The University of Pennsylvania Orthopaedic Journal

Volume 31 June 2021

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The University of Pennsylvania Orthopaedic Journal

Volume 31, June 2021

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Letter from the Editors

Sachin Gupta, MD and Matthew Stein, MD

Sachin Gupta, MD

Matthew Stein, MD

We are delighted to present this year's issue of the UPOJ (University of Pennsylvania Orthopaedic Journal). It is an honor for both of us to take part in such a longstanding tradition, dating back to 1986 under the leadership of Dr. Carl Brighton. We feel privileged to take part in the growth of both the orthopaedics and medical field and feel proud to share our department's achievements with the world. This year's issue is dedicated to one of the hardest workers and most affable members within our department, Dr. Craig Israelite, former Program Director, Co-Director of the Knee Service, Associate Professor of Orthopaedic Surgery, and outstanding Arthroplasty surgeon. Dr. Israelite knows how to make a work day enjoyable and bring smiles to both his patients and his residents. He has contributed so much to the development of this program and he is an invaluable member of the team here at Penn.

This year has not been without its challenges. With COVID-19, faculty and residents alike have had to make many adjustments both inside and outside the hospital. Part of this year's issue is to give a "behind the scenes" look at the changes and adjustments we made as part of this global pandemic. In addition, our faculty and residents led the charge in taking care of complex and very ill patients during the pandemic. Changes our program instituted consisted of virtual conferences, lectures, and meetings in addition to scheduling changes and policies implemented to maintain the safety of patients and providers.

We are truly proud of Dr. Kristy Weber, the first female AAOS president, for leading the orthopedists across the nation during this difficult time. She has truly made an impact both at our institution and across the nation. In addition, Dr. Levin has demonstrated his excellent leadership for our program allowing us to hold our heads high and be proud of the program we call home.

This year's issue would not have been possible without Dr. Levin, our sponsors, and mentors. We are excited to share this year's issue online as well through http://upoj.org and with our online subscriber database. We hope you enjoy this year's issue and thank you again for allowing us to take part in this endeavor.

Sachin Gupta MD
Matthew Stein MD
Editors-in-Chief

Letter from the Chair

L. Scott Levin, MD, FACS

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

As I write the 2021 chairman's letter, I look back with pride at the accomplishments of our Department across our missions of clinical care delivery, orthopaedic education at all stages of learning, and our ever growing and increasingly successful research enterprise. Each year that I have had the privilege to lead this Department, our team has distinguished itself institutionally, nationally and internationally. This year has been no exception.

The COVID-19 pandemic created enormous challenges for all of us in many ways. In March of 2020 a decision was made to stop all elective surgery in order to accommodate patients with COVID and to protect our workforce. I was asked to join the Penn surgery leadership team that create policies with regards to operating room utilization for emergent cases, preoperative scoring of patient profiles, and preoperative testing for patients that would be going to the operating room. The administrative oversight was led by Neil Ravitz who serves as the Department of Orthopaedic Surgery CEO. Working collaboratively with the chairman of otolaryngology, the chairman of surgery and colleagues in anesthesia, our group assured that patients with critical surgical problems had access to the OR and beginning on May 4, 2020 we strategically reopened our operating rooms to resume elective surgery with a variety of constraints and restrictions. At this time our surgical volumes have almost returned to pre- COVID levels despite a second peak in COVID cases that occurred in December. With the exception of our orthopaedic trauma division, all divisions in orthopaedics were adversely impacted by the pandemic. Unlike many academic medical centers around the country, our faculty base salaries and benefits were kept intact, and our health system did not furlough any of our workforce. Our health system weathered the storm of COVID with remarkable courage and conviction and with great pride remains optimistic about our future. The effects of COVID that adversely impacted the financial stability of countless citizens, small businesses, corporations and health systems did not spare Penn Medicine. That being said, our rigorous financial management, government support, and departmental reserves allowed us to remain "open for business" despite the challenges of the pandemic.

Despite the strengths of the pandemic, the Department was able to complete a strategic plan that involved every faculty member. The strategic planning process was facilitated by the Penn Medicine Academy and led by a distinguished core working group that included Neil Ravitz, Kristy Weber, Brian Sennett, Samir Mehta, Lou Soslowsky and Daniel Farber.

The last time that strategic planning had taken place was in 2008. The end product of our work this past year has created a road map that delineate our priorities for the next several years.

We have identified four pillars that will define our execution of the strategic plan. It includes culture, leadership, innovation and growth. The eponym "CLIG" applies to every mission. Continuous quality improvement in every aspect of our enterprise is essential to assure ongoing success.

We have also matriculated several faculty over the last year who will add depth to our clinical, research and educational benches. Casey Humbyrd, MD was recruited from Johns Hopkins and is the newly appointed division chief of foot in ankle surgery. Dr. Humbyrd has a Masters in Bioethics and will add a new dimension to our research mission. Bobby Ndu, MD MBA will join us in May 2021 and contribute to our foot and ankle program. He was a fellow with Keith Wapner and is returning to Penn. Hannah Lee MD, PhD has joined the hand division and as a new surgeon-scientist she will direct basic science efforts in nerve repair and regeneration. David Casper, MD has joined the spine division and will concentrate on spinal deformity and complement the efforts of Vincent Arlet MD. Rush Fisher, MD has returned to the University of Pennsylvania where he completed his training in 1995. As an accomplished spine surgeon, he will contribute to our educational and clinical growth in spine at Pennsylvania Hospital. Ernestina Schipani MD PhD joined us last fall. She is the W.W. Smith Endowed Chair of Orthopaedics and will augment our McKay laboratory program and become the fourth endowed research chair in the department.

Our basic research program is stronger than ever, and our NIH ranking (#3 in the US of all Orthopaedic Departments) is a testament to the leadership of Louis Soslowsky, PhD. In fact, our P30 Penn Center for Musculoskeletal Disorders grant was just renewed for another 5 years with another outstanding score, making it the longest running P30 in history. The research faculty has had tremendous success this past year with regards to NIH funding. Both Mike Hast, PhD and Josh Baxter, PhD were awarded K08 grants. Several R01 grants were awarded despite the increasingly competitive funding levels, a true testament to our investigators and their scholarship.

On Leadership

This year allows me to look back on the two consecutive terms I have had as Chairman of Penn Orthopaedic Surgery. Currently, my leadership is being reviewed by the Dean of the School of Medicine, and I sincerely hope to have the privilege of a third and final term as chairman.

I have said several times that it is the responsibility of leaders to acquire new skills which ultimately improves their ability to

lead. A few months ago I watched the 2009 commencement address given by Jamie Dimon to the graduating students at Harvard Business School. Mr. Dimon is the CEO of JP Morgan Bank and one of the most prominent financiers of our time.

Mr. Dimon's talk is about leadership. I'd like to share his concepts with you which epitomize leadership. His principles are in bold lettering. I have applied them to my observations as an Orthopaedic Chairman. I have also added a few points that have helped me beyond his superb address at Harvard.

1. **Read a lot**. I've learned a lot by studying leaders both their successes and failures. Business books on organizational behavior, team building and communication have helped me.
2. **Talk to people**. I seek out residents and faculty as I walk around the operating room in between cases. It's remarkable what people share, and what you learn about what goes on in your organization when you "walk the floor of the factory."
3. **Watch people**. Whether it's sitting with the other department chairmen in a conference room or these days while participating in a virtual meeting online; you can tell a lot by observing body language, tone of voice, by observing people's behavior. You see good things and you see bad things. Learn from both!
4. **You begin building your brand early in your career**. Your personal demeanor and professional conduct as a medical student, resident or fellow creates a brand. By the time you apply for your first attending job, the "book" on you has already been written.
5. Accomplished leaders **learn how to manage failure and setbacks**. Optimism is a force multiplier. Your team looks to you for guidance-particularly when things are not going well. Remain positive despite the turbulent seas.
6. A certain degree of toughness or GRIT as described in the bestselling book by Angela Duckworth Ph.D is required to endure the long race and to finish strong … whenever your term is over.
7. **One must fight self-deception**. I look at myself in the mirror routinely to ask if I'm doing the right thing. More importantly- what do I need to work on to be a better leader. I run towards trouble and not away from it. For example if our financial performance is suboptimal for a given month or quarter , or if I have a problem with a resident or faculty member – I address the issue directly. Putting off difficult decisions and hoping problems resolved themselves is a recipe for disaster.
8. **Acquiring high emotional intelligence** (EI) is more important than having a high IQ.
9. **Learning to control your anger**, frustration and the urge to retaliate will serve you well. Measure your response before making that phone call or sending an email. Check your emotions often – it will keep you out of trouble. Professionalism is important.
10. **Leadership is personal**. The department represents my family, friends, partners, learners, and the patients we care for. Anything that happens that negatively reflects on the department, I take personally. If a patient writes a letter to me and criticizes care for example, I respond to that patient with a personal letter of apology with a commitment to improve care or the issue that caused the complaint. Fortunately I do not have to write a lot of those letters.
11. **Discipline is important**. Making inpatient rounds to see patients every day of the week is standard on our service. When I arrived 12 years ago-there were patients that were operated on for example on Thursday, and as an inpatient only saw the resident post operatively and did not see a faculty member over the weekend. We changed our standard of care by agreeing that a faculty member would make rounds on Saturday, Sundays and holidays on every patient. My favorite days to make rounds on my patients are Christmas day and New Year's Day. Patients that are in the hospital do not expect to see their physician, but they should be seen by their attending surgeon or another faculty member regardless of the day of the week or if it is a holiday.
12. To lead effectively one must have a **strong work ethic**. I think about Penn Orthopaedics all the time. I ask myself – what can I do to make our team stronger? What new opportunities can we take advantage of? By desire and necessity, I often arrive early and have no problem being one of the last folks to leave the parking lot. You get to know the cars in the lot – who arrives early, and which faculty members are still working as you are leaving the garage.
13. **Continuous quality improvement**. We are data driven. Reviewing re-admission rates, patient mortality, length of stay and complications drive us to improve. Increasing the value of our care means that we have improved outcomes and decreased costs. We can look at outliers regarding physician performance both good and bad. Moving the needle in a positive direction is the underlying principle.
14. **Fortitude** is another characteristic that leaders must possess. Difficult decisions often need to be made about resource allocation, investments in research or education or salary adjustments. There are decisions that leaders make that will be unpopular with some of their constituents. Leadership is not a popularity contest- rather it is the responsibility for an enterprise. Leadership in academic medicine is similar to running a marathon rather than a sprint. For me, each year of my tenure is similar to a mile marker in a 26-mile race. Based on my age and the fact that most chairman at the University of Pennsylvania are limited to three consecutive six year terms, I am now completing my 12th mile. My pace is picking up because of my enthusiasm for what lies ahead over the next six years.
15. **Leaders must set standards** and hold their teammates accountable. Integrity, ethics and unwavering moral compass of doing what's right at all times must guide

behavior. Any deviation from these standards must be dealt with rapidly and harshly if needed which includes immediate dismissal from a training program or faculty in cases where egregious behavior or actions occur.

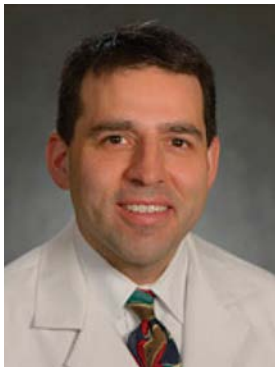
16. **Provide an exceptional product**. Our medical and surgical care must be outstanding at all times. I often say, "if someone wakes up in Melbourne, Australia and has a musculoskeletal problem that no provider can solve in Melbourne or anywhere in Australia – I want their physician to think of Penn Orthopaedics as a destination where the problem can be solved!" More practically, I want Penn Orthopaedics to be the destination for patients in our region seeking the best care for their problem. I have tremendous pride in our team's world class expertise and experience. I have operated with almost all of my partners and have witnessed their skill firsthand. Those that I have not operated with, I have watched them operate as I walk around the ORs and routinely wander into their rooms and observe their skill and surgical execution.
17. **Decision making** should be based on facts, not second hand information or opinions of others that make the issues personal. Get both sides of a story if there is a dispute or controversy and then make a decision about the issue.
18. **There is one truth.** One North star. Follow that star to guide actions and execution.
19. **Kill bureaucracy.** While I believe in the "chain of command" and value the concept of separating "leadership from management," leaders must be accessible to everyone in your organization. An "open door" policy has served me well. My phone is on 24/7/365. I get called about patient referrals to our faculty, resident issues that require my input, and problems that occur with the patients I am caring for. Quoting my mentor J. Leonard Goldner, MD – "Medicine is a lifestyle, and not a vocation".
20. Leaders **develop meaningful relationships** with other leaders. Networking within an institution and outside your institution is helpful. Developing professional working relationships with other department administrators, senior and junior administrators, hospital CEOs and other chairs of Orthopaedics around the country can provide political or social "capital" that can be helpful. Organizations such as the Academic Orthopedic Consortium can help with this.
21. **Engender a culture of "truth tellers."** Do NOT look for people who tell you what you want to hear. Seek out those that are always honest about issues, even if their opinions are contrary to what you thought you would hear with regards to an issue. In faculty meetings I often call upon someone to comment on an issue, knowing that they feel strongly about the issue and that their feelings are diametrically opposite from the majority of the other faculty.
22. **Loyalty is critical**. I encourage faculty members to seek new career opportunities outside of Penn if that is something they care to explore. As a matter of fact, I expect our "superstars" to be considered for positions in other institutions. I like to hear that they are seeking such opportunities *from them* and support them in decision-making and evaluation of the offers they may receive. I do not respond well to sudden faculty departure without knowledge that such a transition will occur. Sudden departures can adversely affect budgets, our educational program and our ability to replace faculty in a timely fashion. Getting a text from a Chairman in another institution that he or she is delighted to matriculate one of our faculty does not sit well with me if I was unaware of the recruitment.
23. **Do not embarrass someone publicly**. As they say in the military—"dress down in private, praise in public". Deliver bad news in person. Never by a phone call or an email.
24. **Morale in an organization comes from fixing problems**. Good leaders recognize problems, make a commitment to address them, and if the problem cannot be solved in a timely fashion—the leader discloses this and provides the reasons for delay.
25. **Treat all folks in your organization with respect**. I know the names of the custodians that empty my trash and clean our building. Knowing the names of personnel in your clinics and operating rooms goes a long way to boost morale and improve teamwork.
26. **Try to get compensation right**. A transparent and formulaic compensation plan is important. There should never be any "special" deals or silent arrangements.
27. **Promote innovation**. Pilot projects should be considered often, with the understanding that not all "great ideas" can come to scale. Failure is expected and should be recognized as a "learning opportunity" rather than a waste of time or resources. Often the "wins" become big wins for the Department and may even be embraced by other departments and the health system. Penn Orthopaedics' motto; "Call us today. We will see you today" has changed our image, and has been adapted by other departments and even our competitors in the market place.
28. **Humility is critical**. I personally believe in servant leadership. Everyone in the organization should work on getting better at what they do and how they do it.

As I complete the 12th year of my tenure as Chair of Orthopaedics, I want to thank our faculty, residents, and staff for their support and hard work. We are poised for continued improvement in Culture, Leadership, Innovation and Growth. I will give you an update in a year!

Warmest regards,
Scott

Letter from the Program Director

Daniel C. Farber, MD



What a year it has been! As I near the end of my first full year as Program Director, I reflect on what has been anything but a "usual" year. Just over a year ago, I took over the official reins of the residency program from the adept and long-standing hands of Craig Israelite, MD. Craig shepherded the residency, with the help of Jaimo Ahn MD, PhD and many others, through many incremental and not-so-incremental changes and challenges, sustaining it as one of the top orthopaedic residencies in the country. Last year's theme was of transition of leadership and the adoption of our newest residents from Hahnemann University Hospital upon its closure. This year's theme (and it is everyone's theme) is COVID. COVID struck shortly after I finished and submitted last year's update. With this pandemic came an opportunity to showcase Penn's strengths. Last year's chiefs, Dan Gittings, Mark Hasenauer and Matt Sloan skillfully re-organized our resident team into platoons to make sure all the hospitals were covered and had back-ups available in case of the unknown. The rotation and call schedules were rapidly revamped to ensure Penn's orthopaedic patients still received the best possible care. I was impressed by our residents who stepped up and volunteered not only to continue treating the orthopaedic patients, but to help in any and all capacities that the hospital system needed during the early days of the crisis. Our outstanding faculty helped transition the educational program into the "zoom" age as our entire didactic program went virtual overnight. The incomparable Shannon Savelloni, our program coordinator, stepped up to facilitate all the logistical challenges that COVID threw our way, all the while preparing for her maternity leave in early May. Lauren Johnson, our (at the time) brand new residency administrative assistant was thrown into the fire just moments after stepping into the frying pan and performed brilliantly during Shannon's maternity leave even with the challenge of fully remote work. With the able help of Vincent Moretti, MD, our Associate Program Director, and many others, we celebrated the Department's first ever virtual "Research Day" featuring Leesa Galatz, MD as our distinguished guest speaker. Soon to follow was our virtual graduation. Certainly not what our graduates had been expecting for the previous 4+ years, but still a heartfelt send-off to honor their accomplishments.

This current year saw the sad absence of any outside rotators to our program due to COVID but we did have the opportunity to really get to know our Penn students who are a fabulous group. The absence of rotators and the decision to keep the entire residency application process virtual completely altered the usual landscape. We arranged multiple online information sessions for students including sessions aimed at those under-represented in medicine arranged by our own Brian Perez, MD and Viviana Serra Lopez, MD along with Larry Wells, MD, the Department's new Vice Chair of Diversity, Equity and Inclusion. We offered students opportunities to be paired with residents and faculty to learn more about our program and for us to learn more about our applicants. Those efforts amongst others led to a strong and diverse class of applicants and interviewees this past January and we hope to see a truly diverse class of interns in just a few weeks. Many thanks to the faculty who combed through the hundreds of applications to help narrow down our interview list and the core group who spent 3 days glued to their computer screens doing virtual interviews of nearly 100 medical students!

This year's administrative chief residents, Chrissy Nypaver, MD, Mike Eby, MD, and Bill Ryan, MD have been an enormous help. Their skilled assistance has allowed us to continue to navigate the in-person restrictions of COVID for education as well as the resurgence program of Penn's Health System which saw most orthopaedic divisions ramp back up rapidly as we learned how to deal with the virus and still provide needed conservative and operative orthopaedic care. We welcome next year's (2021-22) chief residents, Agnes Dardas, Yudi Kerbel, and Liane Miller, who are excited to make their mark at Penn Orthopaedics.

Meanwhile, we have gathered a core group of educators from all divisions to start revamping the orthopaedic curriculum which will incorporate virtual didactics, in-person (COVID safe) labs, hi-fidelity simulation technology, the soon to be released AAOS online curriculum, sub-specialty conferences, and improved feedback mechanisms. We thank Dr. John D. Kelly IV who has generously given his time and money to endow both the yearly Wharton Orthopaedic Leadership Forum and the inauguration of the Penn Orthopaedic Leadership Academy Fellows program with four of our residents. All this aims to keep Penn at the forefront of orthopaedic education and training.

We congratulate our graduating chief residents as they head to some of the top fellowships in the country.

- Gerald Andah, MD—Joints: Montefiore
- Adnan Cheema, MD—Shoulder & Elbow: Mayo Clinic
- Michael Eby, MD—Spine: Emory
- Chelsea Hendow, MD—Spine: Thomas Jefferson University
- Christina Nypaver, MD—Hand: University of Chicago

- William Ryan, MD—Trauma: Carolinas Medical Center
- Christopher Scanlon, MD—Joints: NYU
- Kimberly Stevenson, MD—Joints: University of Utah
- Matthew Webb, MD—Joints: Stanford

We couldn't have such a fantastic program without the brilliant faculty both in the clinic and in the lab that take the time to teach and train our residents. And we certainly wouldn't be where we are without the unwavering support of our chairman, Dr. L. Scott Levin, who is dedicated to making this the best program in the nation.

A final thanks to all of our graduates! You carry the Penn flag and represent us well all over the country and the world, providing first-rate care and leadership in Orthopaedic Surgery. I wish everyone health, wellness, success, and life-long learning.

Letter from the Vice Chair of Inclusion, Diversity and Equity

Lawrence Wells, MD

Dear Colleagues,

I am honored to serve as the Vice Chair of Inclusion, Diversity and Equity and to be a part of the executive leadership board working closely with Dr. Levin, the administrative team and the faculty as we implement our Strategic Plan of Culture, Leadership, Innovation and Growth (CLIG)

It gives me great pleasure to congratulate all of on endorsing our combined mission of increasing diversity in Orthopedic Surgery. Embraced in our strategic plan of Culture, Innovation, Leadership and Growth is Diversity, one of the core ingredients that we champion.

Augustus A, White, III, MD, PhD

We had our first Inaugural Inclusion, Diversity and Equity Visiting Professor lecture featuring Augustus A, White, III, MD PhD, an expert in Cultural Competent Care and the author of "Seeing Patients" and "Overcoming". Resident Survey results revealed 92+% excellent and good scores and content relevance of 95+%. I am happy to see the value noted by our residents and thank each of them for completing the survey.

We had another banner year.

Our commitment and efforts are intentional. Our program participated in the NRMP MATCH PROGRAM, screened over 600 ERAS applications through departmental standard rigorous evaluation. The program director and committee invited 29 exceptionally gifted underrepresented minority applicants (URM) for interview out of a slate of 97 invited applicants. The URM pool represented a 220% increase in 2021, nearly 30% more from previous years. Unusual this year but not uncommon for any other program, all of interviews and interactions were conducted remotely given Covid-19. I am happy and proud of the adaptation that we all adopted yet maintained our departmental principles of pursuing excellence and identifying future leaders in Orthopedic Surgery. I look forward to continuing our efforts to increase diversity next year. Thanks to all of you.

Sincerely,

Lawrence Wells, MD
Associate Professor of Orthopedic Surgery
Standing Faculty, Perelman School of Medicine
Vice Chair, Inclusion, Diversity and Equity

Penn Medicine Orthopaedic Surgery Residency Intern Class 2021–2022

Mohammed Abdullah*
University of Texas

Caroline Granruth
Tulane

Jaret (Mac) Karnuta
Case Western

Erin Kelly
Wake Forest

Sand Mastrangelo
Dartmouth

Bradley Osemwengie
Texas Tech

Eric Schweppe*
Columbia

Weston Smith
Utah

2020-2021 Dedication: Dr. Craig Israelite, MD

Sachin Gupta, MD

It is with the utmost honor and privilege that we dedicate this year's edition of the University of Pennsylvania's Orthopaedic Journal to Dr. Craig Israelite MD, co-director of the Knee Replacement Service, former program director, and Associate Professor of Orthopaedic Surgery. Dr. Israelite's journey within the field of orthopaedics first began when he sustained an ankle fracture while playing tennis the day prior to his orthopaedic rotation. Nevertheless, Dr. Israelite strode in on his first day in crutches, smiling and joking about what had happened the day prior. His jovial personality, his ability to bond with the residents in addition to his passion for surgery, allowed him to fall in love with the field.

He recalled that training during his era was quite different than what it is today. He trained with only two other residents in his year. They labored day and night working on each individual service for three months. As Dr. Israelite was completing his 4th year of residency, Dr. Arnold Berman, his mentor and the chairman of Hahnemann University Hospital at the time surprised Dr. Israelite by offering him a faculty position. Instead of proceeding with the sports fellowship at Penn that had been arranged, he signed on for the position. As a rising faculty member, he found himself doing a wide variety of cases, sometimes performing arthroscopies, arthroplasty, and orthopedic trauma cases in a single day.

Dr. Israelite's transition to the University Hospital of Pennsylvania began in 2002 when he was recruited by Dr. Richard Lachman former chair of the department. His close friend, Dr. Brian Sennett, was instrumental in convincing him to take the leap from Hahnemann to Penn. Both still share a close relationship to this day. While at Penn, Dr. Israelite's ascent to program director began shortly thereafter. At that time, the chairman was the de facto program director. Dr. Israelite attended the monthly resident meetings, developing close relationships with the residents. When Dr. Levin became chairman, he recognized Dr. Israelite's passion for resident education and training, thereby appointing him as the department's first program director.

Dr. Israelite was challenged with the daunting task of building the residency program and reinforcing the infrastructure to allow residents to get top-notch training. His philosophy of taking residents' input and being both fair and balanced when making decisions for the betterment of the program made him a beloved program director. During his early tenure, Dr. Israelite recalled there being less paperwork and milestones. Now the program has grown so much with almost twice as many faculty, but Dr. Israelite ascribes his ability to keep things running smoothly by listening closely to the residents and meeting consistently whether it be late at night or on the weekend. The most rewarding part of the job has been the relationships he has developed and maintained with former residents who he continues to keep close contact with to this day.

Over the years, Dr. Israelite's practice has evolved. Initially, he found himself operating heavily on trauma cases at Hahnemann during his first years of practice due to not having a traumatologist on staff at the time. His first case as an attending was posterior instrumentation and fusion for treatment of an L3 burst fracture. He also recalls the transition of knowing everyone at Hahnemann from the orderlies to the attendings to starting over in 2002 at Penn and building his arthroplasty practice and leading the way as the department's first program director. The three surgeries he misses the most from his early years are tibial plateau ORIF, both bones ORIF, and ACL reconstructions. What Dr. Israelite is most looking forward to in the upcoming years includes the growth of his practice including advances in arthroplasty with navigation and robotics. Upon asking Dr. Israelite what he is most proud of in his career, without hesitation, he states that his family and three wonderful children are his pride and joy. Dr. Israelite gives credit to his wife and recounts that the single best thing is "having your family appreciate your hard work".

Thank you Dr. Israelite for everything you have done for the department, residents, and field of Orthopaedic surgery. We are truly lucky to have such a dedicated, kindhearted, and joyous soul in our department and we Iook forward to your continued teachings and contributions.

Chief's Corner: Academic Chief Update

Michael Eby, MD, Christina Nypaver, MD, and William Ryan, MD

Time continues to pass quickly as another academic year has come and gone. We are honored to have served as the academic chiefs for the 2020-2021 tenure. First and foremost, we would like to express our utmost gratitude to Drs. Levin, Farber, and Moretti for their steadfast support and leadership throughout this year. It has certainly been a unique year as we continue to face the challenges and unforeseen obstacles associated with the COVID-19 pandemic. We would also like to thank the faculty, staff, and our co-residents for their continued hard work and dedication to education albeit living and working in tougher times. Despite the barriers associated with the pandemic, our residency program was still able to pursue and successfully achieve formative changes to our educational curriculum, expand and improve upon our virtual/social media presence, as well as continue the robust visiting professor curriculum from afar.

At the start of the academic year, our daily operations appeared to be back up and running at a near normal pace after an unusual and unprecedented pause in clinical activities in the spring. The addition of new residents from Hahnemann the previous year promoted the implementation of new, desired rotations to the educational curriculum for the residents. Noteworthy additions included a fundamental hand rotation with Drs. Gray and Liu, a supplemental foot and ankle rotation for the more senior residents, as well as an elective rotation for the chief resident class, allowing them to pursue opportunities and experiences in the subspecialty of their choosing.

We became more closely integrated with our colleagues in the Plastic Surgery Department, remodeling our hand call schedule so that both plastic and orthopaedic surgery residents have the opportunity to work and operate with their counterpart residents and faculty. We hope to continue and flourish this working relationship as we value teamwork and educational opportunities from varied perspectives.

The resident education program and Grand Rounds curriculum were also revamped this year and implemented at the start of 2021. Each subspecialty now has dedicated time for conference during the week where faculty, fellows, and residents rotating on that subspecialty engage, debate, and discuss topics in a more intimate and influential environment. These can be in the form of formal lectures, journal clubs, indications conference, or fracture conference and complements what is learned clinically during the rotation. These are supplemented by weekly subspecialty specific, and occasionally multidisciplinary, interactive Grand Rounds lectures which are given by the faculty.

"Fireside chats" or weekly fracture of the night conference continued with our Trauma faculty Drs. Mehta and Donegan, which impressively expanded on the national scale through the Orthopaedic Trauma Association, where residents and fellows interact with Orthopaedic Trauma faculty around the country.

Formal Grand Rounds with visiting professors and Quality Improvement Conference continues to take place on a monthly basis. Indeed, our expansive visiting professor curriculum continued albeit taking place virtually, with national and international leaders in the field giving lectures to and educating the department. We were delighted and honored to have each of these esteemed speakers provide us with thought-provoking and stimulating lectures as experts of their craft. We look forward to a time where we can once again welcome and host our guest speakers and colleagues in person.

It is certainly difficult not to discuss the elephant in the room – the COVID-19 pandemic took its toll on the program, the department, and all of us, as it did to the rest of the world, compelling us to adapt to this new "normal". We are extremely grateful to be in a position where our own careers and livelihoods have been protected during these troubling times where others have not been as fortunate. The introduction of a vaccine which was offered to the department around the Holidays provided new hope that we can return to a state of normalcy once again. We are beginning to reintroduce our cherished in-person cadaver sessions in the Penn Human Tissue Lab and subintern rotations for interested medical students. We also eagerly await the return of international orthopaedic work opportunities and in-person residency interviews this coming year (hopefully) as done in years past.

As our time as academic chief residents comes to a close, we would like to personally thank all of our co-residents at Penn for their enduring dedication, hard work, and perseverance. We would also like to express our sincerest gratitude to our program leadership and faculty who have served as excellent mentors and teachers these past five (plus) years. We wish the best for next year's chiefs and anticipate exceptional achievements and growth for the program in the future.

Sincerely,

Michael Eby, MD
Christina Nypaver, MD
William Ryan, MD

Class of 2012 Alumni Residents—Where are they now?

Matthew Stein, MD

Derek J. Donegan

Fellowship: Traumatology, University Hospital – University of Medicine and Dentistry of New Jersey

Current Employment: Assistant Professor of Orthopaedic Surgery at the Hospital of the University of Pennsylvania

How has training at Penn impacted your practice?

My training at Penn impacts my practice daily. Penn taught me how to be a good surgeon, physician, and educator. Most importantly, it taught me how to be a thinker. My greatest mentors at Penn helped me to internalize what it is I do and strive to constantly improve. This has led me to push the boundaries of turning success into a positive impact on patients' lives.

What have you learned in your first decade of practice?

I have learned that I am constantly learning.

What advice would you give to residents?

My advice is to realize early that everything we do in our job has a direct impact on someone else's life. While we are often looking towards the "next step" or the "next big thing" take the time to appreciate the current moment. This is where you will get the biggest bang for your buck. Take advantage of the incredible faculty that have chosen to be at Penn to dedicate their talents towards helping you become your best self and realize your fullest potential.

Keith D. Baldwin

Fellowship: Pediatric Orthopaedics, Children's Hospital of Philadelphia

Current Employment: Associate Professor of Orthopaedic Surgery at the Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia

How has training at Penn impacted your practice?

I am one of those unusual people that use what they learned at Penn broadly on a weekly basis. My experiences with Mary Ann Keenan of Neuro-orthopedics and Samir Mehta of Traumatology were formative in terms of what I do on a weekly and sometimes daily basis in terms of practical knowledge. Additionally, Penn gave me the thought processes I bring to bear in research and education of trainees in orthopedic surgery. I stayed on and trained under Jack Flynn, and John Dormans two leaders in POSNA and SRS, as well as David Spiegel an internationally known surgeon in cerebral palsy who taught me all I know about scoliosis care. I feel honored to have trained under such greats in the field.

What have you learned in your first decade of practice?

Knowing who to operate on and who not to operate on is equally important to knowing how to do the operation you are doing.

What advice would you give to residents?

You can learn something valuable for your eventual practice in every service. Do not neglect a service because it is far from what you will be doing. Sometimes those services teach you the most valuable techniques and thought processes that can get you out of tight spots in the operating room and in clinical management.

Andrew F. Kuntz

Fellowship: Shoulder and Elbow, Hospital of the University of Pennsylvania, Thomas Jefferson University Hospital

Current Employment: Assistant Professor of Orthopaedic Surgery at the Hospital of the University of Pennsylvania

How has training at Penn impacted your practice?

Without a doubt, my six years of residency at Penn launched me into my current career. I had the opportunity to work with Drs. Williams, Ramsey, and Glaser on the shoulder and elbow service early during residency. Wanting to emulate these individuals, I decided to pursue a career in shoulder surgery. Due to the excellent training that I received during

residency, and thanks to the strong networking of the Penn Ortho faculty, I was able to match into my top-choice for fellowship, and then return to join the Penn Ortho family immediately after fellowship. During my lab year, I solidified my desire to pursue a career as a surgeon-scientist. I also was able to establish wonderful collaborative relationships with Lou Soslowsky and Rob Mauck during my research year, which have continued and grown during these early years in practice. Most of all, though, I can honestly say that I learned something from every faculty member that I worked with throughout residency and have been able to incorporate and build on even little tidbits of knowledge to improve my practice and how I provide care to patients.

What have you learned in your first decade of practice?

I can still remember as a PGY-2 at CHOP, the first time I heard Dr. Wells talking about the importance of being "Available, Affable, and Able." The "3 A's" are critical to successfully building a practice. In addition to these, clear communication is key! Many issues/conflicts can simply be avoided with clear and timely communication. Patients, staff, and colleagues all appreciate effective communication.

What advice would you give to residents?

Truly take advantage of every opportunity – conferences, labs, cases, informal discussions, etc. – during residency. Never again will you have the chance to learn so much from so many talented individuals. Additionally, make sure to build strong relationships with your co-residents, who will be your friends and colleagues for life.

Albert O. Gee

Fellowship: Sports Medicine and Shoulder Surgery, Hospital for Special Surgery

Current Employment: University of Washington Associate Professor of Orthopaedics and Sports Medicine

Amy L. Herz

Fellowship: Sports Medicine, New England Baptist Hospital

Current Employment: Orthopaedic Institute of Pennsylvania, Camp Hill, Pennsylvania

Nick D. Pappas, III

Fellowship: Hand, Microvascular, and Upper Extremity Surgery, Vanderbilt University

Current Employment: Chief of Orthopaedic Hand Surgery and Assistant Professor of Orthopaedic Surgery at Louisiana State University Health Sciences Center, Hand Center of Louisiana

Amit R. Patel

Fellowship: Spine, University of Washington/Harborview Combined Fellowship

Current Employment: OSS Health, York, PA

Ejovi Ughwanogho

Fellowship: Spine, Texas Back Institute

Current Employment: The Core Institute, Phoenix, Arizona

Dr. Kristy Weber Presidential Address and Q&A

Ashleigh N. Bush, MD

Presidential Address

Greetings to all Academy members. I wish I were addressing you in sunny Orlando in a world without Covid-19. The reality is the timing of the virus outbreak and our meeting could not have been predicted, prevented, or ameliorated. The academy board of directors and staff leadership made the difficult but necessary decision to cancel our annual in-person meeting after several weeks of daily, often hourly preparation, contingency planning, and communication with key stakeholders. It was a thoughtful data-driven decision that relied on local, state and national guidance. The pace of disruption due to coronavirus escalated in early March and altered the global landscape. Safety and health concerns are now paramount and must be prioritized for the millions of people directly or indirectly related to the virus. People we know have died, and will die of respiratory compromise. Others will bear mental and physical consequences of the isolation required to flatten a disease curve. The economic impacts imposed staggering burdens on our country, on our workplaces and on our friends and families.

Notwithstanding the bigger societal picture, we must acknowledge the individual disappointments of the college athlete who worked for years to excel in a championship or make it to the pros but now cannot. The first in family college senior denied the chance to walk across the stage this spring to receive her diploma. The families unable to gather to celebrate at a wedding or mourn at a funeral. At the academy level there are many who are disappointed. The staff who worked hard for over a year to execute a successful annual meeting, members starting or ending their leadership terms in Orlando, residents giving their first podium presentation on a big stage, and others looking forward to networking or catching up with friends and colleagues. As for me, I was excited to share with you in person the academys' accomplishments of 2019, new initiatives, programs and creative collaborations. Instead, we will bring this annual meeting week to you virtually to communicate these efforts, and we will roll out CME accredited educational events including ICL's and symposia over the next few months.

Before I continue, I want to thank my extended family who have always reinforced my conviction that there should be no limits to what is possible in work and in life. I'd also like to thank my Penn Orthopaedic work-family, especially my tumor partner Robert Wilson, who supported my increased commitment to the academy this year. It seems like just last week that I addressed over 1,100 of you at the Las Vegas Convention Center. Now, I'm alone in my kitchen in Philadelphia self-recording this video on my iPhone. It is going to be the new normal for a while as the world accommodates to virtual everything from mass gatherings, to journal clubs, to happy hours. Yet the academy will continue to move forward as we have through World Wars and other crises since 1933 because we must on behalf of our patients, our profession and our communities. Let me tell you about what has happened over the past year. We have made remarkable lasting progress that should not be overshadowed by the current state of emergency.

The board of directors has shown both leadership and discipline executing on Year One of our strategic plan and adhering to and building upon governance principles that will sustain the academy through an era of tumultuous change and challenge. It is not easy to stay focused and say no to ideas that while interesting do not align with our commitment, and improve your experience or advance the quality of orthopaedic care. It is however what high functioning organizations and boards must do. We have worked to implement processes that foster year-to-year consistency to ensure that we reach our 5-year strategic goals and avoid personality based leadership so common in our Orthopedic culture. While there is value in knowing our history we cannot be so bound by custom and tradition that it hinders innovation, is contrary to best practice, or limits our organizational relevance to future generations of members.

I will start with progress made on the three goals of the Strategic plan all in support of our vision to be the trusted leaders in advancing musculoskeletal health. Goal number one: deliver a personalized and seamless member experience. In order to deliver, we need to know who you are. We completed over 92% of the data fields on our domestic numbers up from 78% in 2018. We can now say with confidence for example, that the United States segment of the academy is composed of 2,673 women, 1,452 Foot and Ankle surgeons, and 2,633 who self-identify as private solo practitioners. Substantial investments in technology were made to upgrade our systems. Have you logged into the updated website at aaos.org? It is easier to navigate, with better response time and more relevant information. Our Academy Educational Learning platform had nearly 17,000 unique users in 2019, a 17% increase from 2018 and members who claimed nearly 130,000 CME credits. The vast majority of digital education is now free to members. An expanded Orthopedic Video Theater now includes member requested practice management modules and opportunities for academic, industry and specialty society unique channels. Orthoinfo.org had 33 million visitors and has been updated with surgical videos for patients, and a series of downloadable PDF handouts about common conditions and treatments. The new Health E-Center job board helped over 6,700 members connect with potential employers: twice as many as in 2018. Our board approved nearly 5 million dollars to develop a comprehensive, visionary resident curriculum led by Paul

Tornetta, and our education council. Finally, our governance structure was not aligned with a focus on you, so we changed it! A new membership council joins our councils on education, quality, and advocacy. This new group, led by Liz Matzkin, will develop a membership strategy that provides value and understands the different needs and transition stages for residents, practicing surgeons, international members, and emeritus members.

Goal number two: equip members to thrive in value-based environments and advance the quality of orthopaedic care. Bob Quinn and the Council on Research and Quality, with input from multiple member stakeholder groups, developed a new academy definition of quality and value related to musculoskeletal health. Clinical practice guidelines, appropriate-use criteria and performance measures continue to be updated based on the new evidence and the process remains best-in-class among medical and surgical societies. I'm thrilled to announce a new partnership between the academy and the Orthopedic Research and Education Foundation, OREF, to leverage the strength of each organization to raise funds and support clinical researchers who design projects that will answer critical questions relevant to patient care. One key example of an area of clinical concern to our members and patients is biologics and regenerative medicine. The academy along with OREF, the Orthopedic Research Society, orthopaedic speciality societies and other stakeholders is in the process of defining a current evidence related to scope, safety, and the efficacy of these treatments in a credible and reliable way.

Orthopaedic registries are another focal area. The academy's family of registries expanded to include a new partnership with the American Association of Neurological Surgeons for an American Spine Registry. Our American Joint Replacement Registry now captures 40% of the hip and knee replacements in the United States. The Shoulder and Elbow Registry expanded to include modules on rotator cuff repair and elbow arthroplasty, and the Musculoskeletal Tumor Registry expanded beyond the pilot stage. I want every surgeon watching this video to be part of the registry effort so that you and your practice benefit from Center of Excellence status from the Joint Commission, maintenance of certification, self assessment exam credits, and compliance with the merit-based incentive payment system or MIPS. You can track your outcomes compared with national and institutional benchmarks, or submit requests for registry data to be analyzed to answer critical research questions. Finally, the academy has elevated its participation in the Choosing Wisely national campaign to educate patients on procedures and treatments not supported by existing evidence. Moving forward we will all need to focus on high-value care if we want to do right by our patients and personally thrive in this changing healthcare environment.

Goal number three: evolve the culture and governance of AAOS's board and volunteer structure to become more strategic, innovative and diverse. The board is more strategic. Each yearly agenda is focused on board defined key initiatives that are directly aligned with the strategic plan to ensure consistency over time. Meetings are more streamlined. There are robust discussions and a willingness to tackle difficult issues. Even before covid-19, we were using a lot more video conferencing to make member participation and committee work more convenient, and inclusive. A governance committee, led by Brad Henley, is critically evaluating the academies current government structure and what it will take to evolve toward best practice for nonprofit boards. The board adheres to the governance principle of being strategic with centralized authority and decentralized council and committee decision making. In May we defined new academy core values: leading to serve, shaping our future, and excellence together. You will see a focused effort to promote these values and supporting behaviors throughout the volunteer structure. Decision-making must be guided by these new core values and behaviors.

For example, we will use data and evidence rather than opinion to stay a step ahead. We must empower and seek input from all people, not just the majority. And we will collaborate based on mutual respect and trust. Accepting these values and putting them into practice will require a cultural change to be successful. The board also approved a nimble innovation process for moving ideas more quickly through the approval structure based on their merits and alignment with the academys' strategy. Finally we are implementing a multi-pronged strategy to develop a more diverse academy volunteer structure, which requires more frequent and more substantive communication with our partners at the Ruth Jackson Orthopaedic Society, the J. Robert Gladden Orthopaedic Society and the American Association of Latino Orthopaedic Surgeons. We need to make it clear to members, new and old, the mechanics of applying for volunteer positions and we also need greater transparency about how selections are made with feedback to applicants and required implicit bias training for all academy volunteers and staff.

In 2019, 12% of our volunteers were women, and 7% were from under-represented racial minority groups. Those percentages are doubled on the new 2020 board of directors. We will be successful over the next four years in improving diversity, inclusion, and equity among our volunteer leaders. Our key enablers of communication, advocacy, partnerships and technology remain fundamental. Jennifer Weiss and her team made member communications more personalized in both traditional, and social media formats and started the FAAOS campaign to recognize academy members. Wilford Gibson and our tireless advocacy team remain effective on the legislative and regulatory fronts promoting fair arbitration for surprise billing, assuring that 30 million dollars is directed to research funding for extremity war injuries, and for reinforcing the fact that orthopedic surgeons are leaders in advancing value-based musculoskeletal care. Our leading Ortho PAC raised 1.9 million dollars in 2019 and a new online advocacy action center generated more than 3,500 letters to members of Congress. The academy maintained or expanded collaborations with specialty societies in areas of mutual benefit related to advocacy, quality, and education based on our partnership principles.

In closing, I would like to share a few personal observations accumulated over my year as president of the academy. In 2018, the board of directors determined the academy was in real danger of losing relevance to current and future members, patients, and other partners in the healthcare space. Rather than bury our heads in the sand, the board acted and implemented year one of the new strategic plan in 2019. I am incredibly proud of each board member for his or her teamwork and decision-making and of our CEO Tom Arond and his staff for implementing the board strategy. I am particularly grateful to my next two successors Joe Bosco and Danny Guy, who helped lead with courage and humor. The academy's future is bright with their capable leadership. I personally enjoyed hearing the stories of so many members of state societies, specialty societies, and international members who each have their own sagas of challenge and triumph in this great profession of orthopaedic surgery. Our annual member survey shows that the academy is moving in the right direction in terms of member satisfaction and value, and I expect that to continue. We have moved from personality to process on the board, knowing that consistency of year to year is how we will maintain lasting change. However, there is no denying that change is hard and that it makes some people fearful, threatened or angry. In my academy travels this year I have observed that many orthopedic surgeons of my generation, mid-50s and older, are often uneasy about change and lean toward the comfort and predictability of tradition. By contrast, I have found that younger surgeons particularly residents and early career professionals embrace change and frankly do not believe change at the academy is happening fast enough. Instead of longing for the old academy where history, seniority, and tradition were preeminent they look to a new academy for innovation, diversity, inclusion and values come first. I am most humbled to be not only a woman leading this organizational change, but the first woman. I have endeavored to be a model for young women and men who might have once been seen as outsiders in the traditional academy culture and who will someday follow me in this or other leadership roles, where new voices and views must be heard. Thank you and please be safe over the next several weeks and months, as you do your part to lead your communities and responsibly care for your patients and families throughout this defining crisis.

Kristy Weber, MD, FACS
AAOS Past President
Vice-Chair of Faculty Affairs
Director of the Sarcoma Program,Abramson Cancer Center
Chief, Orthopaedic Oncology
Department of Orthopaedics
Hospital University of Pennsylvania

Q&A

Kristy Weber, MD served as the 87th president of the Academy of Orthopaedic Surgeons from 2019-2020. She was the first female president of the AAOS. She earned her medical degree from the Johns Hopkins School of Medicine in Baltimore, Maryland. Dr. Weber completed her orthopaedic residency training at the University of Iowa in Iowa City and a two-year research/clinical fellowship in orthopaedic oncology at the Mayo Clinic in Rochester, Minnesota. Prior to serving as a faculty member at the University of Pennsylvania, she served on the faculty at the University of Texas MD Anderson Cancer Center and Johns Hopkins. We had the honor and distinct opportunity to conduct a Q&A with her regarding her outstanding achievements and guidance for orthopaedic surgeons.

