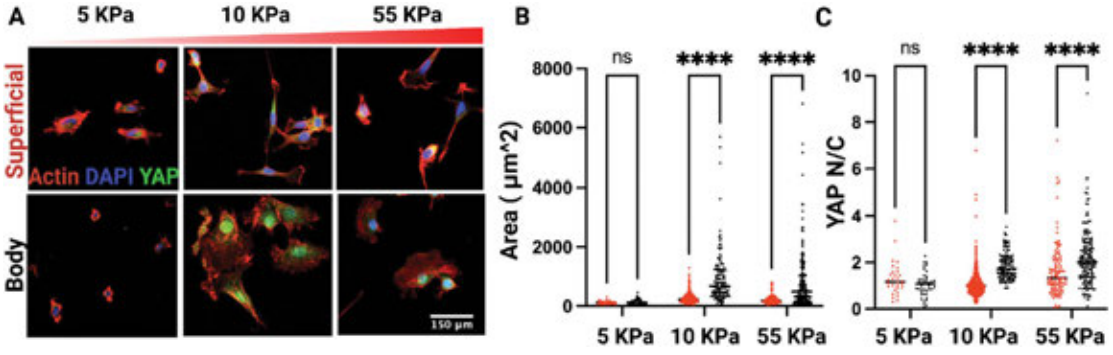

Figure 2. Response to Mechanical Environment. Superficial cells did not show a significant change in area or nuclear YAP with an increase in stiffness, unlike cells of the meniscus body. N/C: Nuclear/Cytoplasmic, sample number: 5 per group, ****$p < 0.0001$. Scale bar: 150 m.

Superoxide Dismutase-Loaded Porous Polymersomes as Highly Efficient Antioxidant Nanoparticles for Osteoarthritis Therapy

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Introduction

Oxidative stress and the reactive oxygen species (ROS) have important roles in osteoarthritis (OA) development.[1] Scavenging ROS by exogenous antioxidant enzymes could be a promising approach for OA treatment. However, the direct use of antioxidant enzymes, such as superoxide dismutase (SOD), is challenging due to a lack of effective drug delivery system. This study utilized a highly efficient antioxidative nanoparticle based on SOD-loaded porous polymersome nanoparticles (SOD-NPs) for delivery of SOD to mouse knee joints and tested their therapeutic efficacy in OA mice.

Methods

SOD-NP synthesis

SOD was encapsulated within the aqueous interior of polymersomes made from a mixture of two amphiphilic diblock copolymers, 75 mol% poly (ethylene glycol)-polybutadiene copolymer (PEG-PBD) and 25 mol% poly (ethylene glycol)-poly (propylene oxide) (PEG-PPO) (Figure 1A). The retention assay was performed by one-time intra-articular (IA) injection of 10 μl IRDye 800CW-labeled SOD or SOD-NPs, the fluorescence intensity in the joint was quantified over a period of 28 days.

Cartilage and Synovium explants

Cartilage and synovium explants were obtained from human knee joints after total knee arthroplasty surgery. Explants were treated with PBS (Untreated), IL-1β in combination with PBS, empty NPs, SOD or SOD-NPs for 8 days.

Cell culture

Chondrocytes and synovial fibroblasts were harvested from mouse knee joints by enzymatic digestion and subjected to viability and flow analysis

Animals

All animal work was approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania. Male C57Bl/6 mice at 3 months of age received destabilization of medial meniscus (DMM) at right knees. They were then divided into 4 groups, receiving 10 μl PBS, empty NPs, SOD (500 U/mL), or SOD-NPs (500 U/mL) IA injections once every 2 weeks for 12 weeks (n = 6 mice/group). An additional group of mice (n = 6) received sham surgery with PBS injections.

Histology

Knee joints were processed for paraffin sections followed by H&E, Safranin-O/fast green (SO/FG), 8-OHdG, Mmp13 and Adamts5 staining. MicroCT- Femurs were scanned from the epiphyseal end at a ± μm resolution by microCT 35. The subchondral bone plate thickness (SBP. Th) of distal femoral end was quantified.

Statistics

Data are expressed as means±SEM and analyzed by one way ANOVA and unpaired, two-tailed Student's t-test.

Results

SOD-NPs up to 500 U/mL (SOD concentration) did not affect viability of mouse chondrocytes (Figure 1B). Joints receiving IRDye 800CW-labeled SOD-NPs injection had much higher fluorescence intensity than those receiving IRDye 800CW-labeled SOD injection. Moreover, the retention of SOD-NPs in DMM joints was longer than that in healthy joints (Figure 1C). Interestingly, biodistribution assay indicated that SOD-NPs were largely retained in synovium and minimally located at articular cartilage surface (data not shown). In vitro, synovial fibroblasts endocytosed SOD-NPs and their production of ROS marker H2DCFDA after TNFα treatment was greatly reduced by SOD-NPs co-treatment (Figure 1D). SOD-NPs treatment protected cartilage (data not shown) and synovial explants (Figure 2A-F) from IL-1β-induced OA-like degeneration. IA delivery of SOD-NPs attenuated DMM-induced OA cartilage erosion and degeneration (Figure 3A, B), synovitis (Figure 3C,

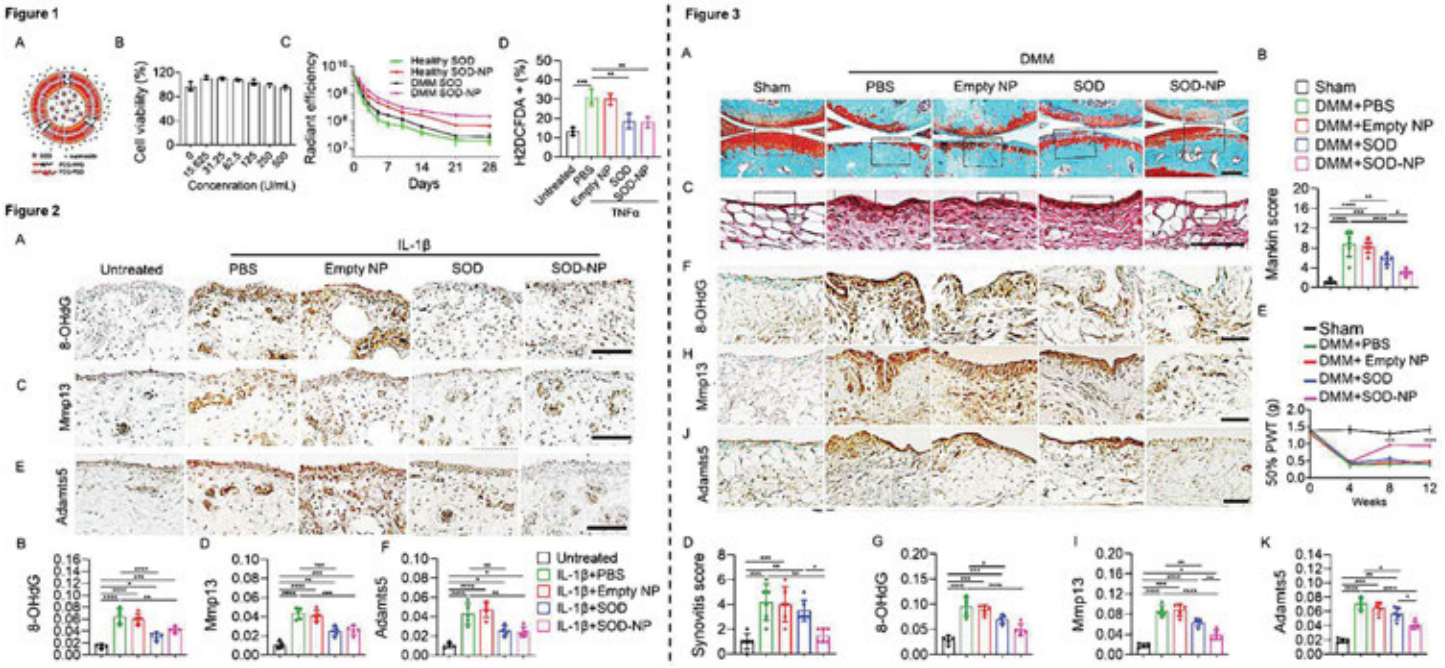

Figure 1. SOD-NP synthesis and characterization. (A) Schematic diagram of SOD-loaded polymersomes. **(B)** The cell viability of primary chondrocytes after incubation with SOD-NPs at various concentrations. (n = 3/group). **(C)** Quantitative analysis of time course radiant efficiency within knee joints over 28 days after IA injection of IRDye 800CW–labeled SOD or SOD-NPs. (n = 6/group) (D) Measurement of H2DCFDA levels in mouse SFs after treatment with TNFα plus PBS, empty NP, SOD, or SOD-NP for 24 h. (n = 3/group).

Figure 2. SOD-NP protects synovium explants from OA injury. (A, C, E) Representative IHC images of 8-OHdG, Mmp13 and Adamts5 in human synovial explants with indicated treatment. Scale bar, 100 μm. **(B, D, F)** Semi-quantitative evaluation of 8-OHdG, Mmp13 and Adamts5 amount represented as IOD/area. (n = 5/group).

Figure 3. SOD-NP attenuates joint destruction in DMM induced mouse OA model. (A) SO/FG staining of knee joints at 12 weeks after surgery. Scale bars: 200 μm. **(B)** The OA severity of knee joints was measured by Mankin score. (n = 6/group). **(C)** von Frey assay at 4, 8 and 12 weeks after DMM surgery. PWT: paw withdrawal threshold. (n = 6/group). **(D)** HE staining of synovium tissue (Black boxed areas). Scale bar: 200 μm. **(E)** Synovitis scores were quantified. (n = 6/group). **(F, H, J)** Representative IHC images of ROS marker 8-OHdG, Mmp13, Adamts5 in synovium tissue. Scale bar: 50 μm. **(G, I, K)** The amounts of 8-OHdG, Mmp13, and Adamts5 in synovium tissue were quantified as integrated optical density to area (IOD/area). (n = 6/group). *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.

D), subchondral bone plate sclerosis (data not shown), and joint pain (Figure 3E). Mechanistically, SOD-NPs treatment significantly reduced amounts of 8-OHdG (ROS marker, Figure 3F, G), Mmp13 (Figure 3H, I) and Adamts5 (Figure 3J, K) in synovium of DMM knees. On the contrary, SOD or empty NPs alone did not alter OA progression after DMM. Similar results were also obtained when SOD-NPs treatment starts at 4 weeks after DMM surgery (data not shown).

Discussion

The therapeutic utility of the antioxidant enzyme SOD is largely hindered by inadequate delivery, stability, and retention at its intended site of action, due to rapid degradation and/or clearance. Our study demonstrates that SOD-loaded porous polymersomes are more efficacious than free SOD in treating OA. Besides the breakdown of articular cartilage, synovial inflammation is also an important risk factor in OA initiation and progression. Our data showed that SOD-NPs can be endocytosed into synovial fibroblasts, leading to attenuated ROS reaction and proteinase production, as well as reduced synovitis symptoms and OA pain relief. Targeting key aspects of synovium inflammation holds great promise for OA therapy.

Significance

This proof-of-principle study demonstrates the therapeutic efficacy of SOD-loaded porous polymersomes for OA treatment.

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The Effects of Hydroxyapatite Coating on Poly(caprolactone) Micromechanics and Mesenchymal Stem Cell Behavior

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Introduction

Robust osseointegration is a critical component in the success of many orthopaedic interventions from fracture healing to spinal fusion. Of particular interest to our group is the osseointegration of our endplate-modified disc-like angle ply structure (eDAPS), a tissue engineered total disc replacement designed for the treatment of end-stage disc degeneration[1]. Hydroxyapatite (HA) coating has long been an established method to improve osseointegration. However, disagreement exists as to whether scaffold macro- or micromechanical properties dictate successful bone tissue regeneration. Some studies report increases in scaffold stiffness following HA coating[2,3]. Other studies report only increases in local stiffness[4,5], indicating that stiffening at the cellular level may primarily drive osteogenesis. In this study, we investigated the effect of two different HA coatings on the mechanical behavior of salt-leached poly(caprolactone) (PCL) porous scaffolds as well as the scaffolds' ability to induce osteogenesis of MSCs *in vitro*, with or without growth factors.

Methods

PCL scaffolds (5 mm in diameter x 1.5 mm in height) were fabricated according to a previously established salt-leaching protocol[6]. Constructs were hydrolyzed in 2M NaOH for 28 hours and immersed in 10x simulated body fluid (SBF) for up to 7 days (0.25, 1, 3, and 7 days) to create materials with varying degrees of hydroxyapatite surface functionalization. The formation of hydroxyapatite crystals was characterized using μCT and SEM imaging (n = 9). To characterize the scaffolds' macromechanical properties, constructs were compressed for 3 cycles up to 3 N (n = 5). To characterize the scaffolds' micromechanical properties, constructs were indented using the Optics11 Piuma system and a 4.33 N/m probe with a radius of 51.5 μm (n = 3).

PCL scaffolds hydrolyzed for 28 hours and subsequently incubated in SBF for 1 or 7 days were selected for *in vitro* experimentation. Prior to cell seeding, PCL only scaffolds and HA-coated PCL scaffolds were hydrated and sterilized through an ethanol gradient and coated overnight in fibronectin. Each construct was seeded with 41,500 P2 bovine MSCs on both the top and bottom surfaces and then divided into groups fed with either basal or osteogenic media. Every other week, cellular metabolism was quantified using an Alamar Blue assay (n = 6). At 5 and 10 weeks, ± scaffolds from each group were removed from culture. Half of the sample was used to quantify alkaline phosphatase (ALP) activity (n = 3-6). Cryosections from the second half of the scaffold were utilized for immunohistochemistry (IHC) using osteocalcin and osteopontin primary antibodies, or Von Kossa and Draq5 staining (n = 3-6). Data was analyzed using parametric or nonparametric One-Way ANOVAs based on normal/non-normal distribution. Significance was defined as $p < 0.05$.

Results

Longer periods of SBF immersion correlated with greater depths of HA crystal infiltration into the scaffolds' interior (Figure 1B) as well as increases in surface crystal size (Figure 1A). Macromechanically, hydrolyzed scaffolds experienced a reduction in linear modulus followed by a significant increase in stiffness after both 1 day and 7 days of HA coating with no differences between coated groups (Figure 1A). Micromechanically, PCL only scaffolds were significantly stiffer than 7 day HA-coated constructs. *In vitro* studies revealed an upregulation in cellular proliferation on scaffolds fed basal media compared to scaffolds fed osteogenic media (Figure 3A), in addition to cell migration further into the depth of the scaffold.

By 10 weeks, 7 day osteogenic HA-coated scaffolds had significantly increased ALP activity compared to both basal HA-coated scaffolds and PCL only scaffolds. Minimal differences in ALP activity existed between 1 day HA-coated scaffold groups (Figure 3B). Von Kossa staining

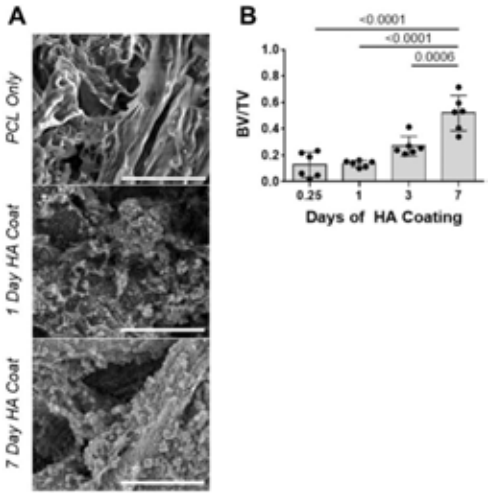

Figure 1 (left and above). (A) Representative SEM images of PCL scaffolds immersed in SBF for 0, 1, and 7 days. **(B)** Scaffolds hydrolyzed for 28 hours and immersed in SBF for 0.25, 1, 3, and 7 days (scale bar = 15 μm).

suggested an increase in calcium deposition homogeneously throughout the osteogenic HA scaffolds and concentrated around the very exterior of osteogenic PCL scaffolds for both coating durations. Von Kossa staining was heterogeneous in basal HA constructs and minimal in basal PCL scaffolds. Osteocalcin IHC in 1 day HA-coated scaffolds revealed an upregulation only in osteogenic constructs, while 7 day HA-coated scaffolds also showed an upregulation of osteocalcin in basal HA scaffolds (Figure 3C).

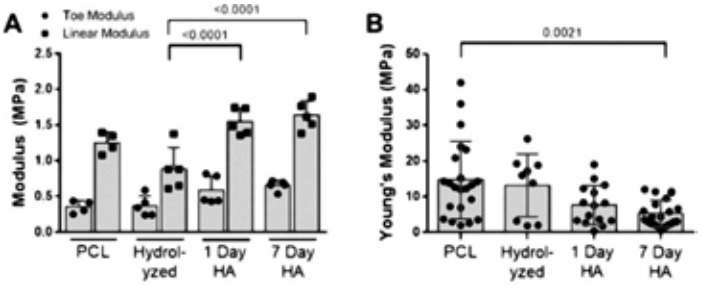

Figure 2 (right). (A) Macromechanics and **(B)** microcmechanics (5-9 indentations of each scaffold, n = 3) of PCL only, hydrolyzed, and HA-coated scaffolds.

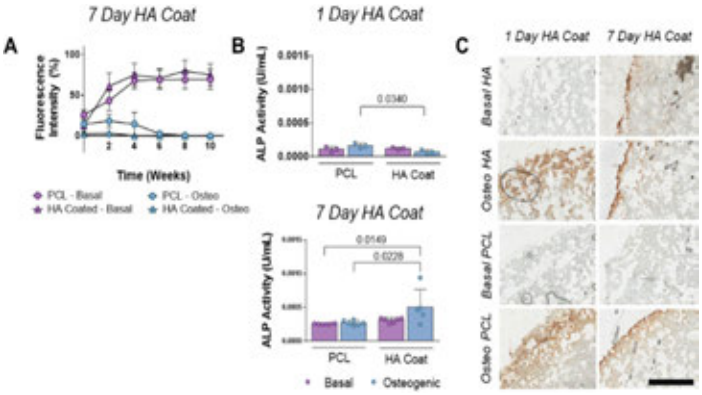

Figure 3 (above and right). For MSC-seeded PCL only and HA-coated PCL scaffolds at 10 weeks: **(A)** Alamar Blue assay, **(B)** ALP activity, and (C) osteocalcin IHC (scale bar = 500 μm).

Discussion

The immersion of scaffolds in SBF for 7 days led to increased osteogenic behavior of MSCs, both without and in concert with osteogenic media. Overall, MSCs on PCL only scaffolds fed basal media exhibited minimal to no osteogenic behavior, whereas PCL only scaffolds fed osteogenic media exhibited an upregulation of osteogenic markers at their external edge. Decreased cellular metabolism in osteogenic media scaffolds suggests a decrease in proliferation that most likely correlates with cell specialization. For HA-coated scaffolds cultured in basal media, increases in osteocalcin and Von Kossa staining were observed primarily in the 7 day coating group. It is unlikely that macroscopic mechanics are driving this upregulation, as no significant differences in compressive modulus between coating groups were observed. Although there was a trend of decreasing micromechanical stiffness as coating time increased, this may be attributed to the heterogeneous surfaces of PCL only and hydrolyzed PCL scaffolds in addition to the limited indentation depth achieved with the 4.33 N/m stiffness probe utilized. The increase in osteogenic behavior of MSCs between the 1 day and 7 day HA-coated scaffolds may be attributed to the mechanobiologic effects of larger, more homogeneously distributed HA crystals. Although osteogenesis was more significantly upregulated in HA-coated scaffolds fed osteogenic media, our data suggests that the coating alone (after 7 days of SBF immersion) can have an osteogenic effect. This supports our group's strategy to implant HA-coated PCL scaffolds, as part of our eDAPS, to drive osseointegration with native bone *in vivo*.

Significance

Understanding how hydroxyapatite influences cellular differentiation is critical to the successful osseointegration of our lab's tissue-engineered disc replacement and can inform approaches for improved osteogenesis for other applications, such as fracture healing and spinal fusion.

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Muscle, Tendon, and Ligament

Mouse Supraspinatus Tendon Mechanical and Structural Properties Are Dependent on Region and Age

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Introduction

Musculoskeletal pathologies such as rotator cuff tendon disorders of the shoulder are prevalent in the aging population[1]. Dysregulation of tendon homeostasis due to aging can result in premature sub-rupture damage accumulation, degeneration, and ultimately injury. Such changes occur primarily in regions of high and complex stresses, such as at the supraspinatus tendon insertion site of the shoulder[2]. While recent studies in patellar tendons showed inferior dynamic structural response to load, reduced elastic and viscoelastic mechanical properties, and altered fibril structure with aging[3], region and age dependent changes in the rotator cuff of the shoulder remain unknown. Therefore, the objective of this study was to elucidate region-dependent mechanical and structural differences in aging mouse supraspinatus tendon. We hypothesized that aging would result in region-specific mechanical and structural changes, such as inferior elastic and viscoelastic mechanical properties as well as altered collagen fiber realignment and fibril morphology, with larger alterations at the insertion site due to the complex functional demands in this region[2].

Methods

Animals

Forelimbs were collected from male wildtype mice sacrificed at either 300 (P300, n = 20) or 570 (P570, n = 20) days of age (UPenn IACUC approved), corresponding to ~40 and ~65 years of age in human[4], respectively.

Elastic and Dynamic Viscoelastic Mechanics

All mice for mechanical testing were frozen at −20ºC until the day of testing. Mice were thawed at room temperature and the supraspinatus tendon-humerus complex from the left limb of each mouse was carefully dissected to remove extraneous tissue. Stain lines were applied for optical strain tracking of the insertion and midsubstance regions and a laser device was used to measure cross-sectional area of the supraspinatus tendon. The myotendinous junction was placed between two sandpaper tabs with cyanoacrylate glue to prevent slippage. The humerus was secured in a custom construct with polymethyl methacrylate and the construct was mounted on a material testing machine (Instron 5848). All testing was conducted in a phosphate buffered saline bath at 37ºC. Each sample was preloaded to 0.025N. The testing protocol consisted of 10 cycles of preconditioning, followed by stress relaxations at 3%, 5%, and 7% strain. Following each stress relaxation, frequency sweeps of 10 cycles of 0.125% amplitude sinusoidal strain at 0.1, 1, 5, and 10 Hz were performed. Following a 10-minute rest at zero displacement, a quasistatic ramp-to-failure at a strain rate of 0.1%/s was completed. Data were collected at 100Hz. Elastic parameters stiffness, modulus, maximum load, and maximum stress were quantified. Viscoelastic parameters dynamic modulus (E*), phase shift (tan δ), and percent relaxation were quantified for each stress relaxation and frequency sweep.

Fiber Re-Alignment

Throughout mechanical testing, dynamic collagen fiber realignment was quantified using cross-polarization imaging, and regional fiber alignment data was interpolated in MATLAB with a polynomial fit as a function of strain from the load-displacement data. Images were also used to optically measure strain and modulus in the insertion and midsubstance regions.

Transmission Electron Microscopy

Supraspinatus tendons (n = 4/age group) were isolated, fixed, and embedded in epon resin blocks. 85nm sections were cut using an ultramicrotome, stained with uranyless and phosphotungstic acid, and imaged at 60,000x using a transmission electronic microscope (JEOL 1010). Fibril diameter frequency distribution was quantified.

Statistics

Region-specific tendon elastic mechanical properties and collagen fiber realignment were compared using two-way ANOVAs across age and region followed by Bonferroni post-hoc tests. Viscoelastic properties were compared using two-way ANOVAs across age and strain levels followed by Bonferroni post-hoc tests. Fibril

diameter distributions were compared using Kolmogorov-Smirnov tests. Significance was set at $p < 0.05$.

Results

Elastic and Viscoelastic Mechanics (Figure 1)

Cross-sectional area was greater at the insertion than in the midsubstance region in both age groups. Stiffness and modulus were lower at the insertion than in the midsubstance region in both age groups. Midsubstance modulus had an interaction and decreased with age. The viscoelastic response was preserved with aging across strain levels. Specifically, there were differences in stress relaxation and dynamic modulus at 5 and 7% strain relative to 3% strain with aging. P300 tendons exhibited more relaxation at 3% relative to both 5 and 7% strain than P570 tendons. Phase shift was not altered across strain levels for either age group. As expected, all supraspinatus tendon samples failed at their insertion sites.

Collagen Fiber Realignment (Figure 2)

Collagen fiber realignment had a significant interaction with region, but not age, in both age groups. Specifically, normalized circular variance was greater in the insertion than in the midsubstance region (indicative of less fiber alignment) between 3 and 9% strain in both the P300 and P570 age groups.

Fibril Morphology (Figure 3)

Fibril distributions were significantly different across region and age with smaller diameter fibrils at the insertion compared to the midsubstance within each age group. Insertion region fibrils had narrower distributions compared to the

Discussion

We studied regional properties in aging mouse supraspinatus tendons. Supporting our hypothesis, insertion regions exhibited inferior elastic mechanical properties and reduced collagen fiber realignment compared to midsubstance regions. Additionally, insertion region fibril size distributions

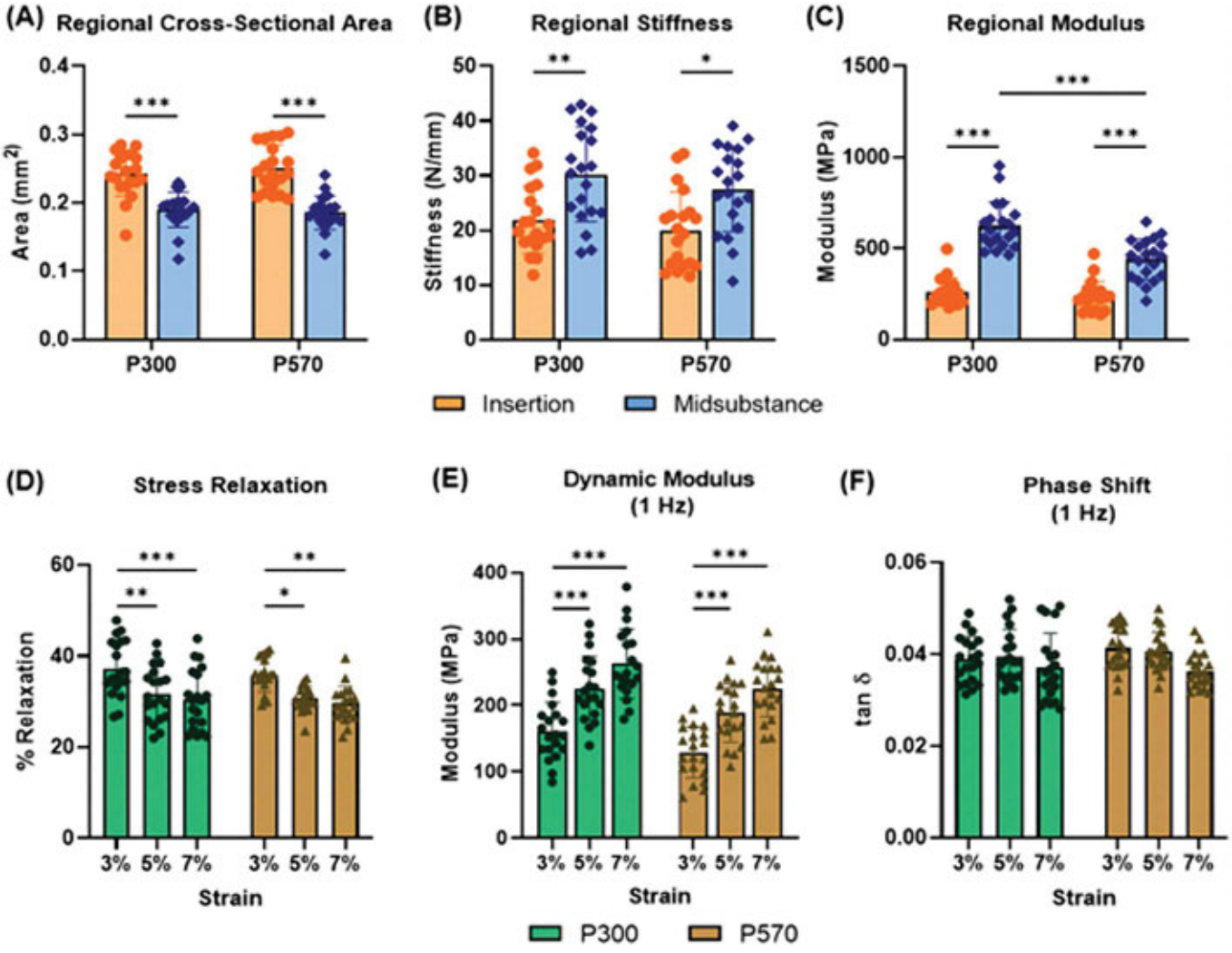


Figure 1. Insertion regions demonstrated greater **(A)** cross-sectional area while midsubstance regions had greater **(B)** stiffness and **(C)** elastic modulus for both age groups. Elastic modulus was **(C)** reduced with aging. Viscoelastic properties were conserved with aging with similar differences across strain levels in **(D)** stress relaxation and **(E)** dynamic modulus and no differences across strain level in **(F)** phase shift in both age groups. Data as mean ± standard deviation (*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$).

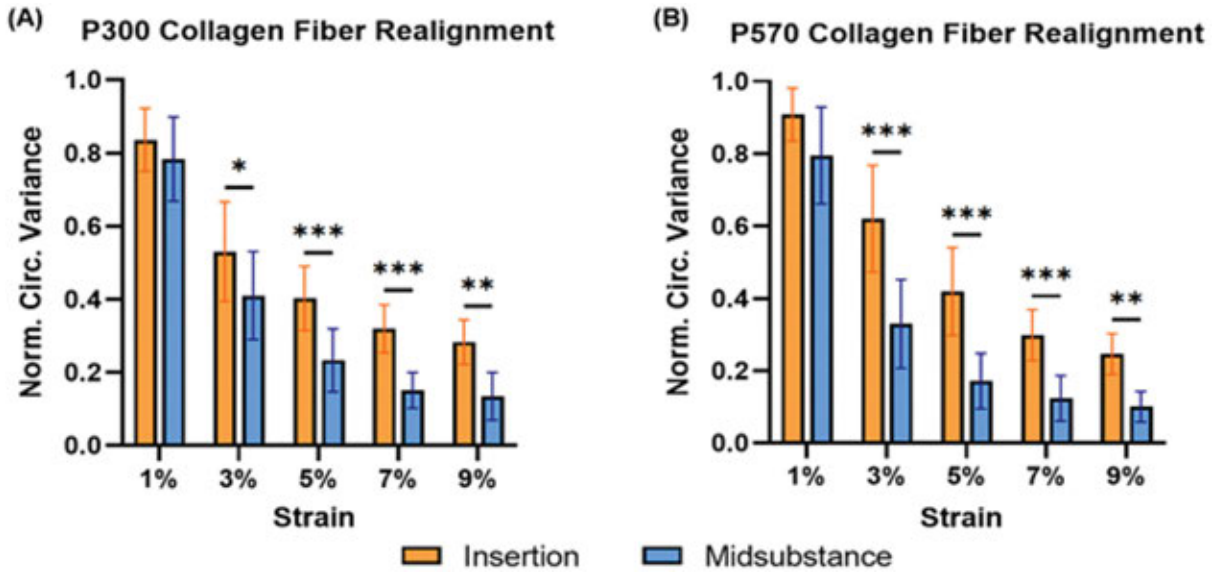
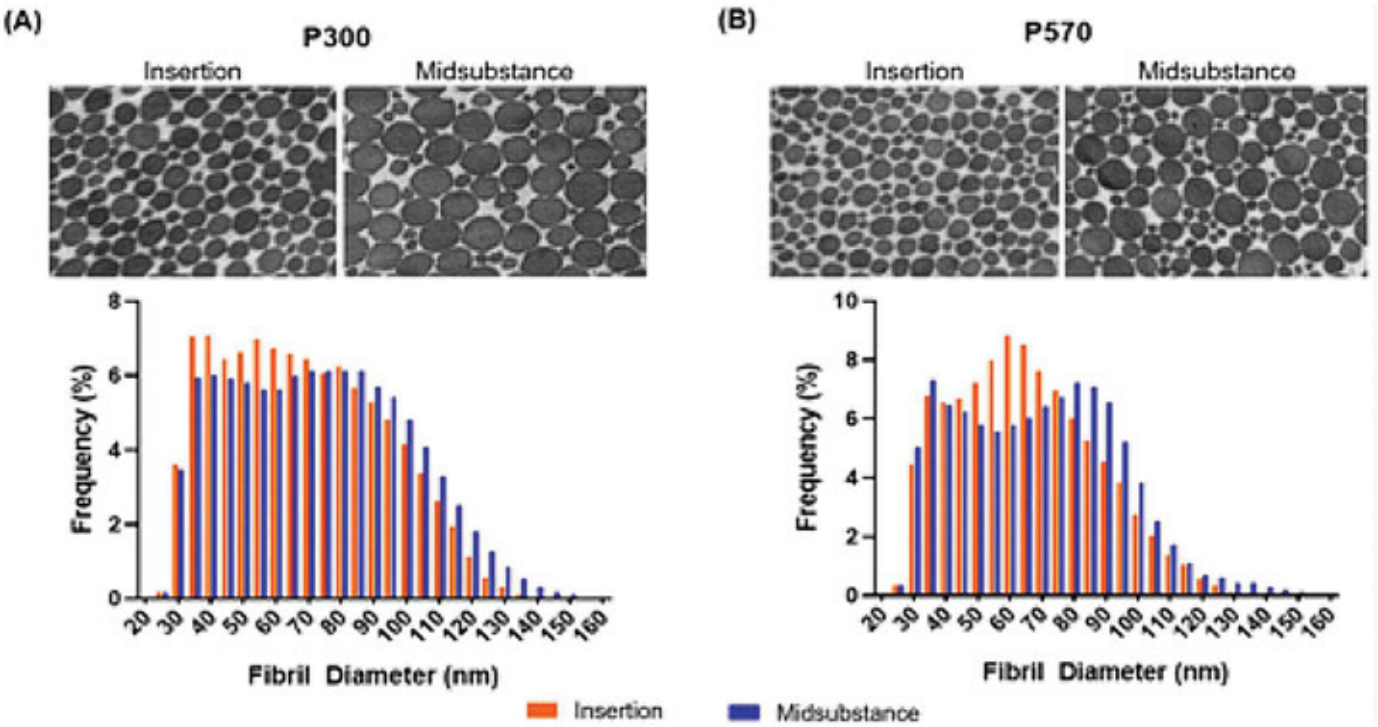


Figure 2. Insertion regions demonstrated lower collagen fiber realignment (greater normalized circular variance) at strain values between 3 and 9% in the (A) P300 and (B) P570 age groups. Data as mean ± standard deviation (*p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001).



	Insertion	Midsubstance
Mean	68.4 nm	72.9 nm
Median	66.4 nm	71.9 nm
Q1	47.9 nm	50.6 nm
Q3	86.9 nm	92.7 nm

	Insertion	Midsubstance
Mean	64.9 nm	68.6 nm
Median	63.2 nm	68.5 nm
Q1	47.6 nm	47.1 nm
Q3	79.9 nm	86.6 nm

Figure 3. Fibril diameter distributions for **(A)** P300 and **(B)** P570 age groups are similar with shifts towards smaller diameter fibrils in the insertion compared with the midsubstance region. Aging also resulted in a shift towards smaller fibrils in the midsubstance.

shifted towards smaller fibril diameters. Previous studies in flexor tendons demonstrated that mechanical properties and fibril diameter distributions can differ from the bone-tendon junction to the myotendinous junction[5]. Interestingly, aging did not influence regional and whole tendon elastic and viscoelastic properties and collagen fiber realignment but did influence fibril morphology.

Multiscale regression analyses have shown that two strong predictors of mechanical properties at the insertion and midsubstance regions were collagen fiber realignment and fibril diameter[6]. Our results suggest potential multiscale structure-function mechanisms relating macroscale tissue mechanical behavior to microscale collagen fiber realignment and nanoscale fibril morphology. Specifically, in the insertion regions, decreased collagen fiber realignment, indicative of a reduction in dynamic structural response to load, in conjunction with smaller diameter fibrils unable to withstand the same loading magnitude results in inferior mechanical properties relative to the midsubstance region. This induces earlier accumulation of damage at the fiber and fibril levels propagating to the macroscale, ultimately leading to premature tendon failure at the tendon insertion[2], as observed in all supraspinatus tendon samples. Clinically, these structure-function mechanistic findings may further explain why supraspinatus tendon tears predominantly occur at its insertion on the proximal humerus[7].

Significance

This study reveals critical mechanical and structural differences in supraspinatus tendon region and age. Future studies will consider additional region-specific multiscale structural, functional, and compositional mechanisms in aging supraspinatus tendons.

Acknowledgments

We thank Ashley Fung and Thomas Leahy for their assistance. This study was supported by NIH/NIAMS (AR070750) and the Penn Center for Musculoskeletal Disorders (NIH/NIAMS, P30 AR069619).

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Tracking Day-To-Day Achilles Tendon Loading Progression During Rupture Recovery

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Introduction

Achilles tendon ruptures have increased 10-fold in the past 30 years. Although state-of-art treatments can reduce re-rupture rate to $< 5\%$[1], two-thirds of patients still suffer long-term functional deficits[2]. An effective strategy to improve tendon healing is via progressive loading[3]. Yet, targeted Achilles tendon loading has rarely been prescribed in rehabilitation, largely due to difficulties to reliably measure and track tendon loads outside of clinics.

Recent advances in wearable sensors, including instrumented shoe insoles, provide powerful platforms to measure real-world biomechanics. Using simple algorithms our group developed, these instrumented insoles can quantify Achilles tendon loads in an accuracy comparable to lab-based analysis[4,5]. Despite these technical advances, the feasibility of using wearables as a tool to enhance targeted Achilles tendon therapeutics remain unknown, partly due to the cost and logistics to obtain continuous data over the long recovery process on many subjects. Therefore, our goal was to leverage a case study to verify whether instrumented insoles are able to track the longitudinal progression of Achilles tendon loading in daily life, and relate to clinically relevant events that are otherwise difficult to capture beyond controlled settings.

Methods

A patient (F, 30y/o) who suffered a rupture of her right Achilles tendon was enrolled and provided consent in this IRB-approved study. The tendon was repaired $\pm$ days after injury, followed by a standard rehabilitation protocol[3]. An immobilizing boot fit with a 3-sensor instrumented insole (Loadsol) was worn starting from week 4 post-surgery. The insole remained in the footwear after it was changed from boot to subject's own shoe at week 9. Data collection continued until week 22. The patient recorded at least 10 seconds of gait data from the insole each day, and logged daily step count using her mobile device. Patient also documented any specific event that may be related to the health of the healing tendon, including pain, discomfort, notable daily living activities, and clinical visits. We also obtained clinical logs from such visits.

We extracted all steps from the daily insole data. For each step, we estimated Achilles tendon loads using our established algorithm[4,5] and calculated 4 mechanical variables: load peak, impulse over a step, average load rate from heel strike to peak, and maximum load rate. We compared the daily average of these load variables longitudinally to step counts, self-reported events, and clinical events to explore their inter-relationships. We also correlated the 4 load variables to determine whether they provide unique insights into Achilles tendon loading versus each other.

Results and Discussion

The insole recorded up to 70 steps each day on a total of 116 days. In general, peak Achilles tendon loading increased gradually over the course of rehabilitation, but in a non-linear manner with large variations especially between week 12-19 (Figure 1). Many "sharp" changes in peak load corresponded to events possibly causing or resulted from altered tendon health. For example, rapid load increases in late week 12 was immediately followed by days of reported pain and swelling. A particularly high step count (20k+) was followed by a large decrease of the Achilles tendon peak load measured at the end of the same day. The insole was also able to identify tendon load changes according to patient instructions. For example, by intentionally "trying to push off' during gait, the patient increased her peak Achilles tendon load by 65% and peak load rate by 45% (Figure 2). This result supports the feasibility for Achilles tendon load to be modified instantly and interactively via instructions or biofeedback. Finally, Achilles tendon load rates and impulse strongly correlated with peak loads ($R^2 > 0.85$). The strong correlations with other mechanical variables suggest peak load is sufficient for tracking Achilles tendon loading.