What is the most valuable piece of advice you have received in your career?

Remember why you went into medicine and specifically orthopedics. Hopefully it is because you want to help patients and it is one of your prime areas of focus and commitment. Work incredibly hard. Orthopedics is not an 8-5 job. There will be demands from our job which pull us in off hours. To be successful in this job, it generally requires work outside of the standard work hours.

What advice would you share with orthopedic surgeons just beginning their careers?

Be so good they can't ignore you. You should strive for excellence in all pursuits in this field, from being an excellent doctor, surgeon, researcher, or leader.

Have a really good work ethic. Don't cut corners. Keep focused on the goal: taking care of the patients who come to you for help. Keep up with your commitments and finish things you commit to on time.

Professionalism- this is of utmost importance. You must be professional to patients, colleagues, and members of the health care team. To be a leader of the surgical team and the musculoskeletal care team providing for the patient, you must value everyone's opinion.

Have a plan. Set a goal of what you want to accomplish over the next 1-3 years and the next 5 years. Stick to this plan. Figure out what you need to do to accomplish your goals and execute.

How has being active in the Academy helped you in your career?

Being a member of the Academy and other national societies has helped me meet people, network, gain new perspectives, understand new ways of doing things, and develop leadership skills.

Within the Academy, I started at the ground level on educational committees. I worked hard and was appointed to roles with more responsibility that helped me develop skillsets including leadership, organization, managing an agenda, and completing projects on time. I moved onto working on and eventually leading Quality initiatives as the Chair of the Council on Research and Quality which helped me continue to develop skills in leading a team.

In addition, the volunteer leadership roles helped me get a sense of the goals and mission of the AAOS and see if this

organization resonated with me. It took years of learning about the AAOS to feel I understood the organization and how it worked.

I was lucky to be nominated for a member at large position on the Board early in my career which was a stepping-stone to later being considered to serve as president of the Academy. Being chosen to serve in the leadership line was likely due to the tangible contributions I had made and my leadership qualifications.

Who is someone whose leadership style you admire? How have you tried to emulate him or her?

There is not only one single person whose leadership style I admire, as I do look up to so many people and enjoy reading about and watching leaders in action and learning from them.

One person that comes to mind is a mentor from residency- Dr. Stuart Weinstein. He was and still on the faculty at the University of Iowa specializing in pediatric orthopedic surgery. He has served as a past president of many orthopedic organizations including the AAOS. He has served as a mentor and sponsor for me and has become a good friend. I admire his work ethic in that he works incredibly hard and takes responsibility for his actions. He is competent at his craft and I love to watch him prepare to solve difficult problems by considering multiple different angles.

I am also interested in women leaders not only in orthopedics, but in medicine and in other fields. I like to learn how they navigate the challenges of leadership and excel at their roles. For example, some women here within Penn Medicine that come to mind are:

- Deborah A. Driscoll, MD who was appointed Senior Vice-President for the Clinical Practices of the University of Pennsylvania and Vice Dean for Professional Services at the Perelman School of Medicine in October 2019 after serving as Chair of the Department of Obstetrics and Gynecology and Director of the Center for Research on Reproduction and Women's Health for 14 years.
- Regina Cunningham PhD, RN, who serves as the CEO of HUP. She is an accomplished nurse executive, scientist, and educator who has made impactful contributions to advancing nurse practice and clinical care.
- Lynn M. Schuchter, MD a faculty physician at HUP who serves as the Chief of the Division of Hematology and Oncology, Director of the Tara Miller melanoma Center, and is the C. Willard Robinson Professor of Hematology-Oncology.

As Academy president, what is an example of a leadership challenge you faced? What did you learn from it?

A goal of mine as AAOS president was to change leadership from being 'personality'-based to 'process'-based. In prior years, each individual president would have personal priorities and pet projects that would influence the organizational goals for that year. However, priorities would vary year to year and make it difficult for the organization to consistently move forward. I led the development of a 5 year strategic plan from which the Board determines the key initiatives for each year. This plan is accountable, documentable, and related to tangible goals.

Additionally, culture is something that is important to me. Part of this means questioning traditions and asking: are these traditions inclusive? Why do we do things this way? Additionally, the Board approved including culture and governance into the strategic plan with some of the specific metrics related to increasing diversity in the volunteer leadership.

What achievements in your career are you the proudest of?

There are a few of achievements in my career that make me proud. One would include the Academy presidency. Another would be my Quality related work with the Academy which included leading the development of clinical practice guidelines and appropriate use criteria which were not terribly popular when we were rolling these out in 2008. Finally, I was awarded the Duncan Van Dusen award for Professionalism from the Perelman School of Medicine in 2019, which was a great honor. I am also proud to be able to serve as a role model to young women and aspiring orthopaedic surgeons.

What is your favorite memory from residency?

I don't know that I have a specific favorite memory; more so a collection of impressions. I truly loved residency. There was a sense of comradery among the residents and a commitment of the faculty to our training and careers that was special. I loved my time on the tumor services as well as the trauma team. We frequently had social activities where faculty, residents, and their families would spend time together. Each year, we would have a pig roast at a faculty members farm. These inclusive social gatherings were special because we would set aside the work roles to some degree and enjoy each other's company as friends.

Is there a single memorable case you can recall from residency?

There was a woman with metastatic renal cell carcinoma. When you're a resident, you often spend more time with the patient in the hospital than the faculty member. I had time to get to know this patient. I sat with her and got to know her goals and fears. Ultimately this patient died of cancer while I was on the tumor service. I try to remember that, even when I am busy as an attending with a myriad of responsibilities, I cannot stray too far from these interactions with patients.

Another case I remember was as a PGY2 on the tumor service. The case was a superficial malignant tumor resection and I cut into the tumor. I remember feeling mortified. The tumor faculty fixed my mistake and made sure we got the entire tumor out with a wide margin (including my skin incision). It reminded me that when you make a mistake, you should own it and take responsibility. If you feel bad after making a mistake, it probably means that you care and have the drive to learn from this mistake and not make it again.

Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment Update

Hannah M. Zlotnick, BS[1,2,3], Tomasina M. Leska, BS[4], Divya Talwar, PhD, MPH[4], Jay M. Patel, PhD[1,2], Jonathan H. Galarraga, BS[3], Jason A. Burdick, PhD[3], Theodore J. Ganley, MD[4], Robert L. Mauck, PhD[1,2,3], James L. Carey, MD, MPH[1]

[1]Department of Orthopaedic Surgery, University of Pennsylvania, [2]Translational Musculoskeletal Research Center, CMC VA Medical Center, [3]Department of Bioengineering, University of Pennsylvania, [4]Children's Hospital of Philadelphia

Introduction

In January 2013, the proposal to create a Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment was supported by L. Scott Levin, M.D., Chair of the Department of Orthopaedic Surgery, and then officially endorsed by J. Larry Jameson, M.D., Ph.D., Dean of the Perelman School of Medicine at the University of Pennsylvania. This Penn Cartilage Center operates as a Type-1 Center within the Department of Orthopaedic Surgery—promoting targeted, inter-disciplinary science and education spanning basic, translational, and clinical research. Over the last year, the Cartilage Center has excelled in this mission.

Cartilage Symposium

We adapted the 8th Penn Cartilage Symposium to a virtual platform, and held this meeting on September 11-12th, 2020. Due to support from our generous sponsors, we were able to offer this educational opportunity for free to anyone interested. While we missed the human teaching lab portion of the program that is typically associated with the in-person symposium, the virtual platform allowed us to hear from speakers around the United States, and abroad. The symposium included basic, translational, and clinical science presentations with the overarching theme of "Enhancing the Quality and Value of Cartilage Repair". The translational science keynote was given by Alan J. Grodzinsky, Sc.D., a leader in cartilage biomechanics, tissue engineering, and drug delivery from Massachusetts Institute of Technology. Dr. Grodzinsky spoke about the delivery of novel therapeutics for cartilage repair and regeneration. The clinical keynote was given by Tim Spalding, FRCS Ortho, a surgeon and pioneer in meniscal transplantation from England. Mr. Spalding covered the cost-effectiveness of fresh osteochondral allografts and meniscus transplants. These keynote presentations were accompanied by 14 other talks by leading scientists and clinicians. In addition to the talks, there were numerous posters submitted and presented by trainees. We finished the symposium with a virtual mural arts tour of Philadelphia hosted by Mural Arts Philadelphia. Overall, the 8th Penn Cartilage Repair Symposium was a success, and we look forward to meeting in-person next time.

Basic Science and Translational Research

Magneto-driven cell gradients for cartilage tissue engineering

We recently developed a novel cell patterning strategy using magnetic fields to position unlabeled cells in three dimensional hydrogels (Figure 1). A provisional patent has been filed for this invention through the University of Pennsylvania and the Philadelphia CMC VA Hospital (Application No. 63/009,419). We applied this magneto-patterning strategy to create engineered cartilage tissues with native-like cell gradients. This advance permits us to engineer tissues with greater complexity than previously possible. Our findings were recently published in Advanced Materials1, and showcased as the cover image on December 3rd, 2020. In addition to this cover article, Hannah Zlotnick was interviewed on KYW NewsRadio, and a summary of the paper was featured in Advanced Science News, and Penn Medicine News. We are very excited about this work and we look forward to implanting our magneto-patterned cartilage tissues in a preclinical cartilage defect repair model in the coming year.

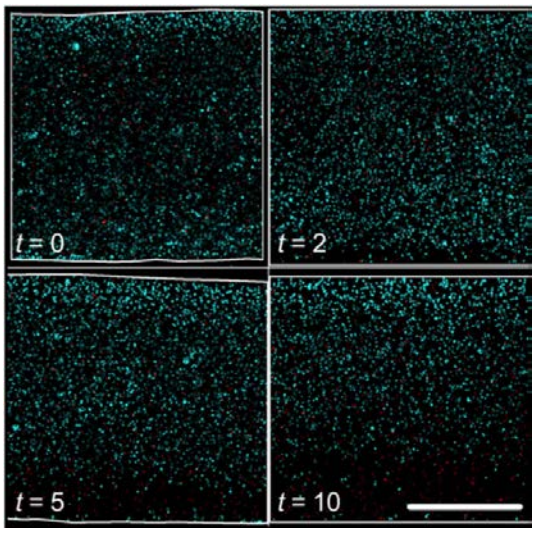


Figure 1. Cell magneto-patterning. Over time the cells (cyan) move upward, away from the magnet positioned underneath. t = time exposed to magnetic field (minutes). Scale bar = 500 μm.

Hydrogel-mediated reinforcement and sealing of cartilage defects

Over the past few years, we have developed a novel biomaterial system to stabilize damaged cartilage tissue. Our modified hyaluronic acid system is applied to cartilage tissue, diffuses in, and is crosslinked into place with a light source, fortifying the existing tissue. Moreover, we can introduce various biochemical and biophysical cues to this new environment. For example, we conjugated a peptide sequence that enhanced the adhesion and response of stem cells at the damaged cartilage surface and guided these cells towards the formation of a sealant layer with the intent of preventing further cartilage deterioration. Recently, with the support of the Penn Health-Tech Pilot Funding program, we conducted a pilot study in a large animal model (Yucatan minipig) and are currently finishing evaluation of the therapeutic benefit of our approach. This multi-phasic system (Reinforcement and Sealing) has already displayed promising outcomes, resulting in a pending patent application and the formation of Forsagen LLC, a startup company attempting to further translate and commercialize this technology.

Improving marrow stimulation techniques for cartilage repair

We have recently formed a new collaboration with sports medicine surgeon Jason L. Koh, M.D., from NorthShore Medical Group in Glenview, IL, and the team at Marrow Access Technologies. This group has recently developed a spring-loaded needle device (SmartShot) to improve upon traditional awl-based microfracture. Their device creates repeatable marrow stimulation holes that are smaller in diameter and deeper than awl-based holes. This collaboration has allowed us to compare the current clinical marrow stimulation strategies (mallet and awl, drill and K-wire) to the Marrow Access Technologies' needle-based device. For this study, we utilized a large animal model of cartilage defect repair. We found that the needle-based device reduces bone resorption typically observed post-microfracture (Figure 2). We also discovered that drilling with a K-wire leads to significant bone compaction around the hole site, and this compaction leads to delayed bony healing. The results of this study were presented at the recent virtual Orthopaedic Research Society Meeting in an abstract entitled, "Marked differences in local bone remodeling based on marrow stimulation technique in a large animal."

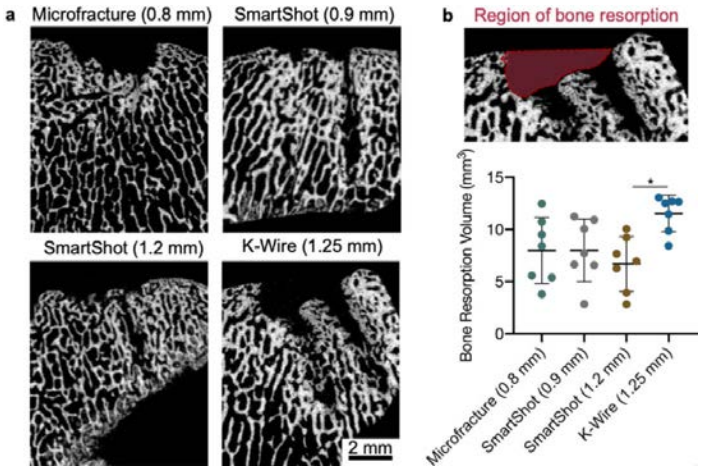


Figure 2. Global bony response underneath cartilage defects treated with different marrow simulation techniques. **(A)** Representative μCT images from each marrow stimulation group. **(B)** 3D quantification of bone resorption 4 weeks post-surgery. * $p < 0.05$.

Bioprinted composite scaffolds for cartilage repair

As part of a research consortium with the AO Foundation, we have recently developed fiber-reinforced hydrogels with the requisite mechanical properties and physiochemical properties to promote cartilage repair within focal defects. To create these composite scaffolds, we leverage melt electrowriting (MEW) to first form polycaprolactone (PCL) meshes composed of microscale fibers. Thereafter, precursor hyaluronic acid (HA) hydrogel components are filled within these PCL meshes before being cured via visible light crosslinking. The resultant composites possess compressive properties that are <50-fold larger than hydrogels alone and ,10-fold larger than PCL meshes alone. Since the HA hydrogel prevents PCL fibers from buckling under compression, the total load-carrying capacity of the scaffolds synergistically increases when hydrogels and meshes are combined together. Moreover, mesenchymal stromal cells embedded within these composites readily form and disperse extracellular matrix towards the formation of neocartilage. We are currently evaluating the therapeutic potential of these composite scaffolds in a large animal model (Yucatan minipig) of articular cartilage damage, and preliminary results for this ongoing study were recently presented at the 2020 World Biomaterials Congress Virtual Meeting in an abstract entitled, "Engineering MEW-Reinforced Hydrogels to Enhance the Mechanics of Cartilage Constructs."

Clinical Research

ROCK (Research in OsteoChondritis of the Knee) Prospective Cohort Study

The ROCK Prospective Cohort was created by the osteochondritis dissecans (OCD) study group, ROCK. ROCK is dedicated to determining the optimal treatment for OCD—a focal, idiopathic alteration of subchondral bone with risk for instability and disruption of adjacent articular cartilage that may result in premature osteoarthritis. Since its inception in 2013, the ROCK Prospective Cohort has become one of the largest cartilage cohorts in the world. This study aims to develop a comprehensive database of predictors and outcomes for patients who are diagnosed with OCD of the knee by following their course of care for up to 50 years. In addition to prior ROCK publications on the novel and reliable classification of OCD lesions and healing using x-rays[2,3] and arthroscopy[4], the ROCK group published a substantial work on the reliability of MRI features[5] last year. The Institutional Review Board-approved home of the cohort is the University of Pennsylvania under Principal Investigator James L. Carey,

M.D., M.P.H., and the study is now comprised of 26 surgeons and 29 research coordinators at 19 institutions across the country and throughout the world. Management of the study has also expanded to Children's Hospital of Philadelphia (CHOP) under Principal Investigator Theodore J. Ganley, M.D., who also currently serves as President of the ROCK study group. Penn serves as the compliance center for the ROCK Prospective Cohort and CHOP serves the data coordinating center. To date, there are over 1400 knees enrolled in the cohort. As enrollment continues, additional studies and analyses are underway, including a recently submitted descriptive epidemiology study of the first 1000 patients.

PEAK (PEdiatric Autologous cultured chondrocytes treatment of cartilage defects in the Knee)

As thought leaders in research on osteochondral defects, Dr. Carey and Dr. Ganley were invited by Vericel to lead a trial in accordance with the Pediatric Research Equity Act and to serve as Steering Committee members. The purpose of this investigation is to compare the efficacy and safety of MACI (autologous cultured chondrocytes on porcine collagen membrane) versus microfracture for treating patients with symptomatic articular chondral defects or osteochondral defects of the knee. The prospective, multicenter, open-label, parallel group FDA clinical trial will include 45 patients aged 10 to17 years who are randomized to receive either MACI or microfracture treatment. Randomization will be done in 2:1 ratio where 30 patients will be enrolled for MACI and 15 for microfracture. Currently, the accepted standard of care treatment for treating smaller osteochondral defects is microfracture. MACI treatment includes two steps where first a screening arthroscopy and cartilage biopsy are performed after ensuring at least one symptomatic knee lesion with a size of more than 2 cm2. The biopsy cells are sent to Vericel to culture chondrocytes and ultimately to seed them on the collagen membrane. The second step is implantation of MACI via arthrotomy within approximately 5 to 12 weeks from the initial biopsy visit. Patients within both arms are followed prospectively for 2 years post-treatment. Enrollment has been underway and, currently, CHOP has enrolled 8 subjects and Penn has enrolled 1 subject. CHOP leads nationwide enrollment of the trial despite delays and restrictions due to the COVID-19 pandemic.

Clinical Volumes

With respect to clinical care, the Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment remains one of the highest volume centers for autologous chondrocyte implantation and for meniscus allograft transplantation in the world. In addition, surgeons perform many cases of fresh osteochondral allograft transplantation, osteochondral autograft transfer, and microfracture (including autologous matrix-induced chondrogenesis). Second-look arthroscopy is performed when appropriate to assess healing and to refine function. The cartilage center attracts patients on a national and international level, which has been facilitated over the past year by implementation of virtual telemedicine visits.

Summary

Despite the challenges of a pandemic, the Penn Cartilage Center continued to serve as an intellectual common space for interdisciplinary education and research, linking basic science, translational studies, and clinical research.

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Medical Education in a COVID Era: The Role of Virtual Conference

Matthew Stein, MD, Samir Mehta, MD, L Scott Levin, MD, Derek J. Donegan, MD

The University of Pennsylvania Department of Orthopaedics has been at the cutting edge of both telemedicine as well as conferencing advancements since the drastic adjustments COVID required. A quick google search of "disruptive innovation + COVID" offers approximately 23 million hits—needless to say the COVID-19 virus was a disruptor of epic proportions. It did however serve as the genesis for unprecedented medical innovation. Within a matter of weeks, the standard operating procedures of hospitals needed to be recreated out of thin air with only the barest bit of information available concerning COVID itself. An entire discussion of this is outside the scope of this brief update. We will discuss the salient points of virtual conferencing and the beneficial effects we have noted it to have on both resident orthopaedic education as well as resident leadership and professional development.

As a result of the COVID-19 pandemic, many residency and fellowship programs implemented unique and creative solutions to continue required graduate medical education[1] while adhering to social distancing guidelines. These strategies include utilization of Google Hangouts for daily surgical lessons in anatomy and clinical practice[2], "platooning" residents into "active duty" and "working remotely" factions that allow focus on service and education respectively[3], attending-led discussions of high-quality surgical videos[4], and weekly morning, afternoon, and evening educational teleconferences[5]. It was unclear, however, how these virtual educational initiatives compared to traditional educational activities, how effective they were in accomplishing their educational goals, and how satisfied residents and faculty have been with those efforts.

At Penn, daily fracture conference and weekly subspecialty educational conferences that traditionally met in person were disrupted by social distancing restrictions in mid-March 2020. In order to continue educating our residents, we implemented both morning and evening teaching via a screen-sharing software platform on personal computers and mobile phones (BlueJeans or Zoom) (Figure 1, 2). The evening fracture conference at our institution was met with active participation and the resident response was enthusiastic. For this reason, we expanded the conference format with the support of the Orthopaedic Trauma Association. The conference was organized as a case-based imaging presentation similar to traditional fracture conference, supplemented by "chalkboard" discussions led by a rotating group of orthopaedic trauma faculty across the country. Virtual real-time polling questions were incorporated to assess learner knowledge during the case and to create discussion. Though we felt that the national conference was being well received we were unsure if this was simply a case of confirmation bias due to high attendance and enthusiasm of certain faculty and residents.

For this reason, we conducted a national survey to gauge resident and faculty perceptions of virtual fracture conference with very compelling results. The overwhelming majority (88%) responded that participation in the virtual fracture conference improved their overall educational experience;

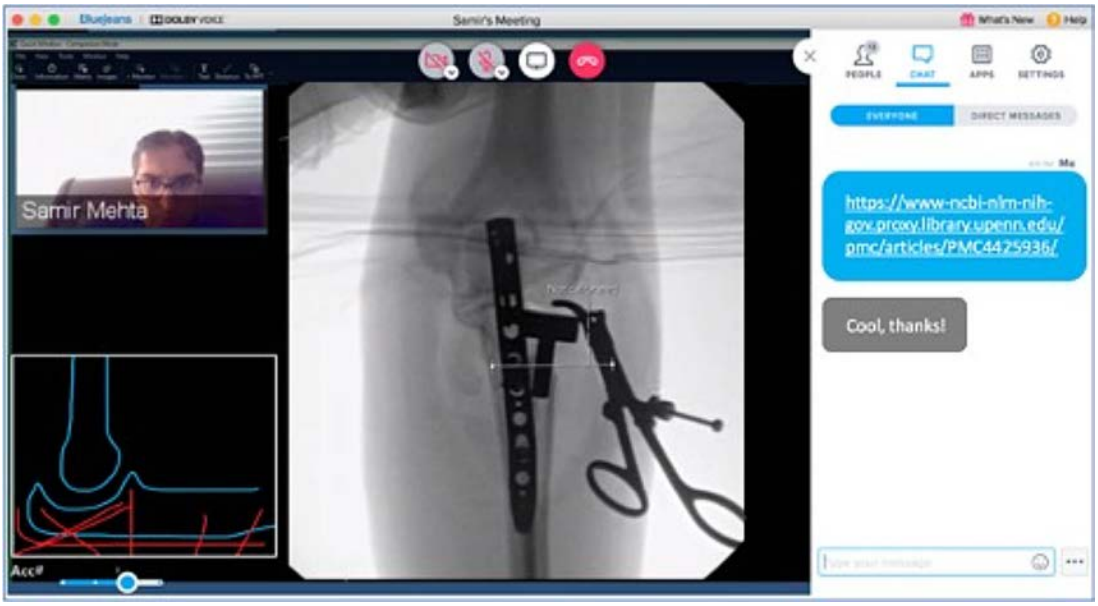

Figure 1.

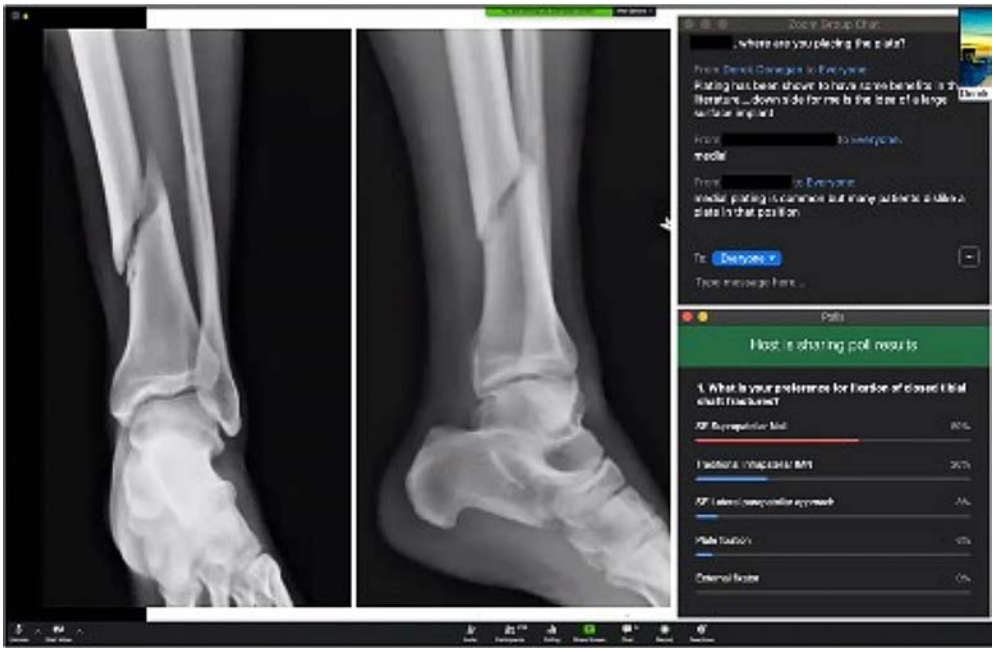

Figure 2.

47% noted moderate improvement and 41% noted significant improvement. Additionally, 100% of participants were likely to recommend this virtual conference to their colleagues, with 100% of participants also recommending continuing this conference even after the COVID-19 issues resolve[6].

Our yearly leadership forum also occurred virtually during 2020. In an effort to promote leadership as part of residency training, we have had the privilege of engaging and collaborating with the Wharton School at the University of Pennsylvania since 2017 to create an annual leadership program, with topics rotating on a four-year cycle. Over the course of two days, the program provides didactic training in leadership that provides an overview of leadership to residents. The formal program is supplemented by periodic grand rounds speakers in addition to a quarterly leadership 'journal club'.

In a serendipitous turn the first year we decided to collect data on the value of our leadership conference, it was forced to go virtually as a result of COVID. Early results were very promising. Survey of our residents' perspectives on the annual leadership conference showed that 100% of residents found value in the program, with 71% of participants finding it be of either excellent or very good value overall. In terms of value to their career development in particular 93% found it to be useful. 64% found it the career development potential to be extremely or very valuable. A majority of residents also found the speakers to be engaging with a high level of comfort in asking them questions concerning their specific content[7].

It remains to be seen if interest in our virtual conferences will remain as COVID-19 recedes, elective surgery resumes, and demanding clinical duties resurface. Unfortunately, we cannot predict either the future of COVID-19 or how learners will respond in a post-COVID learning environment. The COVID-19 disruption has accelerated our adoption of clinical innovations that have been years in the making. For example, rapid telehealth expansion has met a positive reception[8,9]. Evolution does not always occur in a steady or gradual manner but is more aptly characterized by eras of dramatic leaps and advances in times of unprecedented stressors. These innovations are re-shaping the realm of education as well. In the domain of orthopaedics this has led to the successful implementation of a weekly, national fracture conference, and leadership conference which residents find both educational and of high professional value. Even as clinical practice has resumed our national fracture conference continues to average 120-150 participants every Wednesday evening—another sign that virtual conferencing may remain a mainstay in the education of surgeons in-training.

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Providing Orthopaedic Care During a Pandemic

Andrew Kanoff, MHA[1], Sean Looby, MHA[2], Eric Hume, MD[3]

[1]Administrator of Practice Operations, [2]Director, Service Line & Network Integration, [3]Associate Professor, Director of Quality & Safety

As a specialty with primarily elective surgeries and a majority of patient issues that can be postponed in the short term, orthopaedics came to a screeching halt in mid-March 2020. To ensure we could continue to provide safe access to quality care, our clinical and administrative teams pivoted quickly, working tirelessly to reimagine our business model and re-engineer workflows and protocols. While elective surgeries at Penn Medicine were postponed in March and April, our steadfast efforts allowed us to begin rebounding in May when they reopened. Several key efforts helped us get back to business fairly quickly and continue to provide care throughout the pandemic.

Telemedicine

Prior to the pandemic, we had implemented a telemedicine pilot with several of our surgeons for post-operative visits. At the time, there was limited payer coverage and reimbursement for telemedicine services, and some questioned where and how it was appropriate in a hands-on specialty like Orthopaedic Surgery. We had some but limited traction, and most patients opted for in-person visits when offered telemedicine. But when March 2020 came along seemingly overnight payers, providers and patients all embraced telemedicine. We quickly pivoted to providing over seventy percent of our total visits via telemedicine for much of March and April. This allowed us to meet patients where they were, provide safe and efficient care, and continue to see new patients. While we have since transitioned back to primarily in-person visits, we have continued to examine the optimal use of telemedicine for the long term. Permanent payer policies and reimbursement will heavily influence how we move forward, but telemedicine in some fashion is here to stay.

Practice Operations

In May we began shifting back to more in-person visits, with strict practice protocols removing almost all patient interactions with support staff and streamlining everything other than the actual visit with a provider. The traditional flow of clinic was reimagined and we recognized almost all steps could be done fully remotely or with a hybrid model that significantly decreased face to face time. As shown in the flowchart below (Figure 2), we identified nine key steps in a patients' journey through the office and were able to convert five of those to fully remote, one to a hybrid approach, and eliminate one step almost completely. Before the pandemic it would have been unthinkable to run a day of visits with no one sitting in the waiting room, however we achieved and sustained this for months. Social distancing, masking, limiting support persons, and screening questionnaires were strictly enforced and effectively prevented the spread of COVID-19 between patients and our team, and amongst colleagues.

Surgeries

From mid-March through the beginning of May, elective surgeries were postponed, with only urgent and emergent orthopaedic cases being performed. During this period, a backlog of close to 1,500 surgeries built up across the Department of Orthopaedics. While elective surgeries weren't being performed, there was a fury of activity in the month of April in determining when and how to safely return to elective surgery in the face of COVID-19.

Much of this was informed by a scoring system developed by a team of investigators at the University of Chicago, which incorporated 21 factors balancing the patient's need for surgery and the risk of contracting COVID-19. The system, called

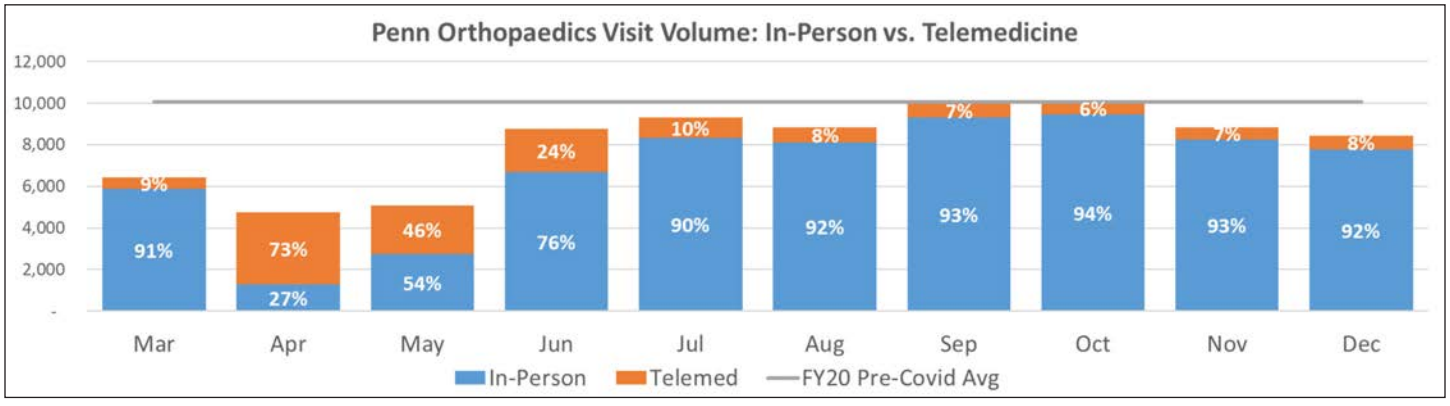


Figure 1

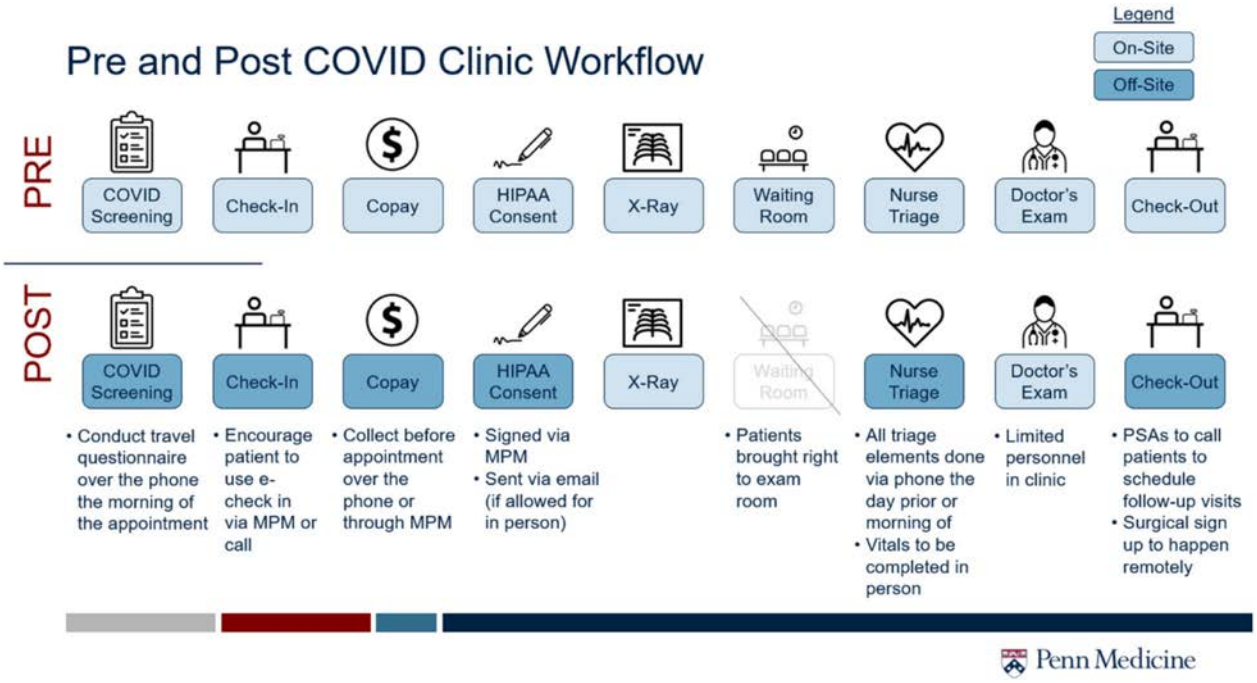


Figure 2

Medically Necessary Time-Sensitive (MeNTS) Prioritization, was published as an "article in press" on the Journal of American College of Surgeons website ahead of print on April 14. It quickly became a national standard and was widely adopted for empowering surgery departments to prioritize medically necessary operations that should not be delayed because of concerns about hospital resources or risk associated with COVID-19. Additionally, on April 17, the American College of Surgeons (ACS) published local resumption of elective surgery guidelines to help facilities to not only optimally provide safe and high-quality surgical patient care, but also to ensure that surgery resumes, and doesn't stop again. The 10 principles are highlighted in Figure 3.

Penn Medicine incorporated MeNTS and the ACS guidance and restarted elective surgery on May 4, 2020. A manual process was initially required for MeNTS scoring of each patient, which eventually became an on-line, Epic integrated tool. Figure 4 shows the number of backlog cases by division and the overall MeNTS score distribution across the Department of Orthopaedics.

Through the MeNTS scoring, optimal patients with fewer comorbidities and those likely to be discharged to home were prioritized. This allowed us to move forward while minimizing stress on the hospitals, post-acute facilities, and entire healthcare system. Pre-surgical COVID-19 testing was also implemented for all patients. Surgical cases during May through July were primarily these lower risk patients. With decreased risk of COVID-19 in Philadelphia and decreased stress on hospital systems, as of August 11 elective patients were scheduled based on our usual preparation and preoperative evaluations. Patients during this time period who had expectations for prolonged inpatient stays were

American College of Surgeons: Local Resumption of Elective Surgery Guidance (Released 4/17/20)	
COVID-19 AWARENESS	Know your community's COVID-19 numbers, including prevalence, incidence, and isolation mandates Know your COVID-19 diagnostic testing availability and policies for patients and health care workers
PREPAREDNESS	Promulgate personal protection equipment (PPE) policies for your health care workers Know your health care facility capacity (beds, intensive care units (ICUs), ventilators), including expansion plans (e.g., weekends) Ensure OR supply chain/support areas Address workforce staffing issues Assign a governance committee
PATIENT ISSUES	Patient communication Prioritization protocol/plan
DELIEVERY OF SAFE AND HIGH-QUALITY CARE	Ensuring safe, high-quality, high-value care of the surgical patient across the Five Phases of Care continuum

Figure 3

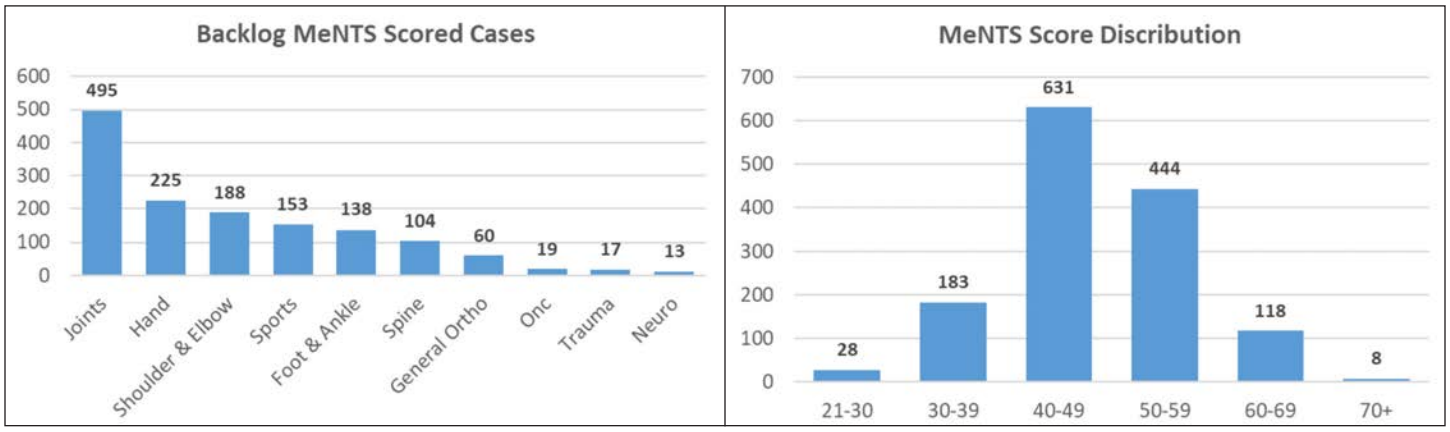
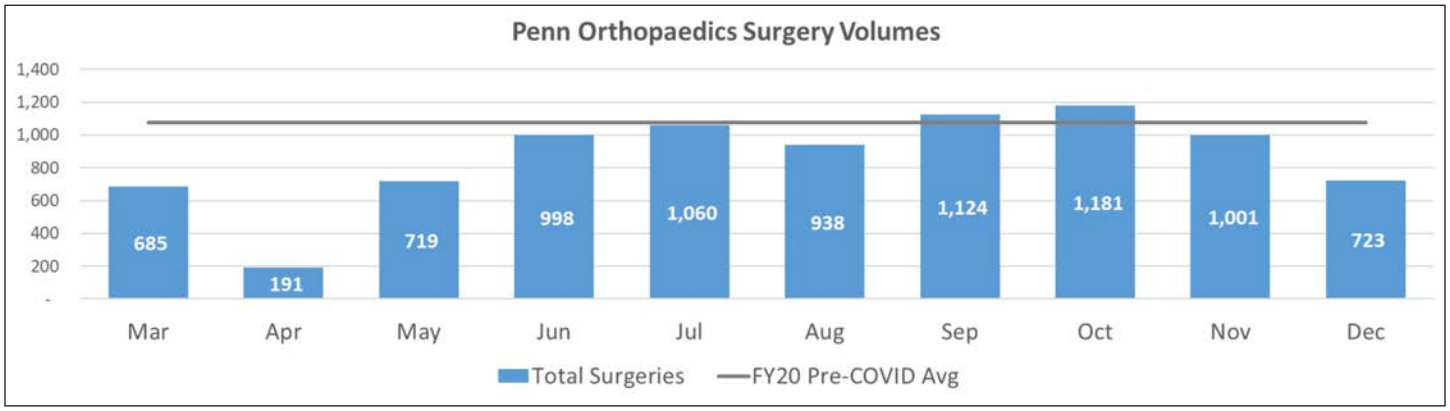


Figure 4

slowly phased back in, allowed for by a lower SNF census of COVID-19 patients. SNFs required COVID-19 testing inpatient before an admission even though all patients were tested preoperatively. With this the ability to operate on most of the available active patients was improved.

As COVID-19 cases increased in the early fall into winter, MeNTS prioritization was once again put in place effective December 1, 2020. Implementing this process through two major COVID-19 case spikes allowed us to safely treat our surgical patients while minimizing risk. These systems were effective in managing elective surgery through a complex year, with many protocols and innovations being harnessed long term.