Significance

Longitudinally monitoring Achilles tendon loading is challenging because 1) it is limited by the scarce frequency of clinical visits, and 2) lab-based gait measurements do not faithfully

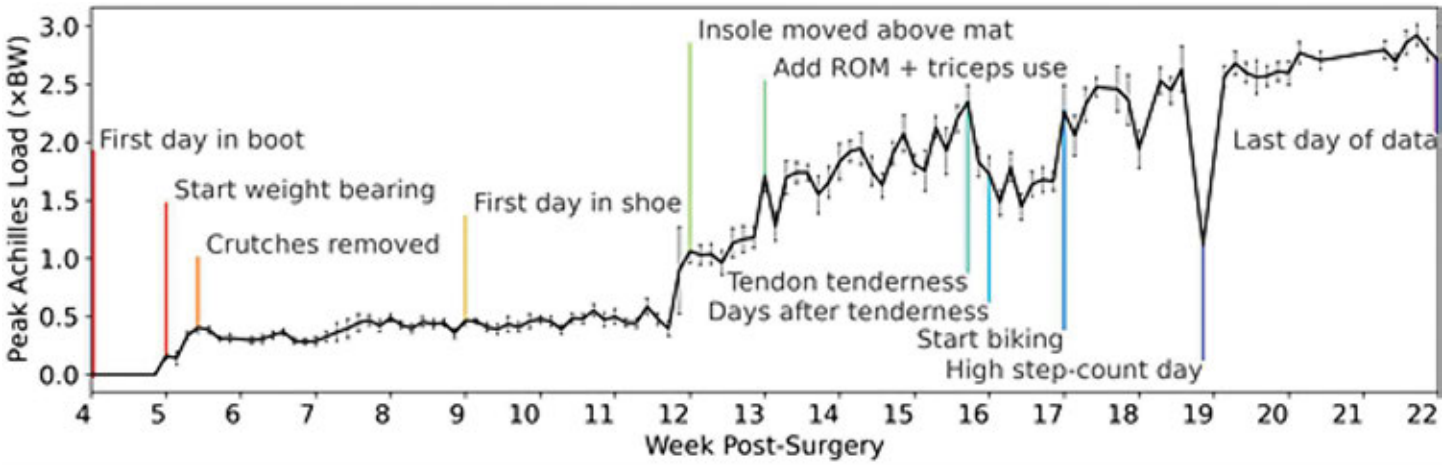

Figure 1. Achilles tendon peak load progression, annotated with selected representative clinically relevant events. Error bars = ± 1 standard deviation (SD) across steps on the same day.

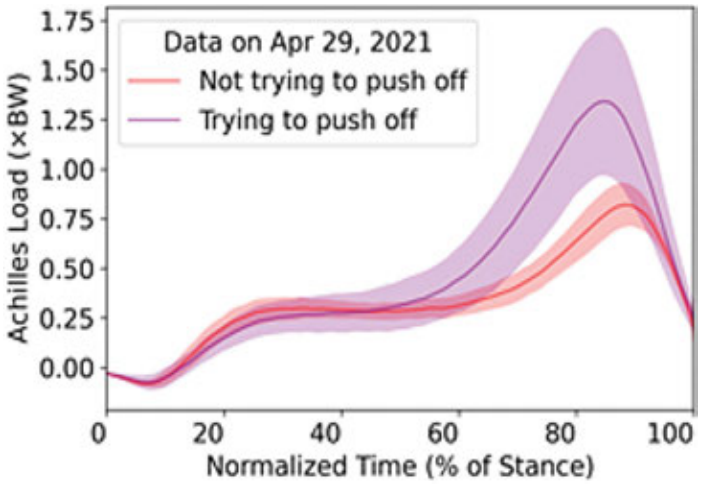

Figure 2. Achilles tendon load over a step with vs without intentional push-off. Shades = ± 1 SD.

reflect real-world biomechanics [6]. This first-of-kind case study shows the value and feasibility of using instrumented insoles to track day-to-day Achilles tendon loading in the real world. Our innovative paradigm can empower future studies to leverage accessible tools (e.g. biofeedback systems) and deliver personalized rehabilitation according to quantitative guidance, thereby optimizing long-term Achilles tendon healing and functional recovery.

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Knockdown of Decorin and Biglycan During the Early Proliferative and Remodeling Phases of Tendon Healing Alters Gene Expression and Fibril Morphology

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Introduction

Tendon matrix consists of highly organized collagen fibrils with small leucine rich proteoglycans (SLRPs) bound to the fibril surface. The SLRPs decorin (gene: *Dcn*) and biglycan (gene: *Bgn*) play a critical role in regulating fibrillogenesis during tendon development and following tendon injury.[1-3] Previous studies have demonstrated that *Bgn* knockdown alone or in tandem with *Dcn* knockdown during healing resulted in improved tendon mechanical properties, regardless of knockdown induction timepoint.[4-5] Surprisingly, *Dcn* knockdown alone had no measurable effect on healing tendon mechanical properties. While these prior studies demonstrated that knockdown of SLRPs could improve tendon mechanical properties, they did not define the mechanism by which SLRP knockdown altered the biological processes and matrix structure within the healing tendon. Therefore, the objective of this study was to define the roles of decorin and biglycan in modulating tendon morphology, gene expression, and collagen ultrastructure throughout the phases of tendon healing. We hypothesized that *Bgn* knockdown alone or in tandem with *Dcn* knockdown would lead to faster recovery of healthy tendon properties, including increased tendon-specific extracellular matrix gene expression, reduced scarred matrix, and a return to an uninjured distribution of collagen fibril sizes.

Methods

Study Design

Female wildtype (WT, n = 36), $Dcn^{flox/flox}$ (I-$Dcn^{-/-}$, n = 36), $Bgn^{flox/flox}$ (I-$Bgn^{-/-}$, n = 36), and compound $Dcn^{flow/flox}$/$Bgn^{flox/flox}$ (I-$Dcn^{-/-}$/$Bgn^{-/-}$, n = 36) mice with a tamoxifen (TM) inducible Cre, (B6.129-Gt(ROSA)26Sortm1(cre/ERT2)Tyj/J, Jackson Labs) were utilized (IACUC approved). At maturity (120 days), mice underwent bilateral patellar tendon injury surgery as described.[1,3] Following surgery, Cre excision of the conditional alleles was induced via two consecutive daily IP injections of TM (2 mg/40g body weight). WT mice received TM injections at 120 days and were divided between the uninjured control group, which was sacrificed at 150 days, and injured groups sacrificed at 3 or ± weeks postinjury. Mice from inducible knockdown genotypes underwent surgery and were evenly divided between Cre-induction during the early proliferative period (TM injections beginning at 5 days post injury, termed TM5) or during the remodeling period (TM injections beginning at 21 days post injury, termed TM21). TM5 animals were sacrificed at 3 or ± weeks postinjury, while TM21 mice were sacrificed at ± weeks postinjury (n = 16/genotype/induction timepoint/sacrifice timepoint).

Gene

Injured patellar tendons were isolated for RNA extraction and cDNA reverse transcription. Pre-amplified cDNA was loaded into a Fluidigm 96.96 Dynamic Array with Taqman assays to probe expression levels of 96 target genes relevant for tendon healing (n = 4/genotype/sacrifice timepoint).

Histology

Whole knees were fixed, decalcified, paraffin embedded, sectioned in the transverse plane, and stained with toluidine blue (n = 4/genotype/sacrifice timepoint). Images were used to quantify scarred area within the injured patellar tendons.

Transmission Electron Microscopy (TEM)

For TEM, injured patellar tendons were fixed, embedded in epon, sectioned at 85 nm, stained, and digitally imaged at 60,000x. Collagen fibril distributions were quantified from images captured within the healing region (n = 4/genotype/sacrifice timepoint).

Statistics

For gene expression and scar area, comparisons were made at each induction-sacrifice timepoint combination using three separate one-way ANOVAs with Tukey post-hoc

tests (significance at $p \leq 0.05$; trends at $p \leq 0.1$). For collagen fibril size distributions, comparisons were made at each induction-sacrifice timepoint combination with Kolmogorov–Smirnov tests (significance at $p \leq 0.05$).

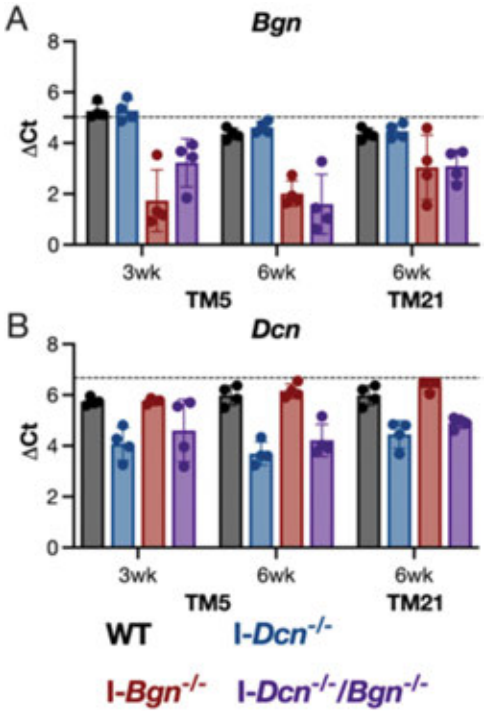

Figure 1. (A) *Bgn* and **(B)** *Dcn* demonstrated expected decreases in expression when targeted for knockdown with at least a trending difference relative to other groups, except for WT vs I-Dcn$^{-/-}$/Bgn$^{-/-}$ at TM5-3wk ($p = 0.15$). ΔCt was calculated by subtracting the gene Ct from average housekeeping Ct (Abl1 and Rps17).

Results

All knockdown groups demonstrated expected decreases in the targeted genes (Figure 1). Further analysis at 3 weeks postinjury revealed increased expression of genes associated with matrix remodeling, inflammation, and activated fibroblasts in the TM5 I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ group relative to all other groups (Figure 3). At ± weeks postinjury, the TM5 I-*Bgn*$^{-/-}$ and I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ groups displayed increased expression of matrix remodeling genes, including Adamts5, Fbn1, Loxl2, and Mmp2, relative to the TM5 WT and I-*Dcn*$^{-/-}$ groups. In the TM21 groups, the increased expression of similar matrix remodeling genes was maintained in I-*Bgn*$^{-/-}$ tendons but not I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons. While there were no differences in relative scar area between groups (data not shown), fibril size distributions were significantly different between all groups compared (Figure 2).

Discussion

Consistent with our hypothesis, the I-*Bgn*$^{-/-}$ and I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons demonstrated increased expression of matrix remodeling genes relative to WT and I-*Dcn*$^{-/-}$ tendons at ± weeks postinjury, which is consistent with improved mechanical properties in these groups.[4,5] Interestingly, increased expression of these genes depended on induction timepoint, as this was observed in both I-*Bgn*$^{-/-}$ and I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ groups at TM5 but only in the I-*Bgn*$^{-/-}$ group at TM21. This suggests that *Dcn* has a more prominent role between 5 and 21 days postinjury. Contrary to our hypothesis, we did not observe reduced scarred matrix nor a return to an uninjured distribution of collagen fibrils in I-*Bgn*$^{-/-}$ and I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons. While the I-*Bgn*$^{-/-}$ group exhibited a narrower

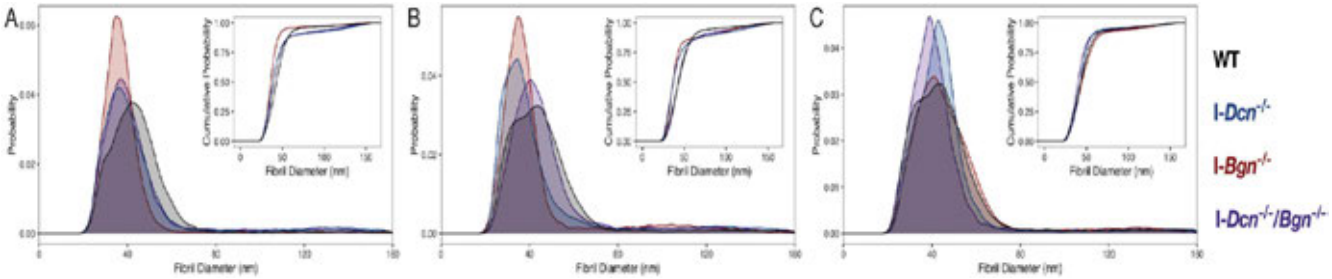

Figure 2. Probability density and cumulative distributions (insets) plots for **(A)** TM5-3wk, **(B)** TM5-6wk, and **(C)** TM21-6wk.

Figure 3. Gene expression summary table. Genes listed are significantly increased in the column group relative to the row group.

distribution of fibrils at TM5 compared to WT, the lack of difference at TM21 suggests that the improved mechanical properties previously observed at both TM5 and TM21 are not due to changes in collagen fibril size distributions. Instead, we speculate that superior healing in these groups is due to changes in the non-collagenous tendon matrix, which then influences matrix synthesis, deposition, and organization. This is supported by observed increases in gene expression for non-collagenous matrix components and matrix remodeling proteins in these groups.

Significance

This study investigated the roles of the SLRPs decorin and biglycan during the early proliferative and remodeling phases of tendon healing. This data indicates that *Bgn* knockdown increases non-collagenous matrix and matrix remodeling gene expression following injury, which is consistent with improved mechanical properties previously observed with knockdown of *Bgn* in healing tendons.

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A Double Cortical Button Technique Yields Similar Biomechanics as the Traditional Docking Technique for Ulnar Collateral Ligament Reconstruction

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Introduction

Ulnar collateral ligament (UCL) ruptures are debilitating injuries primarily incurred by high-level throwing athletes. The docking technique is widely used for UCL reconstruction due to its high failure torque and reliable clinical outcomes[1] This approach uses an autograft palmaris longus tendon, which is looped through bone tunnels and held in place with sutures on the humerus (Figure 1A). Failure of the docking technique is often attributed to bone tunnel failure. Recently, a double cortical button technique has been described, in which the graft is fixated using cortical buttons (Figure 1B). Advantages of this approach include greater control in graft tensioning and elimination of bone tunnel failure. Currently, it is unclear whether a double button reconstruction provides the same repair strength as the docking procedure. The goal of this study was to compare the biomechanics of docking and double button UCL techniques using cadaveric specimens. We hypothesized that there would be no difference in post-operative joint stiffness and reconstruction strength between the two techniques.

Methods

This study was performed on eight matched pairs of cadaveric arm specimens (7M, 1F, 74-87 years of age) randomized into docking and double button groups. Palmaris longus tendons were harvested when present; a sectioned portion of flexor carpi radialis was used when palmaris longus was absent. To model a pitching motion in the cocked position, humeri and forearm bones were secured to a test frame with the elbow flexed 90°, the forearm in neutral position, and a valgus torque applied to the humerus (Figure 2). 3D marker clusters were attached to bones to facilitate the measurement of strain between graft insertion points during testing. Similar to previous studies, controlled valgus rotations were applied to the humerus to develop a reaction moment at the elbow joint[2-4]. Specimens underwent a 4-step non-destructive protocol (Intact, Injured, Initial Repair, 1000 cycles) followed by a destructive ramp to failure test. The stiffness in the toe region and elastic region of torque-rotation curves were calculated. Additionally, maximum torque, and insertion point strain were calculated for all tests. Paired t-tests were used to compare longitudinal measures within the same specimen, and two sample t-tests were performed to determine differences ($p < 0.05$) between the docking and double button groups.

Results

The docking and double button reconstruction techniques provided similar values for torsional stiffnesses in the toe and elastic regions (Fig 3A&B), percent torque recovered (Figure 3C), and graft insertion point strain (Fig 3D) immediately after surgery (10 cycles) and after cyclic loading (1000 cycles). Reconstructed elbows displayed similar restoration of toe and elastic stiffness ($p = 0.483$, $p = 0.754$), regardless of technique used. Both groups had similar decreases in these measures after cyclic loading. Similarly, the docking and double button groups recovered 68.91% and 65.08% of their resistive torque ($p = 0.777$), which also decreased after cyclic loading ($p = 0.918$). Insertion point strain was also similar between groups during the 10-cycle ($p = 0.645$) and 1000-cycle ($p = 0.921$) tests. Ramp to failure testing showed no significant differences in ultimate torque for the docking

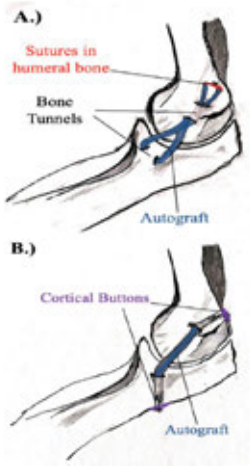

Figure 1. Illustrations of the **(A)** docking; **(B)** double button reconstructions used to restore UCL function.

Figure 2. Photograph of an elbow during mechanical testing. A valgus humeral torque (red arrow) applies stress to the medial elbow.

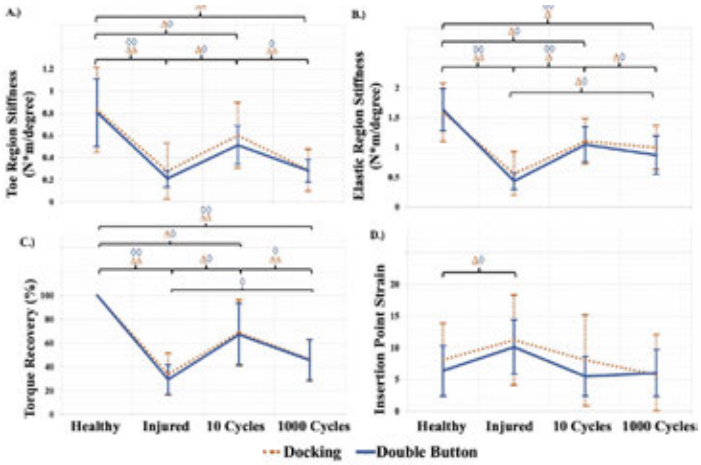

Figure 3. Graphs of **(A)** toe region stiffness; **(B)** elastic region stiffness; **(C)** percent torque recovered; **(D)** insertion point strain. Δ and ◇ symbols indicate $p < 0.05$ for measures within docking and double button groups, respectively. ΔΔ and ◇ ◇ indicate significant differences of $P < 0.001$.

(8.93 ± 3.9 Nm) and double button (9.56 ± 3.5 Nm) groups ($p = 0.739$).

Discussion

Results of this study confirmed our hypothesis, that the double button technique provides elbow biomechanics that are comparable to the docking technique. This experiment indicates that both reconstruction techniques restore a degree of joint function, but pre-injury joint stiffness is not recapitulated with either surgical repair. It is unclear if additional graft tensioning during the reconstruction would provide improved post-operative biomechanics. The loss of stiffness and strength during cyclic testing may not be indicative of clinical experience, as patients are asked to wear a sling and guard the joint to allow for healing. Finally, it should be noted that this model only simulated one motion and the advanced age of the donors in this study is not indicative of the younger patient population that typically suffers this injury.

Significance/Clinical Relevance

The results of this study support the hypothesis that the double button technique for UCL reconstruction is non-inferior to the docking technique. This data also suggests that while both reconstruction techniques restore joint stability, neither can fully restore pre-injury joint stiffness.

Acknowledgements

Arthrex, Inc. provided surgical materials used in this study.

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Knockdown of Decorin and Biglycan at Time of Tendon Injury Alters Gene Expression and Fibril Morphology

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Introduction

Tendon healing follows a typical wound healing process, including inflammatory, proliferative, and remodeling phases, though outcomes following tendon injury remain poor. The small leucine-rich proteoglycans (SLRPs), decorin (Dcn) and biglycan (Bgn), are critical regulators of fibrillogenesis and matrix assembly, but their specific roles in tendon healing are not fully understood. We previously showed that knockdown of Bgn or both Dcn/Bgn resulted in increased tendon modulus 6-weeks post-injury, suggesting improved function due to Bgn knockdown.[1] However, the mechanisms driving these differences remain unknown. Therefore, the objective of this study was to define the biological and structural regulatory roles of Dcn and Bgn in tendon healing using conditional knockdown of Dcn, Bgn, and both Dcn/Bgn at the time of injury. We hypothesized that induced knockdown of Bgn and both Dcn/Bgn would improve healing resulting in increased tendon extracellular matrix gene expression, reduced scarring, and superior fibril structure compared to wild-type mice.

Methods

Study design

Female $Dcn^{+/+}/Bgn^{+/+}$ control (WT, n = 44), $Dcn^{flox/flox}$ (I-$Dcn^{-/-}$, n = 32), $Bgn^{flox/flox}$ (I-$Bgn^{-/-}$, n = 32), and compound $Dcn^{flox/flox}/Bgn^{flox/flox}$ (I-$Dcn^{-/-}/Bgn^{-/-}$, n = 32) mice with a tamoxifen inducible Cre (B6.129-Gt(ROSA)26Sortm1(cre/ERT2)Tyj/J, Jackson Labs) were used (IACUC approved).[2] At 120 days old, Cre excision was induced via two (injured) or three (uninjured) consecutive daily IP injections of tamoxifen. At time of induction, injured groups underwent bilateral patellar tendon (PT) injury surgery as described and were sacrificed 1-, 3- or 6-weeks later. Uninjured groups were sacrificed at 150 days old.[3]

Gene Expression

PTs (n = 4/group) were homogenized, and RNA was extracted. RNA was converted to cDNA, pre-amplified, and loaded into a Fluidigm 96.96 Dynamic Array. The 96 target genes included categories of collagens, non-collagenous matrix, matrix remodeling, cell-ECM proteins, and cell and inflammatory markers. ΔCt was calculated by subtracting the gene cycle threshold (Ct) from average Ct of the housekeeping genes (*Abl1*, *Rps17*).

Histology

Knee joints (n = 4/group) were fixed, decalcified, and paraffin sectioned in the transverse plane of the PT at 10μm. Sections were stained with toluidine blue, and scar tissue was measured in the wound site adjacent to the native tissue.

Transmission Electron Microscopy

PTs (n = 4/group) were isolated, fixed, and processed as described.[4] Sections were cut at 85nm, stained, and imaged at 60,000x in the wound area. Fibril diameter distributions were quantified.

Statistics

For gene expression and scar area percentage, one-way ANOVAs with Tukey post-hoc tests were conducted at each timepoint. Fibril diameter distributions were compared using Kolmogorov-Smirnov tests. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

Gene Expression

Dcn and *Bgn* expression demonstrated efficient knockdown at each healing timepoint. *Dcn* was significantly reduced (4-6 fold) in I-$Dcn^{-/-}$ and I-$Dcn^{-/-}/Bgn^{-/-}$ tendons compared to WT and I-$Bgn^{-/-}$ mice (Figure 1A). Similarly, *Bgn* expression was 4-6 fold lower in I-$Bgn^{-/-}$ and I-$Dcn^{-/-}/Bgn^{-/-}$ tendons (Figure 1B). Further evaluation of gene expression profiles revealed subtle changes during early tendon healing. At 1-wk post-injury, *Col12a1*, *Tnmd*, and *Igf1* (Figure 2A) expression were significantly reduced in I-$Dcn^{-/-}$ tendons compared to WT. By 3-wks, *Igf1* expression in the I-$Dcn^{-/-}$ group was significantly greater than WT tendons, contrasting the difference at 1-week. And by 6-wks, there was no difference in *Igf1* expression between

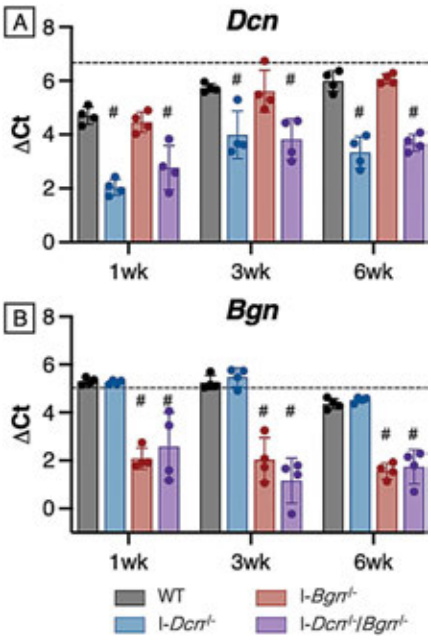


Figure 1. Induced knockdown of **(A)** *Dcp* and **(B)** *Bgn* expression resulted in a significant reduction in expression levels. (#: $p \leq 0.05$ from WT). Uninjured WT expression level is shown as a dashed line.

WT and I-*Dcn*$^{-/-}$ tendons, while expression was significantly higher in the I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ group compared to WT tendons (Figure 2A). Contrasting the subtle changes at 1- and 3-wks post-injury, several significant gene changes during late tendon healing at 6-wks were observed in I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons. For example, there were no differences in *Fmod* at 1 or 3 wks, but *Fmod* was significantly increased at ± wks compared to WT (Figure 2B). Similar trends were observed across several target genes, and those exhibiting increased expression in the I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ group compared to WT at 6-weeks are listed in Figure 2C.

Histology & Fibril Morphology

No differences in scar area percentage were observed at any healing timepoint (data not shown). However, fibril size distributions were significantly different between all groups at each timepoint with a shift towards smaller diameter fibrils in the I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ at both 3- and 6-wks post-injury compared to WT and I-*Dcn*$^{-/-}$ (Figure 3A,B). Additionally, the fibril diameter distribution was narrower in I-*Bgn*$^{-/-}$ tendons compared to WT and I-*Dcn*$^{-/-}$ at 6-wks (Figure 3B).

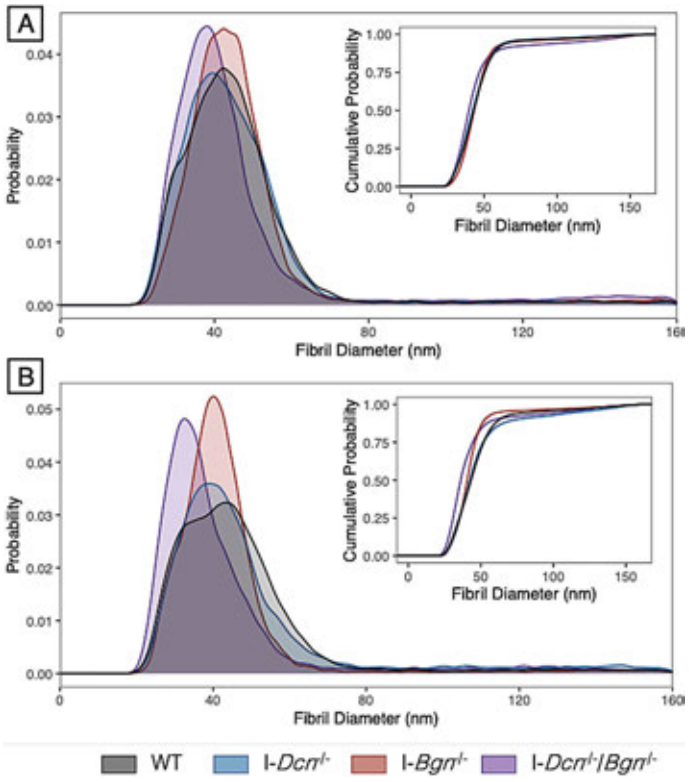
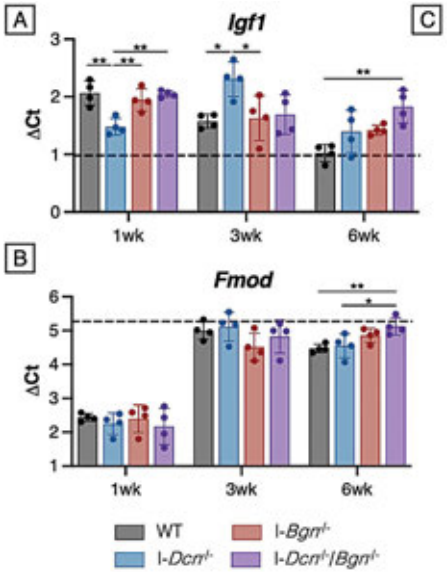


Figure 3. Probability density and cumulative distribution (inset) plots of fibril diameter demonstrated a moderate shift towards smaller fibril diameters in the I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ group at **(A)** 3-weeks and **(B)** 6-weeks post-injury. I-*Bgn*$^{-/-}$ tendons also had a narrower distribution of fibril diameters at 6-weeks compared to I-*Dcn*$^{-/-}$ and WT tendons.

Discussion

Using our novel inducible models to minimize compensation typically present in traditional models, our findings support biological and structural regulatory roles of Dcn and Bgn



C

Gene	ΔCt diff	p-value
Collagens		
Col1a2	0.67	0.006
Col6a1	0.55	0.008
Col11a1	0.58	0.02
Non-Collagenous Matrix		
Fbn2	1.97	0.005
Fmod	0.65	0.01
Hspg2	0.49	0.01
Thbs4	0.83	0.009
Tnc	0.48	0.05
Matrix Remodeling		
Adamts2	0.42	0.006
Mmp2	0.73	0.007
Mmp3	1.38	0.001
Mmp14	0.96	0.003
Cell-ECM		
Itga11	0.65	0.01
Ptk2	0.36	0.005

Gene	ΔCt diff	p-value
Signaling		
Bmp2	0.5	0.02
Igf1	0.81	0.003
Mtor	0.47	0.001
Pdgfa	0.55	0.009
Pdgfb	0.59	0.009
Pdgfrb	0.47	0.04
Tgfb1	0.51	0.006
Tgfb3	0.66	0.005
Vegfb	0.57	0.01
Cell Cycle/Proliferation		
Cdkn1a	0.61	0.02
H2afx	0.49	0.02
Inflammation		
Ccl4	1.61	0.02
Pge2	0.33	0.05

Figure 2. **(A)** I-*Dcn*$^{-/-}$ tendons exhibited an altered healing profile of *Igf1* expression with a significant decrease at 1-week and increase at 3-weeks post-injury compared to WT tendons. At 6-weeks post-injury *Igf1* and **(B)** *Fmod* expression were significantly increased in I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons compared to WT tendons. Uninjured WT expression level is shown as a dashed line. (*$p \leq 0.05$, **$p \leq 0.01$) **(C)** Target genes exhibiting increased expression in I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ tendons compared to WT tendons at 6-weeks post-injury. The signaling category had the greatest number of differentially expressed genes. ΔCt diff represents the increase in mean ΔCt of I-*Dcn*$^{-/-}$/*Bgn*$^{-/-}$ compared to WT.

during tendon healing, as evidenced by alterations in gene expression profiles and fibril structure. In addition to their structural roles in fibrillogenesis and matrix assembly, Dcn and Bgn regulate inflammation and growth factor activity.[5] Though only moderate changes were observed in 1- and 3-weeks post-injury, increased expression of several growth factors and matrix proteins at 6-weeks post-injury suggest that Dcn and Bgn play more critical roles during the remodeling phase of healing.This may be due to the role of Dcn and Bgn in regulating signaling pathways such as Igf, Pdgf, and Tgfb, which results in downstream effects on matrix synthesis and remodeling.[6] While no compensatory changes in *Dcn* or *Bgn* expression were observed, the most pronounced effects in the I-$Dcn^{-/-}$/$Bgn^{-/-}$ group indicate overlapping functions of Dcn and Bgn and that functional compensation may occur in the single knockdown models.[7,8] Contrary to our hypothesis, induced knockdown of Bgn in both the single and double knockdown groups resulted in a narrower distribution of fibril diameters at 6-weeks post-injury, which deviates from an uninjured distribution. Therefore, increased modulus in the I-$Bgn^{-/-}$ and I-$Dcn^{-/-}/Bgn^{-/-}$ groups is likely not due to superior fibril structure and may instead be driven by alterations in the non-collagenous matrix.[1] Future work is necessary to elucidate the roles of decorin and biglycan in regulating growth factor activity and evaluate the composition of the healing matrix.

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Regional FDL Tendon Development Involves Differential Pericellular Matrix Expression and Presence

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Introduction

Tendon requires highly aligned collagen I fibrils to aid in mechanical strength in response to tensile loading. Regions of tendon that wrap around bones or joints, however, experience additional compressive loading and display a complex, fibrocartilaginous tissue phenotype[1]. Fibrocartilage and resident chondrogenic cells rely heavily on the collagen VI-rich pericellular matrix (PCM) for proper mechanosensation and homeostasis[2]. While the fibrocartilage matrix within wrap-around tendon regions has been characterized[3], the development of this unique tissue region and its PCM content remains unknown. Therefore, the objective of this study was to define differential PCM expression and presence within the highly aligned (tensile) tendon matrix and the wrap-around (compressive) fibrocartilage matrix during murine FDL tendon development. We hypothesized that PCM expression and synthesis is increased in the compressive region compared to the tensile region as early as two-weeks postnatally due to compressive joint loads from ambulation at this age.

Methods

Animals

Wild-type P7 (n = 9), P14 (n = 7/sex) and P21 (n = 7/sex) mice were used in this study (IACUC approved). At sacrifice, mouse hindlimbs were harvested, fixed in 4% RNAse-clean PFA for 3hr, then embedded and flash frozen in OCT. Embedded limbs were cryosectioned at 20μm for gene expression or at 8μm for histological staining.

Gene Expression

Tensile and compressive regions of sectioned FDL tendon were microdissected and separated using 25G needles. Regional samples were digested with proteinase K, and RNA was extracted with Zymo Quick-RNA MicroPrep kits. cDNA was reverse transcribed and preamplified for 15 cycles with *Col6a(1-3), Bgn,* and *Abl1* Taqman assays. RT-qPCR was performed on preamplified cDNA for those target genes. ΔCt values for each gene were calculated based on corresponding *Abl1* Ct values.

Histology

After fixation, samples were decalcified with EDTA for 4-5 days prior to embedding and sectioning. Sections were stained with rabbit anti-collagen VI antibody (Fitzgerald, 70R-CR009x) and Hoechst nuclear stain prior to being imaged on a Zeiss Axio Scan.Z1. The tensile and compressive tendon regions were segmented, and mean antibody intensity was quantified for each region using FIJI.

Statistics

Paired t-tests were used to compare ΔCt values for measured genes and mean staining intensity between the tensile and compressive region. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

In P7 FDL tendons, the compressive region showed increased expression of *Col6a1*, with trending increases in *Col6a2* and *Bgn*, compared to the tensile region (Figure 1). At P14, the compressive region exhibited increased expression of all measured *Col6* genes and of *Bgn* compared to that of the tensile region. At P21, *Col6a3* and *Bgn* had trending expression increases in the compressive region compared to the tensile region. Quantification of collagen VI antibody staining revealed no regional differences in P7 FDL tendons (Figure 2). However, mean staining intensity was increased in the compressive region compared to the tensile region at P14 and P21.

Discussion

Results demonstrate that regional differences in PCM begin at early postnatal ages in the FDL tendon. The tendon PCM is comprised of collagen VI α-chains[4], and evidence suggests that biglycan helps organize the tendon PCM[5]. While the compressive region exhibited some increases in PCM gene expression compared to the tensile region at P7, this increased expression was consistently observed across all measured

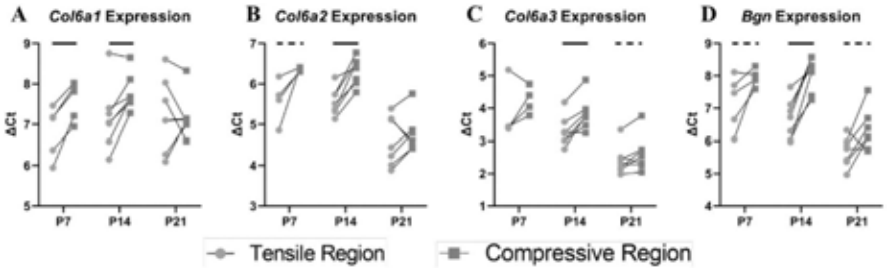

Figure 1. Region-dependent PCM gene expression peaks at P14. Expression of Col6 genes **(A-C)** and of Bgn (D) was higher in the compressive region compared to the tensile region by P14. Most of these regional differences were not present at P21. Solid lines denote $p < 0.05$, dotted lines denote $p < 0.1$.

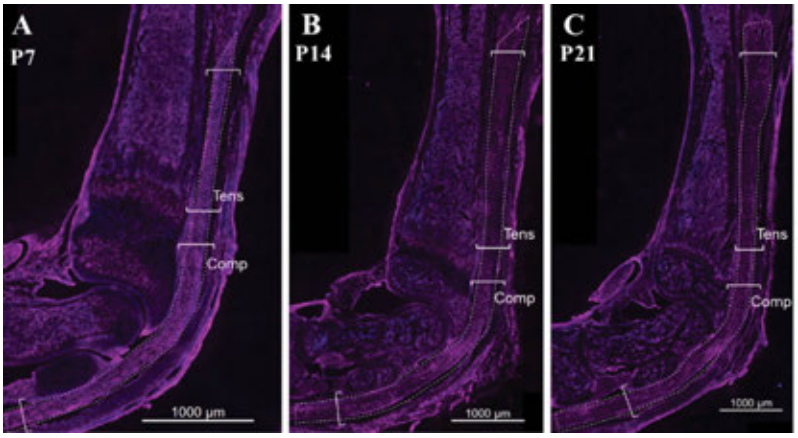

Figure 2. Region-dependent PCM presence is apparent at P14. Collagen VI staining (pink) reveals no differences in intensity between the tensile (Tens) and compressive (Comp) regions of the FDL tendon at P7 **(A)**. By P14 **(B)**, the compressive region contains higher intensity staining compared to the tensile region, which persists at P21 **(C)**. Signal intensity quantification shows that these changes are significant (D). Solid lines denote $p < 0.05$.

genes by P14. This expression pattern was supported by elevated PCM content in the compressive region at P14, which persisted at P21. Supporting our hypothesis, this result suggests that increased PCM expression and synthesis in the compressive region is driven by complex joint loads during murine gait. Mice begin walking quickly by two weeks of age[6], which would lead to increased joint flexion and loading on wrap-around tendons. Tendon cells respond to these forces by producing a fibrocartilaginous, GAG-rich matrix[7] with thickened PCM staining (Figure 2). As a result, the tendon PCM is likely a critical regulator of tendon cell phenotype. A limitation of this study is the inability to precisely define tensile and compressive tendon regions, as there are likely no regions that experience purely compressive or tensile loading. However, prior studies demonstrate that regional differences in wrap-around tendons are exacerbated by compressive loading[7,8], supporting our definitions of tensile and compressive tendon regions. Anatomical markers were used to segment these regions, making them consistent across samples and age groups. Future work will analyze the differential response of these FDL tendon regions to knockout of PCM molecules.

Significance

This work defines temporal regional development of the PCM within the murine FDL tendon. Understanding the differential development of these tendon regions provides insight into how tendon cells respond to physical cues, which is critical for treatment paradigms.

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Aging Alters Epigenetic and Mechanobiological Status in Murine Tenocytes

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Introduction

Age-related fibrous connective tissue degeneration (e.g., tendinosis) is a significant and costly clinical problem. While the increased prevalence of tendinopathy in older populations is well known, the molecular mechanisms by which this degeneration occurs is less well understood[1]. Degeneration alters the bio-physical environments of fibrous tissues, including changes in stiffness and changes in mechanical loading conditions.[2] These changes alter the biophysical inputs to resident cells (called tenocytes), impacting their phenotype and contributing to pathology. Chromatin organization, which is regulated by epigenetic changes, plays an important role in gene expression and cell differentiation.[3] Moreover, altered bio-physical environments with tissue degeneration regulate epigenetic status in cells. For instance, in tenocytes, epigenetic changes in genome architecture that contribute to pathology may be explained by a stiffening environment that occurs with age.[4] However, this is not yet fully understood in the context of tendon aging and degeneration. Here, we investigate the underlying age-dependent epigenetic and chromatin structural changes in tenocytes and their baseline mechanobiological status.

Methods

Tenocytes were harvested from young (< 5 wks) and old (> 40 wks) mouse tail tendons (four donors per group) and cultured in basal growth media until passage 2. Cells were seeded and fixed (after two days) on 8-well chambered cover-glasses and stained for transcriptional repression markers (H3K27me3: the tri-methylation of lysine 27 on histone H3), activation markers (H3K4me3: the tri-methylation of lysine 4th of histone H3), and histone-H2B (for super-resolution STORM imaging). H2B staining and Voronoi cluster analysis-based chromatin density were determined using our established protocols[5, 6]. Baseline cellular contractility was determined by traction force microscopy (TFM) carried out on 10 kPa poly-acrylamide gels with cells seeded for 1 day[7]. A wound closure assay (WCA) was performed on cells seeded in a 6-well dish with imaging via brightfield at 4-hour increments. Wound closure was quantified by percent closure of a predefined area at time of scratch using Image J. Dynamic tensile loading (DL) was applied to cells seeded on aligned poly ε-caprolactone (PCL) nanofibrous scaffolds using a custom bioreactor[3] at 5% strain, 1Hz, for 5 hours—cell seeded scaffolds were immediately placed in Trizol for mRNA extraction. RT-PCR was performed to assess GAPDH, Type-I collagen (Col1), Scleraxis (Scx), Matrix metalloproteinase 3 (Mmp3), and Tumor necrosis factor-α (Tnfα). Fold change is calculated by the delta-delta-C_T method, relative to Young-Control. Statistical analyses were performed using a student's t-test or two-way ANOVA with Tukey's post hoc testing.