Current Residents

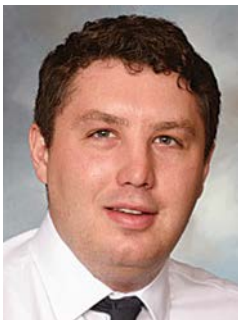
Clinical Year 5 Resident Spotlight

Gerald Andah, MD
Hometown: Pittsburgh, PA
Undergraduate: University of Pennsylvania
Medical School: Perelman School of Medicine University of Pennsylvania
Residency Highlights:
Future Directions: Arthroplasty at Montefiore

Chelsea Hendow, MD, MS
Hometown: Roslyn, NY
Undergraduate: Univ. of CA—Los Angeles
Medical School: New York Medical College
Residency Highlights:
Future Directions: Spine at Rothman Institute

Adnan Cheema, MD*
Hometown: Philadelphia, PA
Undergraduate: University of Missouri-Kansas City
Medical School: TUniversity of Missouri-Kansas City School of Medicine
Residency Highlights:
Future Directions: Shoulder/Elbow at Mayo Clinic

Christina Nypaver, MD
Hometown: Portsmouth, RI
Undergraduate: Univ. of Notre Dame
Medical School: Loyola Univ.—Chicago Stritch School of Medicine
Residency Highlights:
Future Directions: Hand at University of Chicago



Michael Eby, MD, MS*
Hometown: Springvale, ME
Undergraduate: University of Pennsylvaniat
Medical School: Georgetown University School of Medicine
Residency Highlights: .
Future Directions: Spine at Emory

William Ryan, MD
Hometown: Rochester, NY
Undergraduate: Muhlenberg College
Medical School: Drexel University
Residency Highlights:
Future Directions: Trauma at Carolinas Medical Center

*Indicates Resident is in the 6-year Research Track

Christopher Scanlon, MD, MS

Hometown: Beverly, MA
Undergraduate: Univ. of So. Carolina—Columbia
Medical School: Drexel University College of Medicine
Residency Highlights:
Future Directions: Arthroplasty at NYU

Matthew Webb, MD

Hometown: Atlanta, GA
Undergraduate: Harvard College
Medical School: Yale School of Medicine
Residency Highlights:
Future Directions: Arthroplasty at Stanford

Kimberly Stevenson, MD, MS

Hometown: Dallas, TX
Undergraduate: Univ. of Delaware
Medical School: Georgetown University School of Medicinel
Residency Highlights:
Future Directions: Arthroplasty at Utah

*Indicates Resident is in the 6-year Research Track

Clinical Year 4 Residents

Sarah Blumenthal, MD
Undergraduate:
Harvard University
Medical School:
University of California–Los Angeles

Matthew Counihan, MD, MS*
Undergraduate:
Univ. of Richmond
Medical School:
Drexel University College of Medicine

Agnes Dardas, MD, MSc
Undergraduate:
Harvard University
Medical School:
Washington University in St. Louis

Martin Griffis, MD
Undergraduate:
Temple University
Medical School:
Drexel University

Brandon Haghverdian, MD
Undergraduate:
University of California–Irvine
Medical School:
University of California–Irvine

Yehuda Kerbel, MD
Undergraduate:
La Salle University
Medical School:
Drexel University

Liane Miller, MD*
Undergraduate:
Univ. of CA—Santa Barbara
Medical School:
Univ. of CA—San Francisco School of Medicine

Eric Pridgen, MD, PhD
Undergraduate:
University of Delaware
Medical School:
Stanford University

Ivan Zapolsky, MD, MS
Undergraduate:
Tulane University
Medical School:
Tulane University

*Indicates Resident is in the 6-year Research Track

Clinical Year 3 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

George Fryhofer, MD, MTR*

Undergraduate:
Harvard University

Medical School:
Perelman School of Medicine at University of Pennsylvania

David Falk, MD

Undergraduate:
University of Michigan

Medical School:
George Washington University

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

Undergraduate:
James Madison University

Medical School:
Tulane University

Research Year

Brian Perez, MD

Undergraduate:
Rutgers University

Medical School:
Albert Einstein

Sachin Gupta, MD*

Undergraduate:
George Washington University

Medical School:
George Washington University

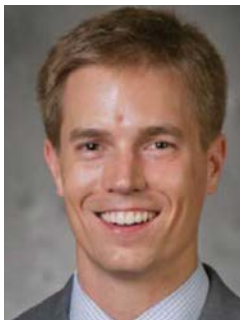
Matthew Stein, MD, MS*

Undergraduate:
Univ. of Maryland

Medical School:
Georgetown University

*Indicates Resident is in the 6-year Research Track

Clinical Year 2 Residents



Stephen Barchick, MD

Undergraduate:
Harvard University

Medical School:
Duke University

Jordan Cohen, MD*

Undergraduate:
University of Maryland

Medical School:
George Washington University

Joung (Richard) Kim, MD

Undergraduate:
University of Rochester

Medical School:
Icahn School of Medicine at Mount Sinai

Kendall Masada, MD*

Undergraduate:
University of Texas

Medical School:
University of Texas Health Science Center

Charles Lucas Myerson, MD

Undergraduate:
University of Southern California

Medical School:
Tulane University

Andrew Summers, MD

Undergraduate:
Portland State University

Medical School:
Oregon University

Kelsey Young, MD

Undergraduate:
Cornell University

Medical School:
Cornell University

Steven Zhang, MD

Undergraduate:
Cornell University

Medical School:
Stanford University

*Indicates Resident is in the 6-year Research Track

Clinical Year 1 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*

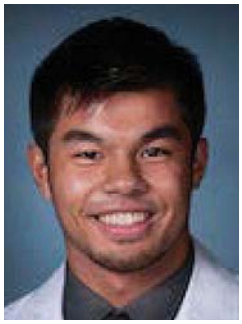
Undergraduate:
Perelman School of Medicine at the University of Pennsylvania

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

U·P·O·J

Current Fellows

August 1, 2018–July 31, 2019

Germanuel Landfair, MD
Adult Reconstructive Surgery

Christopher Odom, MD
Adult Reconstructive Surgery

Zachary Shirley, MD
Adult Reconstructive Surgery

Sunny Gupta, MD
Foot & Ankle Surgery

Corey Clyde, MD
Hand Surgery

John Roberts, MD
Orthoplastics & Limb Salvage

Alexnder Govshievich, MD
Shoulder & Elbo Surgery

Christine Piper, MD
Spine Surgery

Bilal Qutteineh, MD
Spine Surgery

Jay Reidler, MD
Spine Surgery

Thomas Byrnes, MD
Sports Medicine

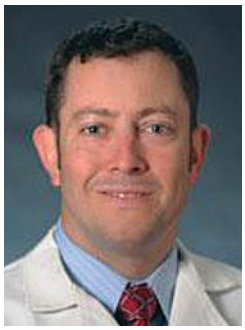
James Redshaw, MD
Sports Medicine

Orthopaedic Trauma & Fracture Service

Samir Mehta, MD

Orthopaedic Trauma Faculty

Samir Mehta, MD



Derek Donegan, MD, MBA

Susan Harding, MD

"Your Pace or Ours"

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

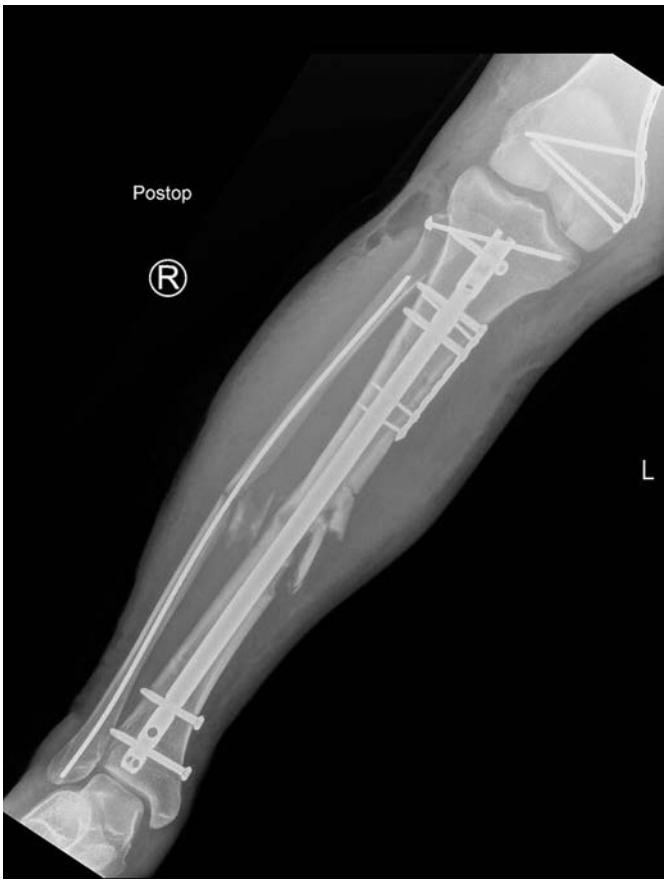


Figure 1

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 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. Additionally, the orthopaedic trauma service through the support of Dr Levin and the Health System is an integral part of the new Penn Orthopaedic Limb Salvage Center (POLSC). The orthopaedic trauma service is offering 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.

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 in 2020-2021, there are plans to continue our efforts in the Dominican Republic starting in 2022. 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 2). 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 transition. Dr Susan Harding, who was at Hahnemann University, transitioned 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. In addition, Dr Ahn has established himself at the University of Michigan as Chief of Orthopaedic Trauma and Vice-Chair of Education. We are not surprised at how quickly he has become successful there and hope he has carried a piece of the Penn Orthopaedic Trauma spirit with him.

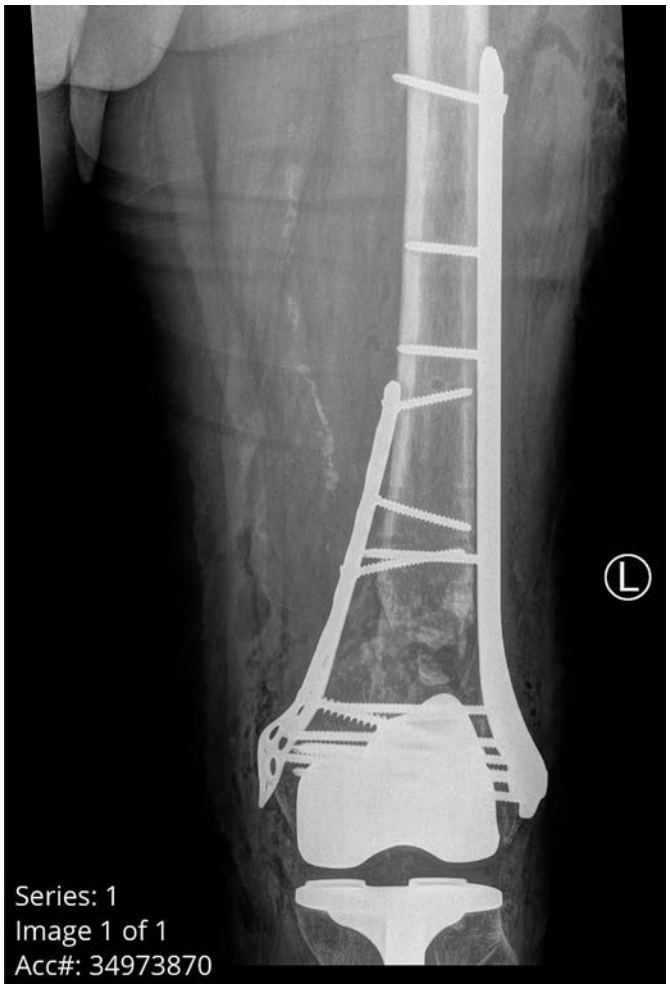


Figure 2

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 Division continues to grow, and, despite the challenges (of COVID) and the changes, we are looking forward to another momentous year of patient care, innovation, research, outreach and education.

Spine Division Update

Harvey Smith, MD

Spine Faculty

Harvey Smith, MD

Vincent Arlet, MD

Amrit Khalsa, MD

Comron Saifi, MD

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

Clinical Growth

Over the past year Drs. David Casper and Rush Fisher joined our division.

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.

Academic Productivity

Penn Ortho Spine has been represented in over 20 peer-reviewed publications, abstracts and presentations. Our faculty chair committees at North American Spine Society, 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. The spine fellows participate in the outreach program.

Spine Fellowship

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

Penn Sports Medicine Division Update

Brian Sennett, MD

Sports Medicine Faculty


Brian Sennett, MD


James Carey, MD, MPH


John Kelly, MD


Miltiadis Zgonis, MD


Kevin McHale, MD

The Sports Medicine Division at Penn Orthopaedics was challenged with the pandemics as youth, college, and professional sports moved to the sidelines for an extended period of time. Despite the effect of the pandemic on sports, the Division has continued to excel in their pursuit of clinical care, education and research, the year has been a banner year of relationships and contributions. While the Division of Sports Medicine has traditionally provided medical coverage for Penn Athletics, the University of the Sciences, and many local high schools, the Philadelphia Flyers and the Philadelphia Eagles have reached out to Penn Orthopaedics and the Division of Sports Medicine to provide care for their athletes. In addition, the Division now provides orthopaedic care for Drexel University as well.

Penn Medicine enters its second year as the medical and orthopaedic consultants for the Philadelphia Flyers and Wells Fargo Center. Penn Medicine provides medical services, including on-ice, orthopaedic, and general practice, and is also the preferred provider for Comcast Spectacor.

In addition to the partnership with the Philadelphia Flyers, the Philadelphia Eagles continue to be cared for by Arsh Dhanota. He serves as both the Head Team Physician and Chief Medical Officer of the Philadelphia Eagles. He was initially signed to a 3-year agreement which has already been extended to a 5-year commitment. He has been the guiding medical force behind the Philadelphia Eagles. In his first two years at the helm, he significantly decreased soft tissue injuries and improved the team's ranking in the category of "games missed due to injuries". He has done a stellar job not only in decreasing injuries but in transforming the medical care provided.

While the new professional team affiliations have dominated the news around the division, the cornerstone of cartilage restoration has continued to be one of the primary focuses with respect to all three areas of clinical care, research, and education. Dr. James Carey, Director of the Penn Cartilage Center currently serves as the lead Principal Investigator and Chairperson of the Clinical Steering Committee for the MACI Pediatric Study—PEAK (PEdiatric Autologous cultured chondrocytes treatment of cartilage defects in the Knee). In addition, Dr. Carey and Dr. Mauck ran the first virtual Penn Cartilage Repair Symposium in September with the greatest attendance ever

Other areas of expansion have continued with the addition of orthopaedic and sports medicine coverage to Drexel University and expansion at Penn Medicine at Radnor and local high schools. With the new expansion of Penn Medicine at Radnor, the footprint of sports medicine is growing. Dr. John Vasudeven, who along with Alexis Tingan provide coverage of our largest running events, will expand clinical and educational experiences for patients at the new Radnor facility. In addition, Penn Medicine, under the direction of Drs. Tingan and Vasudeven will be the official medical providers for the Broad Street Run to be held this October 2021. Lastly, Dr. Vasudeven also now serves as the Head Team Physician for the Archbishop Caroll Catholic High School.

It has been a busy year in the Division of Sports Medicine and we are glad to be back on the ice, fields, and courts. No matter what comes our way, we are ready to be teammates for Penn Medicine and all athletic individuals across the Tri-State region.

Hand Division Update

David Bozentka, MD

Hand Surgery Faculty


David Bozentka, MD


David Steinberg, MD


L. Scott Levin, MD, FACS


Hannah Hoeun Lee, MD


Robert Carrigan, MD


Apurva Shah, MD, MBA


Stephen Liu, MD

The Covid-19 pandemic has brought challenging times to the world this past year with the Penn Hand and Upper Extremity Service embracing the opportunity and emerging stronger in our clinical, research and educational programs.

We welcome Dr. Hannah Lee to the Penn Hand Surgery family. Dr. Lee joined the group as a clinician scientist this summer. She attended Cornell University obtaining her bachelors of science degree cum laude with a major in chemical and biomolecular engineering and a minor in biomedical engineering. Dr. Lee obtained her M.D./Ph.D. at the University of Pittsburgh working with Dr. Constance Chu M.D. She went on to complete her orthopaedic surgical residency and hand surgical fellowship at the University of Pittsburgh. Her laboratory work has included Cellular Approaches to Tissue Engineering and Regenerative Medicine with a focus on cartilage tissue engineering and an emphasis on cartilage repair and regeneration. Her research interest in translational regenerative medicine will be an excellent fit with the Penn musculoskeletal research group.

We congratulate our chairman, L. Scott Levin MD, who has been named the new Chair of the Board of Regents of the American College of Surgeons. Dr. Levin is the first hand surgeon in this role. He will work with the executive directory and board members of the ACS in formulating policy, while providing strong representation for hand surgery in the college.

The hand surgery fellowship continues its strong tradition under the leadership of David R. Steinberg MD as the director and Ines Lin MD as the associate program director. Our hand surgery fellows have had a solid clinical and academically productive year. Dr. John Roberts completed his plastic surgical residency at the Penn State Milton S. Hershey Medical Center in Hershey, PA. Following his fellowship year, John plans to continue his career in an academic setting with a goal of obtaining his master's in education. Corey Clyde MD completed his medical school training at the Sidney Kimmel Medical College at Thomas Jefferson University and orthopaedic surgical residency training at the University of Buffalo in Buffalo, NY. After his training, Corey also plans to pursue a position with his interests in clinical, academic and teaching endeavors. Our fellows from prior years keep in touch regularly. Dr. Jonathan Lundy MD, who recently completed his fellowship, has been working as a hand surgeon for the United States Army Institute for Surgical Research Burn Center and joined the upper extremity team at the adjoining San Antonio Medical Center. John was recently deployed to Iraq. We are all very proud of John. We know he embodies all the skills and knowledge to be successful and safe as we surround him with our thoughts and prayers during this admirable service to our country.

Although at the height of the pandemic elective clinical work was curtailed, the hand section continued to treat urgent traumatic injuries as well as 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 on-line format allowing members throughout the country to attend. We welcome all alumni to join the virtual conferences and add to our educational sessions.

The hand and upper extremity research team includes Annamarie Horan PhD, Director of Orthopedic Clinical Research, and our Clinical Research Coordinators Mary Dooley, Ashley Iwu and Evan Bannister. The team has been instrumental in advancing the numerous ongoing clinical research projects. The group is completing patient enrollment to evaluate digital tomo-synthesis for the detection and case management of scaphoid and distal radius fractures with a comparison to MRI or computed tomography. Enrollment has completed for the Axogen-sponsored study: A Multicenter,

Prospective, Randomized, Subject and Evaluator Blinded Comparative Study of Nerve Cuffs and Advance Nerve Graft Evaluating Recovery Outcomes for the Repair of Nerve Discontinuities.

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

The practice at Penn Medicine Radnor has moved across the street into a new state of the art multi-specialty outpatient facility. The building provides expanded office space and medical services with plans to open outpatient operating rooms in the future. Dr. Stephen Liu's practice at Chester County Hospital continues to expand. He will be increasing his work at Pennsylvania Hospital and outpatient surgery at the Tuttleman Center. Dr. Benjamin Gray has accepted a position at Kaiser Permanente in San Diego. We wish him well in his new endeavor.

The hand and upper extremity service could not function without the outstanding support from our superb advance 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

G. Russell Huffman, MD, MPH

Andrew Kuntz, MD

Gabe Horneff, MD

Despite the challenges brought by the pandemic, our division has had an outstanding year. The section's tertiary referral network has dramatically increased along with the complexity of cases. The pandemic provided an opportunity for us to expand our service, and solidify our academic and clinical missions. I am pleased to announce that Gabe Horneff, one of our former executive chief resident, and an established shoulder and elbow surgeon at The Rothman Institute joined our team. While growing his clinical practice, Gabe has immediately taken ownership of resident education for our division. Our indications conference has been expanded to include a nationwide group of our past fellows. Through a virtual platform, the group of talented sub-specialists re-unite monthly to discuss complex cases, opportunities for research and catch up on important life events.

Andy Kuntz is leading our research effort, setting a high standard for both research and clinical outcomes. With close collaboration with Lou Soslowsky and others in the McKay Research Laboratory, we help form one of the largest research laboratories in the world. 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, translation and basic science. We are currently rolling out an integrated research platform that will be able to seamlessly, 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 are working on several sponsored clinical trials, including two stemless reverse arthroplasty IDEs, an arthroplasty outcome study, a cementless elbow arthroplasty IDE, and 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. In conjunction with Mike Hast, we are testing biomechanical characteristics of a novel elbow ligament reconstruction technique. For Andy's efforts, he has been elected to 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.

Under the guidance of Russell Huffman, the fellowship has continued to thrive, attracting the most competitive candidates. 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. Additionally, now in its fourth year, and in collaboration with our French colleagues, we offer our fellow an opportunity to visit world leaders in shoulder surgery. Current fellow Christy Piper (F'21) will follow Greg Gomez (F'19), Josh Rogozinski (F'18), and Chad Myeroff (F'17), and spend three weeks visiting academic centers in Monaco and France. Robert Williams (F'20) was stuck with us during the shutdown. We have consistently matched our top choices. Past fellow, Mohit Gilotra (F'15) won the 2018 ASES Charles Neer award and several 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 Update

Charles Nelson, MD

Arthroplasty Faculty

Charles Nelson, MD

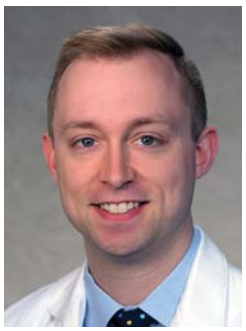
Craig Israelite, MD

Eric Hume, MD

Christopher Anthony, MD

Gwo-Chin Lee, MD

Neil Sheth, MD



Christopher Travers, MD

Vincent Moretti, MD

The 2020/2021 academic year has been a productive year for the Penn Orthopaedics Adult Reconstruction Division. Despite many of the challenges related to COVID-19, the adult reconstruction division has continued maintain high surgical volume and provide high quality despite caring for very high risk patients with innovative quality and safety measures. The annualized surgical volume this year for the total joint division remains over x primary and revision joint replacement procedures at the two down town hospitals.

In addition to clinical excellence, our faculty have remained active in 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 the American Associaton of Hip and Knee Surgeons, the American Orthopaedic Association, and the American Board of Orthopaedic Surgeons. Our faculty participated in more than 50 peer reviewed publications in 2020 and more than 50 scientific presentations or lectures by invitation. We have expanded our robotics program with two different robotic options at both of the downtown facilities expanding beyond robotic partial knee replacement to increased experience with robotic total knee and hip replacement procedures. The division remains active in clinical research with both significant federal and industry funding.

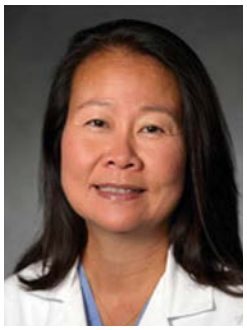
Despite the challenges of the COVID pandemic, our Adult Reconstruction has continued to grow. With the recent recruitment of Dr. Christopher Anthony with a special emphasis on Adult and Pedriatric Hip preservation, our division provides comprehensive Hip clinical care from cradle to grave. We have also recently recruited Dr. T. David Tarrity, a complex reconstructive fellow at the Hospital For Special Surgery, with an interest in complex revision joint replacement to further complement our faculty. The adult Reconstruction faculty members include Professors Charles L. Nelson, MD and Gwo Chin-Lee, MD, Associate Professors Eric Hume, MD, Dr. Craig Israelite, MD and Neil Sheth, MD and Assistant Professors Christopher Travers, MD, Christopher Anthony, MD, Vincent Moretti, MD and will soon also include T. David Tarrity, MD.

Foot and Ankle Division Update

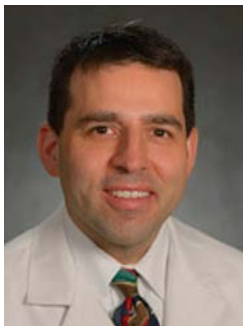
Casey Humbyrd, MD

Foot & Ankle Faculty

Casey Humbyrd, MD



Wen Chao, MD



Daniel Farber, MD

Anthony "Bobby" Ndu, 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 Update

Kristy Weber, MD

Orthopaedic Oncology Faculty

Kristy Weber, MD, FACS

Cara Cipriano, MD

Musculoskeletal Oncology at Penn: Continuous Evolution toward Excellence

The Orthopaedic Oncology clinical service at Penn is currently comprised of Dr. Kristy Weber as well as Sasha Mendez, Administrative Coordinator; Kate Barrie, PA-C; and Chrissy Vanella, RN. We are a key part of a larger multidisciplinary team who care for patients of all ages with bone and soft tissue tumors in all anatomic areas of the body. This includes the care of patients with benign and malignant primary tumors as well as patients with metastatic bone disease.

The multidisciplinary clinical team that treats patients with bone or soft tissue sarcomas now meets weekly in a virtual setting for a clinical care videoconference to discuss the presentation and differential diagnoses of new patients as well as the ongoing multimodal therapy for existing patients. Given the COVID gathering restrictions this year, we've actually increased participation in the virtual conference with ~25 different team members from Penn and its affiliated hospitals who are interested in bone and soft tissue tumors. A Sarcoma leadership group meets monthly to work on quality initiatives and clinical pathways to improve the overall delivery of care to our patients. Our primary quality metric this year is 'collection of pre-treatment biopsy samples for research' as we build a tissue bank of valuable 'untreated' specimens to study sarcoma. This can be compared to surgical resection specimens of sarcoma which have often been treated with preoperative radiation or chemotherapy. We also track other metrics such as 'time to biopsy' and 'time to new patient appointment'. Many of our patients can now get a 'same day' biopsy facilitated by our musculoskeletal radiology team which is a big patient satisfier.

Our Penn Sarcoma team profile has changed this year. Dr. Robert Wilson left Penn Ortho in December, 2020 to take a new position in Jacksonville, Florida that is affiliated with MD Anderson Cancer Center. We are sorry to lose a great surgeon-educator and wish Dr. Wilson and his family success in his next chapter. Dr. Ronnie Sebro, our radiology expert in musculoskeletal tumors has also left Penn. To balance these changes in our program, we will welcome Dr. Cara Cipriano from Washington University in St. Louis to be the new Chief of Orthopaedic Oncology on September 1, 2021. She is a nationally recognized expert in the treatment of patients with musculoskeletal tumors and is also fellowship trained in hip and knee replacement. She also has a passion for medical student education and will have a formal role in the Perelman School of Medicine. We welcomed Dr. Saeed Dianat as the new Director of Musculoskeletal Tumor Imaging in the Fall of 2020. Dr. Dianat completed his musculoskeletal radiology fellowship at Brigham and Women's Hospital in Boston and has a passion for quality improvement. In addition, the CHOP team of sarcoma scientists is growing with the addition of Dr. Ted Laetsch in September, 2020. He moved from UT-Southwestern and is the new leader of the CHOP Developmental Therapeutics Program. He previously trained at CHOP and will also be establishing a new Very Rare Malignant Tumors program.

The core sarcoma research team continues their work and has been productive with new publications, grants and awards. Drs. Karin Eisinger and Malay Haldar continue their RO1-funded projects in sarcoma and are constantly looking for additional grant funding. We have a monthly sarcoma research seminar with scientists working on the Penn Med, CHOP, and Penn Vet campuses. There are ongoing clinical trials for patients with soft tissue sarcoma with the SARC trial combining pembrolizamab and IMRT for undifferentiated pleomorphic sarcoma as well as a clinical trial for patients with desmoid tumors using nirogacestat. Additional human trials are in the pipeline for osteosarcoma, soft tissue sarcoma, and chondrosarcoma. The canine trial for dogs

with soft tissue sarcoma using an NFkB inhibitor is slowly accruing patients during the pandemic.

Finally, philanthropic support from grateful patients is critical for our research efforts and we are thankful for their generosity. In 2020, our patient and family Sarcoma Advocacy group raised over $110,000 to support sarcoma research at Penn Med/Penn Vet/CHOP despite changing at the last minute to a virtual event. This year the 6th annual event is May 23, 2021 and will likely be a hybrid live/virtual celebration at Wilson Farm Park in Wayne, PA and online for those who can't attend. www.stepstocuresarcoma.com/

Orthopaedic Oncology sites and upcoming lecture:

Patients are seen in person or via telemedicine 5 days per week with clinic locations at PCAM and Radnor. Surgeries are performed at HUP and CHOP (along with Dr. Alex Arkader). A collaboration with the Philadelphia Shriners Hospital to evaluate and treat patients with bone or soft tissue tumors has continued this year. The Penn Orthopaedic Oncology Visiting Professor for 2020, Dr. Carol Morris, Chief of Orthopaedic Oncology at Johns Hopkins, was postponed until we can have her visit in person.

Recent Publications:

1. **Stadtmauer EA, Fraietta JA, Davis MM, Cohen AD, Weber KL, Lancaster E, Mangan PA, Kulikovskaya I, Gupta M, Chen F, Tian L, Gonzalez VE, Xu J, Jung IY, Melenhorst JJ, Plesa G, Shea J, Matlawski T, Cervini A, Gaymon AL, Desjardins S, Lamontagne A, Salas-Mckee J, Fesnak A, Siegel DL, Levine BL, Jadlowsky JK, Young RM, Chew A, Hwang WT, Hexner EO, Carreno BM, Nobles CL, Bushman FD, Parker KR, Qi Y, Satpathy AT, Chang HY, Zhao Y, Lacey SF, June CH** CRISPR-engineered T cells in patients with refractory cancer. Science. Feb, 2020
2. **Ye S, Liu Y, Fuller A, Katti R, Ciotti G, Chor S, Alam Z, Lorent K, Devalaraja S, Weber K, Pack M, Haldar M, Eisinger-Mathason TSK**: TGFB and Hippo pathways cooperate to enhance sarcomagenesis and metastasis through the hyaluronan mediated motility receptor (HMMR). *Molecular Cancer Research,* 2020, Jan 27 (in press).
3. **Devalaraja S, To TKJ, Folkert IW, Natesan R, Alam MZ, Li M, Tada Y, Budagyan K, Dang MP, Zhai L, Lobel GP, Ciotti GE Eisinger-Mathason TSK, Asangani IA, Weber K, Simon MC, Haldar M**: Tumor-derived retinoic acid regulates intratumoral monocyte differentiation to promote immune suppression. *Cell*, 180:1098-1114, 2020.
4. **Othman S, Bricker JT, Elfanagely O, Azoury SC, Weber K, Kovach S**: Allograft alone vs. allograft with intramedullary vascularized fibular graft for lower extremity bone cancer: A systematic review and meta-analysis. *J Plast, Reconstr & Aesthet Surg*. 73:1221-1231, 2020.

Neuro-Orthopaedics Division Update Comprehensive Complex Care Complex Population

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 Orthopaedics at Penn and is one of a handful of orthopaedic surgeons nationally who cares for the spectrum of neuromuscular disorders in both adults and children. Dr. Baldwin works alongside Kerry Howrey, PA to provide timely care to adults who have suffered a traumatic brain injury, spinal cord injury, multiple sclerosis, cerebral palsy and a variety of other conditions. This includes direct work with well-known rehabilitation services both inside and outside the system including Penn Good Shepard partners, Moss Rehabilitation, Magee Rehabilitation, and Bryn Mawr rehabilitation among others.

On the Pediatric side, Dr. Baldwin works with David A. Spiegel MD to address the musculoskeletal needs in children with a variety of disorders such as Cerebral Palsy, Spina Bifida, Charcot Marie Tooth, Spinal Muscular atrophy, and others. They are supported by Kathy Abel CRNP and Jessica Staschak, who play a key role in serving this challenging population. Treating neuromuscular disorders is a team sport, and the neuro orthopedic team is large. The service partners with many other services within Penn Orthopedics to provide cutting edge and high-level care by partnering in the last year with the Adult Reconstruction service, the Hand and Upper Extremity Service, the Ortho Plastics Service, 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 a physiatry fellow last year and provides a supportive role in the education of Foot and Ankle, Pediatric and hand fellows.

On the pediatric this year we welcome a new partner, Dr. Chrissy Goodbody, MD. We look forward to building the service further with Dr. Goodbody. Additionally we have partnered with the Philadelphia Shrine to offer gait lab services as part of our Nurse Navigator patient outreach service to offer care to patients in other parts of the country and world, a service which, on the pediatric side has borne many fruits. We hope to add this service to our armamentarium on the adult side, as this is a good way to offer access to these unique services that Penn offers. Outreach to outlying institutions has been highly successful. Penn has become the "go to" service for neuro orthopedic care for much of the surrounding area with referrals coming from all major rehabilitations in the area.

The research program in neuromuscular orthopedics has been on the rise with publications in neuromuscular spine published in the Journal of Pediatric Orthopedics, Spine Deformity, and Journal of Bone and Joint Surgery. Publications in Single Event multilevel surgery in Current Orthopedic Practice, and publications in neuromuscular hip surgery in the Journal of Bone and Joint Surgery reviews. 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.

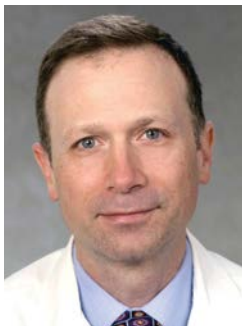
We have faced the challenges of the COVID 19 pandemic to bring care to this disadvantaged and often forgotten population of patients in a safe and effective manner, and look forward to continuing to provide them care to aid in functional recovery in the years to come.

Orthoplastic Approach to Limb Salvage: The University of Pennsylvania Fellowship Experience

Alexander Govshievich MD[1,2] and L. Scott Levin MD, FACS[1]

[1]Department of Orthopedic Surgery, University of Pennsylvania
[2]Department of Plastic Surgery, University of Montreal

Orthoplastic Limb Salvage Faculty



Stephen Kovach III, MD

L. Scott Levin, MD, FACS

Samir Mehta, MD

Reconstruction of complex extremity defects is a challenge for both Plastic and Orthopedic surgeons. Effective management and good patient outcomes rely on joint expertise, meticulous planning and a collaborative surgical approach. Despite being advocated as early as 1993, Orthoplastic limb salvage has not been universally adopted and remains the exception, rather than the norm.1 In most university healthcare centres worldwide, bony and soft tissue components of extremity wounds are being management separately, with little communication between the Orthopedic and Plastics teams and without clear inter-departmental treatment guidelines.

The Orthoplastic and Limb Salvage Surgery fellowship at the University of Pennsylvania is a new and unique training program aimed at bridging this gap. It provides graduating Plastic and Orthopedic surgeons the necessary skills and knowledge to develop a dedicated Orthoplastic division at their home institution. The fellowship covers the entire spectrum of extremity pathologies, including open fractures, chronic infections and osteomyelitis, infected prosthesis, post-extirpative defects, diabetic wounds and vascular wounds. In addition, aesthetic microvascular soft tissue resurfacing, vascularized bony reconstruction of hip avascular necrosis and vascularized composite allotransplantation of upper extremities are covered.

From the Orthopedic perspective, the fellow is exposed to the principles and techniques of skeletal stabilization using external fixation devices, internal fixation systems and intramedullary nailing. In addition, the fellow becomes accustomed to the surgical management of bone and joint infections and the use of antibiotic beads and spacers. From a reconstructive standpoint, restoration of segmental bone defects of using bone grafting and autologous free osseous flaps are implemented. Lastly, in case of failed salvage or patients not being candidates for complex reconstructive procedures, the Fellow is exposed to below knee amputations along with ancillary procedures such as targeted muscle reinnervation and regenerative peripheral nerve interface, which have been shown to decrease neuromas and phantom limb pain. 2

From the Plastic Surgery perspective, the fellow is exposed to the principles and techniques of adequate soft tissue debridement and coverage. There is ample opportunity to utilize the full spectrum of reconstructive techniques, ranging from local flaps, to regional flaps to microvascular free tissue transfer. The reconstructive elevator principle is applied to each case, warranting consideration of all reconstructive options, and choosing the one most likely to achieve the best long term functional as well as aesthetic outcomes.

In nearly 20 weeks of Fellowship, I participated in 26 flap procedures for extremity coverage, including 24 free and two pedicled flaps. The etiology of wounds stemmed from chronic infection / osteomyelitis (9), post trauma (9), infected prosthesis (4), post extirpative (3), diabetes (1). The wounds were located all over the body, including the arm (1), elbow (3), forearm (4), hand (3), knee (3), leg (7) and foot and ankle (5). This allowed familiarization with most major recipient sites, including the brachial, radial and ulnar arteries in the upper extremity and femoral, posterior and anterior tibial arteries in the lower extremity. Flaps consisted of the ALT (13), latissimus dorsi (6), lateral arm (3), radial forearm (1), medial femoral condyle (1), second toe (1) and gracilis (1). Harvesting these flaps provided invaluable experience in perforator dissection and subsequent microvascular

anastomosis, both under loupe magnification and the operating microscope. Limb salvage was successful in all but one patient, who developed persistent distal ischemia due to poor microcirculation, caused by end stage renal disease and poorly controlled diabetes.

In summary, this one-of-a-kind fellowship provides the necessary knowledge and skill in both Plastic and Orthopedic surgery aspects of limb restauration to successfully implement the Orthoplastic approach at an outside institution and develop a designated centre for limb salvage. Due to the complexity of these cases and the many intricacies and nuances they involve, the Penn Orthoplastic and Limb Salvage Fellowship program is an invaluable experience for anyone seeking to push the boundaries of extremity reconstruction.

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Corporal Michael J. Crescenz Philadelphia VA Medical Center

Richard E. Grant, MD

Joseph Bernstein, MD

Richard E. Grant, MD

Eric Hume, MD

Andrew Kuntz, MD

Vincent Moretti, MD

Harvey Smith, MD

David Steinberg, MD

A Series of Updates from the VA Orthopaedic Division

"Our goal was to document a typical period of resident involvement in VAMC PHL Orthopaedic surgical cases. We worked to obtain the surgical case data covering the period of September 2020 thru Feb 2021. We were able to identify 74 miscellaneous Orthopaedic surgical cases during that period, extending well into the relative height of the COVID 19 pandemic. We then searched for specific diagnoses and matching Orthopaedic surgical subspecialty cases completed during the same period. From September 2020 thru February 2021, the dates reflecting 6 months of OR experience, our team of attendings and residents were able to compete 26 carpal tunnel releases, 6 knee arthroscopies, 5 rotator cuff repairs, 4 ORIF of ankle fractures, 22 primary total knee arthroplasties, 28 primary total hip arthroplasties, 22 incisions of finger tendon sheaths, 6 removals of implants/ retained hardware, 4 staged total knee arthroplasty revisions, and 8 ulnar nerve transpositions. Considering the rates of improved vaccination numbers, we surely expect a significant increase in Orthopaedic surgical OR experience for all of our UPenn Orthopaedic residents as more veterans will begin to seek safe Orthopaedic surgical care. We are also excited about the recent faculty addition of Dr. Hannah Lee. Dr Lee is a new member of our VAMC hand and upper extremity services. Dr. Hannah Lee is pursuing innovative 'same day surgery 'techniques of trigger finger release under local anesthesia and minimally invasive CTR using advanced endoscopic technology."

Richard Grant MD
Chief of Orthopaedics

"The VA continues to serve as the home base for the Ortho-200 required rotation, though for the past year we were compelled to employ a Covid-related version of the course, with greater emphasis on distance learning. (Kudos to the education chief resident, Chelsea Hendow, for masterful scheduling and coordination.) The VA orthopaedic service has also implemented Covid-related instruction for residents, centered on the recently acquired arthroscopy simulator (kudos to Dr. Demaio for initiating this and to Dr. Grant for getting the lab up and running). Needless to say, this simulator will be a big part of resident education even when the pandemic ends. Of course it should also be noted that Dr. Joseph Bernstein received a CHERP (Center for Health Equity Research and Promotion) local grant to investigate hip fracture mortality."

Joseph Bernstein, MD
Professor of Orthopaedic Surgery
Sports Medicine,Arthroscopic Knee and Shoulder Surgeon

"I started performing endoscopic carpal tunnel releases and made small procedures under WALANT (wide awake local anesthesia no tourniquet) a norm at the VA. On the research front, I started collaboration with D. Kacy Cullen, a prominent nerve researcher, on peripheral nerve regeneration. Hoping to get national foundation as well as federal grants within a year."

Hannah Lee, MD
Assistant Professor of Orthopaedic Surgery
Hand Surgeon

"We continue to have a weekly shoulder clinic, providing care to veterans with all types of shoulder pathology from the Philadelphia area and surrounding satellite VA facilities. We also continue a weekly didactic teaching session with the residents on shoulder pathology and care. Residents are exposed to arthroscopic shoulder surgery and shoulder arthroplasty in the OR, and now have the ability to further practice arthroscopy skills in the scope lab. From a research stand-point, two separate manuscripts have been published in the past year as the result of research from prior SPiRE and Merit grant funding."

Andrew Kuntz, MD
Assistant Professor of Orthopaedic Surgery
Shoulder and Elbow Surgeon and Director Shoulder Study Group

Pennsylvania Hospital

Neil Sheth, MD

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.

Although the last academic year has presented unique challenges due to the COVID pandemic, 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 are no conducted virtually. We are hoping that in-person conferences will recommence during the 2021 academic year.

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 from various sub-specialties to populate the orthopaedic clinic in the Cathcart Building and the Farm-Journal Building. Among the sub-specialties represented are adult hip and knee reconstruction, foot and ankle, hand/plastic surgery, neuro-orthopaedics, shoulder and elbow, spine/deformity, sports medicine, and trauma. Notable for this past year, Dr. Christopher Anthony (hip preservation), Dr. David Casper (Spine), Dr. Gabe Horneff (shoulder and elbow), Dr. Casey Humbyrd (foot and ankle), and Dr. Rush Fisher (Spine) have been added to the roster at Pennsylvania Hospital. The arrival of these new Attendings 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. As of August 2020, the Adult Reconstruction service have expanded to 3 Fellows, spending 4 month blocks each at PPMC, PAH and Virtua. 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. The PGY-2 resident is still dedicated to Sports Medicine under the guidance of Dr. Miltiadis Zgonis.

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 50-60% of the orthopaedic patient volume coming through PAH. In addition, a new robotics platform is being offered at Pennsylvania Hospital. Pennsylvania Hospital is poised to be successful in the region as we continue to evolve.

Children's Hospital of Philadelphia Update

Divya Talwar, PhD, MPH and John Flynn, MD

Pediatric Faculty


John Flynn, MD


Jason Anari, MD


Alexandre Arkader, MD


Keith Baldwin, MD, MPH, MSPT

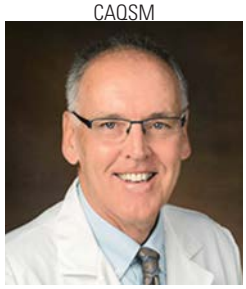

Naomi Brown, MD, FAAP, CAQSM


Patrick Cahill, MD


Robert Carrigan, MD


Benjamin Chang, MD, FACS


Richard Davidson, MD


Vincent Deeney, MD


Malcom Ecker, MD


Theodore Ganley, MD


B. David Horn, MD


J. Todd Lawrence, MD, PhD


Ines Lin, MD


Kathleen Maguire, MD


Christina Master, MD, FAAP, CAQSM, FACSM


Christopher Renjilian, MD

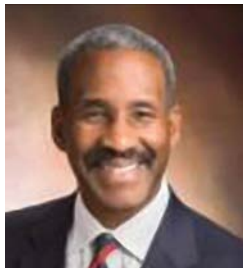

Wudbhav Sankar, MD


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 care to our patients, we have continued to expand our clinical, research, and teaching programs despite challenges due to COVID-19 pandemic. In 2020, US News and World Report ranked the Division of Orthopaedic Surgery 1st in the nation in pediatric orthopaedic surgery.

In 2020, CHOP Orthopaedics welcomed sports medicine pediatrician on our team, participated virtually in major conferences cancelled due to COVID, maintained enrollment of FDA Phase IIIb investigational drug trial and a feasibility device trial, published in more than 200 articles, obtained significant extramural funding from major funding agencies such as National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and National Science Foundation (NSF).

Clinical Program

Our orthopaedics faculty continues to expand and is currently comprised of twenty-nine Faculty, nineteen specially trained pediatric orthopaedic surgeons (fifteen operative and four non-operative), six sports medicine-trained pediatricians, two active plastic surgeons, and three transition-to-adult care faculty. Our division welcomed faculty member, Dr. Mary Daley. She obtained her medical degree from Albany Medical College, Albany, NY. Dr. Daley completed a triple board pediatrics residency from Tufts Medical Center, Boston, MA. She joins our program as a new sports medicine pediatrician with a subspecialty in sports psychiatry on our team.

Figure 1. Mary Daley , MD

Education Program

CHOP Orthopaedics currently funds four one-year clinical fellowships. The 2020-2021 clinical fellows are Chrissy Goodbody, MD (Figure 2); Jessica Heyer, MD (Figure 3); Stephanie Logterman, MD (Figure 4); and Stuart Mitchell, MD (Figure 5). This year's research fellow is Dr. Soroush Baghdadi, MD from Iran (Figure 6). While at CHOP Dr. Baghdadi has focused his research efforts on between basic science projects related to cartilage regeneration and clinical research focused on pediatric trauma, neuromuscular conditions, and sports injuries. We are excited to have Dr Goodbody join our team as an Attending Surgeon in pediatric limb deformity, foot/ankle and neuromuscular disorders in the upcoming academic year.

Due to COVID-19 restrictions, the Division rescheduled the Nicholson Visiting Professor Program and Annual Drummond Rising Star Visiting Professor Program. However, we hope to resume our educational activities in the upcoming year. All educational activities were not impeded and continued to be done remotely. The Division in early 2020 hosted visiting scholars to provide them with an opportunity to observe clinical care of pediatric patients in a high volume, academic setting.

Figure 2. Chrissy Goodbody, MD

Figure 3. Jessica Heyer, MD

Figure 4. Stephanie Logterman, MD

Figure 5. tuart Mitchell, MD

Figure 6. Soroush Baghdadi, MD

Research Program

Basic Science and Translational Research

This past year, our basic and translational medicine researchers led by Maurizio Pacifici, Ph.D. have made impressive progress and generated novel, exciting, and far-reaching insights on key aspects of skeletal biology and growth and pediatric musculoskeletal pathologies. Our pediatric musculoskeletal research lab 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. These biomedical research projects aim to advance current understanding of basic cellular, biochemical and genetic mechanisms that regulate the behavior and function of skeletal forming cells. These basic and key insights and observations are used to predict what may subtend and lead to pediatric pathologies including Multiple Hereditary Exostoses (MHE), Fibrodysplasia Ossificans Progressiva (FOP), Temporo-mandibular 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 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 200 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), Research in Osteochondritis Dissecans of the Knee (ROCK), SCFE Longitudinal International Prospective Registry (SLIP), The Fox Pediatric Spinal Deformity Study (Fox PSDS), Pediatric ACL: Understanding Treatment Operations (PLUTO), Medial Epicondyle Outcomes Multicenter (MEMO) study and International Hip Dysplasia Institute (IHDI). Investigators within the division have been awarded funding from both internal and external sources to conduct these studies. In 2020, the Division published over 200 articles in major orthopaedic journals, including JAMA, JBJS, Lancet Neurology, JPO, and CORR. Members across our division presented more than 130 presentations at international and national conferences last year alone.

The Division successfully continues to award the annual Benjamin Fox Fellowship Award for medical students who are interested in conducting a year of clinical research within orthopaedics. In July, Mitchell Johnson (Perelman School of Medicine at the University of Pennsylvania), Ryan Guzek (Sidney Kimmel Medical College at Thomas Jefferson University) and Max Cornell (Geisinger Commonwealth School of Medicine), were awarded with the fellowship (Figure 7-9).

Figure 2. Mitchell Johnson

Figure 8. Ryan Guzek

Figure 9. Max Cornell

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 co-PI from Penn Institute for Translational Medicine and Therapeutics (ITMAT) titled, "Development and testing of deep learning algorithms for segmentation on 4D MRI to understand changes in normal thoracic dynamics during childhood maturation".

Alexandre Arkader, MD was the Vice Chair for the Pediatric Orthopaedic Society of North America (POSNA) Educational Course Committee. He also serves as subcommittee 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 a number of 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.

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 continues as co-PI on Penn Institute for Translational Medicine and Therapeutics (ITMAT) titled, "Development and testing of deep learning algorithms for segmentation on 4D MRI to understand changes in normal thoracic dynamics during childhood maturation". 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, started his term as the Vice President of the American Board of Orthopaedic Surgery. Dr. Flynn is a co-editor of Lovell and Winter's Pediatric Orthopaedics, Rockwood's Fractures in Children, Operative Techniques in Pediatric Orthopaedics. He is a core member of Pediatric Spine Study Group and Harms Study Group; a multicenter collaboration of researchers studying care improvements for pediatric spine deformity surgery and serves on the Board for the Children's Spine Foundation. In the past year, Dr. Flynn was also invited as Graduation Speaker for OrthoCarolina Residency. 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, continued growth of clinical, research initiatives. Dr. Ganley has continued in several leadership roles with national organizations, such as the chairman for the POSNA Evidence Based Practice Committee, second vice president of the Pediatric Research in Sports Medicine (PRISM) group, co-founder and executive board member for the Research in Osteochondritis Dissecans of the Knee (ROCK) group, executive committee member for the American Academy of Pediatrics, advisory board member for the International Pediatric Orthopaedic Symposium, and program chair for the Philadelphia Orthopaedic Society. Along with his leadership roles, he continues to be actively involved in biomechanical studies utilizing cadaver specimens in collaboration with the Biedermann Lab for Orthopaedic Research and Human Motion Lab. 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. Dr. Additionally, he is the site leader for the FDA clinical trial for studying the efficacy and safety of autologous cultured chondrocytes on porcine collagen membrane (MACI).

John Todd Lawrence, MD, PhD continued his collaborative work with Dr. Leo Han at Drexel University. Funded by the National Science Foundation, the project focused on conducting in vitro studies for a novel cartilage repair strategy. 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 received a new grant as co-PI from NIH titled "A Low-Cost, Collaborative Tool for the Tracking of Youth Activities to Reduce Risk of Physical Injury".