Results

The baseline mean intensity of H3K27me3 (epigenetic repressor) was higher in the aged group. Conversely, basal levels of H3K4me3 (epigenetic activator) decreased with donor age (Figure 1A). Consistently, STORM data showed an increase in Voronoi density (and thus increased nanoscale chromatin density and condensation) (Figure 1B). TFM showed an increase in cellular contractility in old cells, as measured by total force and average traction stress (Figure 2A). WCA results showed an increase in migratory capacity of old tenocytes as compared to young (Figure 2B, C). The application of DL significantly increased gene expression of Col1 in both young and old tenocytes (Figure 3.) and the load-induced Col1 gene expression level was higher in young donors than old donors (Figure .3). Interestingly, only the expression of Tnfα in the young group was significant in response to the mechanical perturbation (Figure 3). No significant changes in Scx1 and Mmp3 expression with DL were observed in either donor (Figure 3).

Discussion

The immunofluorescence of histone modifications broadly indicates a general decrease in transcriptional activity in aged tenocytes. This is consistent with quantitative STORM imaging of H2B – showing an increase in condensed chromatin and reduced levels of gene expression. We used TFM and WCA

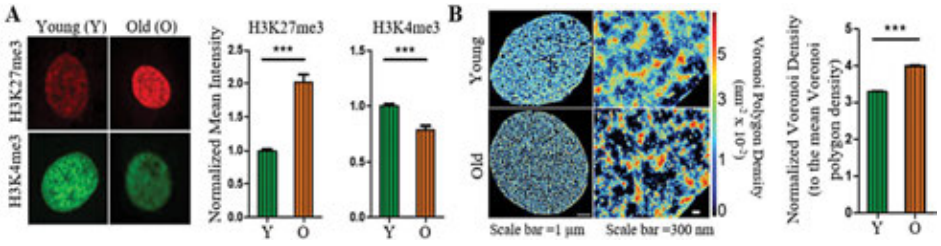

Figure 1. Region-dependent PCM presence is apparent at P14. Collagen VI staining (pink) reveals no differences in intensity between the tensile (Tens) and compressive (Comp) regions of the FDL tendon at P7 **(A)**. By P14 **(B)**, the compressive region contains higher intensity staining compared to the tensile region, which persists at P21 **(C)**. Signal intensity quantification shows that these changes are significant **(D)**. Solid lines denote $p < 0.05$.

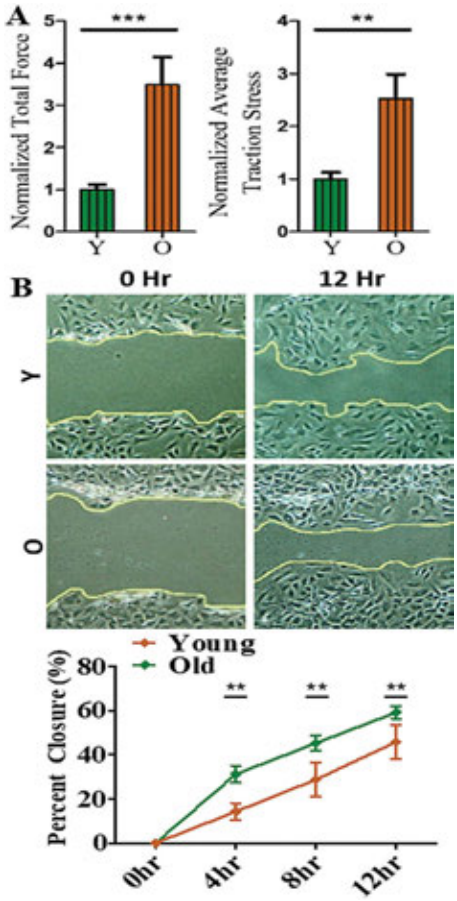

Figure 2. (A) Total traction force and normalized average traction stress (n=37 both groups, $p < 0.05$). **(B)** WCA representative images and results quantified as percent wound closure over time ($n = 3$ both groups, **: $p < 0.01$).

to measure the mechanobiological status of the tenocytes, and the results suggest an altered baseline contractility and migratory capacity in cells with aging. An increase in traction stress in old cells correlates well with the increase in migratory behavior observed in the WCA. Interestingly, Col1 was upregulated in both young and old tenocytes in response to 5% strain DL, but no effects were observed in Scx and Mmp3. More interestingly, Tnfα (a pro-inflammatory cytokine) was significantly upregulated in only the young group in response to DL, but no significance was observed in the old group. The effects of young and old tenocytes to DL are interesting, and ongoing studies are further focused on determining the effects of applying varying strain levels of the DL on young and old tenocytes. Overall, these data indicate age-dependent mechano-sensitivity in tenocytes and ongoing studies are focused on exploring the impact of degeneration on the tenocyte epigenome and in generating a detailed landscape of age-dependent gene expression by profiling accessible chromatin through ATAC-Seq and by understanding the impact of histone modifications through ChIP-Seq.

These findings contribute to a broader understanding of changes in epigenetic and mechanobiological status in tenocytes within aging tendon and its role in tissue degeneration for therapeutic applications. Future work will focus on novel epigenetic methods to rejuvenate tenocytes to promote healthy tissue regeneration and physiological function.

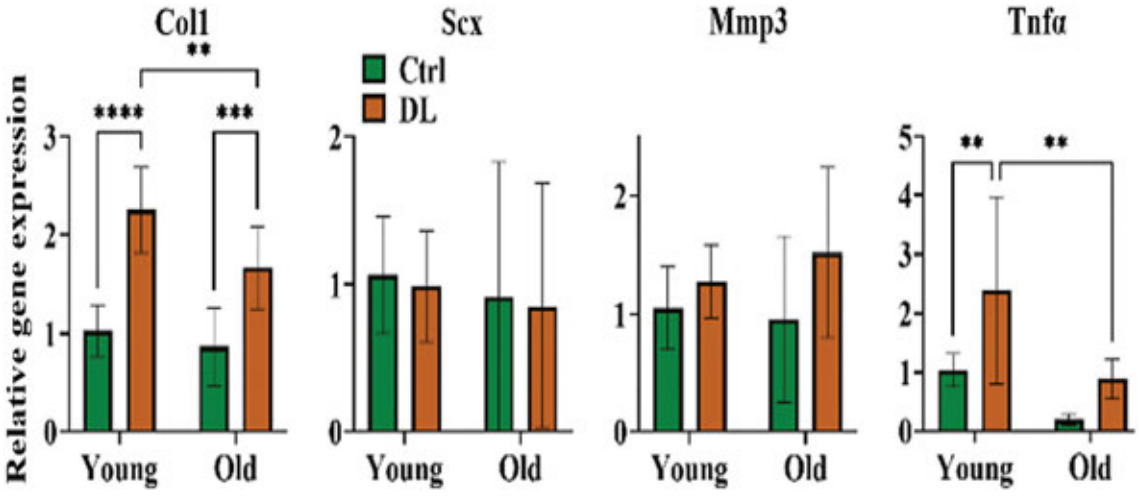

Figure 3. Gene expression levels of Col1, Scx, Mmp3, and Tnfα ($n = 10$ from two donors per group, *: $p < 0.05$). Y: Young, O: Old, Ctrl: Control, DL: Dynamic Loading.

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The Regulation of Tenocyte Differentiation and Morphological Maturation by mTORC1

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Introduction

Tenocytes drive postnatal tendon growth and healing via extracellular matrix (ECM) production and organization. Tenocyte differentiation is a multistep process that requires specific gene expression and unique morphological maturation. Tendon progenitors are marked by the expression of *Scleraxis* (*Scx*), a basic helix-loop-helix (bHLH) transcription factor and differentiated tenocytes express a high level of type I collagen.[1-4] Besides molecular changes, tenocytes undergo unique morphological maturation. Specifically, tendon cells in early postnatal mice are rounder whereas cells in adult mice are elongated to align longitudinally between dense and highly organized collagen fibers.[5,6] Although cellular maturation process of tenocytes is pivotal for tendon ECM maturation and the structural/mechanical properties of tendon, the current paradigm underlining cellular maturation of tenocytes is not fully understood. The objective of this study is to determine the function of mTORC1 signaling in cellular maturation of tenocytes.

Methods

All procedures were approved by UPenn's IACUC. The assessment of morphological changes of tendon cells is challenging because tendon cells assemble into a complex cellular and ECM network that is difficult to quantify accurately without time-consuming electron microscopy. To overcome this limitation, we developed a novel method by which we can measure cell density, cell size, cell shape, and protrusion numbers at a single cell level by using a high-resolution confocal imaging technique with Zo-1 and Phalloidin double immune staining. To further measure the morphological changes in tendon cells, we measured the nuclear aspect ratio (ratio of long and short axes of the nucleus) that indicates the longitudinal shape of tendon cells. To test the effect of genetic manipulation of mTORC1 signaling on cellular maturation, we generated a tendon-specific mTORC1 loss-of-function mouse (*Scx-Cre;Raptor*$^{fl/fl}$) and gain-of-function (*Scx-Cre; Tsc1*$^{fl/fl}$) mouse model. To exam the function of mTORC1 in the differentiation of tendon progenitors into the *Col1(2.3)-GFP-positive cells*, we generated *Scx-Cre; Raptor*$^{fl/fl}$*; Col1 (2.3)-GFP* (loss-of-function) and *Scx-Cre; Tsc1*$^{fl/fl}$*; Col1 (2.3)-GFP* (gain-of-function) mouse models. To perform pharmacological rescue experiment, rapamycin, an inhibitor of mTORC1 signaling, was injected into the control and gain-of-function mouse from day 22 to 29 after birth with the dosage of 4mg/kg. All quantitative data were analyzed using students t-test.

Results

Fluorescent imaging analysis showed that loss of mTORC1 increased Col1-2.3GFP-positive cells in patellar tendon at all postnatal developmental stages (Figure 1A) and this phenotype was verified by quantification (Figure 1B). This result suggests that inhibition of mTORC1 enhances the differentiation of tendon cells into the Col1a1-expressing tenocyte population. This enhanced differentiation phenotype in loss-of-function mouse model prompted us to investigate morphological maturation of tenocytes in mTORC1 loss-of-function mouse model. To investigate the morphological maturation of tendon cells, we analyzed tenocyte morphology at a single-cell level using Zo-1 and Phalloidin double immune staining (Figure 2A). Tendon cells displayed the largest cell area at P30, and the

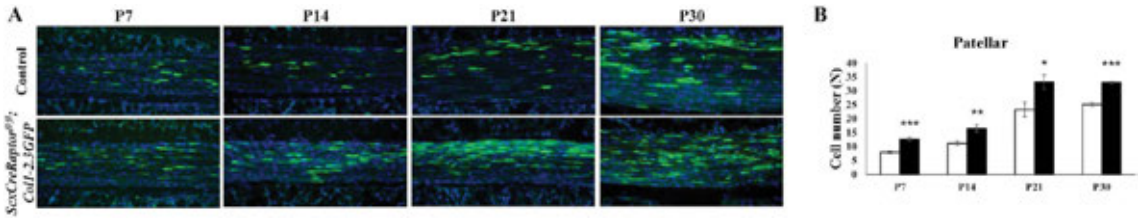

Figure 1. (A) Fluorescent microscopy images for Col1 (2.3)-GFP positive cells in the mid-substance of Patellar tendon from control (Col1 (2.3)-GFP) and mTORC1 loss-of-function (*Scx-Cre; Raptor*$^{fl/fl}$; Col1 (2.3)-GFP) mouse**. (B)** Quantification of Col1 (2.3)-GFP positive cells in Mid-substance of Patellar tendon from each genotype at various stages. Scale bar indicates 100μm *** indicates $P < 0.005$, **** indicates $P < 0.001$ n=3

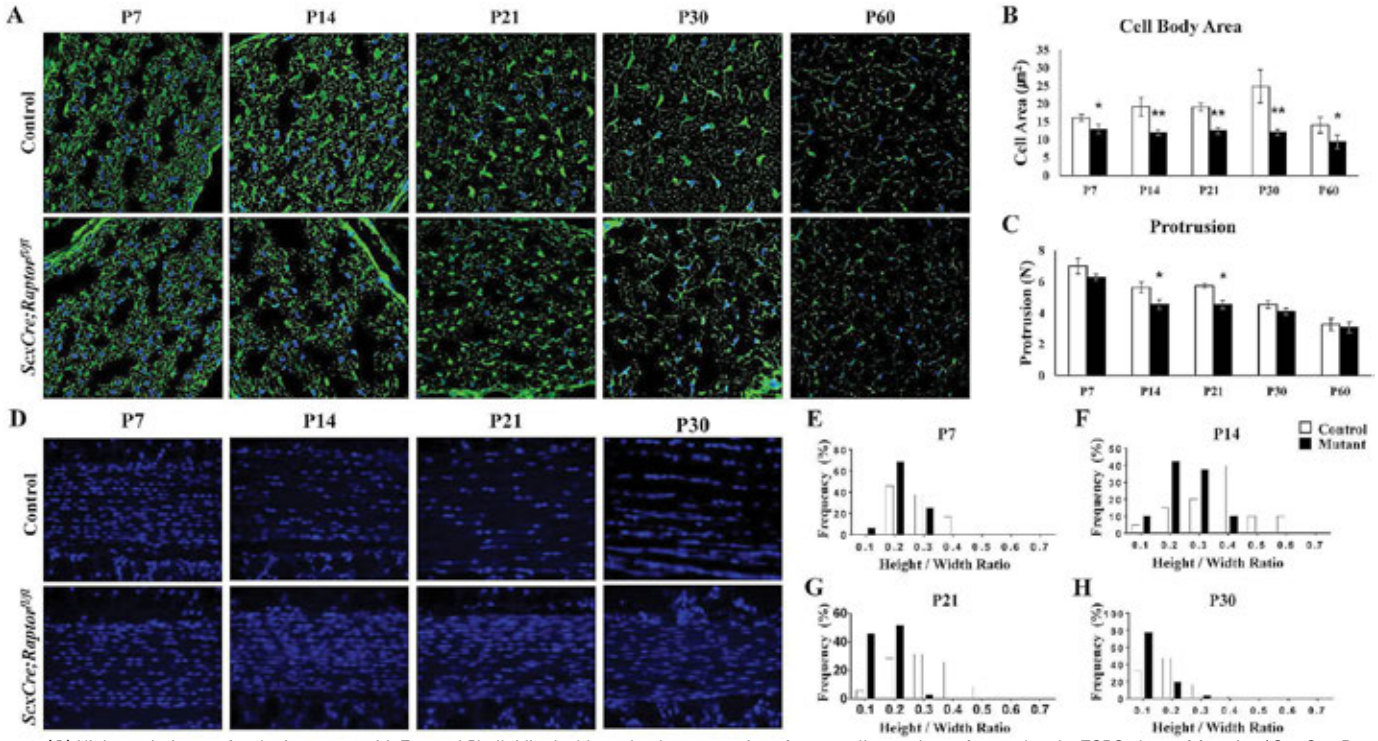

Figure 2. (A) High resolution confocal microscopy with Zo1 and Phalloidin double-stained cross-sections from patellar tendons of control and mTORC1 loss-of-function (*Scx-Cre; Raptor*$^{fl/fl}$) mouse at various stages. **(B and C)** Quantification results of protrusion number, cell body area, and cell density using high resolution confocal images. **(D)** Nuclear imaging with DAPI staining using from control and mTORC1 loss-of-function mouse model at various stages. (E-H) Quantification results of nuclear aspect ratio. Scale bar indicates 10μm **(A)** * indicates $P < 0.05$, ** indicates $P < 0.001$, and *** indicates $P < 0.005$ n=3

cell area was dramatically decreased at P60 in wildtype mice (Figure 2B, white bar), which indicates terminally matured tenocyte population at P60, respectively. Tendon cells in loss-of-function mice exhibited decreased cell area at all stages (Figure 2B, black bar) compared to wildtype. The protrusion is the projections from the cell body that is critical for cell-cell and cell-matrix interaction. The protrusion number was gradually decreased during postnatal tendon development in wildtype mice (Figure 2C, white bar). The *ScxCre;Raptor*$^{fl/fl}$ mice showed significantly reduced protrusion numbers compared with those of wildtype mice at P14 and P21 (Figure 2C, black bar). These morphological analyses suggest that the loss of mTORC1 signaling enhanced the maturation of tendon cells. To further confirm the enhanced morphological maturation, we measured the nuclear aspect ratio (ratio of long and short axes of the nucleus) that indicates the longitudinal shape of tendon cells (Figure 2D). At the early developmental stage (P7), most tendon cells in wildtype were relatively elongated, which was indicated by a lower nuclear aspect ratio (Figure 2E, white bar). And then, tendon cells gradually become rounder at P14 and P21 (Figure 2F and 2G, white bar). Eventually, terminally matured tendon cells become elongated again, as indicated by a low nuclear aspect ratio at P30 (Figure 2H, white bar). Interestingly, tendon cells in loss-of-function mice became very elongated even at P14 and P21 (Figure 2F and 2G, black bar). These data suggest that loss of mTORC1 enhanced the cellular maturation of tendon cells. Our loss-of-function study suggests that mTORC1 signaling negatively regulates differentiation of tendon progenitor cells into col1a1-expressing cells and cellular maturation of tenocytes. To verify this inhibitory function of mTORC1 signaling, we performed a gain-of-function study by generating *Scx-Cre;Tsc1*$^{fl/fl}$ *;Col1*

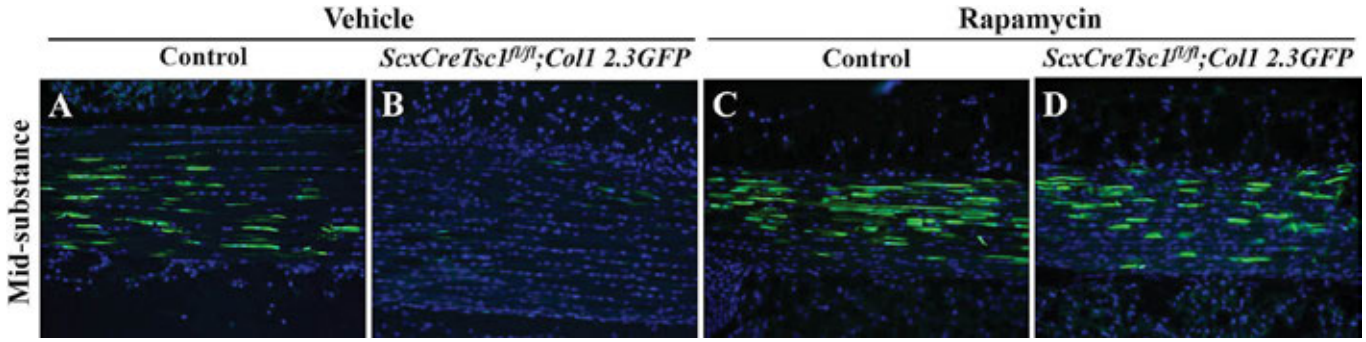

Figure 3. Fluorescent microscopy images for Col1 (2.3)-GFP positive cells in the mid-substance of Patellar tendon from control (Col1 (2.3)-GFP, **(A and C)** and mTORC1 gain-of-function (*Scx-Cre; Tsc1*$^{fl/fl}$; Col1 (2.3)-GFP, **(B and D)** mouse with vehicle **(A and B)** or rapamycin **(C and D)** treatment.

(2.3)-GFP mouse models. As expected, *Scx-Cre; Tsc1$^{fl/fl}$* (gain-of-function) mice showed dramatically decreased Col1 (2.3)-GFP-positive cells in the Patellar tendon (Figure 3B) compared with control mice. To test if the inhibition of mTORC1 signaling can rescue the reduced number of Col1 (2.3)-GFP-positive cells in *Scx-Cre;Tsc1$^{fl/fl}$* mice, rapamycin, a mTOR inhibitor, was injected in both control and *Scx-Cre;Tsc1$^{fl/fl}$* mice. Col1-2.3GFP-positive cells were increased by rapamycin in *Scx-Cre;Tsc1$^{fl/fl}$* mice (Figure 3D). These results verify that mTORC1 signaling inhibits early differentiation of tendon progenitors into Col1a1-expressing tenocytes.