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 the chair of the POSNA Fellowship committee and co-director of the International Hip Dysplasia Institute. He remains active in several study groups including Academic Network of Conservational Hip Outcomes Research (ANCHOR), SCFE Longitudinal International Prospective Registry (SLIP) and International Perthes Study Group (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 received Angela S.M. Kuo Memorial Award from POSNA for his research project "Opioid vs. Non-Opioid Analgesia in Pediatric Supracondylar Humerus Fractures."

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 and Director of Quality, Safety, Value, and Patient Experience in the Division of Orthopaedic Surgery. Dr. Wells currently serves as the President of Board of Directors for the Philadelphia Orthopaedic Society.

Brendan Williams, MD as new faculty member 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.

Penn Center for Musculoskeletal Disorders

Louis J. Soslowsky, PhD

Founding Director of the Penn Center for Musculoskeletal Disorders

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

The overall goal of this Center is to promote cooperative interactions among investigators, accelerate and enrich the effectiveness and efficiency of ongoing research, foster new collaborations and new research, and ultimately, translate our research efforts into better and new therapies for musculoskeletal disorders. The central theme of the Center continues to be "Musculoskeletal Tissue Injury and Repair". This theme is broad (as it includes all musculoskeletal tissue types, such as bone, cartilage, disc, ligament, meniscus, muscle, and tendon), focused (as takes advantage of commonalities in approaches across tissue types), and clinically significant (as it fosters development of assays, procedures and knowledge in pre-clinical animal and human models of translational relevance). It is important to note that our PCMD is not a "bone center" nor is it a "muscle center". Rather, it is truly a "musculoskeletal center" and has emerged as the recognized home for musculoskeletal research across the Penn campus and as a technical and intellectual resource for the broader Philadelphia musculoskeletal research community. Thus, the primary overall aims of this Center are to enhance and advance the research productivity of investigators in musculoskeletal tissue injury and repair by: 1) Providing innovation within critical resource core facilities in areas that cross disciplines, length scales, and hierarchies. These core facilities are mCT 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.

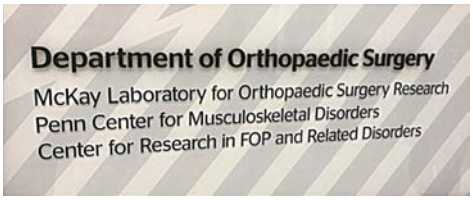
The Center currently has a membership of more than 158 faculty across five schools at Penn (Perelman School of Medicine, School of Engineering and Applied Science, School of Veterinary Medicine, School of Dental Medicine, and School of Arts and Sciences). We also now have 54 affiliate faculty members for more than 16 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 120 full- and part-time staff and trainees now in the labs. McKay is an active, thriving research and educational community committed to advancing basic and translational musculoskeletal research.

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 in which to grow our laboratory space, faculty, and research and training endeavors. We were also excited this year to recruit Dr. Sarah Gullbrand as our newest Assistant Professor, who is developing a program studying mechanisms of spine degeneration and regeneration, supported by both a Career Development Award and SPiRE Award from the Department of Veterans Affairs. We were equally excited, after an exhaustive search, to successfully recruit and welcome Dr. Ernestina Schipani, MD, PhD, in November 2020 as the inaugural WW Smith Professor of Orthopaedic Surgery! Dr. Schipani brings outstanding expertise in cartilage and bone development, hypoxia, and metabolism, and is already establishing herself as a leader in the lab and across the campus. Welcome to McKay, Sarah and Stina! Working in conjunction with the newly formalized departmental strategic plan, we are excited to continue to strategically grow our 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 >12.8% since 2016, despite flat and/or decreasing NIH pay lines. McKay has also ranked in the 'top five' of orthopaedic research for more than a dozen years, with Dr. Soslowsky has ranked in the top 5 individually for over a decade, and several other faculty members now ranked in the top 50 in the field. 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. Boerckel, Mourkioti, Baxter and Dyment together have brought in 6 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, fundable score in March 2021) over just the last two years. As these new research programs continue to mature, we expect that the Department will continue to rank in the top five and will increase in ranking relative to other programs. Finally, our Penn Center of Musculoskeletal Disorders (PCMD),

located within the McKay Labs and supported by an NIH P30, scored a '13' on its most recent renewal application (reviewed March 2021), and we are optimistic for its continued funding for another five years (years 16-20)! 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, Robert Mauck and Lou Soslowsky were named a Fellows of the Orthopaedic Research Society at the 2021 annual meeting. Our trainees also won numerous awards and prizes over the last year, including multiple Section Awards and New Investigator Recognition Awards at the 2021 Orthopaedic Research Society Meeting, Young Investigator Awards at the 2020 American Society for Bone and Mineral Research Annual Meeting, and multiple PhD and Masters' Competition selections at the 2020 Summer Bioengineering Conference, to name just a few. Faculty and trainees also regularly publish high profile papers in the leading journals of the field, and this is 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 year, 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. Likewise, we recently formed a Mckay International Outreach Committee (https://www.med.upenn.edu/orl/international-outreach-committee). This committee's mission is 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. This event provides an opportunity for trainees to present their work to the entire group and develop presentation skills. The goal of our collective work 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.

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

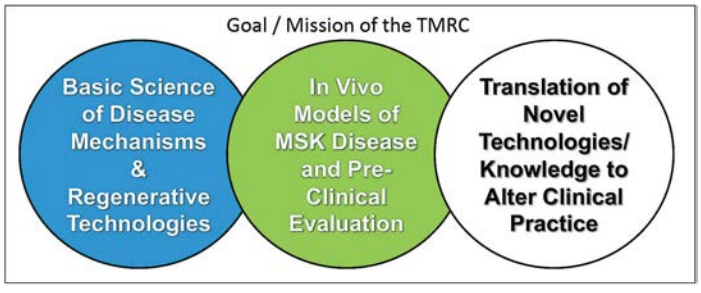
Directors: Carla R. Scanzello, M.D., Ph.D. and Robert L. Mauck, Ph.D.

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, MSK diseases and related disabilities are more prevalent in Veterans than in the general population. While improvements in armor and "in theater" medical care has introduced incredible life-saving technologies, an increasing number of our wounded soldiers return home with damaged limbs and joints. Also, as with any population, when veterans age, there is an increasing tendency to develop arthritis and various degenerative joint diseases, each of which can significantly compromise quality of life. In response, the Department of Veterans' Affairs has focused research efforts to improve our understanding of the function of MSK tissues and injuries that occur to them. 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 to enhance tissue repair, regeneration, and ultimately function. This was named the Translational Musculoskeletal Research Center, which has grown over these past 7 years to be a research enterprise comprised of 18 Principal Investigators including 2 new junior members, 10 full-time VA employees and more than 35 WOC employees.

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 from 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 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 Research Enterprise 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. This year has seen several new grants from both VA and NIH sources including a new Career Development Award-2 (CDA-2) to Dr. Sarah Gullbrand that is focused on novel disc and spine regenerative approaches and a CDA-1 Award to Dr. Jay Patel, focused on cartilage repair. Dr. Robert Mauck was also awarded a VA Career Scientist Award, and both Drs. Sarah Gullbrand and Dr. Mauck were awarded VA SPiRE Awards. Dr. David Steinberg was awarded a new VA Merit Award focused on articular cartilage regeneration and Dr. Harvey Smith renewed a Merit Award focused on disc tissue engineering. Grant funding at the VA TMRC totals more than $2.5 million dollar in direct costs.

The ultimate goal of the TMRC is to develop a focused, internationally recognized research center at the CMC VAMC. 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.

Human Motion Lab

Josh Baxter, PhD

The Human Motion Lab continues to work closely with our clinical colleagues to address unmet clinical needs. Our research focuses on Achilles tendon injuries using small animal experiments and observational patients studies. We use wearable sensors, motion capture, ultrasound imaging, and musculoskeletal modeling to establish and improve exciting new frameworks to continuously monitor structural and functional progress in patients who are treated in the Orthopaedic Surgery clinics at Penn Medicine. Despite the challenges of COVID-19 this past year, our lab has thrived. We were awarded 2 NIH grants, a PCMD pilot grant, and an American Orthopaedic Foot and Ankle Society (AOFAS) research grant. We also started new collaborations with researchers at the University of Delaware and Washington University in St. Louis.

We are excited to begin a new clinical research study on patients with Achilles tendinopathy that is supported by the National Institutes of Health (R01AR078898). This study will investigate the effects of tendon mechanical loading on tendon disease state, healing, and outcomes. Treating Achilles tendinopathy is challenging in part due to the wide range of disease severities and presentations seen in the clinic. To account for this variation, we are leveraging machine learning to identify patient subgroups to better guide treatment. Our recent study published in the journal Medicine & Science in Sports & Exercise ranked common rehabilitative exercises for patients with Achilles tendon pain. By continuously monitoring patients during daily living, we will capture the cumulative tendon loads they experience. This will provide a never-before-seen picture of how our daily activities of real-life impact—for better or worse—tendon health across a diverse group of patients.

In addition to growing our clinical research effort, we also are studying the effects of mechanical loading on Achilles tendon ruptures using a small animal model. Dr. Baxter received funding through the NIH (K01AR075877) and the PCMD (P30AR069619) to investigate how Achilles tendon ruptures stimulate muscle remodeling and tendon elongation. Then, he will determine how joint immobilization can most effectively be used to promote tendon healing and preserve muscle function. We are running a parallel clinical study supported by the AOFAS to characterize tendon loading biomechanics throughout healing in patients. We expect these studies will identify rehabilitative loading guidelines and ultrasound imaging benchmarks to inform personalized treatment.

Our group published 6 papers this past year. We have developed new techniques to monitor patient function outside of the traditional laboratory setting, which we expect will expand our reach and impact on musculoskeletal patient research. We also teamed up with researchers and the University of Delaware and Washington University in St. Louis to understand the varying implications of Achilles tendon ruptures on function. In this study, we found that although patients restore most of their functional strength during tasks like jumping, their ankles can operate through a reduced range of motion. These findings highlight the importance of rehabilitative care to restore plantar flexor function that will translate to improved return to activity outcomes.

We are excited to continue our clinically-relevant research to improve patient care, advance our fundamental understanding of musculoskeletal biomechanics, and educate the next generation of leaders in clinical care and research.

Recent Work

1. **Schmidt EC, Hullfish TJ, O'Connor KM, Hast MW, Baxter JR.** Ultrasound echogenicity is associated with fatigue-induced failure in a cadaveric Achilles tendon model. J Biomech [Internet]. 2020 May 22;105:109784. Available from: http://dx.doi.org/10.1016/j.jbiomech.2020.109784 PMID: 32278525
2. **Drazan JF, Hullfish TJ, Baxter JR.** Novel isodamping dynamometer accurately measures plantar flexor function. J Biomech [Internet]. 2020 Oct 9;111:110015. Available from: http://dx.doi.org/10.1016/j.jbiomech.2020.110015 PMID: 32891810
3. **Hullfish TJ, Baxter JR.** A simple instrumented insole algorithm to estimate plantar flexion moments. Gait Posture [Internet]. 2020 Jun;79:92–95. Available from: http://dx.doi.org/10.1016/j.gaitpost.2020.04.016 PMID: 32388057
4. **Hullfish TJ, O'Connor KM, Baxter JR.** Instrumented immobilizing boot paradigm quantifies reduced Achilles tendon loading during gait. J Biomech [Internet]. 2020 Aug 26;109:109925. Available from: http://dx.doi.org/10.1016/j.jbiomech.2020.109925 PMID: 32807329
5. **Baxter JR, Corrigan P, Hullfish TJ, O'Rourke P, Silbernagel KG.** Exercise Progression to Incrementally Load the Achilles Tendon. Med Sci Sports Exerc [Internet]. 2021 Jan;53(1):124–130. Available from: http://dx.doi.org/10.1249/MSS.0000000000002459 PMID: 32658037
6. **Zellers JA, Baxter JR, Gravare-Silbernagel K.** Functional ankle range of motion but not peak Achilles tendon force diminished with heel-rise and jumping tasks after Achilles tendon repair. Am. J. Sports Medicine. [Accepted—ahead of print].

Clinical Research Section

Annamarie D. Horan, MPA, PhD

The Year 2021 has been a year of change, adaptation, and resilience for the Penn Orthopaedics Clinical Research Program in parallel with the Department, the Institution and the larger community. Clinical Research activity at Penn Orthopaedics was brought to a temporary halt in March of 2020 preparatory to the clinical response to the COVID19 pandemic. Staff worked with Sponsors and faculty to ensure the safety of our research participants during this unprecedented time. We the clinical research staff echo all the pride that has been directed at our clinical and administrative staff in response to the pandemic and its impact on clinical operations and the continuity of patient care for both emergent and elective populations.

As clinical research always runs parallel to care, the Clinical Research Team and PIs had to overcome significant logistic challenges to keep pace with the ever changing physical and technical barriers of each day. Sponsors once eager to begin new work put new studies on indefinite hold. Existing studies each had to either adapt to virtual visits or suspend activity until in-person contact was permitted. All changes to protocols always require regulatory approval, and the team worked diligently with Sponsors, faculty, and the IRB to achieve operational success. At the same time, the Institution focused effort on prioritizing COVID19 related and other life-saving research.

Staff Update. Each year, our Team changes a little as many of our CRCs mature in their careers and seek other opportunities either to further their education or to take more advanced positions at Penn or in Industry. This year, we have had to adapt to these normal transitions in the wake of a University-wide hiring freeze anticipatory to the financial losses from the pandemic. We are very happy to congratulate the success of Christine Wojciechowicz, former Adult Reconstruction CRC, and Shawn Simmons, former Sports Medicine CRC, for their successful admission into Medical School for Fall 2020. We are also very proud of Evan Bannister who formally served the Department as a CRC for Trauma, Sports Medicine, and Shoulder & Elbow Divisions and informally cross covered studies in every other Division. Evan accepted an Industry position and left Penn in September, 2020. Renee Jurek, long time CRC in the Division of FOP has stayed within Penn but moved on to the Department of Epidemiology & Biostatistics. Most recently, Warren Harding, former CRC at PAH who served Foot & Ankle, Spine, and Adult Reconstruction Divisions, accepted a promotion in rank and has transitioned into the Department of Anesthesiology & Critical Care. All of these Team members will be missed as their contributions to the Department were significant. The search for new staff is underway.

Adult Reconstruction still has 11 active funded studies. All of these were temporarily paused or quickly adapted to the virtual visit model. Helena Moses had been working from home but was one of the first non-clinical people to return to the office when elective surgeries were permitted at PPMC. The myMobility study (NCT03737149) led by Dr. Israelite and the PCORI funded PEPPER study (NCT02810704) led by Dr. Nelson remain our largest projects in regards to targeted enrollment. Other PIs such as Drs. Hume, Lee, Sheth, and Travers also have active funded projects at various stages.

Foot & Ankle has maintained 3 funded projects through the pandemic, though one, the longest running, STAR study (NCT01284283) has come to its planned end with the last subject completing their last visit this year. This Division has welcomed a new Chief, Dr. Casey Humbyrd, and we have already benefited from her presence in the Divisional Research meetings. The Fellows in this Division are engaged and active and work closely with Dr. Mary Dooley to stay on track with compliance. The position recently vacated by Warren Harding will need replacing as the PAH Campus is energetic and poised for productivity. We also look forward to working with Dr. Anthony "Bobby" Ndu who trained in this Division as a Fellow. Dr. Ndu was active in Clinical Research during his Fellowship so we expect he will rejoin us with that same level of energy and engagement!

FOP. It is difficult to say enough about Team FOP. Despite the immediate shutdown of patient contact activities due to the pandemic, the tireless search for every conceivable approach to conquering this disease continues. Drs. Kaplan and Al Mukaddam have wrapped up the Natural History Study (NCT02322255) this year and prepare for additional investigations with Palovarotene (Ipsen https://www.ipsen.com/). They are also about to complete a study using the investigational product REGN2477 (Regeneron Pharmaceuticals, https://www.regeneron.com/) (NCT03188666). The FOP Program is still supported by Katherine Toder, Project Manager, and Kamlesh Rai.

Hand Surgery remains one of our most active and financially sound Divisions. Dr. Mary Dooley and Ashley Iwu continue to support this Division. Mary is known well throughout the Department as she assists in nearly every Division in some capacity. Ashley has also cross covered the Division of Trauma. Dr. Bozentka's Axogen Nerve Cuff Study (NCT01809002) is complete at our site and globally has fewer than 20 patient visits remaining for completion. Dr. Scott Levin is the Global PI on this study. Dr. Levin also serves at the Global PI on the Polyganics Sponsored Protect Neuroma study (NCT02993276) for which Dr. Gray is the local PI. The Polyganics study is complete and Dr. Levin is working on the

manuscript. We are very excited about how this positions our site for future work in Hand Research. Dr. Steinberg recently completed enrollment for an Investigator Initiated Trial funded by GE Healthcare which evaluates the use of Digital Tomosynthesis vs CT or MRI scanning when wrist fracture is suspected. The outcomes will be forthcoming. It is with extreme pride that we also report that Dr. Levin's Team has successfully enrolled all eligible adult Hand Transplant recipients and candidates in screening, into his DOD funded Qualitative Research Study (W81XWH1820067). This groundbreaking work wherein Dr. Levin serves as a partnering PI with Dr. Scott Tintle (Walter Reed Medical Center) and Dr. David Tulsky (University of Delaware) is capturing data that will assist all providers in the Hand Transplant selection, treatment, and recovery process garner a fuller understanding of this complex experience from the clinician and patient perspectives. This work and all of Dr. Levin's ceaseless efforts in this focus area will forever mark Penn Orthopaedics as a foundational leader in the world of Vascularized Composite Allograft Transplantation.

Shoulder & Elbow has developed a strong Clinical Research presence over the past 10 years with 5 funded studies currently ongoing. Currently, all studies in Shoulder & Elbow are led by Dr. Kuntz as PI, though there are pending projects for Dr. Huffman anticipated for FY21. We welcome Dr. Tamara Rial to the Shoulder & Elbow Division as the new Clinical Research Coodinator supporting this Division. Dr. Rial joined us in February 2021 and we look forward to her contributions to the Division and our team.

Spine continues to grow its Clinical Research program. The ViviGen Cellular Bone Matrix study (NCT02814825) is drawing to a close as all patients have completed all visits. "An Assessment of P-15L Bone Graft in Transforaminal Lumbar Interbody Fusion with Instrumentation" (NCT03438747) continues to be open to enrollment and we look forward to new funded work being initiated shortly that is driven by a collaboration between Dr. Smith and Dr. George Dodge (McKay Laboratory). We look forward to reporting on these studies in the next issue. The Spine Division also welcomes Dr. David Casper as the new Chief of Clinical Research. Dr. Casper has jumped into this role with both feet and has been having bi-weekly research meetings.

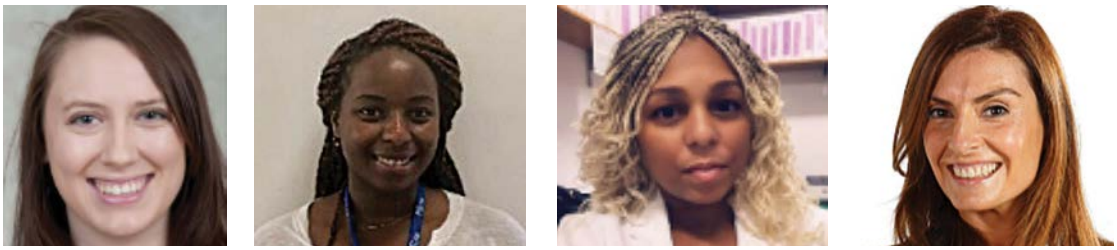
Sports Medicine has maintained the majority of their repertoire of active funded projects and Dr. Carey continues in his role as the Local and Global PI on the Vericel sponsored PEAK study (NCT03588975). The ROCK longitudinal study is transitioning operationally to CHOP. The loss of Shawn Simmons was impactful for this Division and the replacement of his role has been a top priority. A successful match is pending. Dr. Kelly has established a formal collaboration with Dr. Dodge and at least one new study is pending and will start shortly. Drs. Sennett and Zgonis continue to engage in both funded and investigator initiated projects.

Ortho Trauma continues to remain a leader in Clinical Research. Dr. Mehta is the PI on 3 grant funded projects. Two of these projects are funded by the AO Foundation through Virginia Commonwealth University (1 is Investigator Initiated and 1 is AO Initiated). The third, is a PCORI funded project through the University of Maryland which has recently closed to enrollment. We look forward to initiating a new Industry-sponsored, ICU focused project during FY22. During this year the Division has also said farewell to Dr. Jaimo Ahn who will be sadly missed. Dr. Donegan remains active in both clinical and nonclinical research. Dr. Mehta also serves as the Medical Director of Clinical Research and has done an outstanding job of supporting our Team in every area of the research, administrative, and logistical processes that the work requires. We thank him for his indefatigable energy and leadership.

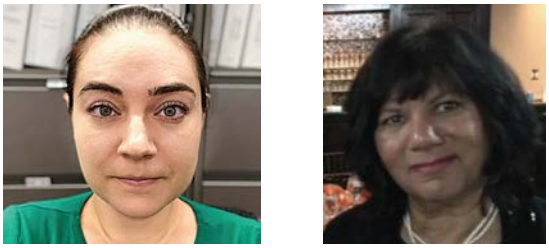
Collaborations. Inter-Divisional and Inter-Departmental collaborations have continued to thrive and new relationships have developed during the past year. The Departments of Orthopaedic Surgery and Anesthesia & Critical Care continue their synergistic relationships. Highlights include recently awarded 1R21NR019047-01A1 (NIH/NINR, PIs Cheatle & Compton,) which features Drs. Charles Nelson and Nabil Elkassabany as Key Personnel on the study team. This project will include the development and preliminary efficacy testing of a targeted cognitive-behavioral therapy (CBT) opioid taper intervention delivered in the 4 weeks immediately prior to planned TKA to mitigate pre-operative risk factors for chronic post-surgical pain. The PCORI sponsored REGAIN Trial (NCT02507505) (PI, Dr. Neuman) trial has reached complete enrollment with randomization of their 1,600th patient on Feb 18, 2021! Congratulations to Dr. Mark Neuman and the REGAIN Team for this amazing accomplishment! Multiple other similar relationships are either being activated or are in discussion.

Thank you to all the named and unnamed staff and faculty on our team, the residents, fellows, and other clinical support staff, and the leadership of Penn Orthopaedics and Anesthesiology & Critical Care for their ongoing support of our team. Specifically, we thank the Chairs, Drs. Levin and Hanson, the Vice-Chairs for Research, Drs. Soslowsky and Eckenhoff, as well as the Chief Operating Officers, Neil Ravitz and Kathryn Stamps, and BAs Cherie Jester and Cindy Bliven for your ongoing support throughout the year.

Orthopaedic Surgery Clinical Research Team



FOP Clinical Research Team



FOP Clinical Research Team

Figure 1. FY21 Orthopaedic Surgery + Anesthesiology & Clinical Research Teams. Top row: Mary Dooley (Cross covering most Divisions), Ashley Iwu (Primary Hand, cross covering Trauma), Helena Moses (Adult Reconstruction, PPMC), Tamara Rial (Shoulder & Elbow). **Middle row.** Katherine Toder, Kamlesh Rai (Not pictured, Giacomo Pazzaglia). **Bottom row:** Aliaksei Basatski, Annie DiLisio (on Active Duty Military Leave at this writing), Cassandra Dinh, Warren Harding.

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 Resarch
Orthopaedic Surgery and Anesthesiology & Critical Care

Staying the Course During COVID-19 MSKR Service Line

Sean Looby, MHA

Director, Service Line & Network Integration, Musculoskeletal & Rheumatology Service Line

The Musculoskeletal and Rheumatology (MSKR) Service Line is driven by multidisciplinary partnerships across departments, divisions, clinicians, administrators and various other supporting cast members. Our disease team structure and the regular meetings for each are the primary vehicles and forum that drive quality and cost efficiency goals and efforts forward on a continuous basis. Our annual goals, set at the beginning of each new fiscal year, provide a roadmap and guide to the primary objectives we set our sights on and hope to achieve throughout the year.

Like every other facet of our lives, much of this well-oiled machine came to a halt in March 2020. March and April were largely consumed with pivoting to telemedicine and determining how we could safely provide care to patients. Across the service line, comprised of orthopaedics, rheumatology, pain medicine, physical medicine & rehabilitation, and musculoskeletal imaging, there are inherent differences that dictated how each underlying service had to adjust their business model. During these initial months of the pandemic, certain service line priorities appropriately took a backseat to more pressing issues.

But once the initial flurry subsided, the health system rallied with a clear focus on getting back to business and continuing to push the envelope in driving care advancements. We found that a return to focusing on bigger picture and longer term goals was welcome by all, as providers and administrators alike were fatigued with the day-to-day of providing care in the pandemic environment. We also found that certain initiatives could be moved forward more quickly due to the positive impact on outcomes or reduced risk they could provide during the pandemic. This included reductions in length of stay as we got patients out of the hospital more quickly, and an increased rate of discharge to home as we reduced the use of skilled nursing facilities (SNFs) where appropriate. We also harnessed this momentum to implement same-day discharge hip and knee replacement surgery on a faster timeline than originally anticipated.

We look forward to a day when the pandemic is in the rear view mirror, but we will not forget the health system's impressive and steadfast response, and the care innovations that were put into place that will be harnessed for the long term. We will also remember how quickly we were able to pivot to meet the needs of our patients, and leverage this acute awareness of what we are capable of to accelerate the advancement of the service line.

Ready to Rebuild

Neil Ravitz, MBA

Chief Operating Officer
Chief Administrative Officer, Musculoskeletal Service Line

When I wrote my last update article for UPOJ, it was February of 2020 and I titled the article "Poised for Growth and Expansion." Wow, clearly I missed the freight train that was coming at us the form of COVID-19 and the year that would ensue! It is hard to believe that it was 12 months ago that we stopped doing non-emergent surgeries, closed down clinics to most patients, tried to figure out what telehealth visits would look like in orthopedics, and began trying to find every closet that contained personal protective equipment. All of those things happened, buts most importantly, we all are reading this article today knowing that we survived one of the most tumultuous years of our personal and professional lives. Like many of you, I have gotten through this time by looking forward to a better time in the future with more vaccines and less disease. From a business perspective in the Department, that starts with our budgeting process for next year and our plans to rebuild our volume. In order to rebuild that volume I want to share with you our large investments in both people and locations.

We had several new clinical faculty members join the Department in the past year. In the Adult Reconstruction Division, we welcomed Dr Chris Anthony in August of 2020. He recently completed his fellowship in hip preservation at Washington University and is practicing at Pennsylvania Hospital. In the Shoulder and Elbow Division, we welcomed back Dr Gabe Horneff who had previously graduated from our residency. He is practicing at Pennsylvania hospital and seeing patients at several places in the suburbs. The Hand Division added Dr Hannah Lee in September of 2020 after a fellowship at University of Pittsburgh. She has a both a Veteran's Administration and a research component to her practice. The Spine Division added two new faculty this year with Dr Dave Casper joining us in September of 2020 after completing his fellowship at Cleveland Clinic and Dr J. Rush Fisher joining us in February of 2021 after practicing in the Delaware market for more than 25 years. Both are great additions to the department and enable us to grow the presence and access of spine care in the region. Finally, our Foot & Ankle Division has gone through tremendous change. In January of 2021, Dr Casey Humbyrd joined as the new division chief as Dr Keith Wapner steps down and towards retirement. She has been a wonderful addition to the department and made an immediate impact by helping us to recruit Dr Anthony "Bobby" Ndu from a local competitor. He had done his fellowship in F&A with us at Penn and we are glad to have him joining us in May of 2021. All of these recruits are key as we look to rebuild. They bring the energy, enthusiasm, and the power for growth and expansion!

The department, as part of the MSKR Service Line, also had long planned an expansion of services at Radnor with the recent launch of a new space in June 2020. The goal of expansion was to bring all members of the service line under one common workspace, expanding from a smaller fragmented experience, to an 18 room suite, with embedded radiology and procedure space. Patients can now see multiple specialties that they would historically need to receive care from under one roof and with one consistent workflow. In addition, cross-collaboration between care providers enhances care and interdisciplinary treatment plans. Year to date Orthopaedics has seen over 9,000 visits in the expanded space with year over year growth between 20-30% each month since going live. Similar volume and growth in all areas of the service line has exceeded early expectations alongside a rapidly changing environment during a global pandemic. Radnor now features state of the art multi-disciplinary care in many areas in addition to MSKR including Women's Health, Cancer, Primary Care, Neurosciences, and Heart and Vascular. With the growth in Radnor, we have now positioned ourselves to be the premier leader in musculoskeletal care in the community that needs our services most.

While we cannot control the number of pick-up basketball injuries that will happen this year in the Philadelphia area or the number of people that may delay care from their fear of the virus, we can control certain things. We are committed to building the most talented and accomplished faculty here at Penn and the people I mention above are proof of that commitment. When we combine highly talented people like that with modern and state of the art facilities like we built in Radnor, then we have a recipe for rebuilding and success that will carry us into the future.

Human Tissue Lab

Lorianne Kish-Burdsall

2020 was a historical point in time for mankind. The scientists and medical professionals faced a challenge unlike any before in history.

Science and medicine are succeeding in their persistence and dedication.

As a result of the pandemic and necessary shut downs, the Human Tissue Laboratory stopped its educational events in March.

Prior to the temporary closing, the laboratory was in full use and serving all genres of medicine.

After receiving permission to open lab activity and following new Covid-19 related protocols, the Human Tissue Laboratory reopened in the fall of 2020.

As the Covid-19 vaccination is becoming more widely administered, the lab interest and activity is growing.

The Human Tissue Laboratory did acquire a new C Arm in 2020. This will be most helpful for our fixation, arthrosplasty and image guided curriculum.

We look forward to resumption of all lab activity and welcome any and all inquiries.

Advanced Practice Provider Update

Christine McAndrew, PA-C

Penn Orthopaedic Surgery Advanced Practice Providers (APP) have been an integral member of the Orthopaedic team for many years. They have supported the department's ability to increase access to quality healthcare for the patient's we serve.

The last year was a challenging one for all with the Covid-19 pandemic changing our lives. The work place was different for all and especially difficult for those in healthcare. We had to quickly find ways to continue to care for our patient population in ways that are safe to all. The APP's in Orthopaedic surgery played a tremendous role in continuing to provide safe access to our patients. They were the first called to scrub all clinic schedules to determine who could be seen by telehealth and who needed to be seen in person. They worked with other members of the care team to coordinate telehealth and clinic schedules. In addition to the physicians doing telehealth, the APPs also ran their own virtual schedules. This group was also the one who took all surgery cancellations and tiered the patients so that once elective surgeries started, we knew the priority of each case. They spent tireless hours ensuring that we were prepared as a team to restart elective surgeries in a safe manner. Since the time we have been able to safely open clinics again, the APPs have worked very hard to increase volumes to pre-Covid numbers. They continue to assist the department in increasing our volumes and access to care. The APP's showed flexibility, adaptability and dedication more than ever this year!

Within the department of Orthopaedic Surgery, our APP group continues to grow year by year. We currently have 38 APPs within our department. In the past year, we have added several new APP's after coming off of a hiring freeze during the pandemic. Devon Leahy joined our foot and ankle team and now serves as Dr. Humbyrd' s PA. Devon same to us a new graduate who was eager to learn and jump into the field. Nadine Raile has joined us to support Dr. Anthony in his hip preservation practice. She comes with several years of experience as an orthopedic physician assistant. Rachel Jackson has joined us to support our spine physician Dr. Casper. Rachel is a new graduate who has an orthopedic background and strong desire to be in spine. Lisa Kelly joins our Chester County team to support Dr. Sheriff in his spine practice. Lisa comes from Chester County Hospital where she worked as a hospitalist physician assistant. Alissa Norris started with us in March to support Dr. Smith, chief of spine. Alissa is a new graduate who comes with a musculoskeletal background and strong desire to be an orthopedic surgery PA. Natalie Knitowski will soon be joining us in the next couple of months to support our new spine physician Dr. Fisher. Natalie brings to us over 15 years of experience as a spine physician assistant. We are all so excited to welcome our new APP's and to finally have a full spine APP team!

In addition to new hires, we have also had some role changes within our APP's. Kerry Howey has transitioned into the PA for Dr. Neil Sheth and consequently, Shawn Mahoney has transitioned into our float PA. Shawn is currently covering trauma clinics and training for his role. Shawn has a strong desire to run general Orthopaedic independent sessions. July 1st, 2021 Lauren McGarrity will transition to Dr. Dhanota' s physician assistant. We wish Kerry, Shawn and Lauren nothing but the best in their new roles.

With appreciation to Brian Fletcher who covered on the inpatient service at PPMC for several months while there was a gap in APP coverage. Brian then remained on service to train the two new inpatient APP's. We are very grateful to Brian who was not only able to bridge the gap in coverage but also to improve communications between inpatient and outpatient teams.

The Orthopaedic APPs continue to support department initiatives, including access to care. The vast majority of our APPs all run independent sessions which range from post-operative patients, return and new patients; as well as minor procedures. They also do the majority of the history and physicals and prepare the patients for surgery. In FY20 they saw a total of 4,486 new patients and 19,202 established patients. This number is down slightly from last fiscal year due to the pandemic. However, this is an incredible accomplishment!

In conclusion, the advanced practice providers have served as major contributors to the success of the department. As many would say, they are the backbone to our department! They are the glue that keeps our care teams together. It has been very gratifying to work with such an amazing group of advanced practice providers that make me proud day in and day out.

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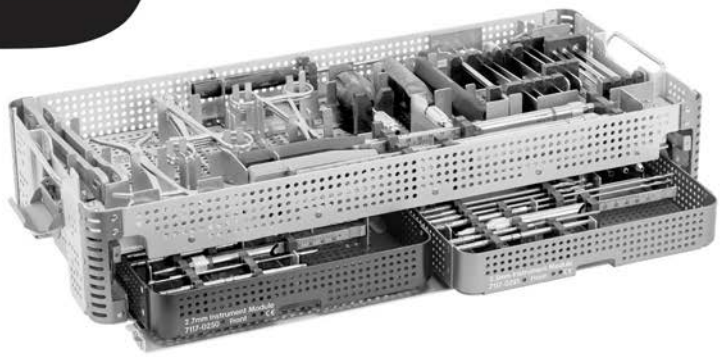

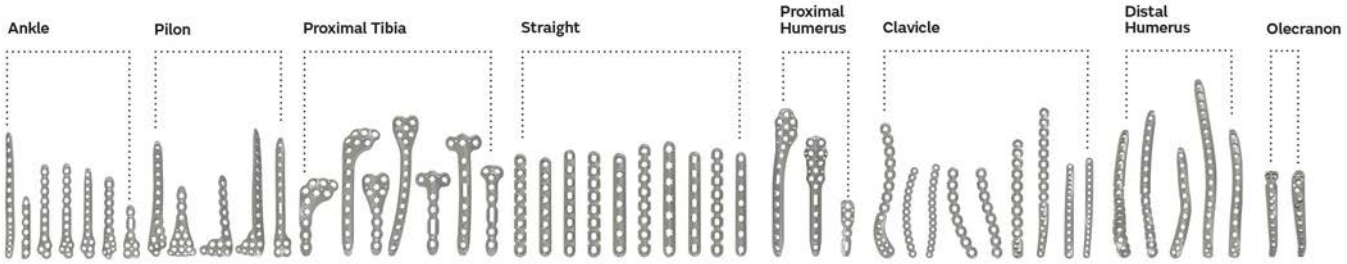

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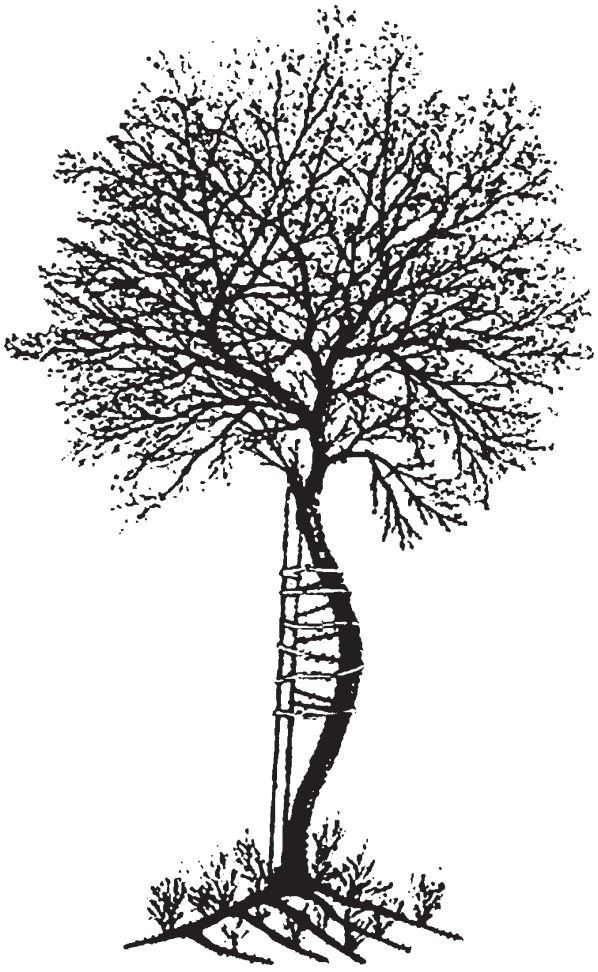

University of Pennsylvania Orthopaedic Journal

2019-2020 Clinical and Basic Science Research

The following sections highlight clinical and basic science research conducted at the University of Pennsylvania in the field of Orthopedics, including work from the Department of Orthopaedic Surgery, The McKay Laboratory for Orthopaedic Research, Children's Hospital of Philadelphia, the Philadelphia Veterans Affairs Translational Musculoskeletal Research Center, The Biedermann Laboratory for Orthopaedic Research, and the Human Motion Lab. In addition to research, each clinical section is preceded with a "Tips & 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.

Tips & Tricks:

Trauma
Spine
Sports
Hand
Pediatrics
Shoulder and Elbow
Arthroplasty
Foot and Ankle
Oncology
Orthoplastics

Clinical Research Sections:

Trauma
Spine
Sports
Hand
Pediatrics
Shoulder and Elbow
Arthroplasty
Foot and Ankle
Oncology
Orthoplastics

Basic Science Research Sections:

Bone
Cartilage
Muscle, Tendon, & Biomechanics

Tips and Tricks

U·P·O·J

Trauma Tips and Tricks: "Kickstand Screw" for Restoration of Volar Tilt in Distal Radius Open Reduction Internal Fixation

Kendall M. Masada, MD[1]
Samir Mehta, MD[1]

[1]Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, Pennsylvania

Background

Distal radius fractures are among the most common fractures in the upper extremity.[1] Multiple treatment options are available including closed reduction and cast immobilization, percutaneous K-wire fixation, volar or dorsal plates, bridge plating, external fixator, or some combination of these techniques. Selection is based on the characteristics of the fracture.[2,3] Restoration of volar tilt is one measure of correct surgical treatment. Correction to a volar tilt to 11 +/− 5 degrees has been shown to restore biomechanical function of the wrist.[4] Current guidelines from the American Academy of Orthopaedic Surgeons recommend surgical fixation of distal radius fractures with dorsal tilt greater than 10 degrees from neutral.[5]

Volar locking plates are a popular method fixation. Use of a volar locked plating system is associated with a small (1.9 ± 3.3 degrees), but statistically significant, loss of volar tilt when comparing immediate postoperative alignment with that seen at 12 months postoperatively.[6] This makes the restoration of the volar tilt intra-operatively particularly important. One method described in the literature is to position and secure the plate on the radial shaft and then reduce the articular block to the plate, which can result in an incomplete reduction or poorly balanced plate.

The use of a "kickstand screw" or "lift-off screw"— a proximal locking screw inserted into the plate prior to plate application perched on the volar cortex— can facilitate restoration of the volar tilt.[7,8,9] Below, we highlight the "kickstand" technique using an example case.

Example Case

The patient is a 23-year-old right-hand dominant female with history of Ehlers-Danlos (hypermobility type), asthma, and obsessive compulsive disorder who presented to the emergency department with left wrist pain after a mechanical fall off of a stepladder. Physical exam demonstrated a closed injury with neurovascularly intact extremity. Radiographs revealed a left-sided comminuted intra-articular dorsally angulated (approximately 22 degrees) distal radius fracture with associated ulnar styloid avulsion fracture (Figure 1). She was stabilized in a sugar tong splint. Via a shared-decision making model, the patient elected to proceed with operative management of her distal radius fracture.

Surgical Technique

The patient was placed supine on a radiolucent hand table. Fluoroscopic imaging was positioned on the ipsilateral side of the table. A modified Henry approach was used. Once the fracture site was debrided, the radius was noted to be short with dorsal angulation of the distal fragment. An AO elevator was used to elevate the articular fragment and restore length. Manipulation alone did not restore the volar tilt. A 6-hole narrow distal, 3-hole proximal distal radius plate (Depuy Synthes, West Chester, PA) was felt to be the most appropriate implant for the patient's anatomy. A locking ("kickstand") screw was inserted into the most proximal locking hole of the plate. The plate was then inserted through the surgical incision, positioned optimally relative to the articular block, and perched on the volar cortex without drilling though the cortex (Figure 2A). The distal portion of the plate was flush with the volar cortex. K-wires were inserted to provisionally secure the plate and verify satisfactory plate balance. Locking screws were then inserted into the most distal holes. The use of non-locking screws in the articular block does not provide adequate compression of the plate to bone due to the quality of the metaphyseal bone in this region. Once fluoroscopic imaging confirmed appropriate placement of the distal locking screws, the "kickstand" screw was removed. The plate was reduced to bone with a non-locking cortical screw in the distal-most proximal hole resulting in restoration of the volar tilt (Figure 2B). Non-locking cortical screws were placed in the remainder of the proximal holes (Figure 2C). The distal radioulnar joint was stressed and found to be stable. Final fluoroscopic evaluation revealed good length, alignment, and angulation of the radius with appropriately placed hardware (Figure 3).

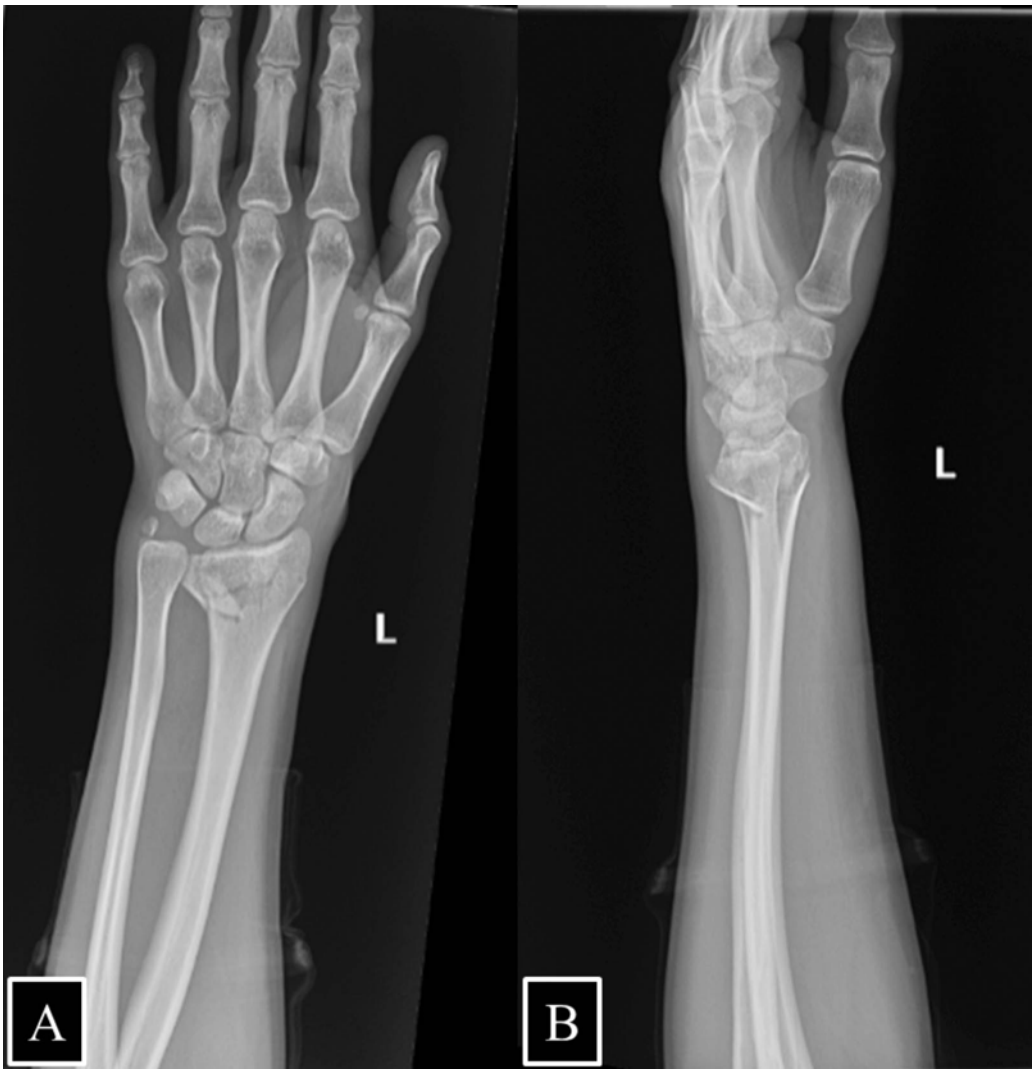

Figure 1. AP **(A)** and Lateral **(B)** radiographs of a left-sided comminuted intra-articular dorsally angulated distal radius fracture with associated ulnar styloid avulsion fracture.

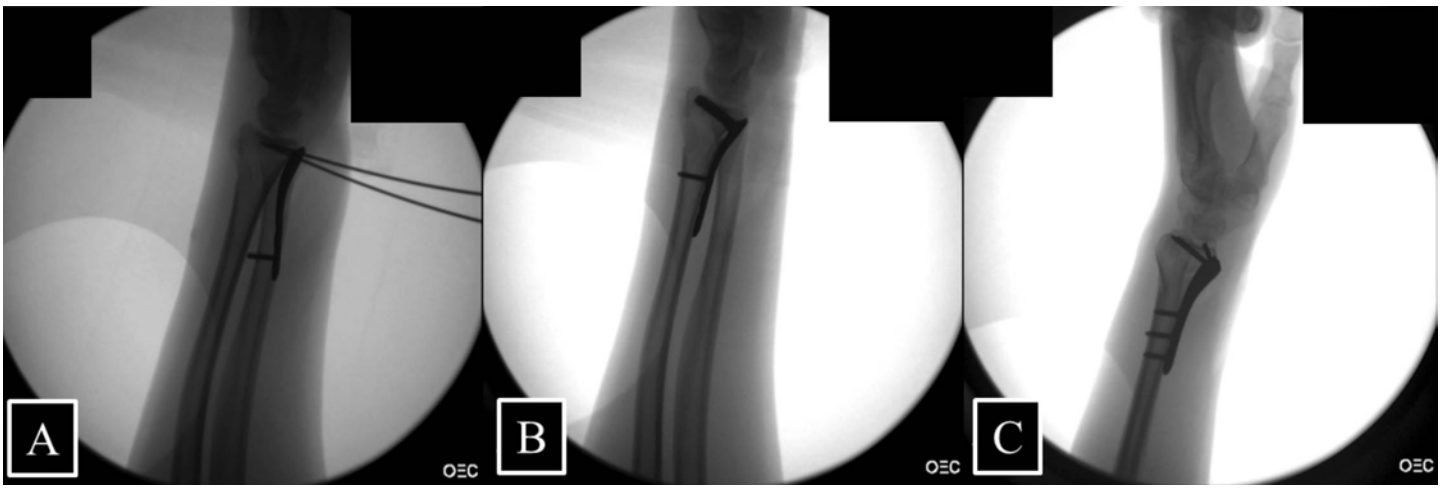

Figure 2. Intraoperative fluoroscopic images revealing **(A)** "kickstand screw" in the proximal locking hole of the distal radius perched on the volar cortex with K-wires in place to provisionally secure the plate distally, **(B)** insertion of distal locking screws securing fixation of the articular block to the plate followed by insertion of a cortical screw through the most distal diaphyseal screw hold, and **(C)** non-locking cortical screws in the remainder of the proximal holes.

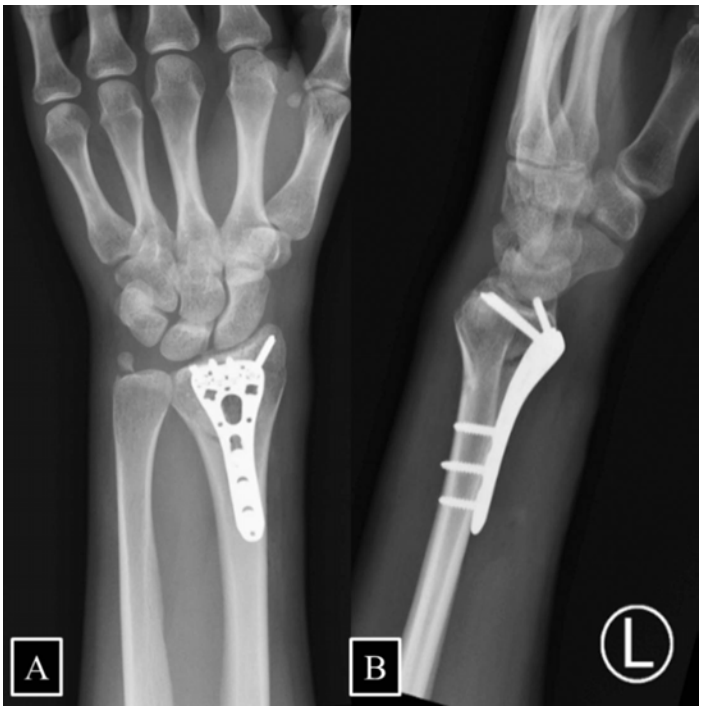

Figure 3. AP **(A)** and Lateral **(B)** final radiographs demonstrating restoration of the volar tilt to approximately 11 degrees

Post-operative Care

The patient was made non-weight bearing in a soft dressing with immediate range of motion. She was then transitioned to physical therapy two weeks after surgery. She was allowed to begin weight bearing at six weeks post-op when interval radiographs demonstrated callous formation without loss of reduction.

Conclusion

In summary, the use of a locking proximal "kickstand" screw through a volar plate offers a simple and reproducible technique for restoring the volar tilt in distal radius fractures to match the volar tilt of the implant being applied.

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Spine Tips and Tricks: Anterior Column Realignment with Expandable Cage in Treating Sagittal Malalignment

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Amrit S. Khalsa, MD[1]

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Introduction

Sagittal balance is a critical measure and reliable predicator of health status in patients with Adult Spine Deformity (ASD). Sagittal imbalance has shown to be associated with pain and worse clinical outcomes.[1-5] Nonsurgical management is often limited in alleviating symptoms in severe sagittal imbalance. Surgery is the standard of care with goal of improving lumbar lordosis (LL) and pelvic tilt (PT) to achieve achieving spinal fusion and restored sagittal balance. Traditional management has consisted of posterior-based surgical approaches with various osteotomy options including Smith-Petersen Osteotomy (SPO), Pedicle subtraction Osteotomy (PSO), and Vertebral Column Resection (VCR), with PSO being the most commonly used in treating fixed deformities.[6] These surgical techniques are successful in the treatment of patients with spinal deformity and restoring alignment goals; however, they carry significant morbidity including prolonged operative time, neurological complications, and risk of intraoperative bleeding.[7-10] Given the significant morbidity associated with such posterior shortening osteotomies, many surgeons prefer anterior-based interbody approaches to restoring sagittal alignment. With recent advancements in minimally invasive surgery (MIS) other options have emerged as promising alternatives in the management of adult spinal deformity including primary as well as revision spinal surgery.[11-14] Anterior column realignment (ACR) is a more recent MIS technique described for the correction of rigid kyphosis of the lumbar spine.[15] ACR is an anterior column lengthening procedure that utilizes the minimally invasive lateral lumbar interbody fusion (LLIF) approach to perform a complete discectomy with deliberate release of the anterior longitudinal ligament (ALL). ACR has been shown to be equally effective and safer alternative to the traditional three column osteotomy.[16] Selecting the appropriate surgical technique is crucial to success.

Indications

Anterior column realignment (ACR) is an emerging minimally invasive (MIS) treatment for sagittal deformity. Surgical indications include progressive focal sagittal deformity and instability, declining neurological status, and declining quality of life secondary to sagittal imbalance. Absolute contraindications include a fused disc space at the affected level, as well as relative contraindications that are shared with any lateral retroperitoneal approach surgery including anatomic access concerns in the lumbosacral spine, retroperitoneal adhesions, and vascular concerns.

Preoperative Planning

Thorough preoperative planning is essential for a safe and effective surgery. Preoperative imaging provides understanding of the spinal deformity. Standing alignment radiographs allow measurement of sagittal parameters and identification of dynamic instability. Advanced imaging such as CT scan allow assessment of bony fusion. MRI identifies any underlying associated neurologic compression as well as anatomical constraints such as vascular anomalies and lumbosacral plexus variants within the psoas musculature. These considerations also help determine the optimal side for approach, with the safest and most effective trajectory. The surgeon can also assess the relation of the great vessels relative to the anterior spine and explore for a safe plane for dissection of the ALL.

Surgical Technique

The approach for ACR as described by Akbarnia et al. in 2014 is through the lateral trans-psoas corridor to access the lateral spine. Patient should be positioned for a standard LLIF approach in the lateral decubitus position. Lateral flank incision at the level of intervertebral disc of interest is made, followed by blunt dissection through abdominal wall musculature and into the retroperitoneal space. This generally allows access to the levels between L1 and L5. Directional EMG is utilized to guide appropriate psoas dissection to allow safe access to the lateral spine while avoiding injury to the lumbar plexus. Once at the lateral spine, careful anterior dissection is performed to create a plane between the ALL and anterior vascular structures, however, the ALL is kept intact

until full discectomy is performed. A retractor is placed in position anterior to the ALL. Then ipsilateral and contralateral annulectomies are performed and complete discectomy is performed. Vertebral body endplates are prepared with cartilaginous removal in anticipation of fusion. Once the discectomy is completed, the ALL is identified and the vascular structures anterior to the ALL are protected, the surgeon can then proceed with direct ALL resection with a scalpel. After the release is complete, an appropriately sized expandable mechanical interbody cage is inserted into the disc space under fluoroscopic guidance. Traditional hyperlordotic 30-degree cages, while providing significant sagittal plane correction, can be difficult to restrict posteriorly within the interbody space without the constraint of ALL intact. Expandable implants in this scenario provide the benefit of being inserted at 10 degrees of lordosis, facilitating safe placement within the interbody space. Another theoretical benefit is decreased insertional stress on the vertebral endplates with less risk of subsidence into bone. Integrated screw fixation is then inserted into the cephalad vertebral body to avoid anterior migration of the cage and a second screw is often fixed into the caudal vertebral body for additional support. The cage, once fixated, can then be expanded to higher degrees of lordosis in-vivo without concern for further anterior migration while still providing significant anterior column lengthening and lordotic correction. Bone graft material can then be inserted to allow for interbody fusion. Posterior instrumented fusion is then performed at least two levels cephalad and caudal to the ACR level for further stability. Posterior column osteotomy (PCO) can be performed concurrently to enhance power of correction if needed.

Example Case

Patient X, 62-year-old female with past medical history significant for HTN and alopecia. Presented to clinic for back pain, progressive lower extremity (worse on the left), and new onset urinary urgency, in the setting for having prior L2-L5 laminectomy approximately 2 years prior at outside institution. Prior to onset of urinary urgency, she had completed interval non-operative treatment (physical therapy, multiple epidural steroid injections) with no relief of symptoms. On examination, her motor strength was 5/5 throughout bilateral lower extremities, except for 4/5 bilateral hip flexion. Sensation was intact bilaterally. X-rays showed progressive post-laminectomy kyphosis with segmental progressive instability at L2-L3 (Figure 1).

Given the progressive deformity with neurologic dysfunction the patient was an appropriate candidate for surgical intervention. She underwent pre-operative testing and was cleared for surgery.

Patient underwent ACR with L2-3 LLIF with expandable cage and L1-L4 PSF (Figure 2). The lateral portion of the case was performed first starting with the discectomy, followed by release of the ALL. The expandable cage was packed with allograft bone graft and patient's left iliac crest bone marrow aspirate. The lateral plate was integrated with the cage and

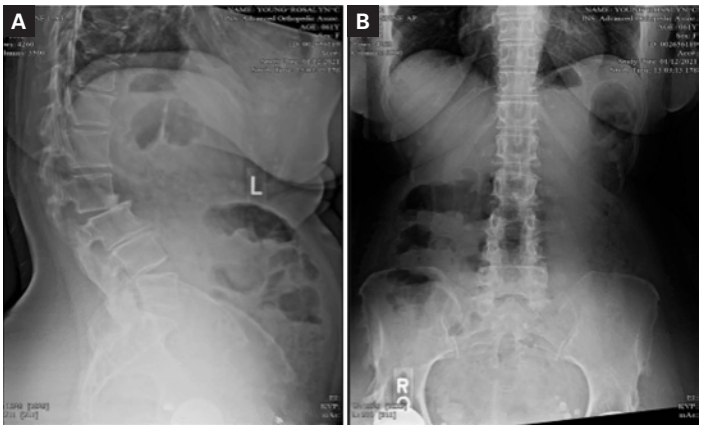

Figure 1. Pre-operative imaging. **(A, B)** AP and lateral X-rays, respectively, demonstrating 30 degrees segmental kyphosis and progressive instability at L2-L3. Pelvic incidence, 35 degrees. Lumbar lordosis, 8 degrees.

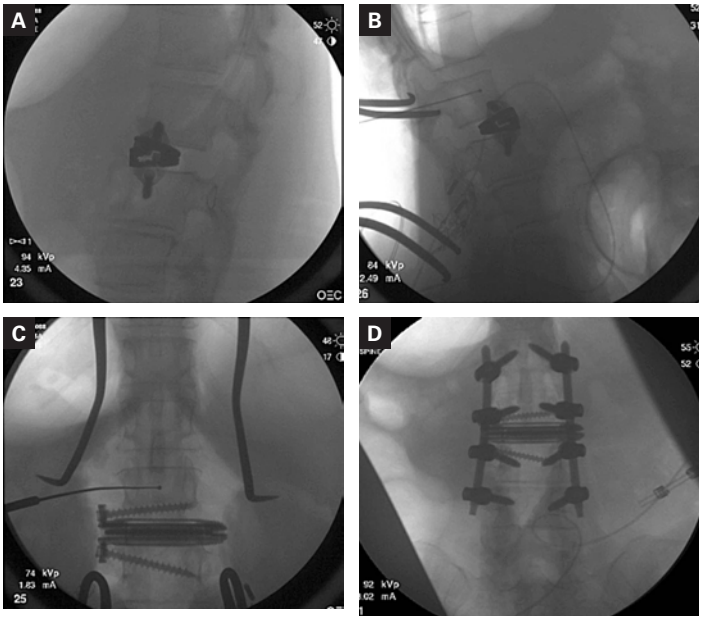

Figure 2. Intra-operative imaging. **(A)** Lateral intraoperative X-ray demonstrating placement of the expandable cage at the L2-L3 level prior to SPO, and **(B)** after the SPO. **(C)** AP intraoperative image prior to instrumented fusion, and **(D)** final AP status post final instrumentation.

screws were placed through the bodies of L2 and L3 to help avoid cage migration. The cage was then expanded from 10 to 30 degrees. Finally, in the posterior portion of the case, patient had a Smith Petersen Osteotomy at the level of L2-L3 for additional sagittal correction and L1-L4 instrumented fusion.

Patient's pain was improved on post-operative day 1, and patient was ambulating with physical therapy. Urinary urgency, in addition to the pain, were improved post-operatively. She received 2 units of pRBC for hemoglobin of 6.7 which corrected appropriately, most likely secondary to dilutional rather than significant blood loss (given that her estimated blood loss during surgery was 200cc). Patient was discharged home on post-operative day 5, her delay in discharge was mainly due to high posterior drain output given the revision

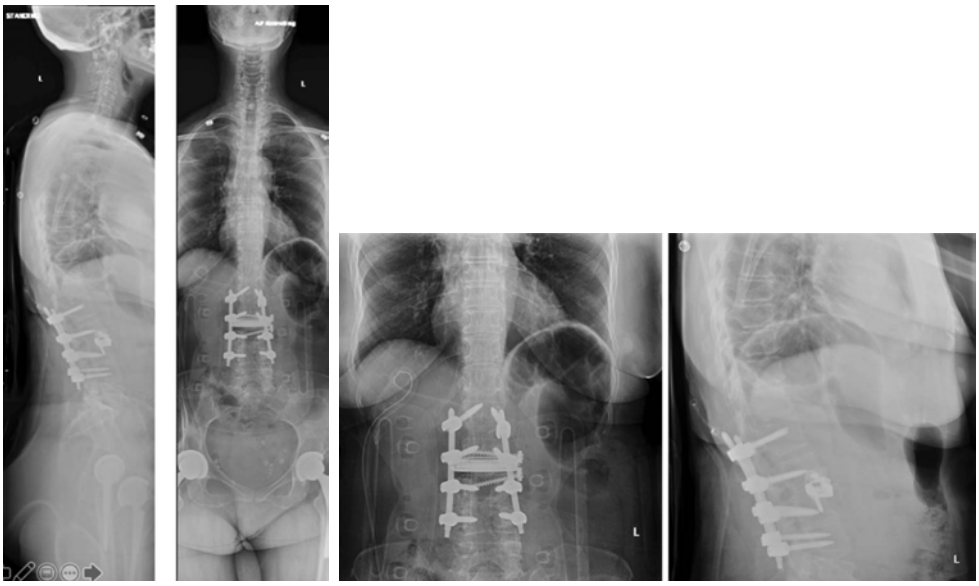

Figure 3. Post-operative imaging demonstrating restoration of lumbar lordosis. L2-3 segmental lordosis, 4 degrees. Lumbar lordosis 42 degrees.

posterior exposure. Post-operative imaging shows restored lumbar lordosis, with the expandable cage positioned properly (Figure 3).

Discussion:

Post-laminectomy kyphosis is more common in the pediatric population than in adults with incidence as high as 26% in children who underwent laminectomy. It more commonly occurs in the cervical spine than the thoracolumbar spine. Higher occurrences have been reported in children undergoing laminectomies for cord tumors, with incidence reported as high as 50% in this population. It is postulated that laminectomy in the skeletally immature spine leads to decreased cartilage growth and anterior wedging of vertebral bodies. While in the adult population, post-laminectomy kyphosis has been shown to be influenced by multiple factors including pre-existing sagittal deformity, more significant facet resection, and muscular insufficiency post laminectomy. Nonetheless, post-laminectomy lumbar kyphosis in adults is not robustly described in the literature. Here, we presented an interesting case with an adult patient with post-laminectomy kyphosis in the lumbar spine.

Traditional 3-column osteotomies (3CO) provide powerful alignment correction of sagittal deformities but come at the expense of increased morbidity. Bianco et al. reported overall rate of major complications (including intraoperative and postoperative complications) of 42% in a retrospective study of 423 patients who underwent 3CO. Smith et al. reported a higher percentage of 78% of patients with at least one complication (including major and minor complications) in a retrospective study of 82 patients with at least 2 year follow up. Most common complications are excessive blood loss, neurological deficits and instrumentation related complications. Neurological deficits were reported as either radiculopathy or motor deficits. Implant-related complications were most commonly rod-breakage. Major blood loss (defined as loss of >4L) has been described in the literature to correlate with increased risk of infections and overall medical complications. Bianco et al. identified major blood loss as a direct risk factor for developing complications in patients undergoing 3CO with patients losing 55% of their blood volume intraoperatively. Such complications include dural tears, deep wound infection, and cardiopulmonary complications (e.g. pulmonary embolism).

The advent of expandable interbody cages over the last several years have presented the theoretical advantages of decreased insertional endplate stresses as well as the ability to "dial in" variable degrees of lordosis.[21] Though first developed for transforaminal interbody fusion (TLIF) devices; expandable technology has more recently been applied to LLIF devices. The larger LLIF cages in general allow for more surface area for fusion as well as the ability to span the more robust apophyseal ring of the vertebrae. The novel usage of expandable hyperlordotic (lordosis greater than 20 degrees) LLIF devices in the setting of anterior column realignment (ACR) is not well explored and warrants further long-term study.

ACR, in general, offers an effective less invasive alternative for sagittal imbalance correction without may of the associated complications of traditional 3CO. Notably, ACR has been shown to be associated with significantly less blood loss compared to the 3CO b obviating the need for extensive bony resection.[18, 19] ACR does present its own approach-specific risk profile. Neurological deficits related to the lumbar plexus have been reported due to the transpsoas approach, however, these deficits were invariably transient.[20] Further larger scale analysis of outcomes and complication's related to ACR is warranted. Thus far, ACR has demonstrated to be an effective procedure for restoring sagittal alignment in appropriately indicated patients with lower rates of complications when compared to traditional 3CO.

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Sports Tips & Tricks: 5 Tips for MRI Evaluation of the Shoulder and Knee

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Introduction

While the history and physical exam provide the bulk of clinical information needed to make a diagnosis in orthopedic sports medicine, advanced imaging techniques such as magnetic resonance imaging (MRI) are increasingly used as diagnostic tools and for surgical planning. Radiology reads are typically readily available, but it is imperative for the orthopedic surgeon to be able to self-interpret MRIs with confidence. The following tips provide a guide for the review of MRI images of common sports injuries of the knee and shoulder. It is not meant to serve as a comprehensive report of pathology but rather a framework for the review of MRI images.

Tip #1 Learn the Vocabulary

MRI is an advanced imaging technique that uses magnets and radiofrequency coils to create three-dimensional representations of relevant anatomy.[1] While the basic science behind this process is interesting to some, it is not needed to properly interpret the MRI. There are a few key terms that are useful to understand. The field strength refers to the strength of the magnet used and is a property of the machine. Higher powered magnets, such as 1.5 tesla (T) and 3T, provide better resolution and are higher quality. The signal to noise ratio (SNR) is also a measure of quality and varies with the different pulse sequence settings set by the MRI technician. Factors influencing SNR include scan time, resolution, and slice thickness. High signal to noise gives a clearer representation of the anatomy.

Tip #2 Understand the Sequences

Different pulse sequences can be used to identify different tissues (Table 1).[1-3] These are settings that are altered by the MRI technician during the MRI scan. T1-weighted images have the highest SNR and are good for detecting anatomy. With T1-weighted images, fat and gadolinium are bright, while water and collagen are dark. T2-weighted images have the lowest SNR but are better at detecting fluid and edema, making them useful for identifying pathology. Fat remains bright and collagen remains dark in T2-weighted images, while water appears bright. Because we are typically looking for fluid/edema in locations where it might not normally be in musculoskeletal imaging, we usually want to suppress the fat brightness to show only fluid. In T2 weighted-images with fat suppression (T2 FATSAT), fat appears dark due to the purposeful suppression, while keeping the signals of the other structures in T2-weighted images the same. Proton density-weighted (PD) images have an intermediate SNR, which maintains the anatomic detail but limits the tissue contrast. Fat is typically suppressed with this type of sequence, and it is used to evaluate fibrocartilage as collagen appears dark and water bright. The final common MRI sequence used in sports medicine is short T1 inversion recovery (STIR) imaging. STIR imaging is similar to T2 FATSAT imaging in regard to the signal of fat, collagen and water. The amount of time it takes to obtain is much shorter than the typical T2 FATSAT, but the quality is not as strong. A basic understanding of the pulse sequences available can assist in the evaluation of various anatomy and pathology.

Table 1. Characteristics of MRI Pulse Sequences

	T1	T2	T2(FATSAT)	PD	STIR
Fat	Bright	Bright	Dark	Suppressed	Dark
Collagen	Dark	Dark	Dark	Dark	Dark
Water	Dark	Bright	Bright	Bright	Bright
Signal/noise	High	Low	Low	Intermediate	Low
Ideal Use	Anatomy		Pathology	Cartilage, ACL	

T1, T1-weighted, T2, T2-weighted, FATSAT, fat saturated; PD, proton density; STIR, short T1 inversion recovery, ACL, anterior cruciate ligament

Tip #3 Determine the Proper Plane

Orthogonal views are essential in the interpretation of images. Certain planes are more helpful than others depending on the joint or region of interest. In general, it is best to stay orthogonal to the structure of interest. For example, in the knee one would assess axial, sagittal, and coronal cuts, which are naturally in line with the joint. For the shoulder, which sits at approximately 30-degree angle due to the plane of the scapula, one would assess the axial, sagittal oblique, and coronal oblique. These oblique views are in line with the axis of the scapular plane and allow for better visualization of key structures.

Tip #4 Consistency is Key

While there are many different ways to approach reading an MRI, the most important factor is consistency. One surgeon may read an MRI "left to right," while another surgeon reads "out to in." There is not one universally agreed upon strategy as the best approach. However, each surgeon should read every MRI with the same approach every single time. This consistency is the best approach to ensure that all structures are appropriately assessed. There are six main groups of structures that should be assessed on every MRI: ligaments/tendons, meniscus/labrum, articular cartilage, bone, fat, and muscle.

Tip #5 Practice Makes Perfect

It is estimated that to become an expert, one must spend over 10,000 hours practicing a skill.[4] It takes time to hone MRI reading skills. For each patient with suspected pathology, systematically approaching the MRI scan will ensure that nothing is missed and provide the surgeon with another repetition. Even when the diagnosis is known, it can be helpful to approach the MRI as if the clinical correlation was unavailable, in order to practice identifying proper sequences and planes to assess both normal anatomy and pathology.

Evaluating an MRI of the Knee

Ligaments/Tendons

When assessing knee injuries, the anterior cruciate ligament (ACL) is one of the most commonly injured ligaments. MRIs are able to accurately detect up to 95% of acute ACL disruptions.[2] Ligaments will generally appear dark with all MRI sequences. The most useful MRI sequence to use to assess the ACL is the proton density-weighted images. The primary plane used to evaluate the ACL is the sagittal plane (Figure 1), although the axial and coronal planes are helpful in assessing the femoral attachment.[2] The PCL is best evaluated on the T2-weighted sagittal images, while the collateral ligaments are best evaluated on the T2-weighted coronal images. The best sequence to evaluate for pathology of the quadriceps tendon is the T2-weighted sagittal and coronal image.

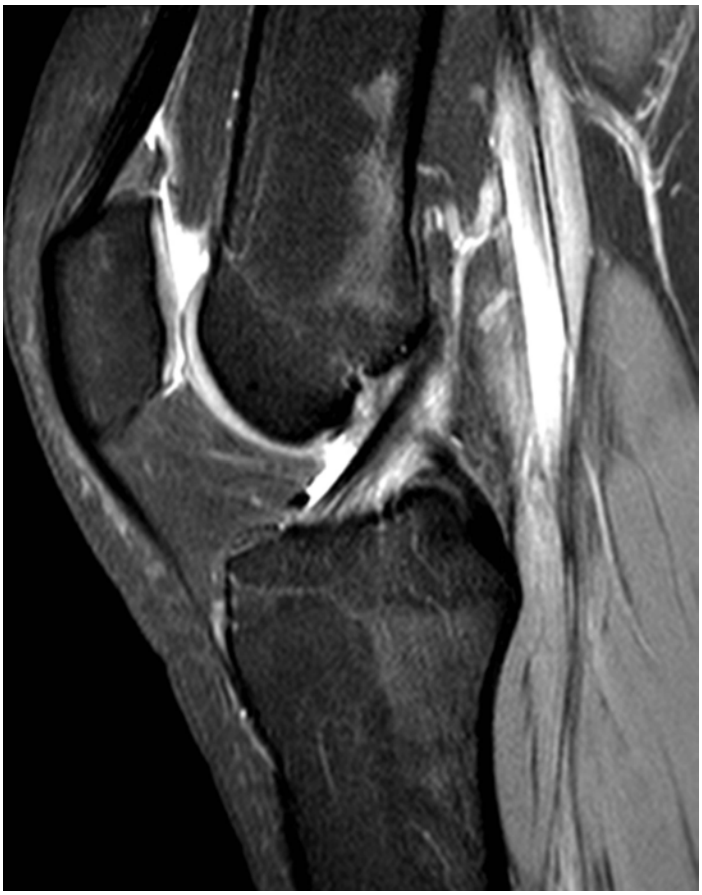

Figure 1. PD sagittal view of an intact ACL.

Meniscus

The meniscus will appear dark in all pulse sequences and will look triangular in cross-section. The PD-weighted image is the best, followed by T2-weighted imaging in assessing for a meniscal tear. The primary planes used to evaluate for a meniscal tear is the sagittal plane and coronal planes (Figure 2). A common pitfall is to misidentify the intermeniscal ligament anteriorly or the meniscofemoral ligaments posteriorly as tears, when in fact they are normal anatomy. Scrolling through multiple cuts and tracing these structures to their anatomic footprints will prevent this mistake.

Articular Cartilage

Cartilage will appear gray (intermediate in signal intensity) on T2 and PD-weighted imaging. These sequences are the best to utilize when assessing for cartilage defects because of the contrast between joint fluid and cartilage.[1] T1-weighted imaging is not a good sequence for evaluating cartilage, because the appearance of water/joint fluid often mirrors the appearance of the cartilage itself. Cartilage defects of the femur or tibia are best visualized on the sagittal and coronal planes, while patellar defects are best seen on the axial plane.

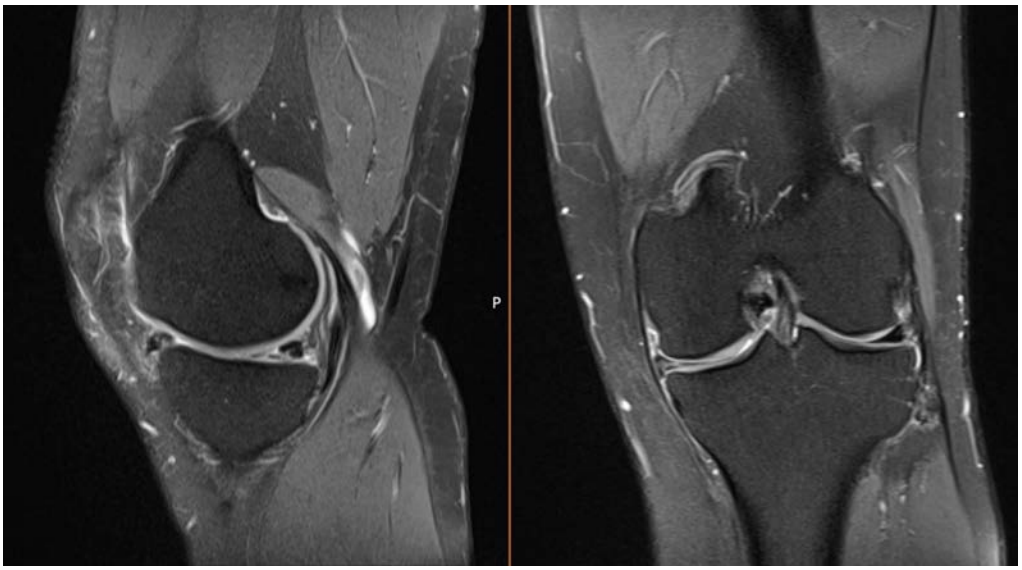

Figure 2. PD sagittal and coronal views of a patient with a medial meniscus tear.

Bone/Fat

Cortical bone is made of mostly calcium (hydroxyapatite) and collagen type I, giving it a characteristically dark appearance in all sequences. However, cancellous bone can appear similar to that of fat since marrow is composed of mostly fat. Thus, marrow will appear bright on T1-weighted images and dark on T2 5FATSAT. Bone marrow edema will appear bright and be contrasted with the dark bone marrow in the fluid-sensitive T2 FATSAT. Bone marrow edema seen in sports-related injuries is typically secondary to trauma and in conjunction with ligament injuries, and is helpful in identifying areas of injury. Sagittal, coronal, and axial planes will need to be assessed when evaluating for bone marrow edema or an occult fracture, and any abnormalities should be present in at least two views to confirm diagnosis.

Muscle

Muscles demonstrate intermediate signal intensity on all pulse sequences and therefore serve as a relative comparison for signal intensity of adjacent structures. T2-weighted images and STIR images highlight muscle edema and fluid collections. T1-weighted images are useful in assessing muscle atrophy, intramuscular hematoma, and distinguishing subacute blood from edema.[1]

Evaluating an MRI of the Shoulder

Ligaments/Tendons

The rotator cuff tendons, being made of mostly collagen type 1, will appear dark on all pulse sequences. The supraspinatus and infraspinatus are best evaluated on the T2 FATSAT or T2-weighted coronal and sagittal oblique planes, while the subscapularis is best evaluated on the T2 FATSAT or T2-weighted axial and sagittal oblique planes. Tendinopathy is depicted as intermediate signal intensity within the substance of the tendon on T2-weighted images. It is important to remember that these findings will also correlate with age-appropriate changes and patients might be asymptomatic.[3] A tear of the tendon will appear as bright fluid within the expected location of the tendon on T2-weighted images (Figure 3).

Labrum

The labrum, again being a mostly collagenous structure, will appear dark in all pulse sequences and appears triangular in cross-section with a smooth transition with confluent glenoid cartilage. Evaluation of the superior labrum is best on T2-weighted coronal oblique images, but axial planes are also helpful. The anterior and posterior labrum are best evaluated on T2-weighted axial images, while coronal oblique planes

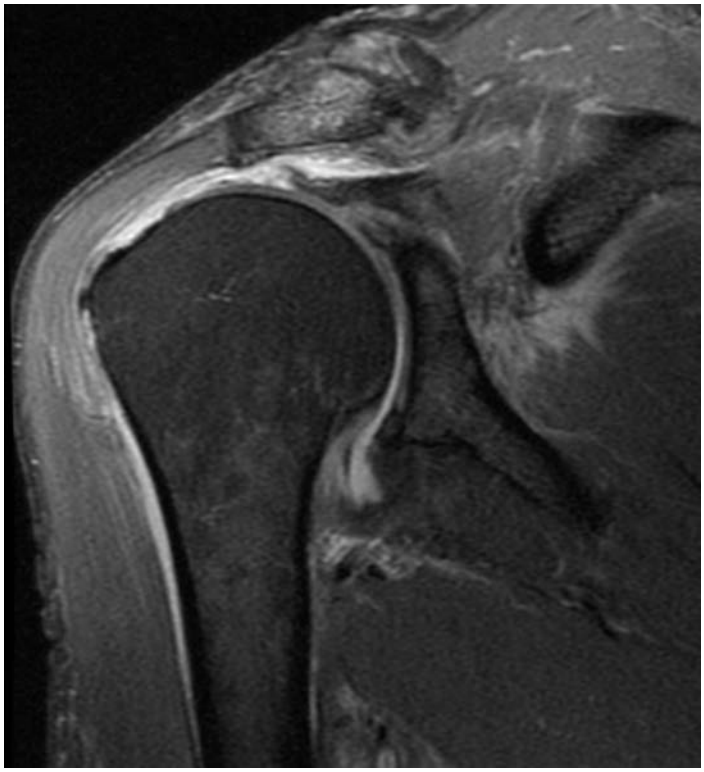

Figure 3. Coronal oblique view of a patient with a large supraspinatus tear.

are complimentary. The use of MR arthrogram has proved to be very helpful in detecting labral pathology, increasing sensitivities and specificities to 91-93%.[3]

Articular Cartilage

Similar to the knee, cartilage in the shoulder will appear as a thin gray uniform layer and have a smooth transition with the confluent labrum. Cartilage defects are best assessed with T2 FATSAT images in the coronal oblique and axial planes and with T1-weighted axial images with MR arthrogram.

Bone/Fat

Bone and fat have a consistent uniform signal and have a similar signal intensity on pulse sequences. They will appear bright on T1, T2, and PD weighted images. They require T2 FATSAT imaging to appear dark.

Muscle

As mentioned before, muscles serve as a relative comparison for signal intensity of adjacent structures. Muscles demonstrate intermediate signal intensity on all pulse sequences. Muscle edema and fluid are best evaluated on T2-weighted images and STIR, while intramuscular hematomas are best assessed with T1-weighted images. Fatty atrophy of the muscles will appear as high signal intensity streaks within the muscle and is best evaluated on T1-weighted sagittal images.

Conclusion

It is important for orthopedic surgeons to be able to self-interpret MRIs. This can be accomplished in five easy steps. Learning the vocabulary, understanding the sequences available, and determining the planes of interest for a given pathology provide a framework for the evaluation. Sticking to a systematic approach and continuous practice and experience will lead to more confident evaluation of MRI.

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Hand Tips & Tricks: Relative Motion Extension Orthosis for Extensor Tendon Injuries

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Introduction

Extensor tendons of the fingers can suffer various injuries over the dorsum of the hand, leading to loss of active extension of the metacarpophalangeal joint (MPJ). The sagittal band can rupture acutely after blunt trauma (Figure 1), or can gradually attenuate idiopathically or in patients with rheumatoid arthritis, leading to extensor tendon subluxation at the MPJ. Occasionally, acute ruptures can be treated with immediate immobilization; however, most patients with symptomatic extensor subluxation require surgical centralization of the extensor tendon followed by immobilization. Extensor tendon lacerations in zones V-VII are treated with tendon repair and post-operative immobilization. Traditionally, all of these conditions have been immobilized with MPJ in full extension for a period of four to six weeks, followed by gradual mobilization. This often leads to loss of finger range of motion secondary to joint stiffness and collateral ligament contractures, as well as tendon adhesions.[1,2] Unlike flexor tendons, extensor tendons pass through interstitial tissue without the protection of synovial sheaths, thus making them susceptible to post traumatic edema and fibrin tethering.[3]

Previous early motion programs utilized high profile dynamic extension orthoses that are time consuming to fabricate and bulky for the patient. These programs integrate gradual range of motion often requiring diligence of the patient, frequent hand therapy visits, and a guided home therapy program.

A more functional protocol, first described by Merritt et al. two decades ago and used at the University of Pennsylvania over the last ten years, was developed to overcome the problems and complications of these other approaches.[4] The Immediate Active Range of Motion (ICAM) program utilizes the low profile relative motion extension orthosis (RMEO) and early, controlled active motion of the fingers, requiring fewer therapy visits and yielding excellent results.[5]

How it works

An RMEO (also referred to as a yoke splint) is often made of thermoplast material and places the injured finger in relative 15 to 20 degrees of extension at the metacarpophalangeal joint compared to adjacent fingers sharing the same common extensor muscle belly (Figure 2).[1,4]

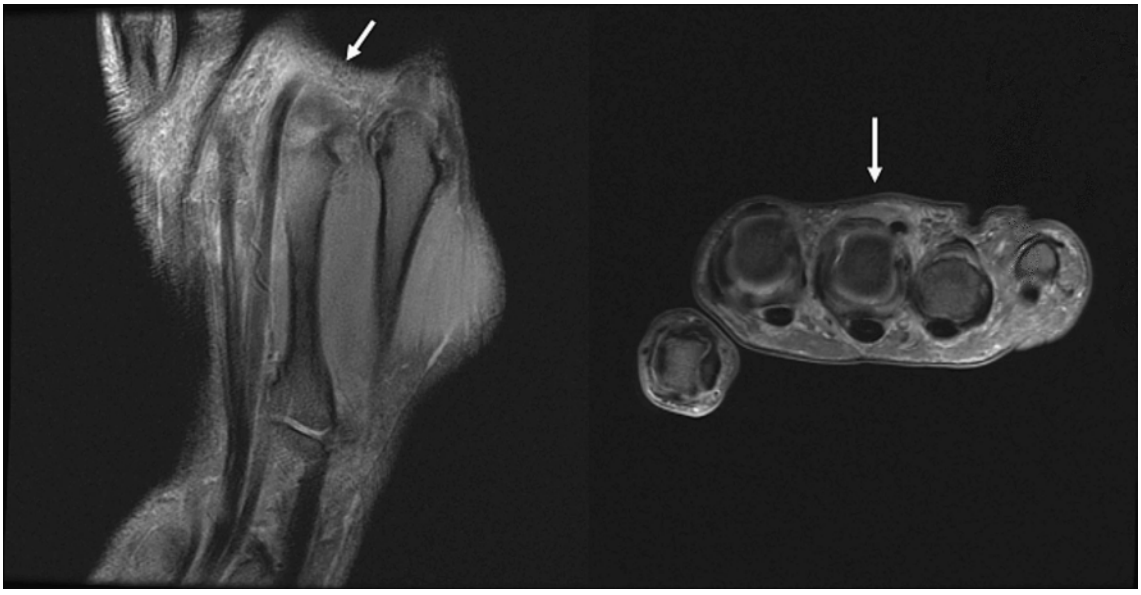

Figure 1. (A) Coronal and **(B)** axial MRI images demonstrate ulnar subluxation of the extensor tendon following closed blunt trauma to the middle finger MPJ.

Figure 2. Relative motion extension splint (RMEO) positioning the injured middle finger in 15-20 degrees in relative extension compared to adjacent digits.

When the finger is restricted in relatively less flexion than its neighboring fingers, less force is exerted on the repaired tendon compared to adjacent tendons, with decreased tendon excursion of approximately 5 mm.[6] This design allows for safe, near full, digital motion without stress that would result in rupture of the repaired tendon.

Additionally, the wrist can be splinted in slight extension to further protect the extensor tendons and suture line from increased passive tension. Both orthoses are worn fulltime, and the patient is encouraged to move the fingers within the confines of the orthoses. At 3 weeks the wrist orthosis is weaned, with continued use of the RMEO until 6-8 weeks postoperatively. It is important to note that these therapy programs are often tailored to individual patients and their progress.[5,7]

Merritt et al. first described this protocol after extensor tendon repairs and for sagittal band injuries.[4] Catalano et al. subsequently reported using a similar relative motion orthosis in slightly more extension (25 to 35 degrees) for nonsurgical treatment of acute sagittal band injuries that result in extensor tendon subluxation and dysfunction.[2] Sagittal bands are primary restraints to radial and ulnar deviation of the extensor tendon at the MCP joint, and injury to the sagittal band results in subluxation of the extensor tendon. The RMEO can be used in nonsurgical management of such injuries or for postoperative protection of surgical repair during rehabilitation.

Benefits

Range of motion

The primary benefit derived from the relative motion extension orthosis is improved passive and active range of motion after extensor tendon injury and repair by preventing joint stiffness and adhesions. Merritt et al. reported near full recovery of full flexion: 98.5% of flexion compared to the contralateral hand at 6 weeks and 96.2% of total active motion.[1]

Therapy duration

Another benefit of relative motion splinting is to allow patients more functional active range of motion of the hand during recovery, with fewer therapy visits required to address the negative effects of prolonged immobilization. with less need for strict supervision from in-person hand therapy. Merritt et al. reported an average of 8 therapy visits during recovery, and a return to work of at an average of 18 days.[1] Howell et al reported that the average discharge from therapy was 7 weeks after surgery.[5] After initial therapy and guidance, the orthosis is typically worn for another 6 to 8 weeks with fewer therapy visits.

Return to work

Immediate controlled active range of motion of the hand allows patients to return to work earlier than with static immobilization. Hirth et al. compared outcomes of relative motion orthosis with immobilization and found that the average number of weeks before return to work was 3.3 weeks compared to 9.4 weeks in the immobilized group.[7]two-way mixed ANOVA

Immediate Active Range of Motion (ICAM) Protocol adopted by Penn Hand Service 5

Phase 1: Postoperative Weeks 1-3

Relative motion extension orthosis is created to hold the involved digit in 15-25 degrees of relative extension (Figure 2). In addition, the patient is placed in a volar wrist orthosis with the wrist in 20-25 degrees of extension. The patient wears both splints at all times and is allowed active range of motion

within the confines of both orthoses. They are restricted from heavy activity or strengthening.

Phase II: Postoperative Weeks 4-5

To progress to phase II, the patient must have full digit active range of motion within the confines of the orthoses. The patient is weaned out of the wrist orthosis for light activity and instructed to continue exercises within the confines of the RMEO. For sleep and medium/heavy activity, the patient should continue to wear both orthoses.

Phase III: Postoperative Weeks 6-8

The patient is weaned out of the wrist orthosis completely. The relative motion extension orthosis is continued, except when performing therapy exercises which include active range of motion out of all orthoses. Once the patient is able to achieve full range of motion of the wrist and digits, the RMEO is discontinued and patient is discharged from therapy with no restrictions.

Conclusion

Relative motion extension orthoses allow for immediate active range of motion of the digits following extensor tendon repair or closed or open treatment of sagittal band injuries. The Penn Hand Service has been using relative motion extension orthoses for both extensor tendon injuries and sagittal band injuries with very good outcomes. Combined with a progressive rehabilitation protocol, these lower profile, functional orthoses offer patients a more comfortable method to preserve range of motion of the digits after these injuries.

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U·P·O·J

Pediatrics Tips and Tricks: Appropriate Use of Medial Pinning for Pediatric Supracondylar Humerus Fractures

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Introduction

Supracondylar humerus fractures are the most common type of elbow fracture in children. The vast majority of these fractures are extension-type injuries that occur in children ages 5-7 years old. Non-displaced (Type I) fractures can be managed without surgery in a cast. However, displaced, angulated or unstable fractures usually require surgical fixation. Closed reduction and percutaneous pinning (CRPP) is the mainstay of treatment in the majority of Type II, III and IV fractures[1,], with open reduction used if there is an inadequate alignment with closed reduction. Classically, CRPP of supracondylar humerus fractures has been accomplished using pins in a crossed configuration. In this method, at least one pin is percutaneously inserted laterally into the capitellar ossification center and another pin is placed medially anterior to the medial epicondyle and the ulnar nerve. The pins are directed to cross proximal to the fracture site and penetrate through the respective far cortex. A medial pin confers additional torsional strength and leads to a more stable construct. However, it also introduces the risk of iatrogenic ulnar nerve injury, leading many to attempt to stabilize these fractures with laterally based pin constructs only. The appropriate indications for use of a medial pin are controversial[13], but understanding the risks and benefits of medial pinning in stabilizing pediatric supracondylar humerus fractures will help clinicians utilize this technique only when necessary.

Biomechanics

Supracondylar humerus fractures tend to fail in extension and/or rotation, and both deforming forces must be accounted for when designing a pin construct. For any transverse fracture pattern stabilized with a smooth pin construct of a given pin size, total pin purchase in each fragment tends to be the most important factor in limiting bending, while pin spread at the fracture site tends to be the most important factor limiting rotation. An ideal pin configuration biomechanically is one that engages as much of each fracture fragment as possible and has as much pin spread as possible at the fracture site. A balance must be struck between maximizing bony purchase and maximizing pin spread, as each will come at the cost of the other.

Consider a fracture fixed with two pins. If the pins are placed with maximal pin spread, they will achieve maximal rotational stability. However, they will engage the fracture fragments so peripherally that they engage minimal bone, and they will sacrifice resistance to extension. The inverse is true if the pins are directed to engage as much bone as possible (Figure 1A-B). In lateral-only pinning, the lateral pins have limited ability to engage the fracture site medially due to their entry site and trajectory, and a more medial trajectory comes at the cost of decreased bony purchase in the proximal segment medially. Crossed pins have traditionally solved this problem because a medial pin's trajectory allows it to cross the fracture site medially while still achieving excellent bony purchase (Figure 1C). It should be noted, however, that even crossed pins can confer minimal rotational stability if they cross at the fracture site (Figure 1D).