Discussion

Our results showed that mTORC1 signaling is a critical regulator of early tendon differentiation and morphological maturation. Our current studies suggest that mTORC1 negatively regulates the differentiation of tendon progenitor cells into Col1a1-expressing cells and cellular maturation of tenocytes. Further morphological analysis using this gain-of-function mouse model will be required to verify the function of mTORC1 in cellular maturation of tenocytes. Further studies with other reporter mice are needed to investigate that the function of mTORC1 in tendon differentiation at various time points.

Significance/Clinical relevance

This study will fill the knowledge gap in tenocyte biology by establishing the function of mTORC1 signaling in tenocyte differentiation and cellular maturation.

Acknowledgements

We thank to Dr. Ronen Schweitzer for providing *Scx-Cre* mouse line.

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FAK Inhibition Attenuates Increased Tendon Cell Nuclear Aspect Ratio with Applied Mechanical Strain *In Situ*

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Introduction

Tendons carry tensile loads via their dense extracellular matrix (ECM), which transmits mechanical strain to the resident cells. Regulatory mechanical cues maintain tendon homeostasis, as unloading and overloading both result in reduced ECM organization and mechanical integrity as well as loss of tendon cell phenotype, including changes in cell and nuclear shape and reduced tenogenic gene expression.[1–3] Focal adhesion kinase (FAK) is an intracellular protein kinase that plays a critical role in regulating cell-ECM attachment as well as turnover of the mechanosensitive actin network that transmits mechanical cues from the plasma membrane to the nucleus. While FAK activation is required for tenogenic gene expression in response to stimulation by growth factors and mechanical stretching,[4–7] the mechanism by which FAK activity regulates the cell's ability to sense mechanical stretching within the *in situ* tendon environment is unknown. Therefore, the objective of this study was to evaluate the effects of FAK inhibition on tendon cell nuclear response to mechanical strain within the *in situ* tendon ECM. We hypothesized that increases in nuclear aspect ratio (nAR) in response to applied macroscale strain would be attenuated in tendons treated with a FAK inhibitor compared to untreated tendons.

Methods

Study Design

Flexor digitorum longus (FDL) tendons from male WT adult mice were freshly dissected and maintained in DMEM supplemented with 5% FBS and 25 mM HEPES. Tendons were randomized to untreated and FAK-inhibited (FAK-I) groups (n = 5-6 tendons per group). For FAK-I tendons, media was supplemented with 10 M PF-573228 (Tocris; Minneapolis, MN) for 1 hour at 37C, while the untreated tendons were maintained for 1 hour at 37°C. Following treatment, cell nuclei were stained with DRAQ5 (1:1000) for 30 minutes, mounted within a custom mechanical loading device, and imaged with confocal microscopy at 0, 5, and 10% applied strain (Figure 1A-B). Nuclei were segmented with FIJI, nAR computed, and manually tracked between strain levels (n = 12-36 nuclei per tendon).[8] Live/dead staining was performed with calcein-AM and ethidium homodimer-1 (ThermoFisher; Waltham, MA) to confirm tissue viability within the loading system.

Mechanical Loading Device

We developed a custom mechanical loading device to apply strain to a tendon sample while being imaged on an inverted confocal microscope. The device consists of 2 linear actuators that apply mechanical strain to the tendon, along with a 20 lb. (88.96 N) load cell to monitor load. Manual stages center the tendon in the x and z directions over the objective and place it within the objective working distance. Custom LabView software was developed to operate the device, including centering the tendon over the objective in the y direction and applying mechanical strain based on the gauge length.

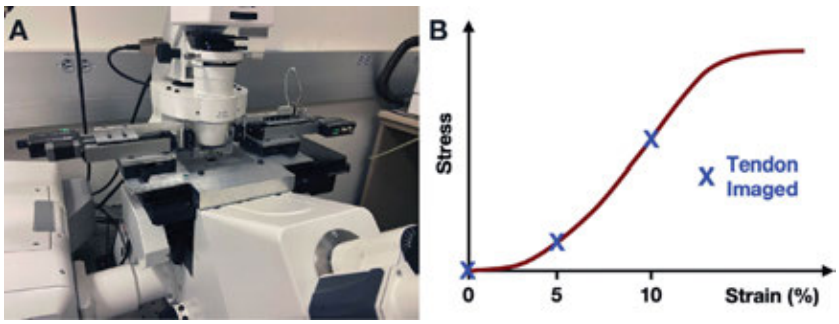

Figure 1. Custom Mechanical Loading Device. **(A)** Fabricated device mounted on a Zeiss LSM 710 inverted confocal microscope. **(B)** Stress-strain curve indicating image capture locations at 0, 5, and 10% strain.

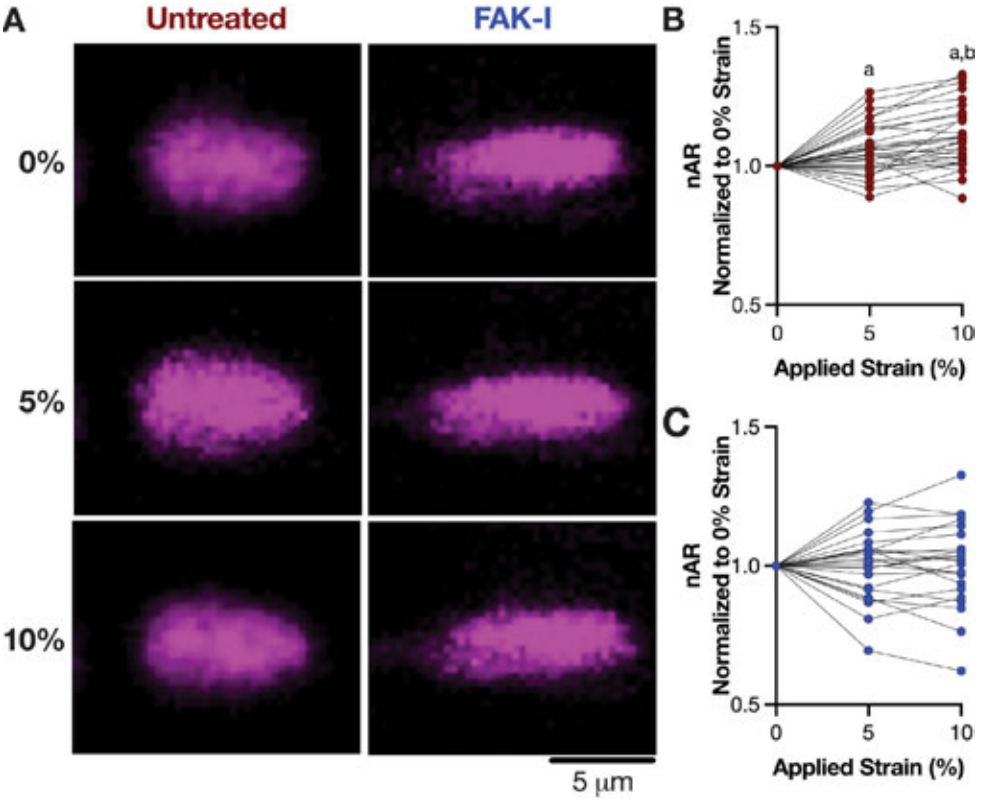

Figure 2. Increases in nAR with increasing applied strain are attenuated by FAK inhibition. **(A)** Representative images for untreated and FAK-I nuclei at the indicated applied strain value. nAR plotted across strain values for **(B)** untreated and **(C)** FAK-I samples. Statistical comparison performed on non-normalized data (data not shown) between strain levels using repeated measures one-way ANOVA with Tukey's post-hoc tests (significance at p 0.05). a, significant increase relative to 0% strain; b, significant increase relative to 5% strain.

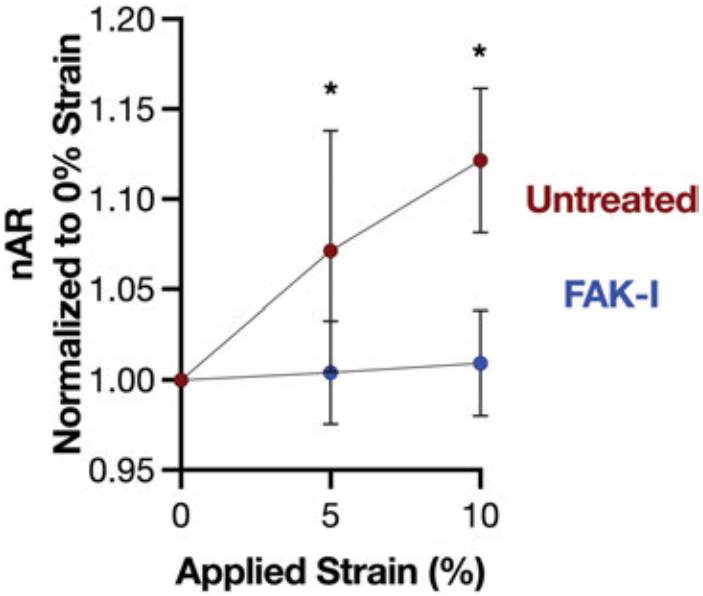

Figure 3. Increases in nAR with increasing applied strain were consistently attenuated by FAK inhibition across all samples. Data is represented as mean normalized nAR ± standard de-viation for each group. Statistical comparison performed using t-tests to compare treatment groups at 5% and 10% strain (significance at p 0.05). *, significant difference between groups at strain value.

Confocal Imaging

Confocal imaging was performed with a Zeiss LSM 710 confocal microscope while the tendon was mounted and maintained at the desired strain level. Imaging was performed with a 633nm excitation laser and 10x objective by imaging through the maximum light penetration depth at a z-stack interval of 5 m.

Results

Live/dead staining indicated that the tissue was viable with no differences between untreated and FAK-I tendons (data not shown). Nuclei tracked across strain levels in untreated tendons became increasingly elongated with applied strain (Figure 2A-B), while the nuclei from FAK-I treated tendons did not elongate across strain levels (Figure 2A,C). Across tendons, normalized nAR was decreased at both 5% and 10% strain in FAK-I tendons relative to untreated tendons (Figure 3).

Discussion

Consistent with our hypothesis, FAK-I treatment attenuated the increases in nAR with applied strain observed in the untreated tendons both within tendons (Figure 2) and across all tendons measured (Figure 3). These results indicate that FAK regulates ECM to nucleus strain transmission in tendon cells. Previous studies demonstrated that intact actin networks are required for maintenance of tendon cell fate, collagen fibril deposition, collagen crosslinking, and re-tensioning the ECM.[9–11] Given FAK's role in establishing focal adhesions to tether actin networks to the ECM, it is not surprising that FAK is required for tenogenic gene expression.[4–7] Results from the present study suggest that the dependence on FAK for tenogenic gene expression may due to its role in regulating nuclear mechanosensitivity. The rapid effect of FAK inhibition on nuclear response to strain suggests that tendon cells regularly turn over their actin networks and reestablish focal adhesions to actively probe their local mechanical environment. This result is particularly interesting in mature

tendon cells encased in established ECMs, where the local mechanical environment is presumably stable.

Significance

This study evaluated the effects of FAK inhibition on nuclear response to mechanical strain within *in situ* tendon ECM. We found that inhibition of FAK attenuated increases in nAR with applied strain, which suggests that FAK is required for tendon cell sensation of its surrounding mechanical environment.

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Mucopolysaccharidosis I and VII Dogs Exhibit Impaired Anterior Cruciate Ligament Mechanical Properties

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Introduction

The mucopolysaccharidoses (MPS) are a family of inherited lysosomal storage disorders characterized by deficient activities of enzymes that degrade glycosaminoglycans (GAGs) due to mutations in associated genes.[1] MPS I and VII are characterized by deficient α-L-iduronidase and beta-glucuronidase activities, respectively.[2,3] Both subtypes accumulate heparan (HS) and dermatan sulfate (DS) GAGs, while MPS VII additionally accumulates chondroitin sulfate (CS).[2,3] MPS I and VII patients commonly exhibit progressive skeletal abnormalities that are associated with chronic pain, impaired mobility, and overall decreased quality of life.[2,3] Synovial joint (e.g., hip, knee, hands and shoulder) disease manifestations are prevalent in both subtypes, which can be traced in part to a combination of developmental abnormalities and chronic inflammation, which accelerates soft tissue degeneration.[4,5] However, understanding of the underlying pathological mechanisms is limited, hampering the development of effective treatments. In particular, there is a poor understanding of how component joint tissues contribute to progressive mechanical dysfunction of the overall joint. The anterior cruciate ligament (ACL) performs a critical role in maintaining the rotational stability of the knee joint.[6] Therefore, the objective of this study was to establish whether ACL tensile mechanical properties are altered in MPS I and VII using the naturally-occurring canine disease models.

Methods

Animals and Sample Collection

The naturally-occurring canine models of MPS I and VII exhibit progressive synovial joint dysfunction similar to human patients, making them clinically-relevant platforms for studying joint disease pathophysiology. With IACUC approval, MPS I (n = 5) and heterozygous control (n = 4) dogs were euthanized at 12 months-of-age, and MPS VII (n = 5) and heterozygous control (n = 6) dogs were euthanized at ± months-of-age. Prior to euthanasia, all animals received physical examinations from a veterinarian. Left stifle (knee) joints were excised postmortem, all soft tissue between the distal femur and proximal tibia except the ACL was carefully removed, and ACL cross-sectional area was measured using a laser-based device.

Mechanical Testing

The femur and tibia were potted in polymethylmethacrylate, mounted in custom fixtures of a servohydraulic mechanical testing system (Instron 8874; Figure 1), and the ACL tested in uniaxial tension to failure. Briefly, following 10 cycles of preconditioning, samples were subjected to a quasi-static ramp to failure at a strain rate of 0.3%/second. Testing was conducted at room temperature and samples were sprayed with saline to prevent dehydration. The following parameters were calculated for all samples: stiffness, modulus, toughness, failure load, failure stress and failure strain.

Statistical Analyses

All results are reported as median and interquartile range. Significant differences in ACL tensile mechanical properties between MPS I or VII and their respective controls were established using Mann-Whitney tests ($p < 0.05$).

Results

MPS I Dogs

By 12 months-of-age MPS I dogs were able to ambulate unassisted but exhibited a hopping gait while running, with moderate effusions and laxity in stifle joints. With respect to ACL mechanical properties, stiffness, toughness, failure load and failure stress were all significantly lower for MPS I dogs compared to controls (65, 56, 45, and 72% of control, respectively, Figure 2), while modulus and failure strain were not significantly different.

MPS VII Dogs

In contrast to MPS I dogs, by ± months-of-age, MPS VII dogs were no longer able to ambulate, and exhibited severe joint effusions and laxity. With respect to ACL mechanical properties, stiffness, modulus, toughness, failure load and failure stress were all significantly lower for

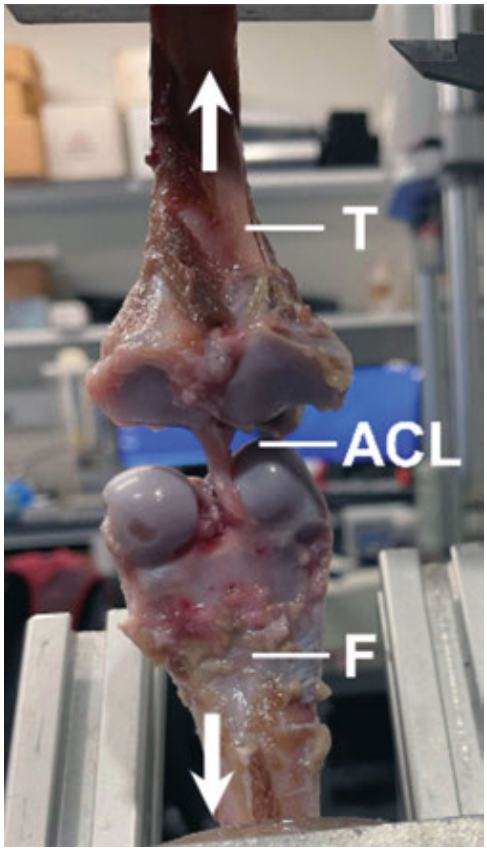

Figure 1. Canjne anterior cruciate ligaments (ACLs) were tested in uniaxial tension to failure (arrows indicate testing direction; F = femur; T = tibia)

MPS VII dogs compared to controls (20, 13, 26, 19 and 16% of control, respectively, Figure 3), while failure strain was not significantly different.

Discussion

In this study we established that impaired mechanical function of the ACL is a key feature of synovial joint disease in both MPS I and VII, implicating pathological changes in this tissue in the overall etiology of joint instability. While we are yet to determine associated changes at the structural and functional levels, they may include extracellular GAG accumulation and resulting abnormal collagen fiber organization, which could reasonably be expected to negatively impact tensile load-bearing capacity. Lower stiffness and modulus may contribute to joint laxity, which was observed clinically in MPS dogs, while diminished failure properties may increase the risk of ACL rupture. Interestingly, mechanical properties of ACLs from MPS VII dogs were significantly worse than those from MPS I dogs, despite the younger age of these animals. Potential explanations may include the fact that MPS VII dogs accumulate CS in addition to HS and DS, which may further exacerbate structural abnormalities. Additionally, prolonged limb disuse in MPS VII animals, which were unable to ambulate at all at the time of euthanasia, may have contributed to diminished ACL mechanical properties. Ongoing studies are focused on establishing the molecular mechanisms of ligament and other soft tissue degeneration in the synovial joints of MPS dogs

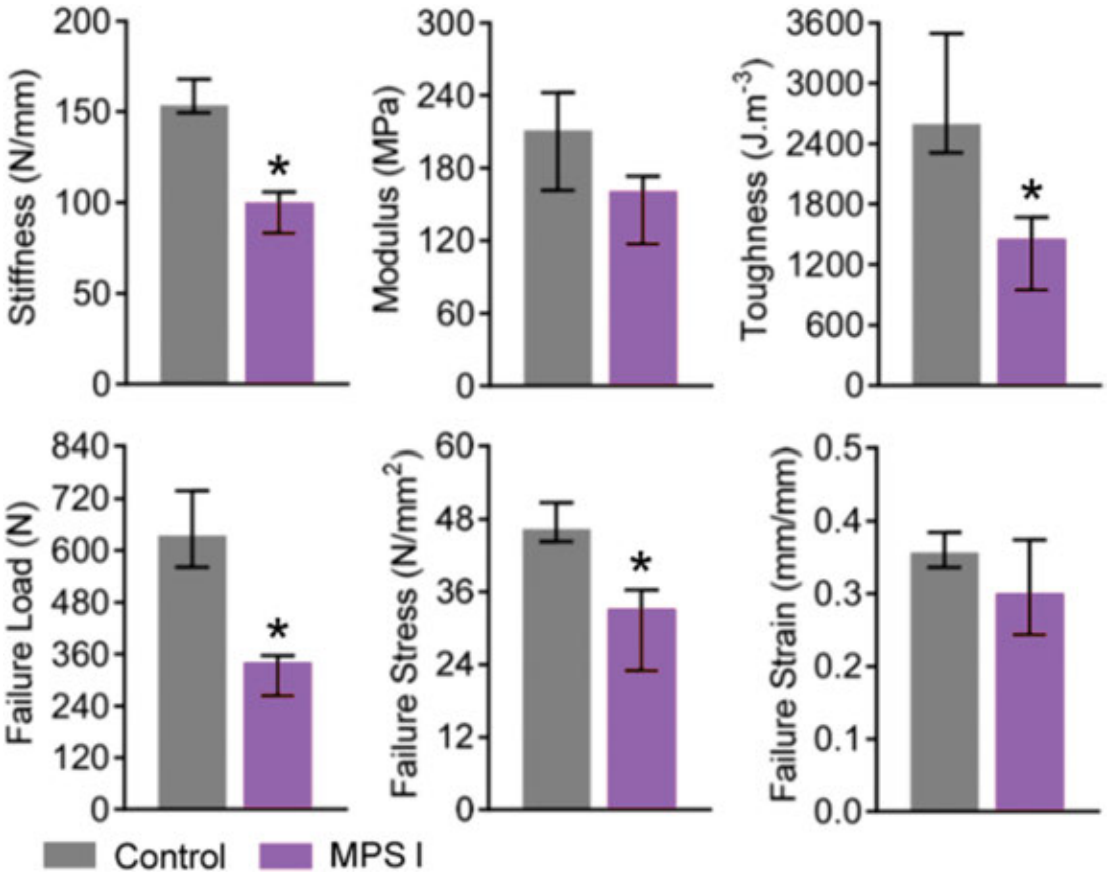

Figure 2. Tensile mechanical properties of anterior cruciate ligaments from control (n=4) and MPS 1 (n = 5) dogs at 12 months-of-age. *$p < 0.05$ vs control.

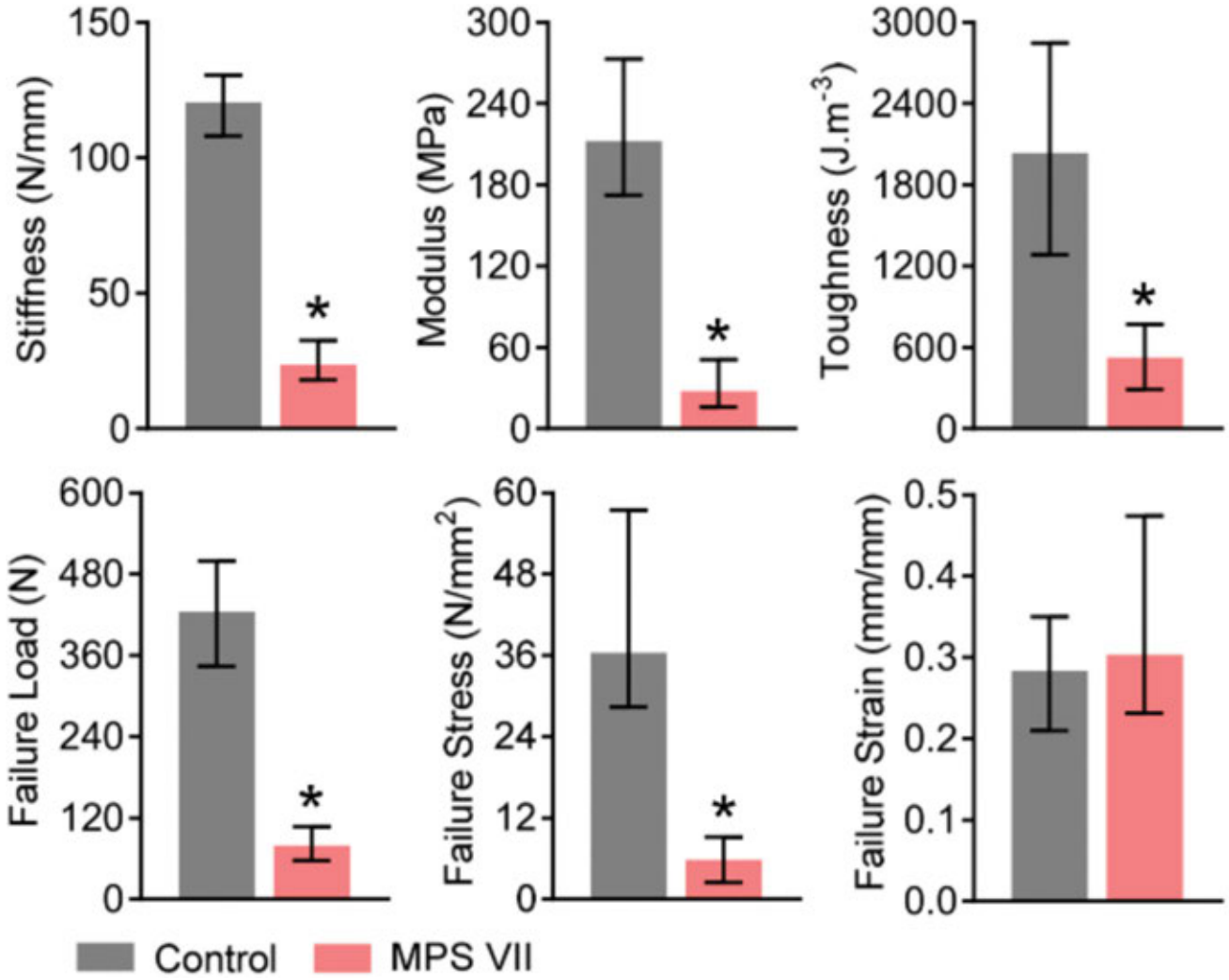

Figure 3. Tensile mechanical properties of anterior cruciate ligaments from control (n=6) and MPS VII (n = =5) dogs at ± months-of-age. *p < 0.05 vs control.

and human patients, with the long-term goal of developing effective, tissue-specific treatment strategies.

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Collagen V Knockdown Alters Collagen Fibril Size, but Not Mechanics, in Mature Female Murine Tendons

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Introduction

Collagen V is a critical tendon matrix regulator that controls collagen I fibril size[1], and collagen V knockdown during tendon homeostasis increased the viscoelasticity of male murine tendons[2]. However, tendons display sex-dependent gene expression changes in response to collagen V knockdown[3] and the effect of this knockdown and differential gene expression on female murine tendon properties remains unknown. Therefore, the objective of this study was to define the effect of collagen V knockdown on mature female murine patellar tendon mechanical properties and collagen fibril size. Based on observed increases in matrix expression following collagen V knockdown[3], we hypothesized that collagen V knockdown would increase the mechanical properties and collagen fibril size of female murine patellar tendons.

Methods

Animals—Female wild-type (WT) and bitransgenic *Col5a1*$^{flox/+}$ and *Col5a1*$^{flox/flox}$ mice with *ROSA26-CreER*^{T2} were used in this study (IACUC approved). At 120 days old, mice received 3 consecutive daily tamoxifen (TM) injections (4mg/40g body weight) for Cre-mediated excision of floxed *Col5a1* alleles, resulting in I-*Col5a1*$^{+/-}$ and I-*Col5a1*$^{-/-}$ genotypes. Mice were sacrificed 30 days post-TM injections. Hindlimbs were harvested, and patellar tendons were isolated and prepared for mechanical testing (n = 15/genotype) or transmission electron microscopy (TEM, n = 4/genotype) as described[4]. *Mechanical Testing*—Tendons were immersed in a 37°C 1x PBS bath and loaded into an Instron 5848. Tendons underwent the following viscoelastic testing protocol: preconditioning, 10 min stress relaxations at 3, 4, and 5% strain, each followed by 10 cycle frequency sweeps at 0.1, 1, 5, and 10Hz, and a ramp-to-failure. Percent relaxation, dynamic modulus, and phase shift were computed from each stress relaxation and frequency sweep. Stiffness, max load, modulus, and max stress were measured from ramp-to-failure tests. *Collagen Fibril Imaging*—Following fixation and processing, tendons were sectioned at ~90nm and imaged with a JEOL 1400 TEM. 10 regions were analyzed per tendon. Collagen fibril diameter was measured across the fibril minor axis with BIOQUANT. *Statistics*—One-way ANOVAs with Tukey post-hoc tests were used to compare mechanical properties across genotypes. Collagen fibril diameter distributions from each genotype were compared against those of the other genotypes using Kolmogorov-Smirnov tests. Significance was set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

No differences in any measured mechanical properties were observed across WT and knockdown genotypes; this included stiffness (Figure 1A), max load (Figure 1B), modulus

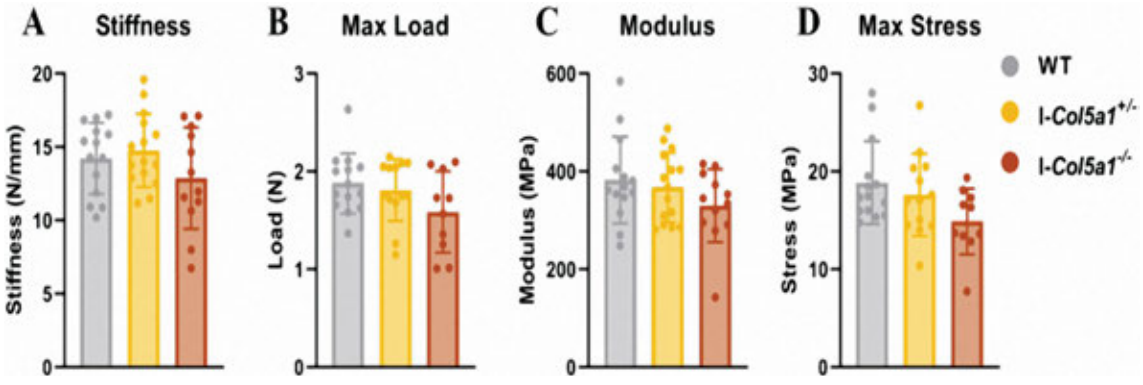

Figure 1. Collagen V knockdown does not impact female tendon mechanical properties. No differences in stiffness **(A)**, max load **(B)**, modulus **(C)**, or max stress **(D)** were observed across genotypes.

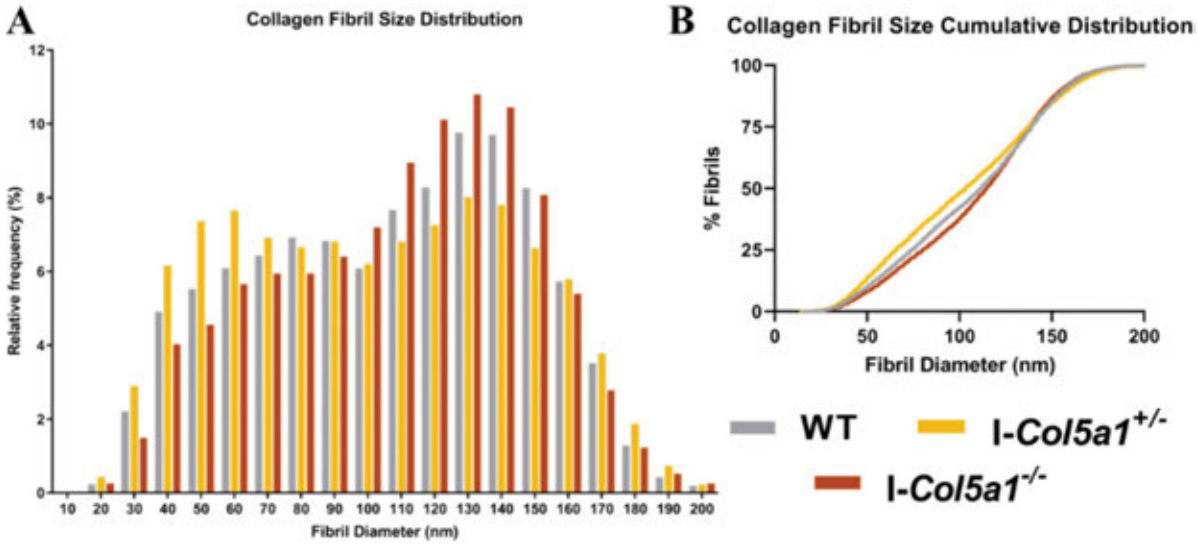

Figure 2. Collagen V knockdown alters collagen fibril size in an allele-dependent manner. WT tendon fibrils demonstrate a characteristic bimodal size distribution. I-Col5a1$^{+/-}$ tendons had a higher proportion of small (< 70nm) and large (> 160nm) diameter fibrils. I-Col5a1$^{-/-}$ tendons displayed a larger proportion of intermediately sized fibrils (100-140nm). All distributions were significantly different from each other ($p < 0.0001$).

(Figure 1C), max stress (Figure 1D), percent relaxation, dynamic modulus, and phase shift (data not shown). Conversely, collagen fibril size distributions were significantly different across all genotypes (Figure 2, $p < 0.0001$). WT tendons displayed a characteristic bimodal fibril size distribution (Q1: 74.3nm, Q2: 111.6nm, Q3: 139.0nm). I-*Col5a1*$^{+/-}$ tendons exhibited a larger spread in fibril size, with increased proportion of small (< 70nm) and large (> 160nm) diameter fibrils (Q1: 65.7nm, Q2: 103.1nm, Q3: 137.2nm). I-*Col5a1*$^{-/-}$ tendons contained an increased proportion of fibrils between 100-140nm in diameter (Q1: 80.1nm, Q2: 114.3nm, Q3: 138.2nm).

Discussion

Contrary to our hypothesis, acute knockdown of collagen V in mature female mice did not significantly alter patellar tendon mechanical properties. Despite the lack of mechanical changes, collagen V knockdown resulted in allele-dependent changes to collagen fibril size distribution. Taken together, these results provide key insights into the sex-linked role of collagen V in homeostatic tendon function. While collagen V knockdown in mature female murine tendons did not impact mechanical properties as shown here, collagen V knockdown did lead to increased viscoelasticity in mature male tendons[2]. Both sexes experienced changes in collagen fibril size in response to collagen V knockdown. This suggests that homeostatic female tendon function is less sensitive to collagen V presence than male tendon function. The decreased sensitivity to collagen V presence in female tendons may be due to observed increases in matrix synthesis expression in response to collagen V knockdown[3]. A limitation of this study is the global nature of the *Col5a1* knockdown model used. While this may lead to confounding effects in other tissues, the short knockdown window employed here likely minimized these effects. Future studies will assess the histological properties of knockdown tendons to further delineate the sex-dependent response to collagen V knockdown.

Significance

This work demonstrates a sex-linked role of collagen V in dictating homeostatic tendon function. Understanding this sex-dependent role can inform therapeutics that treat collagen V-associated clinical disorders.

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U·P·O·J

Collagen XII is a Critical Regulator of Tendon Function: Development of a Conditional Mouse Model

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Introduction

Collagen XII is a fibril-associated collagen with interrupted triple helices (FACIT) that regulates collagen fibril assembly, and mutations in *Col12a1* result in myopathic Ehlers-Danlos Syndrome (mEDS). Patients with mEDS experience excess weakness at birth, hypermobile distal joints, and an absence of deep tendon reflexes[1], indicating impaired tendon function due to the absence of collagen XII. Tendons in a global *Col12a1*$^{-/-}$ knockout mouse model demonstrated disrupted grip strength and tendon fiber structure as well as disordered tenocyte organization[2]. However, secondary effects due to involvement of bone and muscle may occur in this model, and the isolated role of collagen XII in tendon has not been elucidated. To address this limitation, the objective of this study was to create and characterize a conditional *Col12a1*-null mouse model to target collagen XII knockout in tendons using a Scleraxis-Cre driver. We hypothesized that tendon-targeted knockout of *Col12a1* expression would impair tendon function.

Methods

Model Development

A promoter-driven knockout embryonic stem (ES) cell line was obtained from the KOMP Repository (ID: CSD29388, *Col12a1*$^{tm2a(KOMP)Wtsi}$). ES cell clones were injected into wild-type C57BL/6-Albino blastocysts, and resulting chimeric mice were backcrossed to produce mice with the targeted allele, *Col12a1*$^{+/ta}$. *Col12a1*$^{+/ta}$ mice were bred with FLPe mice (B6; SJL-Tg(ACTFLPe) 9205Dym/J, Jackson Labs) to excise the FRT flanked neo sequences. The resulting offspring were crossbred with C57BL/6 mice for ± generations and then intercrossed to obtain conditional knockout mice, *Col12a1*$^{flox/flox}$. *Col12a1*$^{flox/flox}$ mice were bred with Scleraxis-Cre (*Scx-Cre*) mice to obtain tendon-targeted heterozygous (Het, *Col12a1*$^{+/\Delta ten}$) and homozygous (KO, *Col12a1*$^{\Delta ten/\Delta ten}$) collagen XII knockout mice.

Gene & Protein Expression

Col12a1 expression and collagen XII content were assessed in flexor digitorum longus (FDL) tendons from mice at day 10 using qPCR and Western blots, respectively.

Immunofluorescence

FDLs were dissected, fixed in 4% paraformaldehyde, embedded in optimal cutting temperature compound, and sectioned in the transverse plane at 5 μm thickness. Immunofluorescence staining of collagen XII was performed using a rabbit anti-mouse Col XII antibody (KR33, 1:500 dilution) with a donkey anti-rabbit Alexa Fluor 568 (1:200 dilution) secondary antibody.

Grip Strength

Using a grip strength meter, mice were lowered toward the grip platform and upon grasping, mice were pulled away steadily until the grip was broken. The force applied just before the mouse lost its grip was recorded as the peak force.

Tendon Mechanics

FDL tendons from day 60 mice were dissected from the foot, cleaned of excess tissue, and mechanically evaluated as described[3]. Tensile testing was performed using the following protocol: preconditioning, stress relaxation at 5% strain, and a ramp to failure at a rate of 0.5%/s.

Statistics

One-way ANOVAs with Tukey post-hoc tests were conducted. Significance was set at $p \leq 0.05$.

Results

Col12a1 expression was reduced in *Col12a1*$^{\Delta ten/\Delta ten}$ KO mice compared to Cre-littermate control (Ctrl) mice though baseline expression, determined from traditional collagen XII knockout mice[2], was not reached in KO mice (Figure 1A). Furthermore, the α1(XII) chain was present at comparable levels in the control group: Cre-, *Scx-Cre* and *Col12a1*$^{flox/flox}$ mice (data not shown). Collagen XII content was lower in Het mice and just above background in KO mice compared to Ctrl (Figure 1B). Collagen XII immunofluorescence localization demonstrated efficient knockdown in the tendon proper but

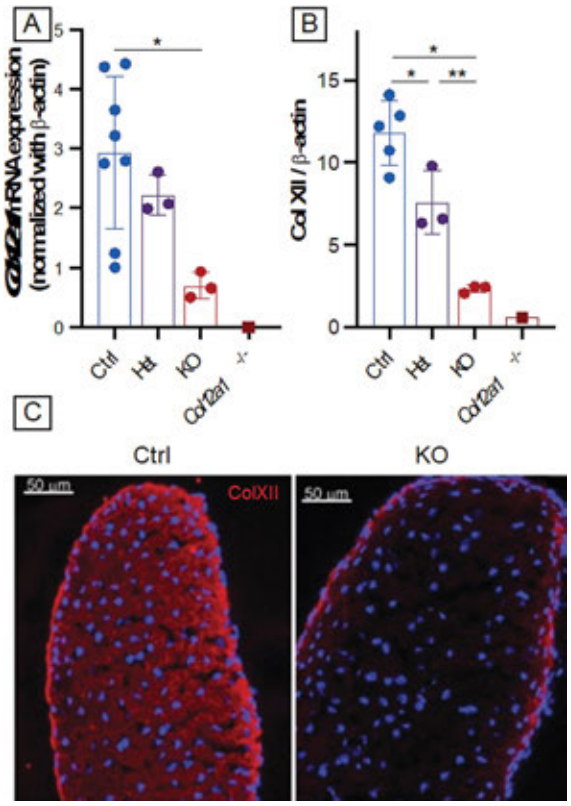

Figure 1. (A) *Coll2a1* and **(B)** collagen XII expression were significantly reduced in *Col12a1*$^{\Delta ten/\Delta ten}$ KO tendons compared to Ctrl though still above the baseline level established from conventional *Col12a1*$^{-/-}$ mice. **(C)** Efficient collagen XII knockdown was achieved in the tendon proper of KO tendons but not the surrounding peritenon. (*p ≤ 0.05 **p ≤ 0.01).

not in the surrounding peritenon as expected (Figure 1C). For joint function, female KO mice had reduced forelimb grip strength compared to Het (Figure 2A) while male KO mice had reduced strength compared to Ctrl mice (Figure 2B). At the tendon level, FDLs from day 60 male and female KO mice exhibited a reduction in mechanical properties. There was no difference in cross-sectional area (data not shown), but stiffness and modulus were both decreased in KO FDLs compared to Ctrl (Figure 2C, D).

Discussion

The overall goal of this study was to create a conditional *Col12a1*-null mouse model and target collagen XII knockout to tendons using a scleraxis-Cre driver. In FDLs of tendon-targeted *Col12a1*$^{\Delta ten/\Delta ten}$ KO mice, both mRNA and protein expression levels were decreased but did not reach the baseline levels of global collagen XII knockout mice. This suggests that cells from a non-tendon lineage are not targeted as expected, and collagen XII immunofluorescence indicates that the surrounding peritenon population likely contributes to the above baseline expression levels.