Crossed pinning, then, is biomechanically advantageous because the increased resistance to rotational deformity will reduce the likelihood of fixation failure. Historically, clinical outcomes of crossed pinning have been very good[2, 3], and biomechanical studies have supported the idea that a medial pin is required for optimal fixation.[4, 5] Zoints at al. used adult cadaveric models to demonstrate that a medial and lateral crossed pin construct is stronger than both 2-pin and 3-pin lateral pin constructs.[4] Lee et al. examined this question usng using a pediatric synthetic bone model and demonstrated that while 2 divergent lateral pins are superior to 2 parallel lateral pins, the crossed medial and lateral pin configuration still outperformed both lateral pin configurations.[5] Based on these data, they recommended crossed pinning when there is concern for instability with lateral pins alone. Notably, however, the fixation techniques used in early biomechanical studies don't reflect modern techniques. The lateral pins placed by Zoints et al. were placed in parallel rather than divergently and Lee et al. did not assess 3-lateral pin configurations of any kind.[4, 5]

Larson et al. were the first to compare three divergent lateral pins, a medial pin with 2

divergent lateral pins (3-crossed pins), and a standard medial and lateral crossed pin (2-crossed pins) configuration (Figure 2). They compared the constructs in two synthetic humerus models: a standard fracture model and a model with a medial wedge cut out to simulate medial comminution. The medial wedge model demonstrated less torsional stability across all pin configurations. The 3-crossed pin configuration was the strongest construct in both models. The three divergent lateral pin construct was stronger than two crossed pins in intact humeri, and statistically similar to 2 crossed pins in the model simulating a deficient medial column.[6] The superior torsional stiffness of 3 crossed pins compared to 3 divergent lateral pins has also been replicated by a more recent biomechanical study.[7]

Ulnar Nerve Injury

The primary disadvantage of medial pinning is that it risks iatrogenic injury to the ulnar nerve, which courses just posterior to the medial epicondyle in the cubital tunnel. Ulnar nerve injury can result from direct penetration of the nerve, but can also result from irritation or compression of the nerve by a medial pin post-operatively. The finding that many children have anterior ulnar nerve subluxation complicates pin placement, as one must be mindful not to damage a mobile nerve. Furthermore, even when the medial pin is appropriately placed anterior to the cubital tunnel, a mobile ulnar nerve may still be prone to irritation as the nerve translates anteriorly and stretches around the medial pin. The reported incidence of ulnar nerve injury with medial pinning has been reported to range from 0-12%.[6] Most ulnar nerve injuries resolve

Table 1. Relative Resistance to Deforming Forces

	A	B	C	D
Extension	+++	++++	++++	++++
Rotation	++	+	+++	+

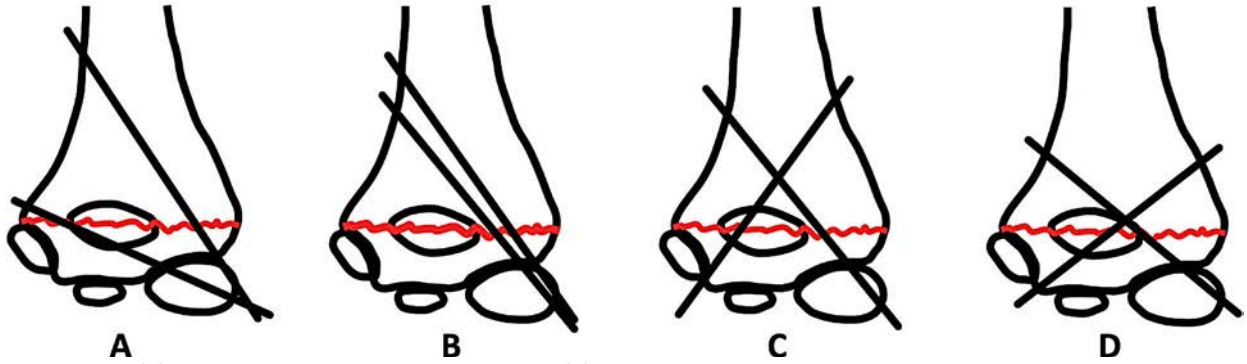

Figure 1. Two pin constructs; **(A)** Ideal 2 lateral pin construct with good separation; **(B)** Less ideal 2 lateral pin construct with poor pin separation but good bony purchase for both pins; **(C)** Ideal 2 crossed pin construct with good bony purchase for both pins and good spread at the fracture site; **(D)** Less ideal 2 crossed pins with no spread.

Table 2. Relative Resistance to Deforming Forces

	A	B	C	D
Extension	+++++	+++	++++++	+++++
Rotation	++++	++++	+++++	+++

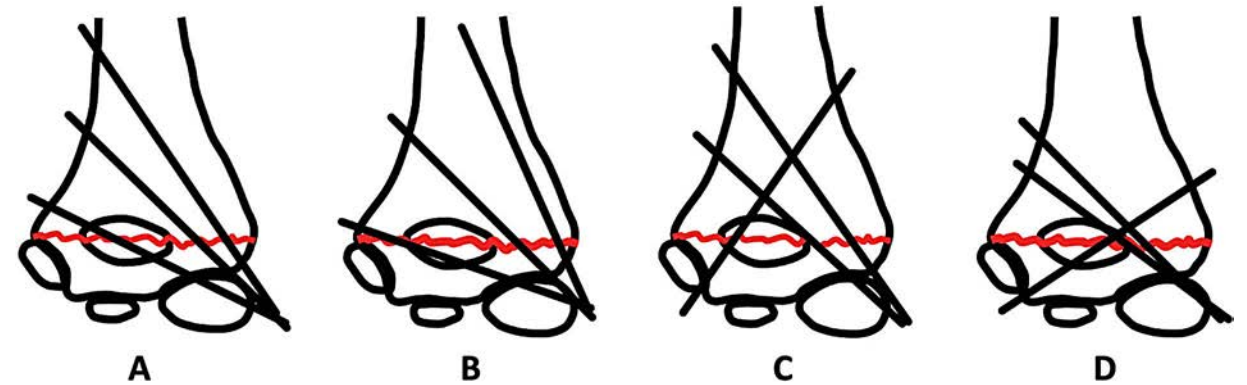

Figure 2. Three pin constructs; **(A)** Ideal 3 divergent lateral pin construct has two lateral pins with good bony purchase and one transverse pin providing good pin spread. **(B)** Less ideal 3 lateral pin construct with one central pin with good bony purchase in both fragments but with two additional medial and lateral pins with good pin spread but less ideal bony purchase. **(C)** Ideal 3 cross-pin construct has two lateral pins and one medial pin all with good bony purchase and good spread at the fracture site. **(D)** Less ideal 3 cross-pin construct with two lateral pins and one medial pin, with good purchase for all pins but with less ideal pin spread at the fracture site.

spontaneously within 6 months, but permanent injuries have been reported and can cause significant disability.[8]

Clinical Outcomes

The ideal pin configuration for supracondylar humerus fractures must balance the need for stable fracture fixation with avoidance of iatrogenic ulnar nerve injury. While early studies suggested that the risk of ulnar nerve injury was minimal, case series in the 1990's brought greater attention to the risk of iatrogenic ulnar nerve injury. Royce et al advocated for the use of lateral-only pinning for fractures that are stable after closed reduction, and recommended medial pins only for comminuted fractures or those that are unstable after closed reduction.[9] In 2001, Gordon et al studied 138 Type II and III fractures and compared three pin configurations: 2 lateral pins, 2 crossed pins, and 3 crossed pins. There was no significant loss of reduction in any group, but they found that the 2 lateral pin construct had slightly more rotational instability. They recommended placing 2 divergent lateral pins, and placing a medial pin only if there is concern for instability on intraoperative stress radiographs.[10]

More recent studies have suggested, however, that lateral pinning provides sufficient fixation of supracondylar humerus fractures if proper technique is used. In 2004, Skaggs et al treated 124 consecutive children with type II and III supracondylar fractures with lateral pinning only.[11] Two divergent lateral pins were placed in all cases, and a third lateral pin was placed when there was concern for instability. There was no loss of reduction, cubitus varus, or loss of elbow motion, and there were no ulnar nerve injuries. They also reported on a separate series of 8 cases of fixation failure after lateral pinning, and highlighted key technical points when placing pins: (1) maximize pin separation at the fracture site, (2) engage the medial and lateral columns proximal to the fracture, (3) engage sufficient bone in the proximal and distal fragments, and (4) have a low threshold for use of a third lateral pin to augment stability.[11] These findings were reinforced by Sankar et al, who evaluated a series of 279 cases found that 8 (2.9%) lost fixation.[12] Seven of eight failures had initially been managed only with 2 divergent lateral pins, and in each case the failure appeared to be due to technical error. They identified the following pin-fixation errors: failure to engage both fragments with at least 2 pins, failure to achieve pin separation >2mm at the fracture site, and failure to achieve bicortical fixation with at least 2 pins (Figure 3). There were no fixation failures when 3 divergent lateral pins were used, and there were no reports of ulnar nerve injury with lateral-only pinning. The data suggest that while a construct consisting of a medial pin and 2 divergent lateral pins is biomechanically stronger than 3 lateral pins, the difference does not impact clinical outcomes. Given these data, Sankar et al recommend against medial pinning due to the risk of ulnar nerve injury with no clear clinical benefit.[12]

Discussion

The decision to use medial pinning remains a subject of controversy, and ultimately depends on surgeon preference and the details of a particular case. Different fracture patterns have different kinds of instability, and thus benefit from different pin configurations. Broadly speaking, the vast majority of extension type 2 SCH fractures are unstable only in extension with little rotational instability, while type 3 fractures are unstable in extension and rotation. Thus, while type 3 fractures may benefit from greater pin spread at the fracture to help control rotation, fractures with no rotational instability only need fixation to resist extension. For laterally based pin constructs, this has led to the suggestion that type 2 fractures can be effectively treated with 2 lateral pins whereas type 3 fractures should get a third pin to help with pin spread at the fracture site and thus rotational control. The biomechanical data would suggest that this pin should ideally be a media pin. However, the clinical data suggests that a third lateral pin placed to engage the fracture site across the medial column works just as well and almost eliminates the risk of ulnar nerve irritation or injury.

There may also be specific fracture patterns that benefit from a medial pin. As Larson et al demonstrated, fractures with medial comminution have significantly less rotational stability because they cannot rely on the intact medial column to resist internal rotation and cubitus varus. Biomechanical studies demonstrate that the most stable way to fix these fractures is with 3 crossed pins (1 medial pin and 2 lateral pins), as lateral pins are less able to stabilize the medial column and prevent rotation (Figure 4A).[6,7] The orientation of a fracture must also be considered. In fractures that run from proximal-medial to distal-lateral, laterally placed pins will run more parallel to the fracture site and achieve weaker fixation (Figure 4B). A medial pin will cross the fracture site orthogonally, greatly augmenting construct strength.

Clinical data suggest that for the vast majority of SCH fractures, lateral fixation can achieve adequate stability and optimal outcomes without risking iatrogenic ulnar nerve injury.[11, 12] However, while there are certain fracture patterns may greatly benefit from or even require a medially based pin for optimal fracture stabilization, some instability patterns are not apparent until the fracture reduction is attempted. In both of these scenarios, the sequence of pin placement is nearly always to place most if not all of the lateral fixation first. We proceed to medial fixation only if there is concern for residual instability based on intra-operative imaging or the fracture pattern. This avoids medial pinning in patients who do not need it. It also provides provisional fixation, allowing for extension of the elbow and placement of the medial pin through a small open approach that enables direct visualization and protection of the ulnar nerve. It is critical that proper technique be used with placing lateral pins, with at least 2 pins engaging both fracture fragments, achieving adequate separation at the fracture site, and achieving bicortical fixation in both fragments.

Conclusion

We recommend that fixation for all supracondylar humerus fractures begin with the placement of the lateral fixation. In

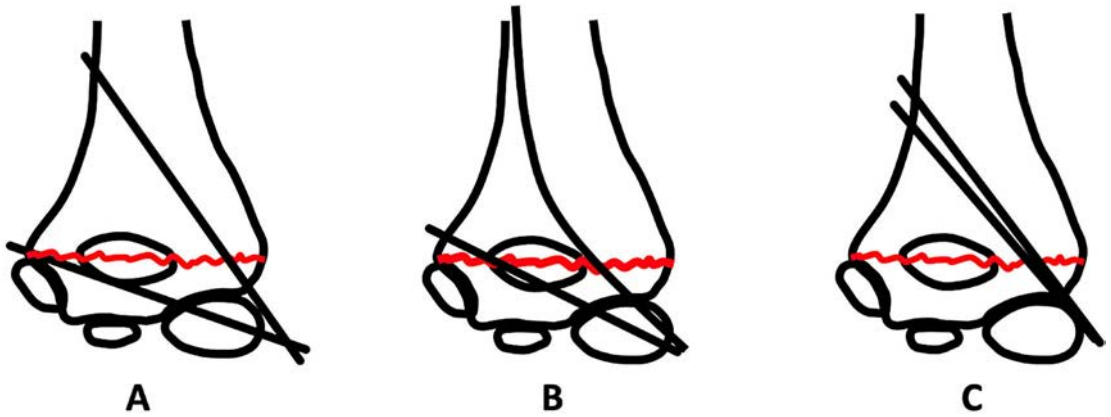

Figure 3. Common technical errors that contribute to fixation failure after lateral-only pinning: **(A)** failure to engage both fragments with at least 2 pins; **(B)** failure to achieve bicortical fixation with at least 2 pins; **(C)** failure to achieve pin separation >2mm at the fracture site12.

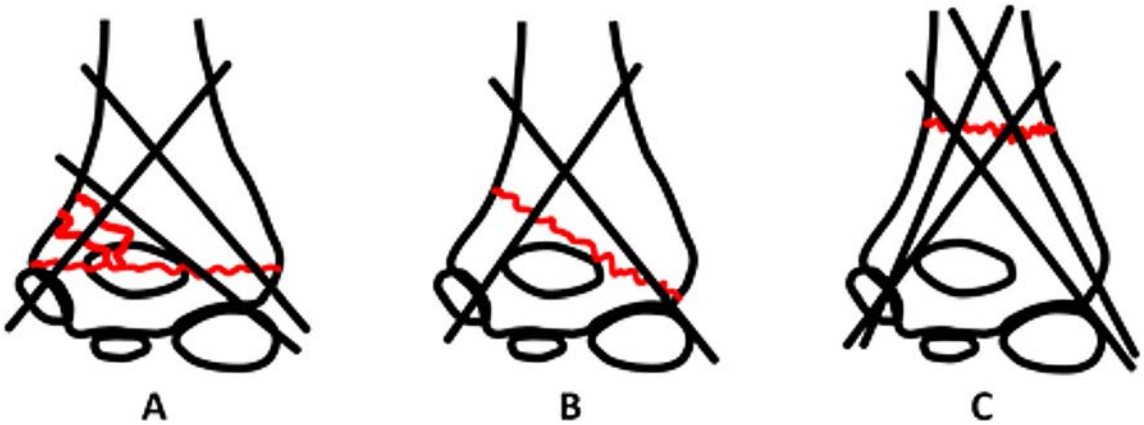

Figure 4. Supracondylar humerus fracture patterns that benefit from a medial pin; **(A)** Medial comminution; **(B)** Oblique fracture line from proximal medial to distal lateral; **(C)** Proximal fractures.

many cases, this will be sufficient. Medial fixation may then be added if there is concern for instability based on the fracture pattern or intra-operative imaging.

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Shoulder and Elbow Tips & Tricks: A Case Study in Shoulder Hemiarthroplasty for Proximal Humerus Fractures: The Importance of Accurate Humeral Head Length Measurements

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Background

Proximal humerus fractures are commonly seen after low energy mechanisms in elderly populations with osteoporotic bone and high energy mechanisms in younger patients.[1] The large majority of these fractures are minimally displaced and can be managed non-operatively with good functional outcomes.[1, 2] Surgical indications for these fractures include multi-fragmentary head-splitting fractures, fracture dislocations, and neurovascular injuries.[1] Surgical management is determined based on patient characteristics, fracture pattern, and how fixation will drive functional outcomes.[1]

For operative treatment of proximal humerus fractures, two broad categories of operative treatment are available: those which preserve the humeral head and those that are humeral-head sacrificing. Preservation of the humeral head includes osteosynthesis techniques using plates or nails, while humeral-head sacrificing arthroplasty refers to reverse total shoulder arthroplasty (RSA) or hemiarthroplasty.[2] Prior to the development of RSA, hemiarthroplasty was the "gold standard" option for proximal humerus fractures in which fracture fixation was unachievable. However, hemiarthroplasty, particularly in older patients with osteoporotic bone and rotator cuff deficiency, showed poor functional outcomes and early re-operation rates.[1] Recently, RSA has become the arthroplasty option of choice for severe proximal humerus fractures[3,4] due to their more reliable and reproducible outcomes. This trend is largely because outcomes of reverse total shoulder arthroplasty are much less dependent on the function of the rotator cuff and therefore less limited by factors such as nonhealing tuberosities or prosthesis height.[5] However, despite the rise in use of RSA, there remains a need for shoulder hemiarthroplasty in the treating surgeon's repertoire.

In current practice, hemiarthroplasty for proximal humerus fractures is reserved for younger or higher demand patients with proximal humerus fractures that are unable to be fixed with osteosynthesis. Patients typically demonstrate adequate bone quality to support healing around the prosthesis, minimal comminution of the tuberosity fragments, and have adequate rotator cuff functions to enable post-operative rehabilitation.[2]

Adequate humeral height, version, and anatomic tuberosity reduction have important implications for success following hemiarthroplasty. Tuberosity reduction correlates with functional results, particularly native shoulder kinematics. Humeral height and version, similarly, correlate to functional outcomes, where improper measurements can lead to persistent pain and stiffness post-operatively.[2]

In order to ensure proper tuberosity reduction, humeral height and version require specific calculations during preoperative planning to restore proper humeral length.[6] Without proper restoration, inadequate humeral height can lead to non-anatomic reconstruction and poor clinical outcomes.

This case study provides an example of the use of hemiarthroplasty in a young female patient after a gun-shot wound to the left upper extremity and demonstrates the importance of accurate measurement of humeral head length when completing the operation.

Case Presentation

A 44-year-old female presents to the Trauma Center with multiple gun-shot wounds, including to the left upper extremity. Radiographs of the left shoulder demonstrated a comminuted left proximal humerus fracture with humeral head displacement and dispersed osseous fragments (Figure 1). The patient was Glascow Coma Scale 3 at the time of arrival and initial physical examination was limited due to her disposition. On examination, there was an entry wound over the lateral shoulder with exit wound near the acromion and clavicle. No motor or sensory examination was possible because the patient was intubated and sedated at this time.

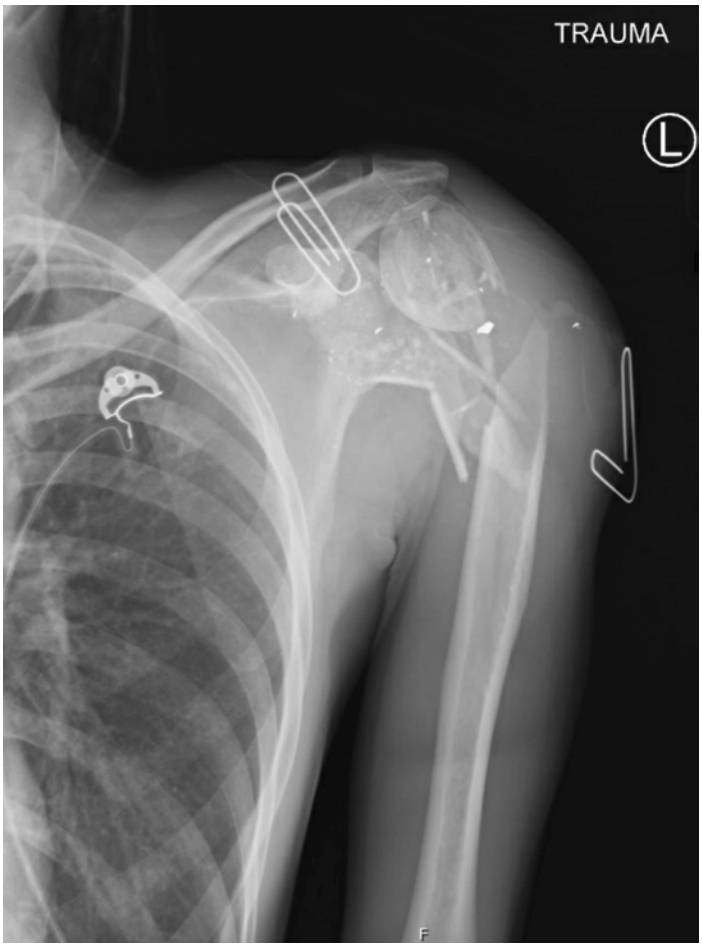

Figure 1. Shoulder x-ray upon arrival to the Trauma Center illustrating a comminuted left proximal humerus fracture with humeral head displacement and dispersed osseous fragments.

The patient was taken emergently to the operating room for a formal irrigation and debridement because of fracture-dislocation of the left glenohumeral joint with joint space violation from her gun-shot wound and concern for possible arterial injury. No arterial injury was identified at the time of surgical exploration.

The patient was extubated post-operatively and able to participate in a neurovascular examination at this time. She was neurovascularly intact in the ulnar, median and radial distributions with overall weakness and diminished sensation. Her axillary nerve was nonfunctioning with no deltoid motor functioning and limited sensation. Definitive operative planning was pending patient stabilization for further surgical intervention.

A post-operative CT scan was performed to better understand the injury pattern and demonstrated a severely comminuted proximal humerus fracture involving multiple portions of the humeral head and medial calcar with significant comminution of the tuberosities (Figure 2). Due to the extensive comminution of the articular surface, open reduction internal fixation was deemed an inadequate option and the decision was made to proceed with a hemiarthroplasty. The indications for hemiarthroplasty included the comminution of the articular surface, the patient's young age, and the concern for deltoid dysfunction in the setting of an axillary nerve injury which would compromise the function of a reverse total shoulder arthroplasty.

Tips and Tricks

The patient was positioned in the modified beach chair position at a 45-degree angle.[6] All areas of bony prominence and possible sites of nerve compression were well-padded and offloaded. At the time of prepping and draping, electrodiagnostic needles were placed for neuromonitoring of the left upper extremity. Due to the patient's symptomatic nerve injury, neuromonitoring was performed to confirm the preoperative status of her nerve function. Neuromonitoring confirmed no signals in the axillary nerve distribution and

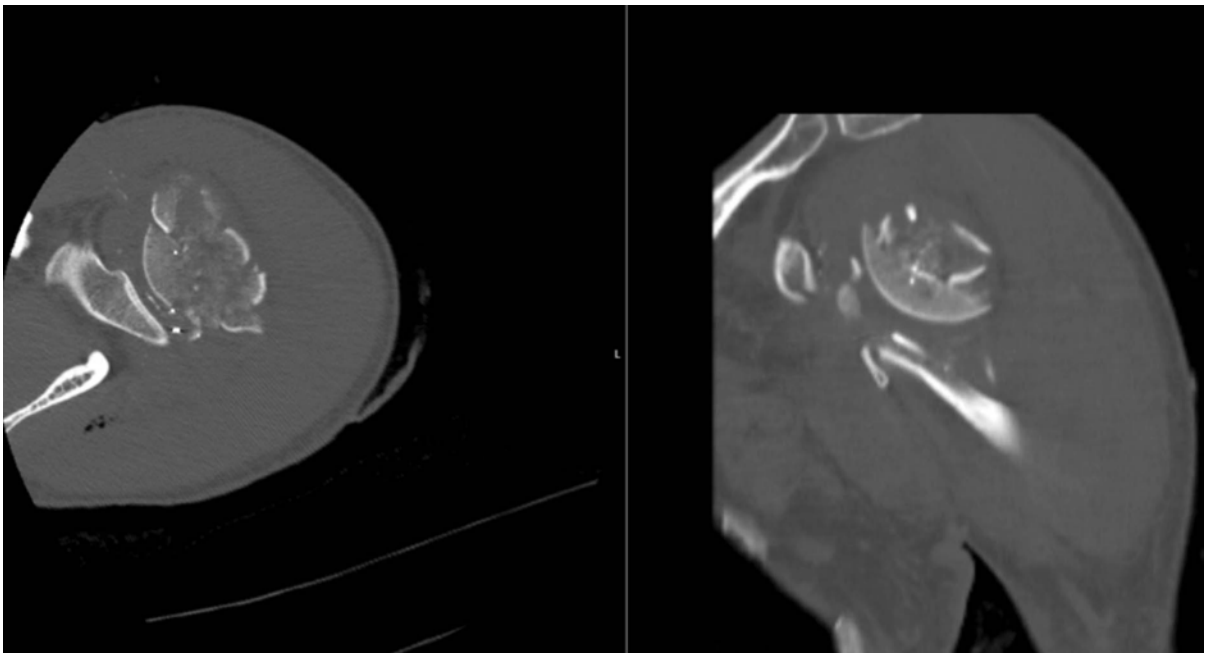

Figure 2. Post-operative CT scan of the left shoulder illustrating severely comminuted proximal humerus fracture.

also demonstrated significant decrease in signals in the other peripheral nerve distributions.

In order to properly restore the humeral length with the hemiarthroplasty, proper preoperative films are obtained of both the injured and contralateral humerus. The films are calibrated using a radiologic marker ball for calibration. In this case, the marker is 30mm in diameter (Figure 3 A-C).

The length of the humerus on the contralateral arm is measured from the superior apex of the articular surface to a fixed point distally. In the case of the AP radiograph, the center of the olecranon fossa is selected. In this particular case, the length of the contralateral (non-injured) humerus for those endpoints measured 299.8mm (Figure 3, A). On the injured full-length humerus film, the measurement is recreated starting from the center of the olecranon fossa distally and measured proximally to the superior-most aspect of the humeral shaft (which in this case was the lateral aspect of the humeral shaft). This distance measured 253.3mm (Figure 3, B). This measurement is repeated but now using the proximal-most aspect of the medial portion of the humeral shaft to the center of the olecranon fossa which measures 216.2mm (Figure 3, C). These two measures from the injured humerus are then subtracted from the length measured on the contralateral uninjured humerus (delta) to help determine how much the humeral prosthesis should be proud from the medial and lateral aspects of the fractured humeral shaft fragment to restore the humeral height appropriately. For the medial aspect, this measured 83.6mm and for the lateral aspect, this measured 46.5mm. A marking pen is then used to mark these delta lengths on the trial and final humeral prostheses as they are measured from the superior aspect of the hemiarthroplasty down the stem. Of note, the large medial calcar fragment that was initially displaced medially included the attachment of the pectoralis major tendon. At the time of surgery, this medial calcar fragment was reduced around the trial humeral stem and cabled into place. Once this was performed, the defect medially was near equivalent to the defect laterally with about 5cm of height needed to be restored. This correlated with the known distance of the pectoralis insertion from the superior aspect of the humeral articular surface.

Cadaveric studies have demonstrated that the average distance of the superior aspect of the humeral head to the superior border of the pectoralis major tendon insertion is 56mm. Murachovsky et. al.[7] described this distance (the PMT) using 20 cadavers (40 shoulders) and showed this measurement with a 95% confidence interval. There was no difference based on patient size and thus, the PMT is a method for accurate humeral length restoration intraoperatively with comminuted fracture patterns when other landmarks are absent. This measure was also used intraoperatively as another check that the humeral height was appropriately restored (Figure 4). Using this anatomical landmark and the preoperative radiographic measurements, a height defect of about 5cm was necessary for restoration of proper humeral length.

Finally, as the trial implant is placed, heavy sutures in the tuberosity fragments were used to reduce to the proximal aspect of the humeral stem. Restoration of the tuberosities to the implant and their relation to each other area also used to judge the height of the prosthesis. In particular, the greater tuberosity should not be proximal to the most superior aspect of the humeral head surface. Intraoperative fluoroscopy was performed at the time of trial reduction to confirm adequate tuberosity reduction with the humeral stem placed at the appropriate height and 30 degrees of retroversion.

Individually or separately, errors in humeral length or version during hemiarthroplasty are associated with non-anatomical reconstruction.[6] Shortening of the humerus can shorten the deltoid causing contracture leading to compromised anterior elevation of the shoulder. This change can decrease the level arm in the operative extremity. Lengthening compared to the contralateral extremity leads to pain and limited range of motion secondary to superior humeral migration and abnormal joint compression forces that may cause anterosuperior impingement.[6] Improper version can place excess tension on the rotator cuff, which can lead to either suture release or posterior migration of the greater tuberosity.

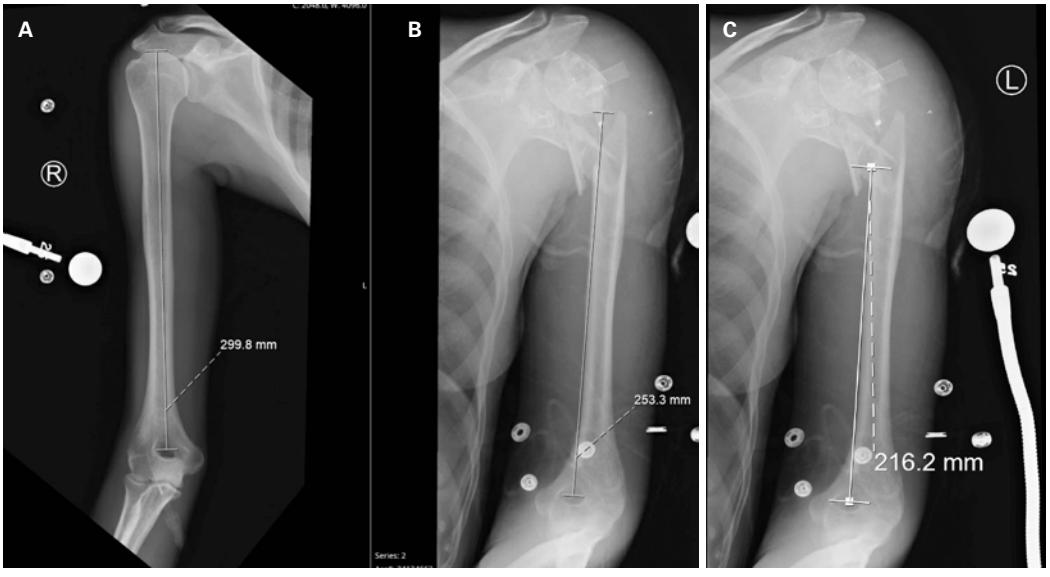

Figure 3. Humerus x-ray measurements. **(A)** Contralateral right humerus measurement with marker ball; **(B)** Left comminuted proximal humerus fracture with lateral measurement; **(C)** Left comminuted proximal humerus fracture with medial measurement.

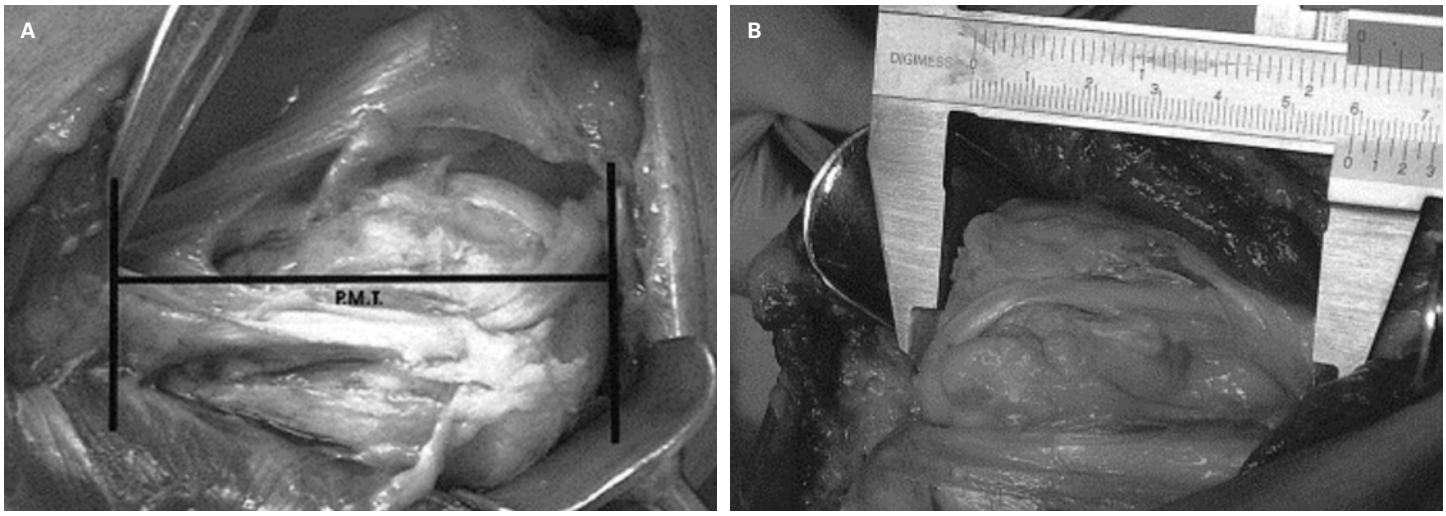

Figure 4. (A) PMT distance showing superior aspect of the humeral head to the superior border of the pectoralis major tendon insertion; **(B)** Intraoperative measurement of PMT of 5cm [images courtesy of Murachovsky et. al.[7]]

Outcome

Following left shoulder hemiarthroplasty with cable fixation and repair of the rotator cuff (Figure 5), the patient was placed in a sling and was started on early passive and active assisted range of motion exercises. However, the patient had increasing pain postoperatively with limited participation in examinations and physical and occupational therapy which delayed discharge.

Three months post-operatively, the patient developed significant deltoid atrophy and persistent axillary nerve dysfunction which was confirmed by MRI. She also had continued weakness in her radial, median, and ulnar nerve distributions. Most recent x-rays of the left shoulder show a well-fixated hemiarthroplasty with some anterior subluxation on the axillary view unchanged from previous x-rays. The implant height is appropriate and well-fixated.

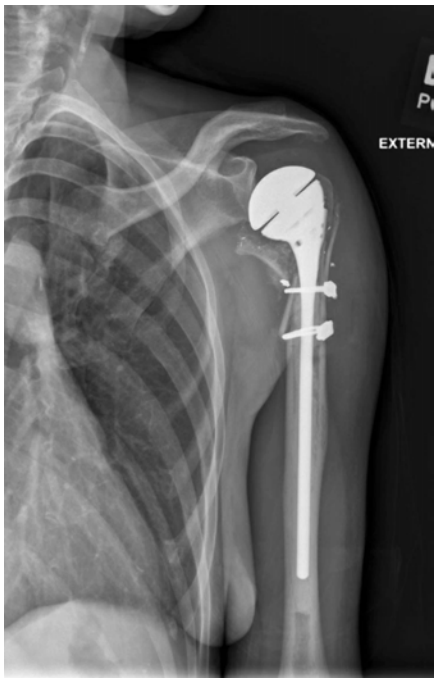

Figure 5. Post-operative x-ray of the left humerus hemiarthroplasty with cerclage wires.

Conclusion

This case demonstrates an example of the continued value in hemiarthroplasty and the need for proper humeral height assessment. Unfortunately, the patient's axillary nerve injury at the time of her trauma resulted in poor deltoid function. However, this was an important thing to consider at the time of her surgical management as a reverse total shoulder would have not been functional and likely would have remained grossly unstable with the deltoid atony.

As with any surgical method, hemiarthroplasty complications occur. These include infection, fracture, nerve injury, and tuberosity malunion/nonunion.[2] However, similar concerns exist with other operative fixation techniques. Thus, with consideration of proper humeral length, version, and anatomic tuberosity reduction in appropriate candidates, hemiarthroplasty is a good surgical option for proximal humerus fractures.[1,2,5] Preoperative radiographic planning and intraoperative measurements using established methods provide good surgical fixation for better patient functional outcomes in younger patients.

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U·P·O·J

Arthroplasty Tips & Tricks: Rapidly Progressive Avascular Necrosis of the Femoral Head Following a Single Intra-articular Corticosteroid Injection

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Introduction

Avascular necrosis (AVN)—also known as osteonecrosis or aseptic necrosis—is the death of bone due to a disruption in its blood supply.[1] It most commonly involves the femoral head, but may also involve other sites such as the femoral condyles, humeral head, or talus.[2] Males are more likely to be affected than females and it typically occurs in patients 30 to 60 years old.[2]

While the pathophysiology of AVN has been studied extensively, there is no general consensus on the specific etiology. The inciting "event" can be broadly classified as traumatic or atraumatic. Such event ultimately leads to disruption of the bone microcirculation *via* three primary mechanisms: mechanical vascular interruption, intravascular occlusion, or extravascular compression.[1,3]

Many of the commonly cited risk factors for AVN—such as trauma or hemoglobinopathy—can be easily understood when considering the mechanisms of osseous vascular disruption. For instance, mechanical disruption typically occurs following trauma. The medial circumflex femoral artery, the main blood supply to the adult femoral head, can be disrupted as a result of fractures involving the proximal femur or hip dislocation.[4] Hemoglobinopathies, such as sickle cell anemia, are classically cited as a cause of intravascular occlusion. The sickled erythrocytes may become mechanically sequestered in the low flow areas of the femoral head, thus leading to vaso-occlusion.[1,5]

A lesser understood phenomenon is AVN resulting from corticosteroid use. Numerous theories exist regarding the exact pathophysiology, but the most accepted theory is that the use of corticosteroids leads to accumulation of fat within the bone marrow resulting in intraosseous hypertension and decreased perfusion.[1,3,6,7] This is most commonly discussed in the context of patients on long term, high dose oral steroids for maintenance of systemic diseases such as systemic lupus erythematous, irritable bowel disease, and rheumatoid arthritis.[8,9] Less often, AVN can be seen after topical steroid use or intra-articular steroid injection; these instances are limited to case reports.[10-16]

We present a case of rapidly progressive avascular necrosis of the femoral head following a single intra-articular corticosteroid injection.

Case Report

The patient is a 74-year-old female with a past medical history significant for lumbar degenerative disc disease who presented to an outside hospital orthopaedic surgeon's office with right groin, lateral hip, and buttock pain. Imaging at that time was consistent with moderate osteoarthritis of the right hip as well as degenerative disc disease of the lumbar spine. Given her concomitant lumbar and hip findings on radiographs, the patient underwent a diagnostic and therapeutic image-guided corticosteroid injection to the right hip at that time.

She reported complete resolution of her pain for approximately two weeks, but the pain gradually returned shortly thereafter. Her imaging was repeated at this time and the findings were unchanged from prior (Figures 1 and 2). Three weeks after the injection, her pain was worse than before her injection and she was unable to ambulate. She returned to her surgeon's office and a bone scan obtained approximately 11 weeks following the injection showed increased uptake in the right hip and pelvis. Magnetic resonance imaging (MRI) of the right hip was then obtained approximately 15 weeks following the injection, showing complete destruction of the femoral head and a fluid collection in the soft tissue anterior to the hip joint (Figure 3). The patient was then referred to our office for further management.

The patient presented to our office approximately 16 weeks following the injection. At that time, plain radiographs demonstrated complete destruction of the right femoral head (Figure 4). Differential diagnoses included septic arthritis, metastatic disease, primary bone malignancy, or Gorham's disease. An infectious work up that included complete blood cell count, erythrocyte sedimentation rate, C-reactive

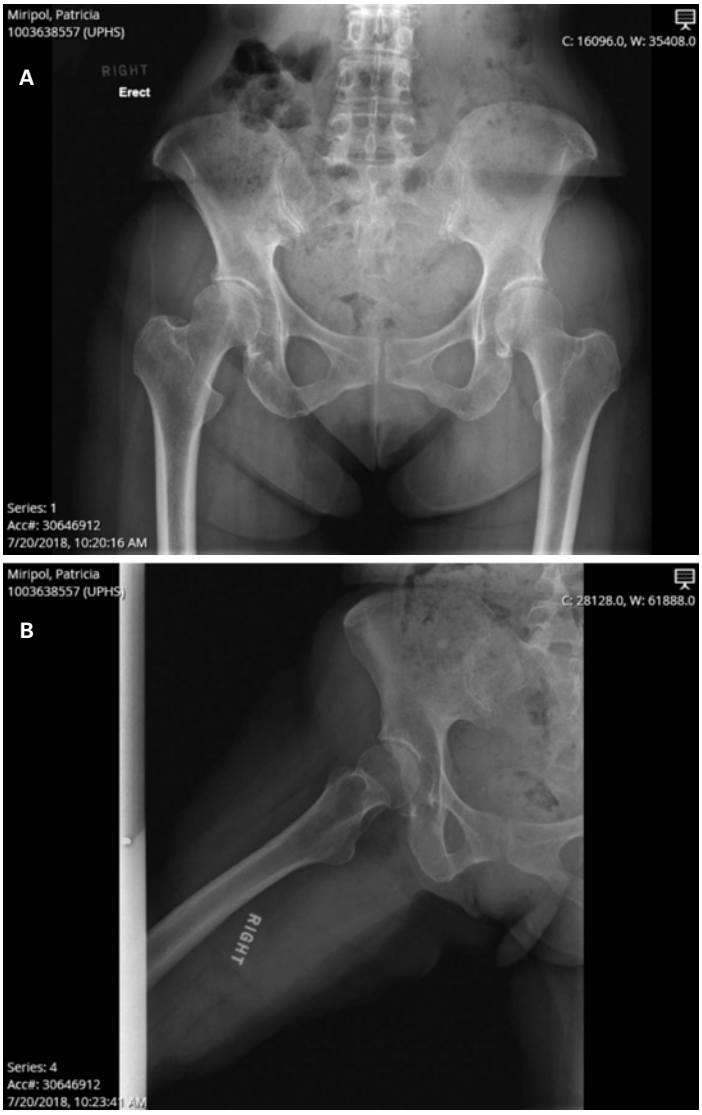

Figure 1. Radiographs obtained 11 days following the right hip injection; **(A)** anteroposterior (AP) pelvis radiograph showing moderate osteoarthritis of the right hip; **(B)** lateral radiograph of the right hip showing moderate osteoarthritis.

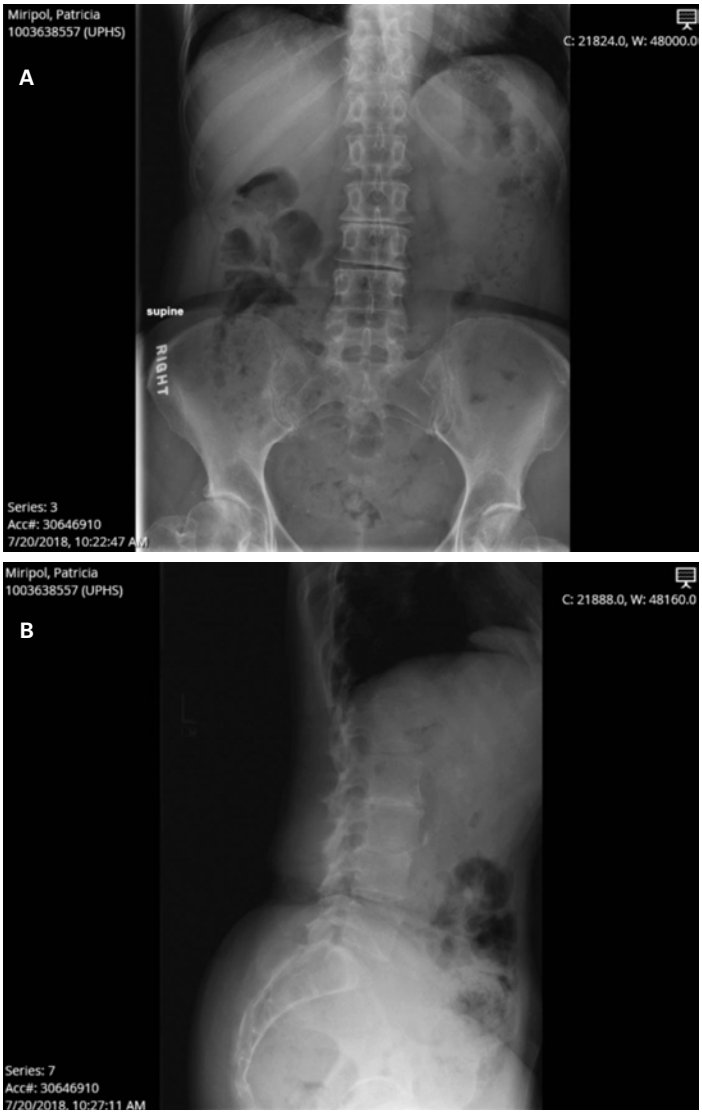

Figure 2. Radiographs obtained 11 days following the right hip injection; **(A)** AP radiograph of the lumbar spine showing disc space narrowing; **(B)** lateral radiograph of the lumbar spine showing degenerative disc disease of the lumbar spine, worst at L2-3.

protein, and subsequent right hip aspiration were all negative for infection. The patient was also discussed at our institution's weekly orthopaedic oncology conference, and there was no concern for an oncologic etiology.

Given the patient's pain and limited function, the decision was made to proceed with right total hip arthroplasty (THA) versus placement of a right hip antibiotic spacer. Despite a negative infectious work-up preoperatively, the patient was advised that intraoperative right hip aspiration and frozen sections would be obtained to guide decision-making.

The patient was taken to the operating room approximately 19 weeks following the injection. Right hip aspiration and intraoperative frozen sections were not consistent with infection. The decision was made to proceed with right THA (Figure 5). The patient's immediate postoperative course was uneventful. The patient was most recently seen over two years following her THA. She reports 0/10 right hip pain with no symptoms of infection or instability. Her Hip disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS, JR.) improved from 43.34 preoperatively to 92.34 postoperatively.

Discussion

Avascular necrosis of the femoral head following intra-articular corticosteroid injection is an uncommon phenomenon. There is a paucity of data surrounding this topic, with case reports comprising the existing literature.[11-16]

There are seven reported cases in the literature for femoral head AVN following a single intra-articular steroid injection.[11] In 2006, Yamamoto et al. reported the first case in a 50-year-old female who received a single intra-articular steroid injection for the management of hip osteoarthritis; the patient developed AVN of the femoral head three months following the injection.[12] In each of the reported cases thereafter, patients developed rapidly progressive

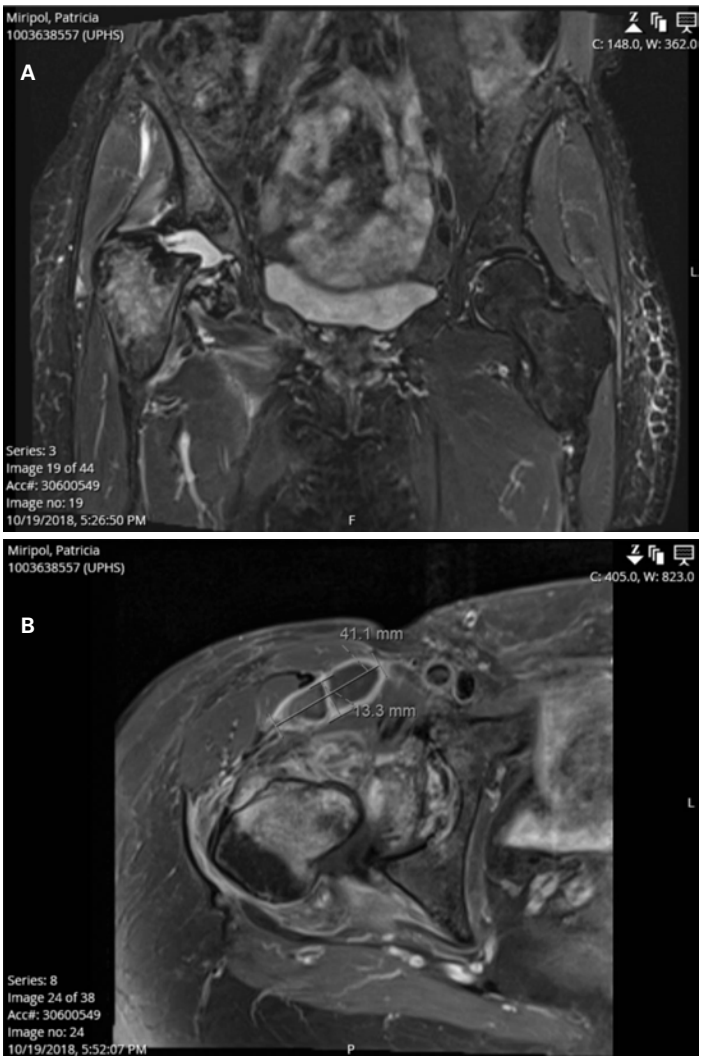

Figure 3. MRI obtained approximately 15 weeks following the right hip injection; **(A)** coronal plane view of a short tau inversion recovery (STIR) MRI of the pelvis showing complete destruction of the right femoral head with associated bone marrow edema in the proximal femur, hip joint effusion, and intramuscular edema; **(B)** axial plane view of a T1 fat saturated MRI of the right hip redemonstrating the destruction of the femoral head as well as a loculated intramuscular fluid collection.

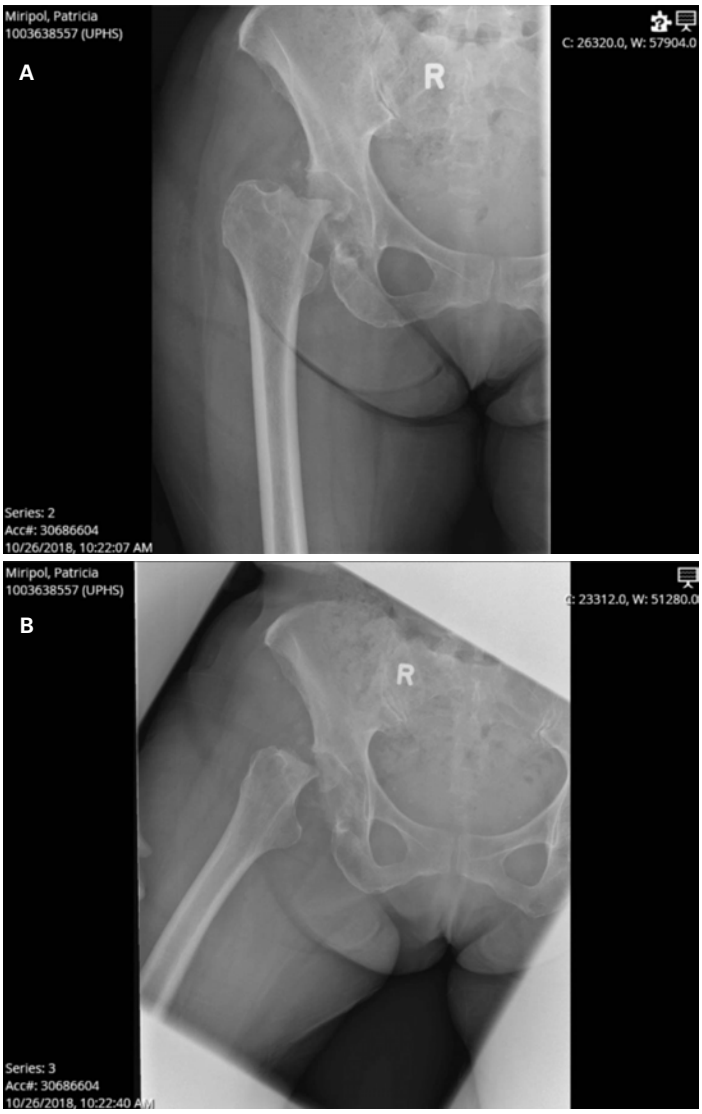

Figure 4. Radiographs obtained approximately 16 weeks following the right hip injection; **(A)** AP radiograph of the right hip showing complete destruction of the femoral head; **(B)** lateral radiograph of the right hip redemonstrating complete destruction of the femoral head.

AVN of the femoral head shortly after a single intra-articular corticosteroid injection with no prior history of steroid use.[11-16] The previously reported cases developed AVN between four and 14 weeks following the injection. The primary treatment modality for these patients was arthroplasty; six patients were treated with total hip arthroplasty and one patient was treated with hemiarthroplasty.

The management of avascular necrosis varies based on radiographic severity and age.[3,17] The initial management for patients with femoral head lesions without collapse is to limit weightbearing using a walker or cane. However, nonoperative treatment is rarely used in isolation due to poor success rates. Mont et al. reviewed 21 studies utilizing nonoperative management as the primary treatment modality for AVN and found only 22% of patients avoided surgery at 34 months.[18] As such, weightbearing modification is typically only one facet of a treatment plan.

As studies uncover more information regarding the pathophysiology of avascular necrosis, researchers have begun looking at pharmacologic interventions to slow or even halt the process. Recent studies have demonstrated the potential benefit from using bisphosphonates, lipid lowering agents, and vasodilators.[7,19,20] However, more robust data from randomized control trials are needed to truly elucidate the utility of these treatment options.

Operative intervention can be broadly classified as joint preserving versus joint replacing. If a patient has a small- or medium-sized femoral head lesion without collapse, this most commonly is treated with core decompression. While the technique can vary, the principle of core decompression is to decrease intraosseous hypertension.[21] The two most common techniques involve using either a trephine or percutaneous drilling to decompress the femoral head lesion and increase blood flow to the necrotic lesion.[22,23] Studies comparing these

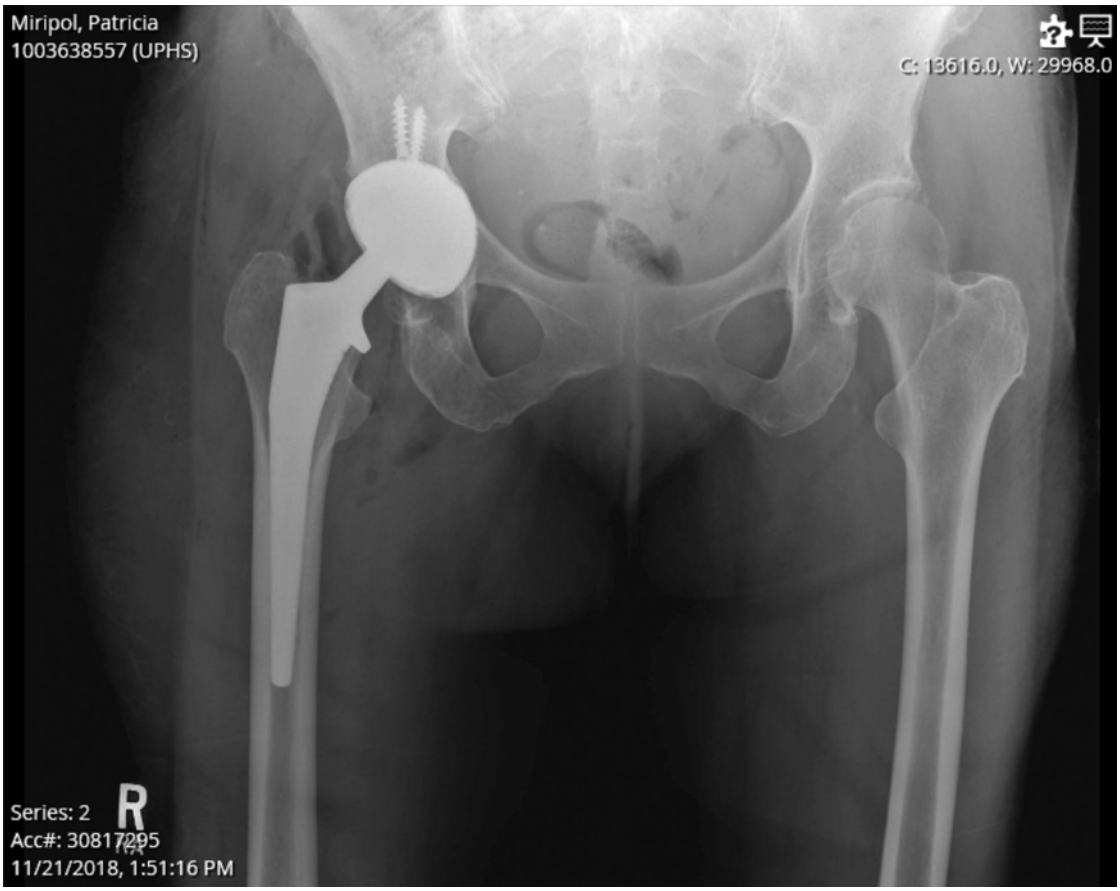

Figure 5. AP pelvis radiograph obtained at time of total hip arthroplasty, approximately 19 weeks following the right hip injection, showing a well-fixed, well-aligned right total hip prosthesis

two techniques in sickle cell patients with AVN have shown equivalent odds of improvement, and the treating surgeon should perform the technique in which they feel the most comfortable.[24]

Core decompression can also be combined with autologous bone marrow grafting.[25] A prospective study by Hernigou et al. followed 189 hips in 116 patients for five to 10 years after undergoing core decompression with autologous bone marrow grafting. One-hundred forty-five patients underwent the procedure prior to femoral head collapse; only nine of these patients went on to a total hip replacement. Twenty-five of the 44 hips that underwent the procedure after femoral head collapse required a total hip replacement during the follow up period.[25]

Bone-grafting—both nonvascularized and vascularized—has shown promise in treating AVN of the femoral head. The theory behind nonvascularized fibular bone grafting was that it would provide structural support to the femoral head and serve as a scaffold for the formation of new bone in the defect.[26] A retrospective review of 39 hips with avascular necrosis treated with nonvascularized bone grafting with supplemental bone morphogenic protein 7 (BMP-7) demonstrated no need for further surgery at 24 months in 80% of small- and medium-sized lesions.[27]

Advances in microvascular surgery have paved the way for vascularized bone grafting, with the thought that vascularized bone grafting not only provides structural support to prevent femoral head collapse, but also the blood supply to encourage healing.[28] A randomized control trial by Cao et al. comparing vascularized free fibula grafting to core decompression showed that patients who underwent vascularized free fibula grafting had improved vascularity and decreased progression of AVN compared to the patients that underwent core decompression.[29] However, at 36 months there was no difference in the rate of THA between the two groups. Although surgeons are optimistic that vascularized bone grafting will be a reliable joint-preserving procedure in the future, further investigation is necessary to identify appropriate candidates.

For the larger, collapsed lesions or if the patient has radiographic findings consistent with arthritic changes of the acetabulum, joint replacement remains the gold standard of treatment.[30] With AVN occurring in younger, more active patients, there were significant concerns regarding implant survivorship. However, with advances in implant technology and surgical techniques, this has been significantly improved. A study comparing THAs performed for osteonecrosis showed an improvement in revision rates from 17% to 3% before and after 1990, respectively.[31] Results continue to be promising, as a recent comparative study examining outcomes for THA performed for AVN versus osteoarthritis showed no significant difference in functional outcomes, implant survival, and rate of complications at ten years when matched for age and sex.[32]

Given our experience with this case, we have several

recommendations for AVN patients with femoral head collapse following an intra-articular corticosteroid injection. The treating physician should utilize all nonoperative modalities to manage the patient's hip osteoarthritis prior to recommending an intra-articular corticosteroid injection. If a patient receives an intra-articular steroid injection and reports worsening pain, radiographs should be obtained at that time. MRI and bone scan can be helpful in making the diagnosis in these cases involving severe bone loss. Infectious etiologies should be ruled out as well. If the patient has persistent pain with radiographic findings consistent with AVN with femoral head collapse, the authors recommend proceeding with operative management. The treating surgeon should obtain intraoperative frozen sections to rule out infection and be prepared to proceed with antibiotic spacer placement if intraoperative frozen section is consistent with infection. If findings are not consistent with infection, we recommend proceeding with total hip arthroplasty.

Given the numerous reports in the literature over the last 15 years, there is a clear link between rapidly progressive avascular necrosis of the femoral head and intra-articular steroid injections. Further studies are required to fully understand this association and the authors advocate for such investigations.

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Foot and Ankle Tips & Tricks: Syndesmotic Screw Fixation—Principles and Technique

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Introduction

Ankle injuries are the most common injury to the lower extremity. Ankle fractures occur at an incidence of roughly 127 per 100,00 adult individuals, and that continues to increase.[1–3] It has been reported that 15% to 23% of operatively managed ankle fractures have associated syndesmotic injuries that require fixation.[4,5] Syndesmotic injuries are a significant source of morbidity and require precise anatomic reduction for successful outcomes.[6,7] It has been shown that the slightest malreduction can foreshadow a poor clinical outcome.[6,7] As little as one millimeter of displacement reduces contact area by up to 42%.[8]

Ankle syndesmotic injuries that require surgical fixation can be treated with a variety of devices. Despite the number of instruments, syndesmotic screws were the historic *gold standard* for fixation of the syndesmosis. However, clinical practice is still highly variable regarding technical aspects of screw fixation. Some of these controversies include the optimal number of cortices needed to stabilize the injury, the size of screw(s), the number of screws, the position of the foot during screw insertion as well as postoperative protocols.

This paper will 1) describe the principles of syndesmotic screw fixation and 2) discuss the technical considerations when inserting syndesmotic screws.

Principles

Anatomy and Biomechanics

The syndesmosis is comprised of five main structures: the anterior-inferior tibiofibular ligament (AITFL), posterior-inferior tibiofibular ligament (PITFL), interosseous membrane, interosseous ligament (IOL) and inferior transverse ligament (ITL).

The syndesmosis functions to maintain integrity between the tibia and fibula by resisting axial, rotational, and translational forces during ankle dorsiflexion and plantar flexion. More specifically, the fibula externally rotates and translates laterally during dorsiflexion in order to accommodate the asymmetric talus.[9,10] Previous studies demonstrate that the syndesmosis widens 1 mm during normal gait, establishing the dynamicity of the tibiofibular syndesmosis.[9,11]

Although the syndesmosis provides stability to the distal tibiofibular joint, the deltoid ligament provides the primary stability. With an intact deltoid ligament, an injured to completely transected syndesmosis demonstrates minimal widening on radiographs as shown in a cadaveric model.[12] The syndesmosis aims to restrain lateral fibular motion with the AITFL and transverse ligaments being the most important. Disruption of the deltoid and syndesmotic ligaments leads to abnormal ankle biomechanics manifesting as lateral translation of the fibula, external rotation of the talus, and increased tibiotalar contact pressures.[7,10]

One novel cadaveric study sequentially sectioned each ligament of the syndesmosis and noted that each ligament imparted varying degrees of stability; the AITFL provided 35%, the AITFL provided 35%, the interosseous ligament 22%, the superficial PITFL 9%, and the deep PITFL 33%.[12] Rupture of two or more of these ligaments may lead to instability.[12]

Stable versus Unstable

The identification of an unstable syndesmotic injury is clinically difficult and requires the use of physical exam findings, radiographic parameters, advanced imaging, and/or intra-operative evaluation to determine whether or not an unstable syndesmotic injury is present that requires fixation.

The most common physical exam findings patients present with are ankle pain, swelling, instability, and pain with walking on uneven surfaces.[13] Patients who have tenderness to palpation over the syndesmosis and/or have reduced ankle dorsiflexion are more likely to have a syndesmotic injury.[10,13,14] Numerous provocative maneuvers can be performed to help clinically diagnose syndesmotic injuries including the Hopkins squeeze test, external rotation test, crossed-leg test, forced dorsiflexion text, and the Cotton test. Despite the number of tests, the clinical diagnosis of syndesmotic injury can be missed up to 20% of the time.[15,16]

When evaluating radiographs for syndesmotic injury, it is important to evaluate certain

radiographic parameters including the tibiofibular overlap, tibiofibular clear space and medial clear space (Figure 1). Cadaveric studies attempted to define the upper limits of normal for the aforementioned parameters. Measurements that should raise suspicion for syndesmotic injuries are tibiofibular clear space greater than 6 mm on the AP and mortise views, a tibiofibular overlap of less than 1 mm on the mortise view and less than 6 mm on the AP view, and a medial clear space greater than 5 mm.[17,18] However, a medial clear space of greater than 4 mm was associated with deltoid and tibiofibular ligament disruption.[17,18]

In addition to static imaging, stress views can help determine the magnitude of instability and thus the need for surgical fixation. Weightbearing and external rotation stress films help identify unstable ankle injuries by displacing the fibula laterally, leading to widening of the tibiofibular clear space (and decreasing the tibiofibular overlap).[19]and an intact ankle mortise underwent an external rotation stress test to confirm injury to the deltoid ligament (stress positive Adjuvant advanced imaging in the form of CT scan or MRI have been shown to be sensitive and specific for detecting syndesmotic injuries and therefore can be used in patients with equivocal radiographic findings or to aid in surgical planning.[20,21]however, can be difficult to diagnose. The purpose of this study was to evaluate both distal tibiofibular articulations using weightbearing computed tomography (CT

In the operating room, two fluoroscopic tests are commonly utilized after rigid ankle fixation to help identify the presence of an unstable syndesmosis: the modified Cotton test and the external rotation stress test. The modified Cotton test, also known as the hook test or lateral fibular stress test, is performed by translating the fibula laterally often with a surgical clamp and visualizing widening of the tibiofibular clear space on fluoroscopy; greater than 2 mm of widening in the syndesmosis is suggestive of an unstable syndesmotic injury. The external rotation stress test, performed similarly during physical exam and obtaining external rotation stress films, is positive if there is talar tilting leading to medial clear space greater than or equal to 5 mm. One prospective study showed that the difference in widening with the stress external rotation stress was significantly greater than the modified Cotton test. This suggests that stress external rotation radiographs are a more reliable indicator of mortise instability than traditional lateral fibular stress.[22] Of note, the fibula is more unstable in the sagittal plane than the coronal plane, and intra-operative direct visualization of stability in the sagittal plane should be determined. This can be completed by placing a reduction clamp on the fibula with a posterior and anterior directed force applied; a 2-mm translation is consistent with instability.[10]

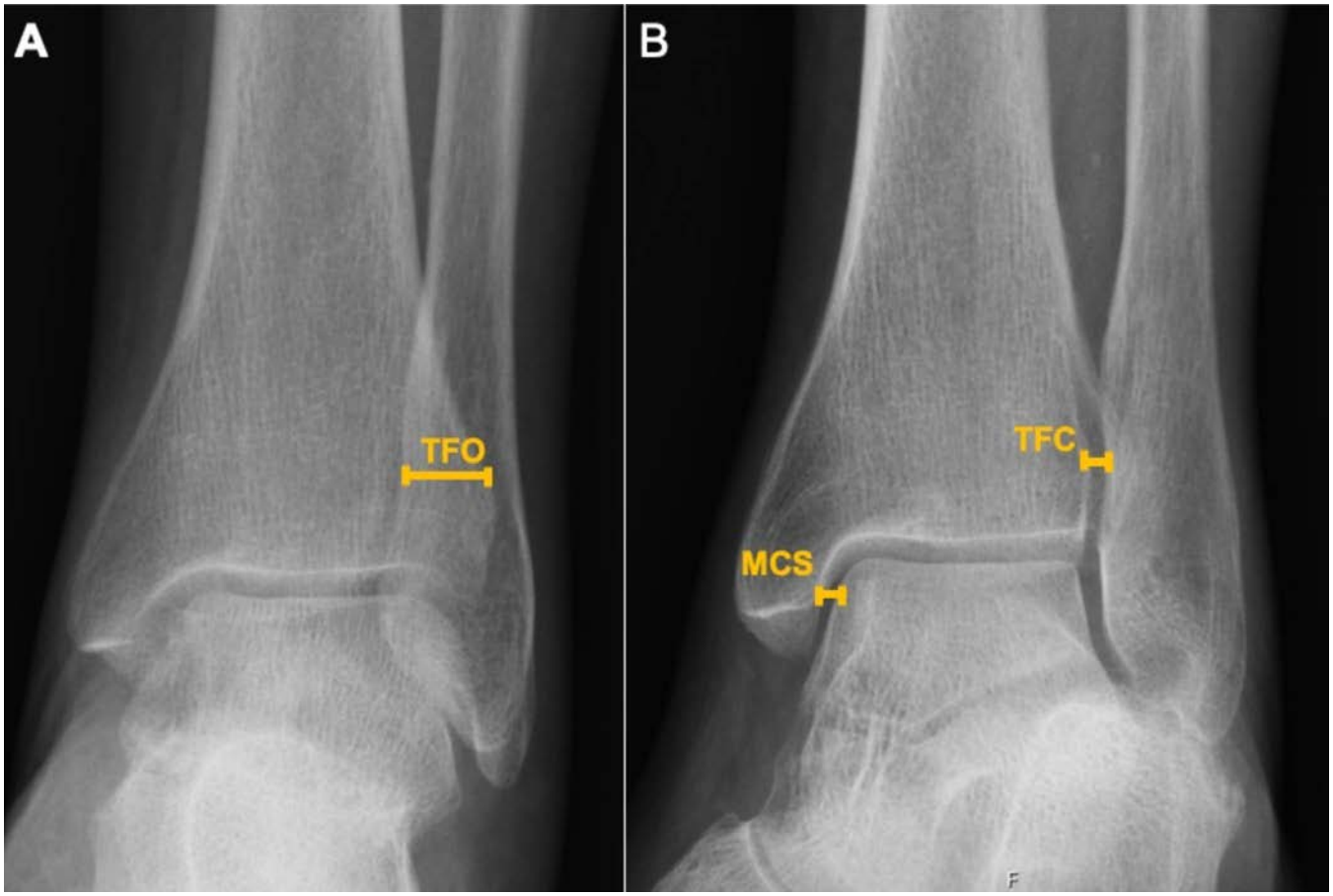

Figure 1. Radiographic parameters of the ankle associated with the syndesmosis. **(A)** Tibiofibular overlap (TFO); **(B)** Tibiofibular clear space (TFC) and medial clear space (MCS).

Importance of Reduction

Syndesmotic injuries are difficult to diagnose, and even when identified and treated, a slightly malreduced syndesmosis can lead to joint destruction and poor functional outcomes.[5,23] Successful outcomes require anatomic reduction of the syndesmosis as a malreduction of just 1.5 mm can portend poor clinical results.[5]

Technical Considerations

Proper Level for Syndesmotic Screw

Syndesmotic screw placement has been described relative to the plafond or syndesmosis. Though technical variability exists, there is no radiographic or clinical difference between trans-syndesmotic and suprasyndesmotic screw placement.[24] However, biomechanical studies frequently use the level of 2.5 cm above the plafond to restore ankle stability.[25,26] A more recent biomechanical study suggests syndesmosis fixation between 30-40 mm above the joint is most advantageous with regards to stress.[27] Caution should be made not to place the screw too proximal as one retrospective cohort study demonstrated that patients with syndesmotic screw placement 41 mm above the joint line had poorer patient outcomes scores.[28]

Hardware

There are numerous considerations and controversies in regard to the hardware and technique for placement of syndesmotic screws. Despite these controversies, numerous studies have demonstrated no clinical difference between one and two screws for fixation, although one study did show less pain and higher functional score at 3 months when comparing a single 4.5 mm screw to two 3.5 mm screws.[29,30] No differences in functional outcome have been demonstrated when comparing the size (3.5 mm vs 4.5 mm) of screws.[30–32] Additionally, numerous studies demonstrated no long-term functional differences between three and four cortices for syndesmotic screw fixation.[30,33–35]

Foot Position during Screw Insertion

Foot position is critical when placing a syndesmotic screw due to the asymmetry of the talus; the talus is wider anteriorly and narrower posteriorly. As the foot goes from dorsiflexes to plantarflexes, the tibial plafond and fibula articulate with anterior and then posterior aspect of the talus. As such, there is fear that over compression of the tibiofibular relationship will occur if fixation is accomplished in plantar flexion because the narrower posterior talus articulates with the tibia and fibula in that position. This would ultimately lead to limited dorsiflexion. However, several studies have demonstrated that maximal dorsiflexion during fixation is not required to avoid loss of dorsiflexion.[36–38] Poor patient outcomes after syndesmotic malreduction may be due to other factors and not loss of dorsiflexion motion.

Authors' Preferred Technique

The authors' prefer to stabilize the syndesmosis most commonly with two, tri-cortical 4.5-millimeter screws placed 2 cm and 3 cm, respectively, above and parallel to the level of the plafond exiting the far medial tibial cortex. It is important to note that these screws are not orthogonal to the sagittal plane of the extremity; they are angulated 20-30 degrees in the axial plane from posterior to anterior to match the orientation of the syndesmosis. Post-operatively, patients are advanced to full weight-bearing at 10 weeks. Routine removal of hardware is not done unless patients are symptomatic.

Suture Button versus Syndesmotic Screw

Suture button fixation is an alternative option for syndesmotic fixation with at least equivalent and possibly better clinical and radiographic outcomes when compared to conventional screw fixation. In one systematic review comparing suture-button versus syndesmotic screws, patients who achieved fixation by suture-button led to a better objective range of motion and earlier return to work.[39] Moreover, the suture-button fixation group had lower rates of implant removal, implant failure, and malreduction.[39] Another systematic review and meta-analysis demonstrated that the suture-button technique showed a significantly lower reoperation rate and tendency towards less malreduction and better American Orthopaedic Foot and Ankle Society scale scores.[40] However, high-quality randomized controlled trials are still needed to determine long-term effects and cost-effectiveness of the suture-button device.

Conclusion

Injuries to the ankle syndesmosis are common and require thorough clinical evaluation via physical examination, radiographs and advanced imaging, as well as intra-operative fluoroscopy for diagnosis. Many controversies exist surrounding syndesmotic screw placement, although no functional or clinical differences have been demonstrated despite numerous studies. The most important factor for obtaining successful patient outcomes is anatomic reduction of the syndesmosis. Reduction can be best achieved through direct visualization and confirmation with intra-operative fluoroscopy and post-operative advanced imaging. Suture button devices have more recently been used as alternatives to syndesmotic screws and have shown promising early results. However, additional high-quality studies are needed to further support these findings.

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Oncology Tips and Tricks: Pathologic Fractures in Metastatic Cancer: Presentation and Workup Considerations

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Introduction

Cancer remains one of the world's leading causes of mortality with an estimated 19.3 million new cases and approximately ten million cancer-related deaths in 2020.[1] The vast majority of cancer-associated deaths occur in those with metastatic disease. With longer survival time in patients with advanced cancers in light of recent advances in treatments, there have been increases in morbidity and disability related to cancer-associated complications.[2]

Among these complications are pathologic fractures, which occur in areas of weakened bone secondary to either primary or metastatic lesions, the latter of which are seen far more frequently. Bone is among the top three most frequent sites of metastases, which include lung and liver. The most common primary cancers to metastasize to bone are breast, prostate, thyroid, lung, and renal cell carcinoma. The relative incidence of bone metastasis by type of tumor is: 65-75% in breast cancer; 65-75% in prostate; 60% in thyroid; 30-40% in lung; and 20-25% in renal cell carcinoma.[3] Multiple myeloma also manifests frequently as lytic bone lesions. Pathologic fractures have been reported in 8 to 30% of patients with bone metastases.[4]

Pathologic fractures cause considerable morbidity and cost to quality of life. A 2020 retrospective study published in JOA comparing pathologic hip fractures to native hip fractures showed that patients with pathologic fractures experience significantly higher rates of death (6.3% vs 4.3%) serious adverse events (17.3% vs 13.5%), extended lengths of stay (30.2% vs 25.9%), readmissions (11.9% vs 8.4%), thromboembolic complications (3% vs 1.6%) and perioperative transfusions (31.5% vs 26.4%).[5]

Level 1 evidence shows that the use of bisphosphonates such as zoledronic acid or bone-modifying agents such as denosumab is associated with a significant decrease in skeletal-related events (SREs) including pathologic fractures.[6] Additionally, in the metastatic breast cancer population, the American Society of Clinical Oncology guidelines recommend treatment of cancer-related bone pain with these agents as part of adjunctive therapy for cancer-related bone pain in addition to additional analgesic therapy, chemotherapy, radiotherapy, or hormonal therapy.[7]

When approaching a patient with a suspected malignancy who presents with new-onset musculoskeletal pain or fracture, a high degree of suspicion and an experienced multidisciplinary team are necessary to accurately diagnose and treat the underlying process.

Presentation and Workup

Pathologic lesions can be discovered in various ways—incidentally found on imaging, in the outpatient clinic during evaluation for hip pain, or as pathologic fractures in the emergency setting. Patients may report progressive pain with inability to bear weight on their affected lower extremity, and often report prodromal pain prior to sustaining a fracture. Workup of pathologic lesions require a thorough history, review of systems, exam, imaging and labwork.

History and Exam

Initial history should include personal and family history of malignant tumors and related treatment, risk factors for cancer including prior smoking history, onset of pain, and mechanism of injury (bone weakened especially by lytic metastatic lesions fracture with much less force than benign bone). A full review of systems should assess for systemic symptoms such as fatigue, fevers, night sweats, shortness of breath, dark urine or hematuria, early satiety and weight loss. Metastatic hypercalcemia occurs when osteolytic metastases cause excessive release calcium from bone, which can cause symptoms such as confusion, muscle weakness, polyuria and polydipsia, gastrointestinal distress, nausea and dehydration.[8] A full physical exam may reveal other signs of metastatic disease such as scleral icterus and jaundice, lymphadenopathy, lung crackles, hepatosplenomegaly, skin lesions, breast masses, enlarged prostate, musculoskeletal tenderness including along the vertebral column, or neurologic abnormalities.

Imaging

Pathologic lesions are most frequently diagnosed on plain radiographs. Metastatic lesions frequently affect proximal aspects of

long bones, and fractures through these lesions often occur commonly in the proximal femur due to the stress from forces placed on the lower extremities during weightbearing. Initial biplanar x-rays should include the joints above and below the lesion, including the pelvis, hip, femur, and knee. Aggressive features suggestive of a pathologic process include lesion diameter > 5cm, cortical interruption, periosteal reaction and associated pathologic fracture.[9] Plain radiographs have high specificity for bone lesions, especially those that appear lytic, and may also reveal osteoblastic lesions which appear sclerotic on imaging.

More advanced imaging such as CT can be used on a case-dependent basis and can be useful in disease staging; they allow for high-resolution cross-sectional views of the bone cortex and periosteum.[10] CT scans of the chest, abdomen and pelvis can help identify possible sources in cases of metastatic cancer with an unknown primary. In women, mammography can be used to evaluate for occult breast masses. The spine is one of the most common sites for metastatic disease to spread, and when physical exam is concerning for neurologic deficit or hyperreflexia, an MRI of the spine can be used to evaluate for neurologic compromise.

Laboratory analysis

A comprehensive laboratory workup is helpful in characterizing the disease process, distinguishes infectious etiologies from cancer, and establishes a baseline from which the disease course can be followed over time. Screening lab studies include a complete blood count with differential and peripheral blood smear, comprehensive metabolic panel, liver function tests, coagulation studies, inflammatory marks (ESR/CRP), electrolyte panel (calcium, phosphorous, alkaline phosphatase), LDH, beta-2 microglobulin, and prostate specific antigen. Other studies include serum protein electrophoresis with quantification of immunoglobulins, 24-hr urine protein electrophoresis, immunofixation, and serum monoclonal light chains for myeloma screening. Tumor markers such as alpha-fetoprotein, carcinoembryonic antigen, CA-19-9, and CA-125 may be useful as a screening test to distinguish skeletal metastases of carcinoma from primary bone tumors.[11]

In patients with an unknown primary carcinoma with a solitary bone lesion, a biopsy is needed prior to any surgical fixation in order to rule out a primary bone lesion such as osteosarcoma, which could jeopardize the chance of limb salvage. Patients who undergo needle biopsy for impending fractures should maintain protected weight bearing status after the procedure. The biopsy should be performed in a location that will permit excision of the biopsy tract should a primary sarcoma be diagnosed.[12] Fixation may precede final biopsy results when metastatic disease may be presumed based on widespread disease to multiple bones and solid organs. Ideally, primary bone sarcoma should be ruled out on pathology prior to the introduction of any internal fixation or instrumentation.

Criteria for prophylactic fixation

In patients with metastatic lesions to long bones that are concerning for impending pathologic fracture, the risk of fracture within 6 months can be predicted using Mirel's criteria, a weighted scoring system based on four objective clinical and imaging risk factors, which include location, size and type of lesion and pain.[13] The system was first established in 1989 following a retrospective study of 78 pathologic lesions that received radiation therapy without prophylactic fixation. Clinical and imaging data were obtained related to each of Mirel's four criteria prior to the follow-up period of 6 months, during which 27 cases sustained fractures and 51 did not. The average score was 7 in the non-fracture group and 10 in the fracture group, which led to the conclusion that lesions with scores higher than 7 have a higher risk of fracture and may be good candidates for prophylactic fixation prior to irradiation.

Internal fixation of pathologic fractures is considered a palliative procedure, to reduce pain and improve mobility by providing stabilization that will outlast the patient's expected survival time. The choice of fixation suited for various types of lesions in each area of bone is a broad and complex topic which is beyond the scope of this discussion. Instead, we will briefly review a case below which discusses one of the most common types of pathologic fractures.

Table 1. Mirel's Classification Scoring System.

Criteria	1 Point	2 Points	3 Points
Site of lesion	Upper limb	Lower limb	Trochanteric region
Size of lesion	<1/3 of bone diameter	1/3-2/3 of bone diameter	>2/3 of bone diameter
Nature of lesion	Blastic	Mixed	Lytic
Pain	Mild	Moderate	Functional limitation

Table 2. Recommendation for fixation based on Mirel score.

Mirel score	Fracture Risk at 6 months post-irradiation	Recommendations
≤7	0-4%	Safe to irradiate with minimal risk of fracture
8	15%	Consider prophylactic fixation
≥9	>33%	Candidate for prophylactic fixation

Radiation Therapy

Radiation therapy has become standard in treatment after internal fixation of a complete or impending pathologic fracture, with evidence supporting that radiotherapy can promote remineralization and bone healing, alleviate pain, improve functional status, and reduce the risk of subsequent fracture or loss of fixation.[14] Compared to surgery alone, radiation therapy is associated with increased regain of use of the affected extremity, fewer reoperations to the same site, and increased overall survival.[15] The area of radiation should include the entire fixation device Radiation therapy can also be used for palliative measures to reduce pain in patients with metastatic disease that are not candidates for surgery.

Brief Case Report

A 38-year-old female with a history of asthma and uterine fibroids was brought to the emergency department after a ground level fall while attempting to get out of a car. She reported severe hip and thigh pain and was unable to bear weight on her right leg. On further history, the patient reported progressively worsening right-sided hip pain for the past four months which had required her to start using a cane. Imaging showed diffuse lytic lesions in the pelvis and femur, especially prominent in the right proximal femur, with a pathologic fracture adjacent to the lesser trochanter. On additional questioning, the patient endorsed early satiety and constipation mixed with loose stools, as well as a mass over her left breast. Exam was notable for significant pain with log roll and palpation of the right hip localizing to the groin, and an 2cm mobile mass in the left upper quadrant of the left breast.

A non-contrast CT of the right hip and femur with axial, sagittal and coronal reconstructions redemonstrated the fracture inferior to the right lesser trochanter, and showed cortical breakthrough and diffuse marrow infiltration of the distal femur concerning for impending pathological fracture. The visualized peritoneum had multiple areas of thickening and nodularity concerning for peritoneal carcinomatosis. Additional CTs of the head, chest, abdomen and pelvis revealed osseous metastases to the clivus, mandibular condyles and upper cervical spine, multiple bilateral pulmonary nodules, numerous hepatic and renal lesions, and widespread lytic and blastic osseous metastases involving the axial skeleton and all visualized long bones. A thorough workup was initiated by a multidisciplinary team including hematology-oncology, radiation oncology, palliative care, and orthopedic surgery.

After discussion with the patient and care teams, the patient was taken to the OR for a right intramedullary nail (Smith & Nephew Meta-Nail) with two proximal and two distal interlocks. Femur reamings were sent for pathology. There were no intraoperative complications. Final pathology results were consistent with HER2-positive metastatic breast cancer.

Final Remarks

Metastatic cancer with skeletal metastasis can cause severe pain and morbidity, reduction in quality of life, and early mortality. The goal for patients with end stage cancer is primarily palliative. Pathologic fractures can be approached

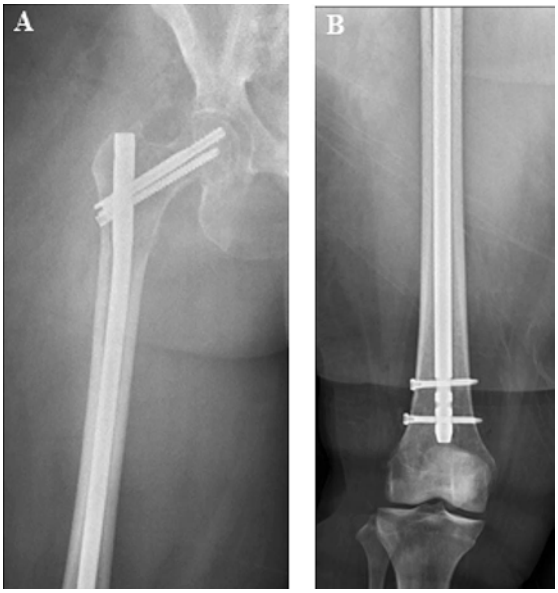

Figure 2. AP Right hip **(A)** and distal femur **(B)** status post right intramedullary Smith and Nephew Meta-Nail.

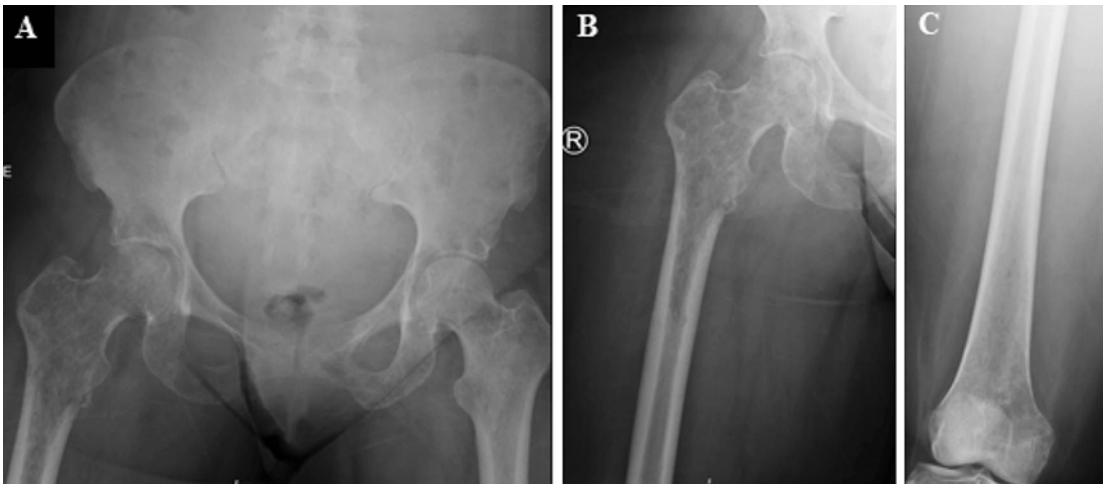

Figure 1. AP Pelvis **(A)** AP right hip **(B)** and AP distal femur **(C)** demonstrating pathologic lytic lesions of the pelvis and right proximal and distal femur.

with a combination of internal fixation and radiation therapy; however, the patient's overall medical course can become unpredictable especially in those with advanced metastases as witnessed in this case. This reiterates the importance of a thorough evaluation and workup and the combined efforts of an experienced multidisciplinary team in order to provide the best possible outcomes for these complex cases.

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Orthoplastics Tips & Tricks: Case Report: Orthoplastic Limb Salvage in a Patient with Chronic Nonunion, Infection, Deformity, and Wound

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Introduction

There are various types of soft tissue coverage options including skin grafting, local tissue rearrangement, rotational flaps such as a gastrocnemius or soleus or a microvascular free flap. For large soft tissue defects in these injury patterns, rotational muscle flaps or free flaps are generally the first choice for soft tissue coverage in the leg. There continue to be, however, some clinical situations in which these flaps are often not possible or the best option for the patient.

Another option for soft tissue coverage is the cross-leg flap. The cross-leg flap was first described by Hamilton in 1854. The cross-leg flap was used extensively for lower extremity trauma prior to the introduction of the free flap in 1970.[1] Since its introduction, the free flap has become the gold standard for post traumatic lower extremity soft tissue reconstruction. While infrequently performed, the cross-leg flap plays a unique role in orthoplastic limb salvage.

This case study describes a patient with a severe initial open tibial fracture which was subsequently complicated by malunion, osteomyelitis, erosion through soft tissue reconstruction, and delayed presentation for and consideration of a cross leg flap for orthoplastic limb salvage.

Case Report

The patient is a male 70-year-old male with a PMH of smoking, coronary artery disease status post stent placement, hyperlipidemia, and AAA status post stent who sustained an open, high-energy left tibial fracture in 1984. This was initially treated with open reduction and internal fixation. Since that time, the patient developed a chronically infected malunion/nonunion. This was complicated by exposed hardware with a chronically draining sinus tract, broken instrumentation, and a significant varus deformity of his left lower extremity. In addition, he had hypertrophy of his fibula.

At the time of his initial visit at our center, the patient had been suffering from this problem for many years prior to referral. The patient wished to have a limb reconstruction rather than amputation. He was seen and evaluated both in the Orthopedic Surgery Clinic and Plastic Surgery Clinic regarding his suitability for limb salvage. At the time of initial evaluation in each clinic, the patient was advised to quit tobacco smoking due to the unacceptably high risk of adverse events.

The patient returned to clinic approximately one year later having quit smoking tobacco. Again, he preferred attempts at limb salvage rather than amputation. Both surgeons had a lengthy conversation with the patient about the risks involved in reconstruction including the very real risk of an amputation. He was seen and counseled on multiple occasions regarding the potential for limb salvage.