Furthermore, in the absence of *Col12a1* expression and therefore collagen XII, *Col12a1*$^{\Delta ten/\Delta ten}$ KO mice have impaired mechanics, as evidenced by reduced forelimb grip strength and FDL tendon mechanical properties. Reduced grip strength is consistent with joint function in the global *Col12a1*$^{-/-}$ knockout model, but interestingly, FDL tendon mechanical properties deviated from previous findings. In the global *Col12a1*$^{-/-}$ knockout model, FDLs had larger cross-sectional area and greater stiffness with no difference in tendon material properties[2]. In this study, however, there were no differences in FDL cross-sectional area in KO mice, but stiffness was significantly decreased, resulting in inferior tendon elastic modulus.

Differences in mechanical properties suggest that collagen XII is a critical regulator of tendon structure-function, and the contrasting findings from the global knockout model may be a result of secondary effects, such as those due to muscle and bone. Additionally, collagen XII knockout did not exhibit sex-specific effects with similar trends in grip strength and tendon mechanics for both male and female mice.

Future studies are necessary to elucidate sex-specific roles of collagen XII in tendon structure and determine the biological mechanisms underlying changes in tendon structure-function. In conclusion, grip strength and tendon mechanical changes in the tendon-targeted *Col12a1*$^{\Delta ten/\Delta ten}$ model support that collagen XII is a critical regulator of tendon function.

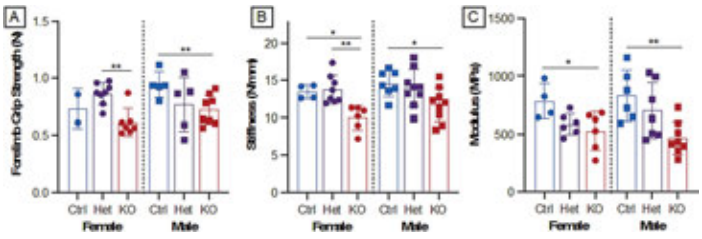

Figure 2. Forelimb grip strength was significantly reduced in **(A)** female *Col12a1*$^{\Delta ten/\Delta ten}$ KO mice compared to *Col12a1*$^{\Delta ten/+}$ Het and in male $^{-}$ KO mice compared to Ctrl. FDL tendon **(B)** stiffness and **(C)** modulus were significantly reduced in *Col12a1*$^{\Delta ten/\Delta ten}$ KO compared to Ctrl in both female and male mice. (*p ≤ 0.05, **p ≤ 0.01).

Significance

Through development of a tendon-targeted collagen XII knockout mouse model, this study demonstrates the critical role of collagen XII in regulating joint and tendon function. Elucidating guiding mechanisms will provide the foundation to leverage the role of collagen XII in therapeutic strategies, providing support for treatments that address conditions such as myopathic Ehlers-Danlos syndrome.

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Collagen III Deficiency Alters Mechanical Properties and Decreases Regulation of Fibrillogenesis Following Injury in Female Murine Tendons

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Introduction

Patients with vascular Ehlers-Danlos syndrome (*v*EDS), a rare genetic disease caused by *Col3A1* mutations, are well-known for severe vascular complications and early death. However, tendon rupture and dysfunction contribute to patient morbidity[1-4], supporting a critical role of collagen III (Col3) in tendon homeostasis and maintenance. Col3 is essential in homeostasis and healing of other collagen I (Col1)-rich tissues (e.g., skin[5], meniscus[6], and bone[7]) due to its role regulating fibrillogenesis, extracellular matrix (ECM) organization, and the formation of cross-links and scar tissue[5,6]. Therefore, the objective of this study was to define the role of Col3 in both tendon homeostasis and in response to injury, regulating collagen fibril deposition and resultant alterations in tendon mechanics. We hypothesized that a reduction in Col3 would result in a more robust, stiffer provisional matrix early in tendon healing, with smaller diameter fibrils when compared to wild-type tendons.

Methods

Female wild-type (WT) Balb/cJ and heterozygous *Col3a1*$^{+/-}$ mice at 30 days of age (n = 48) were used (IACUC approved). Injured mice underwent bilateral patellar tendon injury surgery[8] and were sacrificed 1-week (1w) post-injury in the early proliferative phase of healing. Uninjured sex, strain and age-matched mice were also examined.

Transmission Electron Microscopy (TEM)

Tendons for TEM (n = 4/group) were fixed *in situ* and processed[10] to analyze fibril structure.

Mechanics

Patella-patellar tendon-tibia complexes were prepared for mechanical testing (n = 12/group)[11]. Tendons were subjected to a viscoelastic testing protocol[10,12] 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.

Statistics

Two-way repeated measures ANOVAs with post-hoc Bonferroni tests were used to assess the effects of genotype, injury and their interaction on quasistatic and viscoelastic properties. Collagen fibril diameter distributions were compared by genotype using Kolmogorov-Smirnov tests. Significance was set at $p \leq 0.05$ (solid lines) and trends at $p \leq 0.1$ (dotted lines).

Results

Following injury, tendon cross-sectional area was increased in both WT and *Col3a1*$^{+/-}$ tendons with *Col3a1*$^{+/-}$ tendons having a larger area than WT tendons (trend) following injury (Figure 1). *Col3a1*$^{+/-}$ tendons had increased failure load and stiffness (Figure 2A,B) 1w post-injury when compared to WT tendons, with no differences in uninjured tissues. Additionally, WT tendons had a lower failure load and modulus (trend) 1w post-injury when compared to uninjured, while there was no effect of injury in *Col3a1*$^{+/-}$ tendons (Figure 2A,C). Failure stress (Figure 2D) was decreased in both genotypes 1w following injury. Additionally, TEM analysis showed a shift to smaller diameter fibrils post-injury in both genotypes (Figure 3). Finally, distinctly different distributions for WT and *Col3a1*$^{+/-}$ fibrils post-injury were seen, with *Col3a1*$^{+/-}$ tendons having a larger population of smaller and larger fibrils, and WT tendons having a less pronounced peak and more flat distribution (Figure 3).

Discussion

Our study shows that Col3 deficiency alters both mechanical properties and matrix structure 1w post-injury in a murine patellar tendon injury model in novel and previously unexplored ways. Tendon area increases following injury as healing tissue is deposited into the wound site. The trend toward increased area of *Col3a1*$^{+/-}$ tendons compared to WT tendons post-injury is consistent with an increased deposition of provisional matrix, secondary to increased activation of fibroblasts in *Col3a1*$^{+/-}$ tendons, as decreased Col3 has been shown

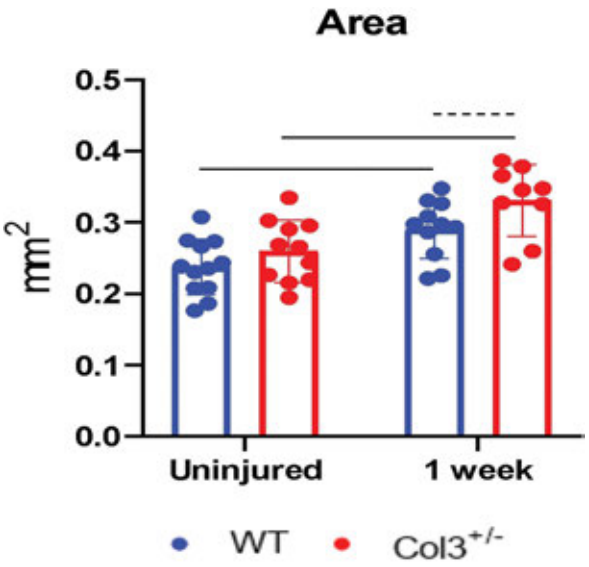

Figure 1. Tendon cross-sectional area was increased post-injury in both genotypes when compared to uninjured tendons.

to cause increased activation[5]. Decreases in failure stress in both genotypes following injury is due to increases in area without concurrent increases in failure load, indicating poor quality tissue following injury in both genotypes as would be expected 1w post-injury. Additionally, TEM analysis showed a more densely packed provisional matrix with smaller fibrils following injury in *Col3a1*$^{+/-}$ tendons likely explaining increased stiffness and further indicating a hypersecretory state of myofibroblasts for Col1 post-injury.

Lastly, the highly skewed fibril diameter distribution with an extended right tail in *Col3a1*$^{+/-}$ tendons indicates dysregulation in fibrillogenesis when compared to WT tendons post-injury. An increased population of larger fibrils reveals increased lateralization of fibrils in *Col3a1*$^{+/-}$ tendons, which is expected as Col3 presence decreases lateral growth during fibrillogenesis[13]. Notably, while *Col3a1*$^{+/-}$ tendons have increased failure load following injury compared to WT tendons at this time point, the poor quality of healing tissue quantified in this study supports the likelihood of an important role of Col3 in dictating cellular activity and healing potential.

Based on these findings, we will examine later time points to understand how fibril growth continues into later stages of healing, along with alterations to the cellular population and activity. Importantly, we will also further evaluate the role of Col3 using a novel conditional Col3 knockdown model to understand the unique temporal role of Col3 throughout

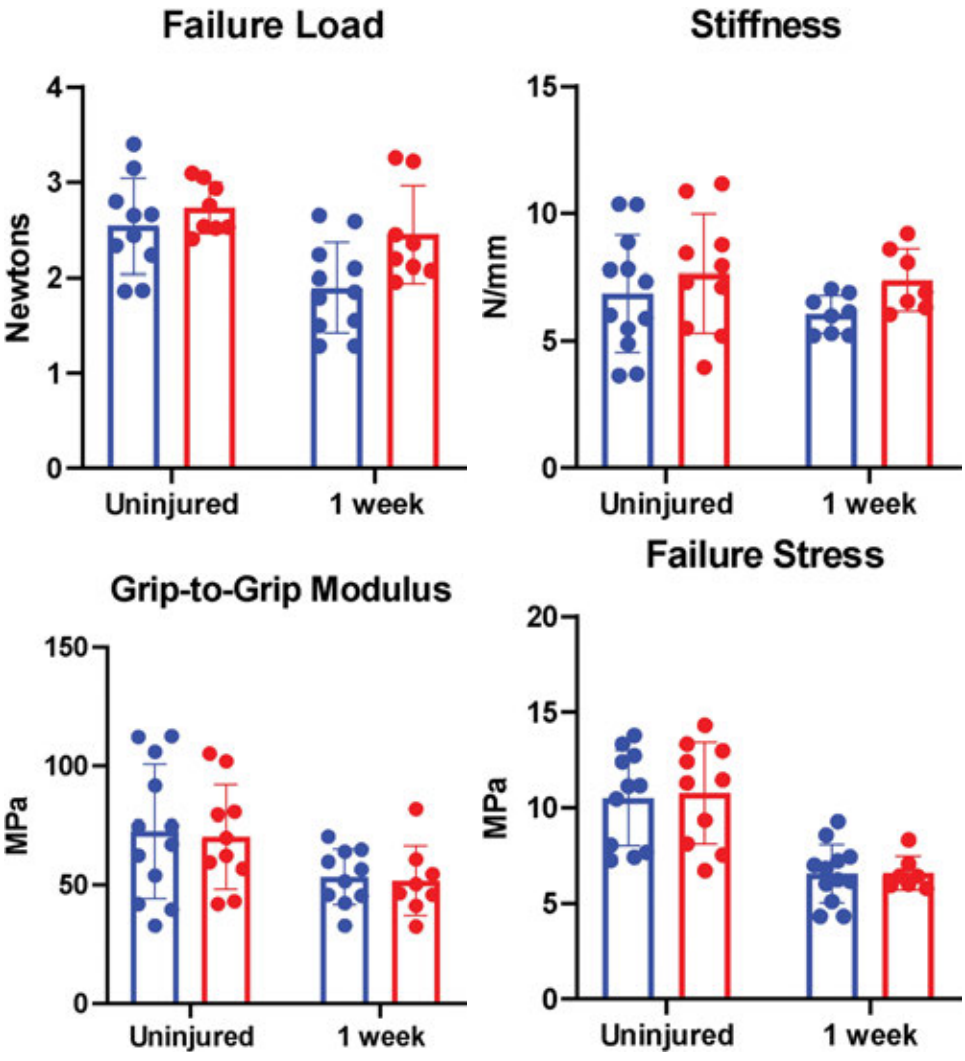

Figure 2. Failure load and stiffness was increased in *Col3a1*$^{+/-}$ tendons 1w post-injury compared to WT. Failure stress was decreased in both genotypes following injury.

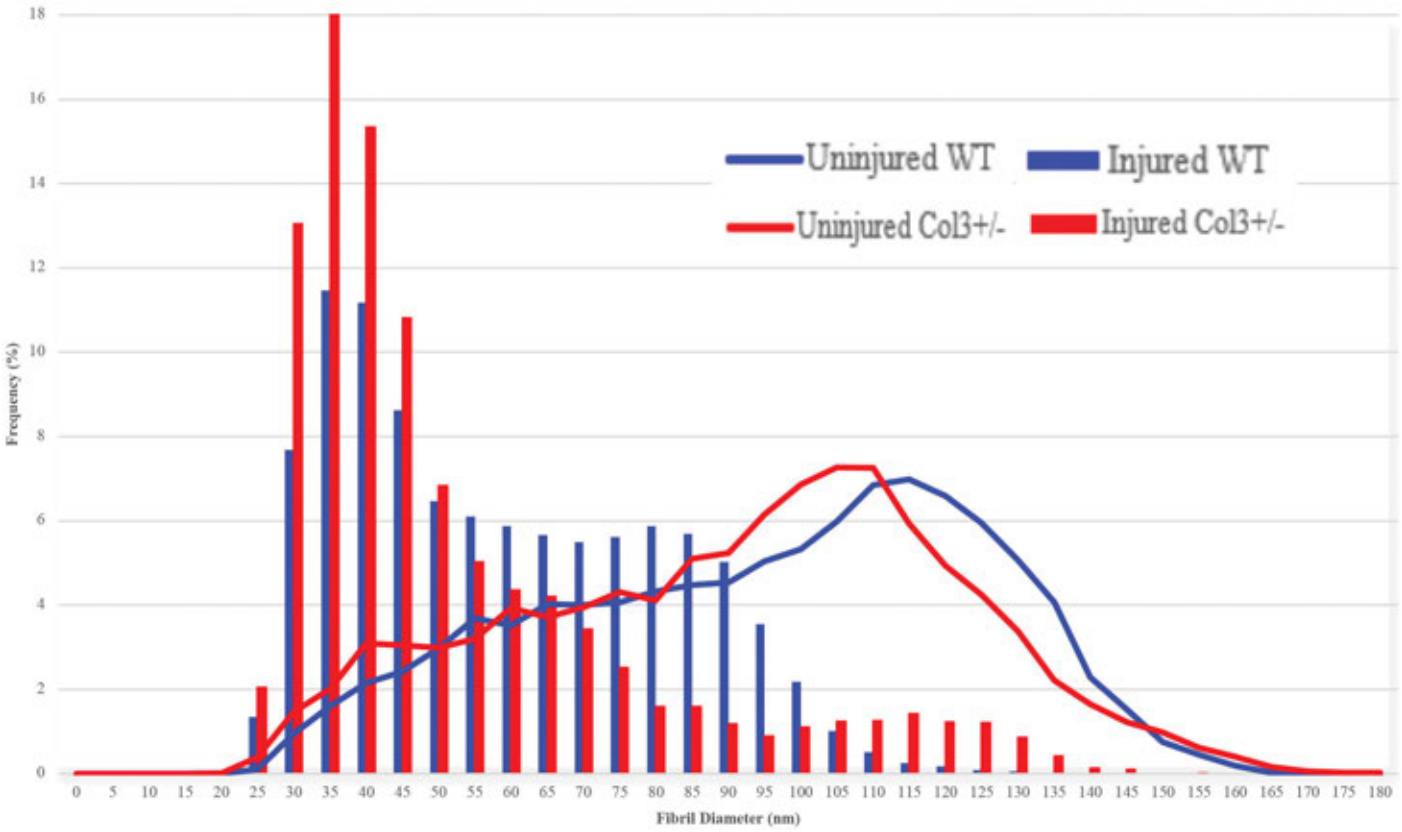

Figure 3. Smaller fibrils were seen in both genotypes following injury. *Col3a1*$^{+/-}$ tendons post-injury had a larger population of smaller fibrils and larger fibrils when compared to WT. Uninjured: line graph, Injured: bar graph.

healing and more specifically, to rigorously analyze the targeted role of Col3 by evaluating the dose response in an otherwise normal matrix.

Significance

Col3 is crucial during early wound healing, affecting matrix structure and function, likely influencing long-term healing. Elucidating the mechanistic role of Col3 throughout healing will provide the necessary foundation for developing Col3-inspired therapies that optimize tendon healing and will ultimately have a profound impact on tendon healing, thereby decreasing healthcare expenditures and improving patient quality of life.

Acknowledgments

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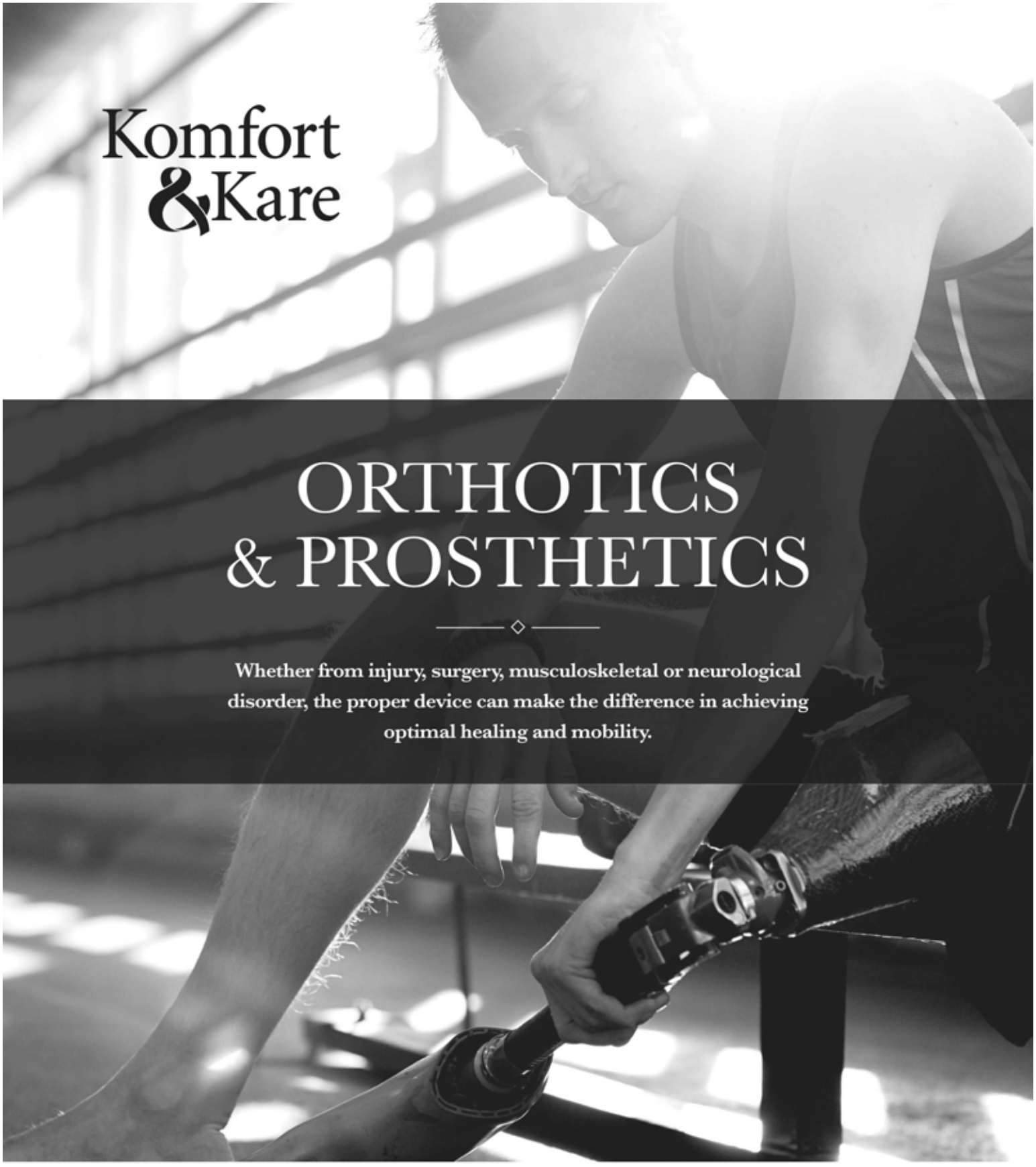

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