To treat this limb, a staged reconstruction was planned to address both the bony and soft tissue challenges. The goals of this reconstruction would be getting the limb straight, allowing him to clear his infection with provisional fixation, getting definitive soft tissue reconstruction, and ultimately reconstructing the bone in a delayed fashion. From a bony standpoint, he had significant loss of length, alignment, and chronic infected nonunion/malunion. From a soft tissue

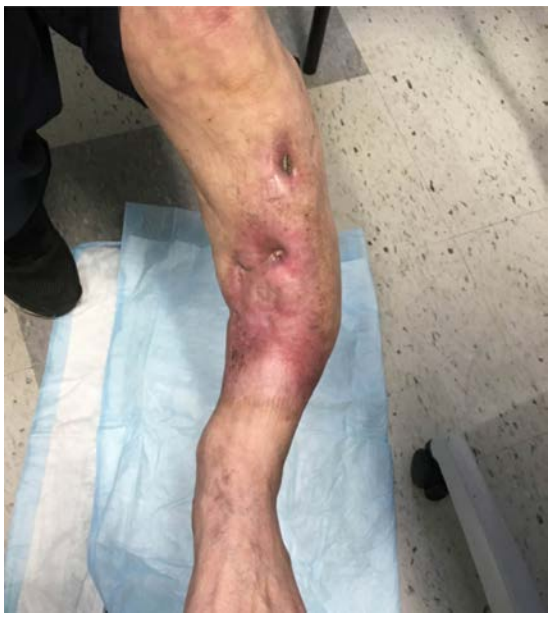
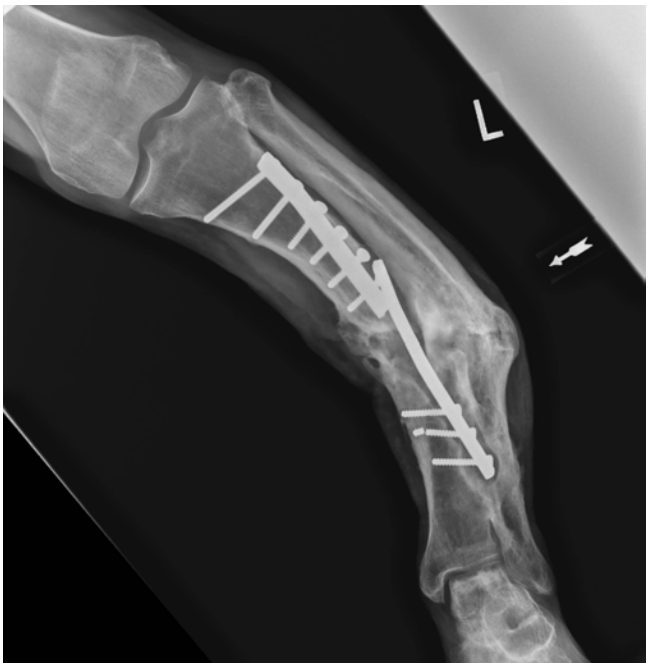
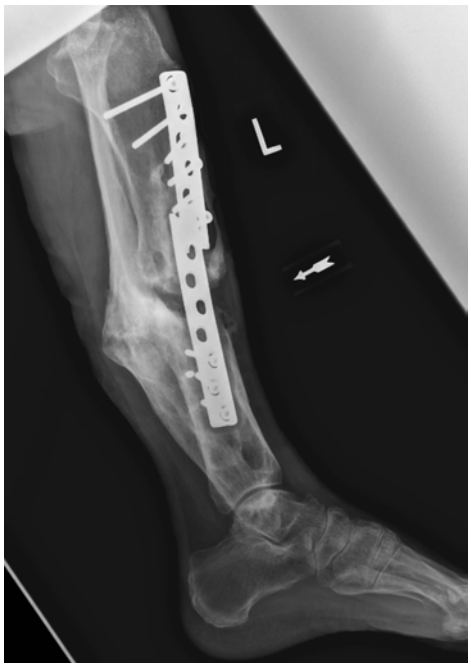


Image 1. Limb at the time of initial presentation to our medical center.



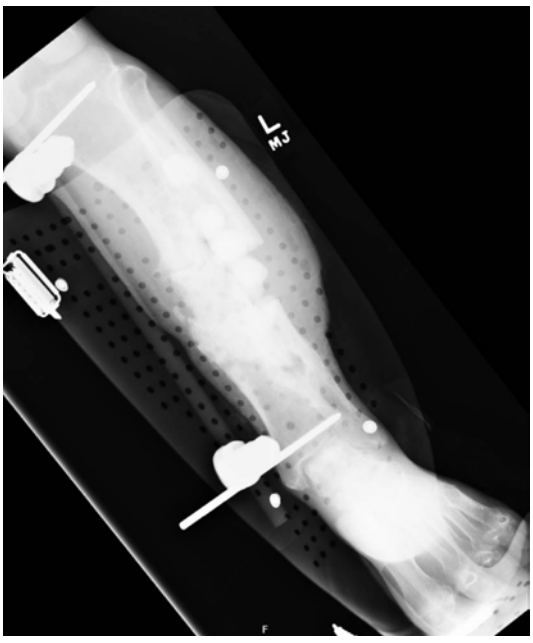


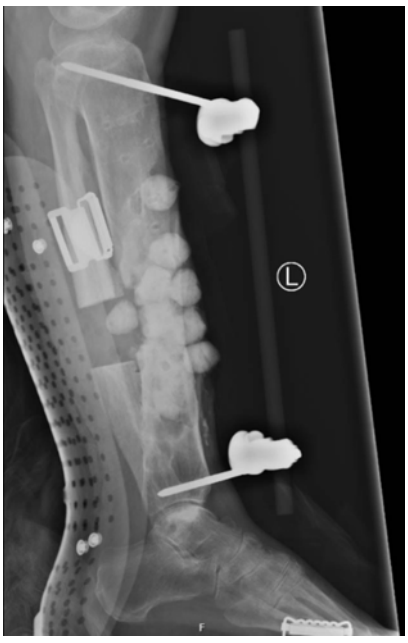
Images 2 and 3. AP and Lateral Xrays of the Left Tibia at the time of initial presentation to our medical center.

standpoint, he had severely fibrotic tissue as well as exposed hardware and soft tissue damage. The chronically infected bone and unstable soft tissue envelope needed to be removed. The surgeons anticipated large tibial intercalary defect and a large soft tissue defect after the removal of the infected bone and unstable soft tissue envelope. After this, the surgeons planned to pursue microvascular free tissue transfer to reconstruct his soft tissue envelope and temporizing fixation to provide stability and bony opposition while continuing to treat his osteomyelitis. Once his bony infection was cleared and he had achieved appropriate alignment, rotation, and soft tissue coverage, he then would undergo bony reconstruction to restore length to the limb.

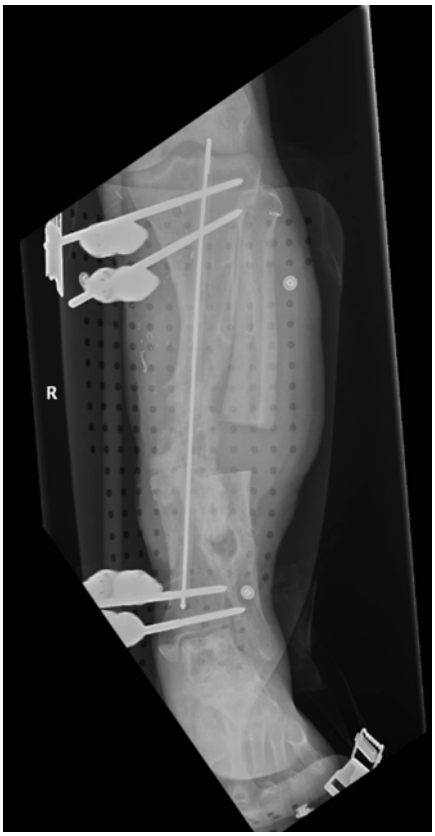
In the first series of operations, he first underwent removal of hardware, excision of the infected tibia and fibula with sequestrum debridement, osteotomy of the tibia and fibula, external fixator application, and antibiotic spacer placement. Five days later, he underwent antibiotic spacer removal, tibial debridement and washout, and antibiotic nail and bead placement. Intraoperative cultures at this time demonstrated methicillin-sensitive Staph Aureus, for which infectious disease was consulted. This patient also had an anaphylactic reaction to cephalexin, thus infectious diseases recommended he be treated with six weeks of intravenous vancomycin therapy.

At this time, he had undergone resection of his fracture, retained hardware, and his limb was provisionally stabilized





Images 4 and 5. AP and Lateral Xrays after removal of hardware, excision of the infected tibia and fibula with sequestrum debridement, osteotomy of the tibia and fibula, external fixator application, and antibiotic spacer placement.



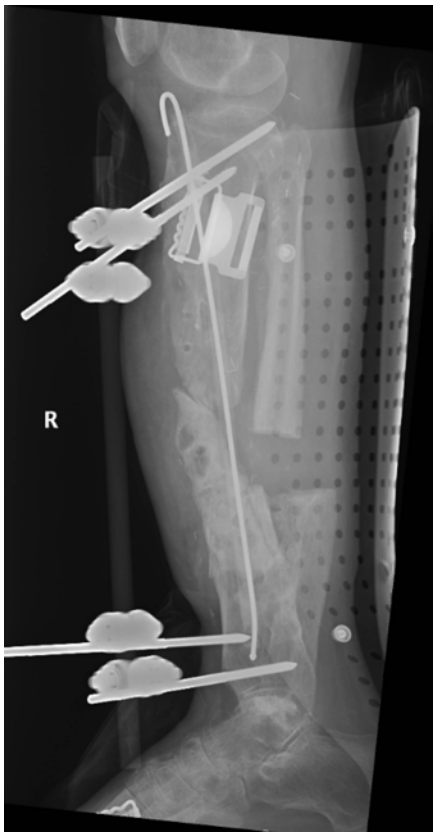


Image 6 and 7. Ap and Lateral Xrays after excision of his infected bony tissue, removal of broken hardware, restoration of alignment and rotation, provisional fixation in the form of an antibiotic nail and external fixator, and free flap reconstruction.

with alignment and rotation restored. However, he still had large, intercalary defect and a massive soft tissue defect overlying his anterior lower extremity. To reconstruct this, microvascular reconstruction was planned. In his preoperative work up, a CT angiogram demonstrated single vessel run off via the posterior tibial artery which emanated high in the popliteal fossa. His anterior tibial and peroneal vessels were occluded in the mid aspect of the lower extremity. This in addition to his severe fibrosis of the affected extremity made soft tissue reconstruction incredibly challenging.

Ten days after his initial operation, he underwent soft tissue debridement and wound excision, antibiotic spacer placements, and Free anterolateral perforator flap to the left lower extremity with right saphenous vein graft harvest

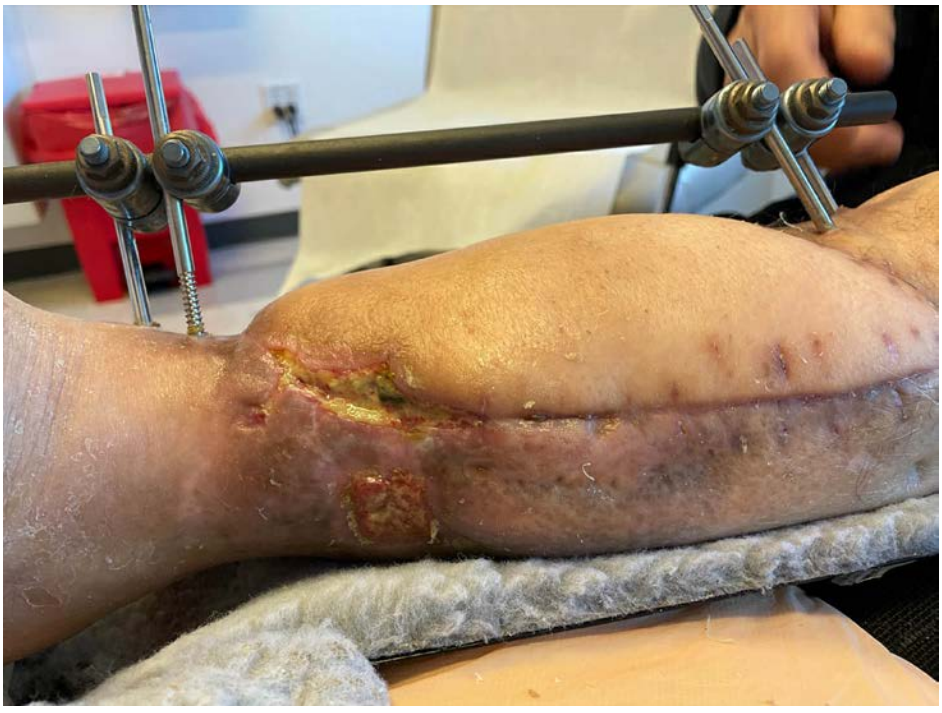


Image 8. Lateral aspect of ALT flap 2 months post operatively.

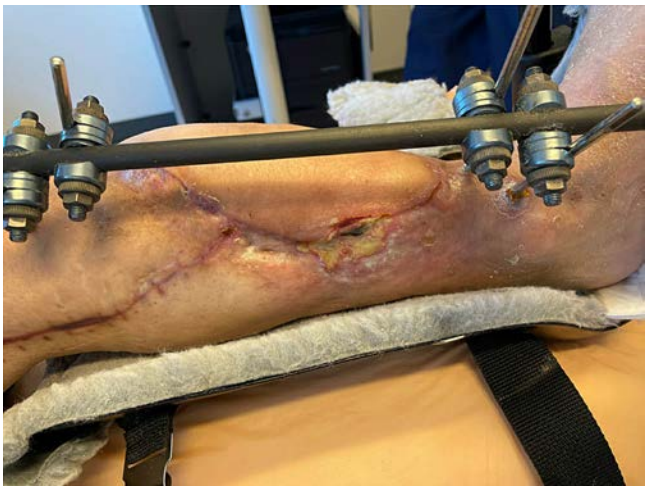


Image 9. Lateral aspect of ALT flap 2 months post operatively.

and for vascular inflow and outflow as interposition arterial and venous grafts. Intraoperatively, the initial plan was to explore the anterior tibial vessels and attempt and end-to-end anastomosis. However, this compartment and his anterior tibial artery were found to be severely scarred in and unable to be dissected for this end. In this case, the posterior tibial artery was identified high in the infrageniculate popliteal fossa and dissected free for microvascular anastomosis with its accompanying veins. With inflow and outflow vessels identified, the skin paddle and its dominant perforator were dissected and prepared. It became clear that the patient would need vein graft to bridge the donor site for his recipient vessel inflow and outflow. Thus, the saphenous vein was harvested from the contralateral side to be used as interpositional vein graft. Prior to leaving the operating room, the flap was found to have excellent arterial inflow, venous egress, and doppler signals.

Having undergone excision of his infected bony tissue, removal of broken hardware, restoration of alignment and rotation, provisional fixation in the form of an antibiotic nail and external fixator, and free flap reconstruction of the affected extremity, the patient was discharged with six weeks of culture directed intravenous antibiotics.

Three months after the index operation, having healed the soft tissue, and being treated with a course of IV antibiotics, he returned to the operating room for placement of a NuVasive magnetically-driven nail for bone transport to definitively manage his limb length inequality and nonunion. The Plastic Surgical Service was consulted regarding management of the soft tissue as well as elevation of his previous free flap reconstruction in order to allow for removal of his existing antibiotic spacer, placement of this intramedullary construct to allow for bone transport.

During this operation, the surgeons found his antibiotic spacer eroded through the soft tissue resulting in a formal defect in the setting of a terribly fibrotic limb and additional soft tissue defect. This residual wound overlying the medial right lower extremity that could not be closed even with his previous free flap reconstruction, therefore negative-pressure wound therapy was placed while preparing to return to the operating room for soft tissue coverage of his underlying bony defect and NuVasive nail.

Planning for soft tissue coverage in his case was challenging given the dense scar burden, one vessel inflow in the form of the posterior tibial artery high in popliteal fossa, and limited veins that could be used for interpositional vein grafts. Thus, the possibility of cross-leg flap was introduced.

He returned to the operating room to undergo a cross leg flap. A random pattern flap was then designed based proximally overlying the medial and posterior aspect of his right lower extremity, taking into account his previous incision and scar from his saphenous vein harvest site. This was raised full-thickness through the deep fascia on top of the gastrocnemius muscle as well. Intraoperatively, the distal flap did appear to perfuse well after being raised, but the surgeons were concerned that they did not want to formally inset this in case there was any chance of distal flap necrosis as this was a portion of the flap that would be necessary. Thus, a decision was made to delay this flap. A sheet of Integra skin substitute was placed on top of the gastrocnemius muscle so that the flap would have no deep tissue contact to the underlying wound bed.

Post operatively, the cross-leg flap was nonviable in the distal aspect and began to necrose. A long discussion was had with the patient regarding pursuing limb salvage and the likelihood of success versus amputation. Extensive discussions were had given the nature of the surgery including the potential for partial or complete flap loss and/or inability to achieve reconstruction based on the amount of available vein graft. He understood the nature of the anticipated surgical procedure as well as the attendant risks and benefits and he wished to proceed with a trial of limb salvage with a second free flap and vein grafts. The patient again wished to pursue limb salvage. He was indicated for a second free flap in the form of an anterolateral thigh flap with interposition vein grafts.

He was taken to the operating room for the second anterolateral thigh flap. The wound overlying his medial and

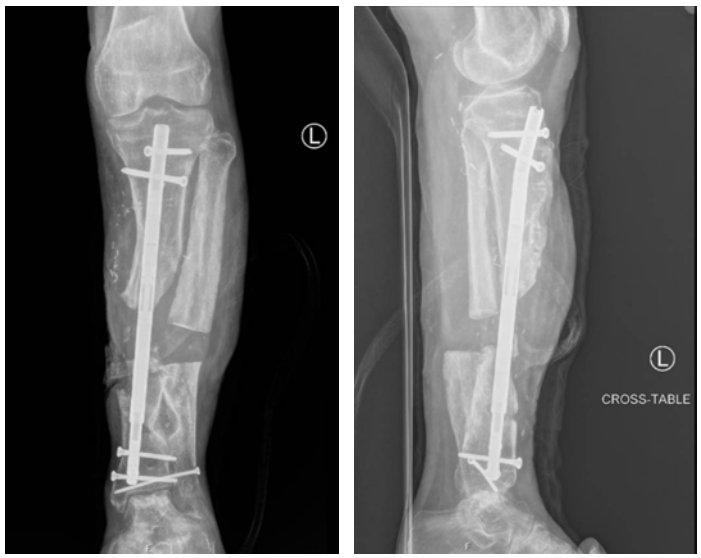


Image 10 and 11. Ap and Lateral Xray after removal of external fixator, removal of antibiotic intramedullary nail, placement of Precice magnetically-driven nail.

anterior left lower extremity was then excised. The proximal posterior tibial artery and large, proximal posterior tibial vein were identified, dissected, and prepared for inflow. For vein graft, the saphenous vein overlying the left thigh was dissected free and prepared from his knee up to his groin crease. Then, the free flap was procured from his right thigh and saphenous vein graft was used as an interposition graft to anastomose the flap to the posterior tibial vein and artery. Finally, the site of the previous delay of an attempted cross-leg flap was debrided and negative pressure wound therapy was initiated. At this time, the patient is approximately six weeks post-operative from second free flap reconstruction.

Discussion

The modern definition of orthoplastics is: "the principles and practices of both specialties applied to clinical problems simultaneously, either by a single provider, or team of providers, working in concert for the benefit of the patient." [2,3,4,5] The combined orthoplastic approach to patients with severe injuries to the lower extremities requiring lower limb salvage has been shown lead to better outcomes including quicker time to bone union, more durable soft tissue coverage, less pain, better function, fewer complications, shorter hospital stays, and higher patient satisfaction. [6]

This is a patient with a complicated extremity who suffered from osteomyelitis, nonunion/malunion, wound, and varus deformity of this extremity for years prior to referral to our orthoplastic limb salvage center. This case demonstrates the importance of early referral to a specialized orthoplastic center with the expertise and facilities to handle the challenges of this case.

The management of long bone defects rely on the principles of distraction osteogenesis which were pioneered by Ilizarov. [7] Newer intramedullary nails which allow surgeons to lengthen magnetically have drastically changed the ability to perform distraction osteogenesis without the need for a bulky ringed external fixator. The PRECICE Intramedullary Limb Lengthening System (Ellipse Technologies Inc., CA, USA) is the nail that was used in this patient. It is a is a remotely controlled, magnetically driven, implantable limb lengthening intramedullary nail system. [8] It has been reported to achieve accurate and precise limb lengthening. [9,10,11,12]

Once a free flap has failed, there are limited options available for soft tissue coverage. Attempts to salvage these extremities can be undertaken with split thickness skin graft or local flaps. However, in these cases, intermittent wound breakdown and drainage of these extremities remain major problems. Thus, these situations indicate that the loss of a free flap significantly affects the overall potential to salvage a lower extremity.[13] Additionally, studies show after failed free flap, the rate of amputation of the affected extremity can vary from 22 to 57%.[14-16]

The cross-leg flap is generally reserved for use when surgeons or medical centers do not have the ability to perform microsurgery. The use of cross-leg flap has previously been limited by the incidence of necrosis, difficulty of immobilizing both legs for 2–3 weeks, joint stiffness, chances of thromboembolism, and concern about donor site cosmetic deformity especially in women. The use of external fixator for immobilization circumvents many of the previous problems with both-leg immobilization. The addition of external-fixator stabilization aids greatly in wound care, as well as for general ease of patient mobility and positioning.[17]

In this patient, had he received a cross leg flap, external fixation would have been used for immobilization. The construct that would have consisted of two pins in the contralateral tibia, one pin in the ipsilateral femur, and one pin in the ipsilateral calcaneus to create a trapezoid-shaped construct. This would avoid placing any pins in the tibia given the magnetically lengthening intramedullary nail as well as the cross leg flap that would have been in place.

The technique of delaying a flap is to allow for enhanced flap length and viability in reconstruction. This has been used nearly 500 years in reconstructive surgery for reliably transferring a greater amount of harvested tissue than one would be able to otherwise.[18] This involves incising the borders of the flap with or without partial subcutaneous elevation and leaving it in situ for a duration of time, usually 10–14 days. After the period of delay, the flap is fully elevated and transposed. Delayed flaps have been shown to have better survival than similar flaps that are raised and transposed primarily.[19]

Conclusion

This is a patient with a challenging limb deformity presenting for limb salvage after a remote history of high energy trauma. His case demonstrates the importance of integrated orthoplastic care, considerations in soft tissue coverage, and restoring length and alignment in a severely shortened and maligned limb.

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Trauma

Statistical Shape Models May Accurately Predict Subacromial Impingement of Shoulder Fractures in the Absence of CT Images

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Introduction

Proximal humeral fractures are a common injury and approximately 20% involve avulsions of the greater tuberosity (GT). Subacromial impingement occurs when a displaced GT fragment becomes wedged between the proximal humerus and the undersurface of the acromion, causing reductions in range of motion, intense pain, and a decrease in overall quality of life. It is difficult for clinicians to predict the likelihood of subacromial impingement, which requires surgical intervention to fix. CT images allow for the creation of patient-specific 3-D dynamics simulations capable of making estimates of impingement; however, CT imaging is typically not performed as a standard of care for proximal humerus fractures. In the absence of CT-rendered models of bones, statistical shape models (SSMs) may serve as reasonable surrogates for use in dynamic simulations of impingement. The goal of this experiment was to evaluate the predictive accuracy of SSMs by comparing specimen-specific outputs to models created with SSMs. We hypothesized that SSMs would be able to predict the occurrence of patient-specific subacromial impingement with at least 80% accuracy.

Methods

Twenty-three intact fresh-frozen upper extremity cadaveric specimens from 17 donors (8F, 9M; mean 81.6 y.o. range 74-89y.o.) were used in this preliminary study. Specimens were scanned with a clinical CT scanner using 0.5 mm axial slice thickness. Humeral and scapular geometries were segmented, flipped if needed to ensure all right-sided specimens, and aligned to the International Society of Biomechanics shoulder coordinate system. Simulated GT avulsions were made by slicing humeral heads in the sagittal plane, 8mm medial to the lateral-most point of the GT. Using a validated OpenSim shoulder model, passive range of motion tests were performed by sequentially simulating abduction from 0° to 180° (Figure 1A) at 18 different elevation planes between −90° (backward reaching) to 90° (forward reaching) (Figure 1B). ROM tests were repeated with all combinations of: 4 GT displacement magnitudes (2.5, 5.0, 7.5, 10.0 mm), 5 displacement directions (0° (anterior), 45°, 90° (superior), 135°, 180° (posterior)) (Figure 1C) and 4 fragment rotations (15°, 30°, 45°, 60°) rotated about the center of mass of the GT fragment along the sagittal axis (Figure 1D). For each of the 1440 unique simulations of abduction per specimen, a binary determination of contact between the GT fragment and the acromion was determined using the OpenSim elastic foundation contact model and 3D shoulder angles were recorded for each impingement event. The same 23 cadaveric specimens were then used as inputs to develop a statistical shape model (ShapeWorks) which output 5 humeral head and 5 acromion geometries, representing a mean shape, ±1standard deviation, and ±2 standard deviations (Figure 2A). All 25 combinations of SSM humeri and acromions were modeled to simulate the same dynamic abduction motions with variable injuries described above. Best-fit pairings of humeral and acromial SSMs for each of the 23 specimens were determined by finding the minimum differences in impingement predictions between SSM combinations and individual specimens.

Results

Best-fit SSMs predicted impingement events within the same elevation planes of CT-based models with 88.5±1.3% accuracy (range 83.2–93.7% for 23 specimens) (Ex: Figure 2B). The majority of subacromial contact events occurred when arms were performing abduction in the 30°-60° elevation planes (CT: 80.5%, SSM 82.4%). Predictions of the timing of impingement (abduction angle achieved before bony contact) only matched exactly 29.3±1.9% of the time. The average probability of impingement for the CT models was 4.3%, 6.8%, 12.4%, and 20.8% for GT fragment displacements of 2.5, 5.0, 7.5 and 10.0 mm, respectively. The probability of impingement for the SSM model was 9.1%, 16.7%, 25.8%, and 31.5% for the same displacements, indicating an overestimation, but similar progression of impingement as a function of displacement.

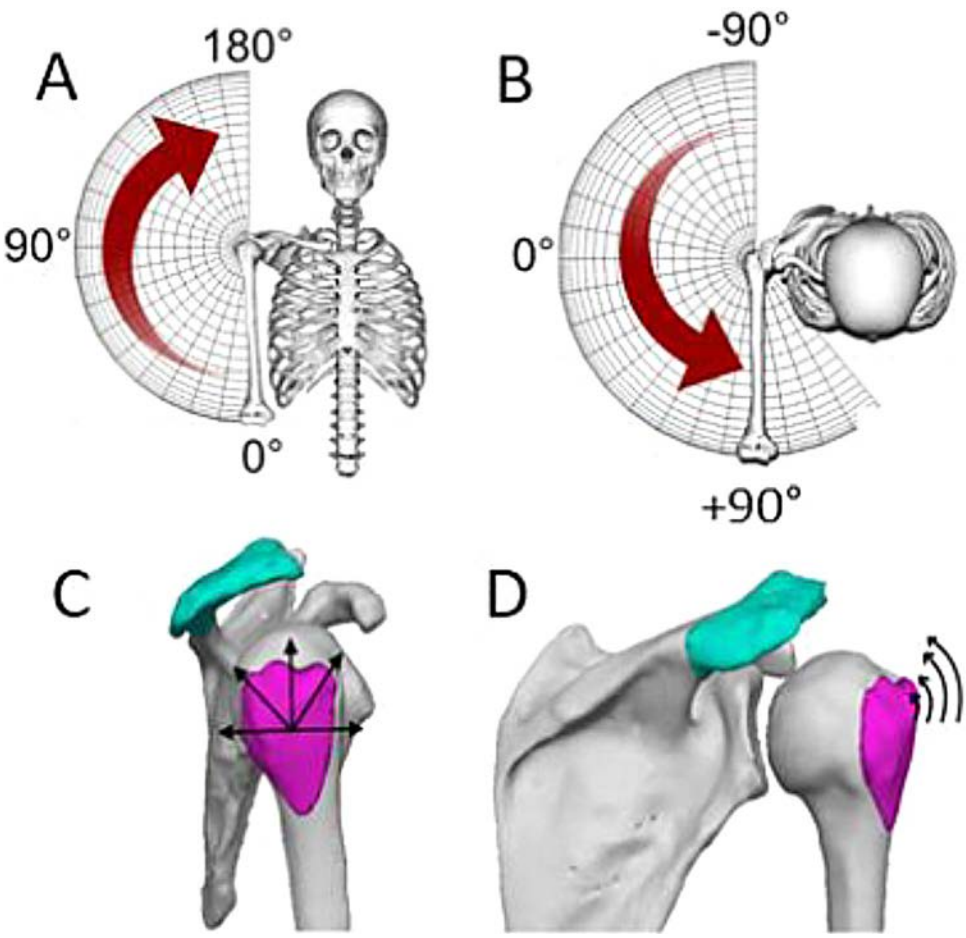

Figure 1. (A) Abductions were performed in **(B)** 18 elevation planes while GT fragments were **(C)** displaced and **(D)** rotated for a total of 1440 unique simulations.

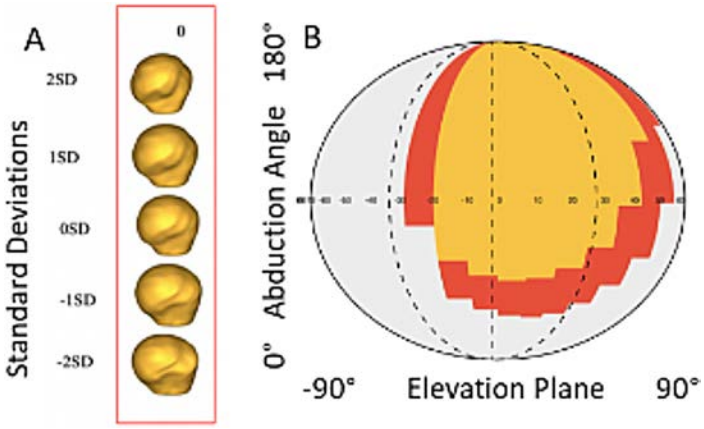

Figure 2. Statistical shape modeling generated **(A)** 5 unique humeral head geometries and acromion geometries (not shown); **(B)** Example of restricted range of motion (10mm displacement at 135o, 0o fragment rotation) shown on a sagittal plane hemisphere SSM models (red) overestimated impingement modeled with CT images (yellow).

Discussion

In accordance with our hypothesis, best-fit SSMs predicted impingement events of patient specific models with greater than 80% accuracy. This preliminary study provides confidence in using statistical shape models of bones as surrogates in dynamic musculoskeletal models. This study has limitations, as the ball joint used to represent the shoulder does not allow for compensatory translations of the humerus or scapula to avoid impingement. Future studies will increase the amount of training data for the SSM software, create algorithms that use 2D measures made on radiographs to assign 3D geometries within the SSM library, and incorporate images and patient-reported outcomes from living patients to further the accuracy and clinical relevance of the models.

Significance/Clinical Relevance

Accurate prediction of subacromial impingement of greater tuberosity fragments is difficult, but statistical shape models may enhance the limited data that is available with 2D radiographs. Continued development of simulations and algorithms capable of leveraging statistical shape models may improve standards of care without the need for CT imaging.

U·P·O·J

Historical and Projected Incidence of Alcohol-related Upper Extremity Fractures

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Introduction

Hand and upper extremity fractures are exceedingly common injuries in the United States population, and have been estimated to comprise 1.5% of all emergency department visits nationwide.[1-3] The most common of these fractures involves the distal forearm (particularly the distal radius), though certain age groups are more likely to be afflicted with certain hand and upper extremity fractures than others.[1,4-6]

These injuries can markedly reduce quality of life. Among the elderly, wrist fractures have been associated with subsequent dependence on caregivers for activities of daily living in addition to the inherent risk for persistent pain and dysfunction.[7-8] Hand and upper extremity fractures also play a major role in disability for younger patients, as they commonly require dedicated time off work with prolonged, aggressive rehabilitation to maximize return to function.[9-10]

A principal goal in healthcare is primary prevention of conditions that result in patient morbidity. Specific to orthopaedic trauma, one critical step in prevention is the identification of associated mechanisms of injury.[11] Falls to the ground on outstretched hands have repeatedly been determined to be the leading cause of hand and upper extremity fractures.[1,6,12-13] Alcohol use and abuse is relatively common[14] and has previously been associated with fractures of the hand and upper extremity via an increased propensity for falls and risky behavior, which could lead to unintentional injury.[15-17] Not only does alcohol use contribute to postural imbalance,[15-16,18] but it also is associated with increased violence and accidents due to impaired judgment. Alcohol consumption has also been identified as a risk factor for both obesity and decreased bone mineral density; this may exacerbate injury risk due to heavier individuals sustaining more forceful impacts on fragile bones.[19-21] To the best of our knowledge, the effects of alcohol consumption on the incidence of traumatic hand and upper extremity fractures has not been reported or investigated.

The purpose of this study is to report national estimates and demographic characteristics of patients presenting to U.S. emergency departments between 2000 and 2017 with traumatic hand and upper extremity fractures associated with alcohol consumption. Our secondary aim is to project alcohol-associated fracture estimates between 2017 and 2030 as well as the annual percentage of the overall number of hand and upper extremity fractures presenting to U.S. emergency departments that are associated with alcohol consumption.

Methods

Data Sources

The Consumer Product Safety Commission's (CPSC) publicly available and deidentified National Electronic Injury Surveillance System (NEISS) was used for this cross-sectional, retrospective epidemiological study. The database is a national representative probability sample of roughly 100 hospital emergency departments that serves the purpose of observing and reliably characterizing the epidemiology of injuries in the United States. It is stratified by both hospital size and geographic location, which allows for statistically validated, weighted national estimates and sampling errors of queried injuries to be derived. The database contains a unique case record for each patient and includes date of treatment, age, sex, race, diagnosis, body part affected, patient disposition, location of injury, as well as narrative fields to provide additional comments. This data is entered into the database by providers and data coordinators and updates (i.e. recognizing and filling in any missing data) are performed daily. The NEISS has previously been utilized in hand surgery studies evaluating the epidemiology of finger amputations[22] and scaphoid fractures.[23] Specific data collection methodologies, quality control precautions, and other general information are available on the CPSC webpage.[24-26]

First, each yearly sample in the NEISS database was queried between 2000 and 2017 using the diagnosis of "fracture" and the affected body parts "finger", "hand", "wrist", and "lower arm" (excluding all injuries at and above the elbow), which were herein considered as "the hand and upper extremity". All hand and upper extremity fracture cases were subsequently identified for

each year during this time period. The narrative sections within these identified case records were then individually analyzed and queried using several keywords to help identify any relevant history of alcohol intoxication or consumption prior to admission and related to the injury event. Examples of these keywords included "alcohol", "drank", "ingested", "consumed", as well as various forms of alcoholic beverages such as "beer", "wine", "vodka", etc. Case records were also included if patients were explicitly noted to be intoxicated with alcohol and had a blood alcohol concentration above 0.08 g/dL. Following the analysis of the narrative section, unique cases of traumatic hand and upper extremity fractures associated with alcohol consumption were subsequently identified for each year during this time period.

As previously described, 27 weighted national estimates were calculated (for total and one-year interval numbers of both total and alcohol associated upper extremity fractures) using a svyset function in a statistical software which uses the NEISS data columns "PSU", "Weight", and "Stratum" as inputs for its sampling unit, sample weight, and strata fields, respectively. The software function then generates weighted national estimates for the given inputs with associated 95% confidence intervals. The incidence of alcohol associated upper extremity fractures out of total upper extremity fractures was then calculated for the total seventeen year time frame as well as one-year intervals. 95% confidence intervals for incidence were calculated using the upper and lower borders from the aforementioned weighted national estimates 95% confidence intervals.

The NEISS database allows for unique case record group analysis and will automatically calculate incidence with respect to various demographic characteristics. Specifically, anatomical location of fracture, age, sex, race, disposition, and location (of injury) were evaluated within our previously identified unique group of hand and upper extremity fractures associated with alcohol. The same svyset function was, again, used to apply standard errors and confidence intervals to the demographic incidence data.

A standard linear regression function (which generates a linear line of best fit for the inputted data and its associated equation) was then used to evaluate trends in the annual national estimate of both total and alcohol-associated hand and upper extremity fractures presenting to U.S. emergency departments over time. Projections were made by applying this regression model forward to the year 2030, by inputting future years into the function to output the predicted national number of injuries if the same linear line were extended forward in time. Significance of trends were determined using adjusted Wald tests. Two-sided p-values < 0.05 were considered significant.

Results

The NEISS database revealed a total of 394,055 cases of patients presenting to an Emergency Department in the United States with traumatic hand and upper extremity fractures between the years 2000 and 2017, which correlated to a total national estimate of 13,544,461 cases. Of these 394,055 cases, 1,541 unique cases of patients whose fracture(s) were associated with alcohol consumption were identified, which correlated to a total national estimate of 62,373 cases. These data by corresponding year, including incidence and their associated 95% CIs are provided in Table 1.

Overall demographics of the patients whose fracture(s) were associated with alcohol consumption can be observed in Table 2. The majority of fractures were located in the hand (37.8%), occurred in young adults between the ages of 20-29 (33.9%), occurred in males (70.9%), occurred in whites (54.7%), were sustained in the home (39.7%), and were also more likely to be treated and admitted to the hospital as opposed to being discharged (60.5%).

The number of total national estimated cases of any cause decreased linearly within this seventeen-year time with a statistically significant p-value of < 0.05 (0.001) and of R2 of -0.79 (Figure 1). Specifically, the number of cases decreased 13% from 788,210 cases in the year 2000 to 686,419 cases in the year 2017 (Table 1).

The number of national estimated cases that were associated with alcohol significantly increased linearly within this seventeen-year time frame with a statistically significant p-value of < 0.05 (0.001) and R2 of -0.86 (Figure 2). Specifically, the number of cases more than doubled from 2,368 cases in the year 2000 or 0.30% to 5,182 cases in the year 2017 or 0.75% (Table 1).

Projected weighted national estimates of traumatic hand and upper extremity fractures associated with alcohol consumption are provided in Figure 3. The existing, current linear trend that has been observed between 2000 and 2017 is projected to continue, with a number of total national estimate cases of 6,802 or 1.04%, by the year 2030.

Discussion

Our main finding was that the number of patients presenting to an emergency department with an alcohol-related hand and upper extremity fracture increased roughly two-fold over the duration study period, from 2,368 annual cases in 2000 to 5,182 annual cases in 2017. This linear trend is projected to continue on the same trajectory into the year 2030, at which point the number of annual cases will reach roughly 7,000, encompassing more than 1% of all hand and upper extremity fractures that present to an emergency department. We demonstrated that these alcohol-related fractures most commonly occur in the hand, more frequently occur in white males between the ages of 20-29 while at home, and are more likely to be admitted to the hospital rather than discharged from the emergency department. Combined, our results suggest that alcohol-related hand and upper extremity fractures, which may be preventable, result in a substantial burden on society in terms of lost productivity and expenditure of healthcare resources.

Our epidemiologic findings are consistent with the literature examining the epidemiology of upper extremity fractures in the United States. In 2001, Chung et al1 studied

Table 1 demonstrates the annual number of national estimated traumatic hand and upper extremity fractures as well as the annual number and incidence of national estimated hand and upper extremity fractures associated with alcohol presenting to emergency departments between the years 2000-2017, and their associated confidence intervals.

Years	National Estimate of Cases Associated with Alcohol Consumption	Total National Estimate of Hand and Upper Extremity† Fractures	Percentage of Hand and Upper Extremity† Fractures Associated with Alcohol Consumption	95% Confidence Interval
2017	5,182	686,419	0.75%	0.55% - 0.96%
2016	5,146	679,653	0.76%	0.57% - 0.94%
2015	4,354	670,753	0.65%	0.45% - 0.85%
2014	3,990	675,055	0.59%	0.44% - 0.75%
2013	3,618	687,686	0.53%	0.35% - 0.70%
2012	3,872	738,941	0.52%	0.42% - 0.62%
2011	3,252	739,063	0.44%	0.30% - 0.58%
2010	3,787	765,177	0.49%	0.35% - 0.64%
2009	3,823	758,601	0.50%	0.38% - 0.63%
2008	3,675	776,862	0.47%	0.33% - 0.61%
2007	3,367	796,817	0.42%	0.33% - 0.52%
2006	3,483	794,358	0.44%	0.32% - 0.56%
2005	2,526	786,556	0.32%	0.21% - 0.44%
2004	2,815	830,509	0.34%	0.24% - 0.44%
2003	2,527	792,243	0.32%	0.21% - 0.42%
2002	2,279	786,606	0.29%	0.21% - 0.37%
2001	2,307	790,952	0.29%	0.18% - 0.40%
2000	2,368	788,210	0.30%	0.19% - 0.41%

Legend:
† - Anatomical locations included in this analysis are as follows: Finger, Hand, Wrist, Lower Arm. Importantly, excludes all fractures/injuries at and above the elbow.

1,465,874 cases of hand/forearm fractures and noted that most fractures occurred in the home (30%) and that whites made up the largest proportion of fractures (83%). While they found that the proportion of all fracture types was evenly divided between genders, they did report that males were more likely to sustain fractures of the hand, and that metacarpal fractures occurred most commonly in the 15-24 year age group, which is consistent with our data. Likewise, Karl et al[2] studied 590,193 upper extremity fractures and found that metacarpal and phalangeal fractures occurred most commonly in the 18-34 year age group. Finally, Ootes et al[3] reviewed 92,601 records of upper extremity injuries from the same National Electronic Injury Surveillance System (NEISS) from 2009, and also found that the majority of cases occurred in the home (45.4%). Though this study included all forms of upper extremity injury, the most common type of injury in their data was fracture (29.2%).

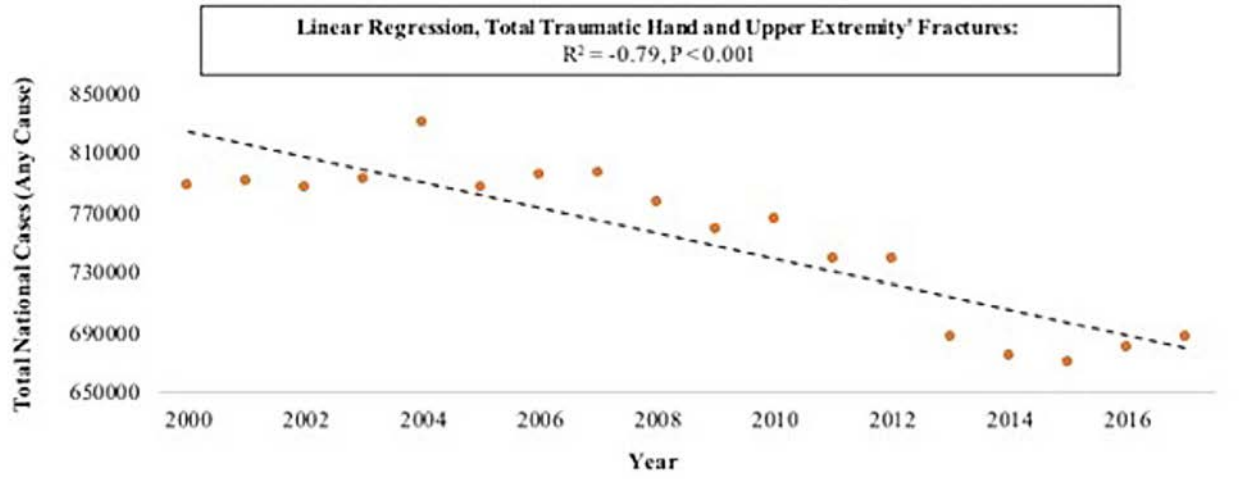
While our epidemiologic data appears to be consistent with previous literature, these studies did not examine alcohol association as our study did. In assessing for a concomitant increase in alcohol consumption, recent surveillance by the National Institute on Alcohol Abuse and Alcoholism28 reported that the per capita alcohol consumption (which is based on reported volumes of alcoholic beverages released to the market for sale) has increased from 1.3 gallons in 1977 to almost 2.4 gallons in 2017. This denotes that the population is consuming more alcohol overall. In addition, other recent epidemiologic studies have noted increases in alcohol use, alcohol use disorder, and high-risk drinking amongst certain population subgroups.[29] The increase in alcohol-related fractures seen in our study thus would correlate with the overall increase in alcohol consumption in the United States.

There are several additional explanations for the linear increase seen in our data. Obesity, of which alcohol use is a risk factor, is rapidly rising in the United States.[21,30-31] This added body mass may contribute to more forceful impacts in a population that is at higher risk of falls.[20-21] These individuals often have decreased bone mass density from alcohol consumption and thus more brittle bones.[19] In addition, with increased awareness of the dangers of drunk driving, more people may be drinking alcohol in their homes. This is supported in our study as most hand and upper extremity fractures tend to occur in the home and was noted in previous studies for all hand fractures.[1,3] Finally, the introduction of newer technologies such as phones and other electronic portable devices have increased the danger of activities such

Table 2 demonstrates the demographic variables and associated categorical percentages of patients presenting to emergency departments with alcohol associated traumatic hand and upper extremity fractures between 2000-2017. Standard error and confidence intervals for each variable are also shown.

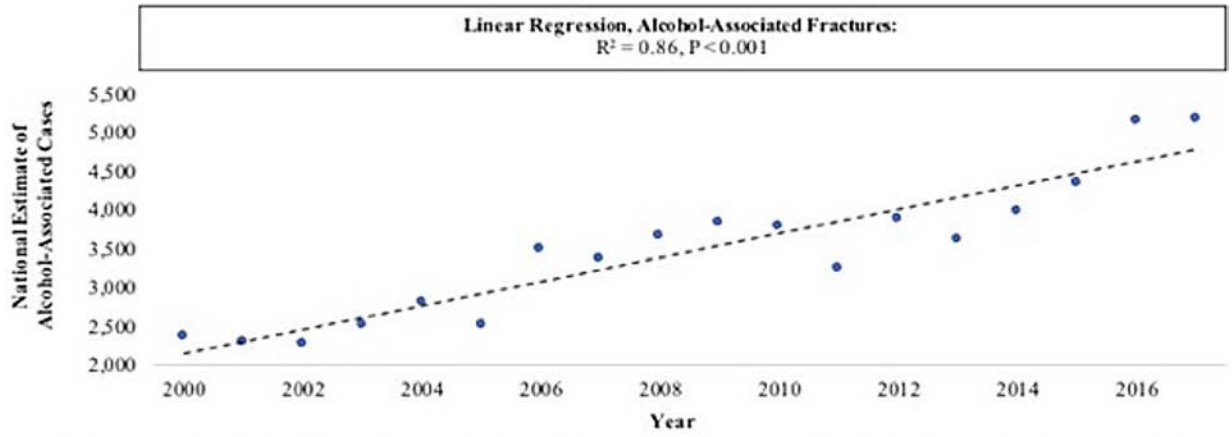
Demographic Variable	Percentage	Standard Error	95% Confidence Interval		
Anotomical Location of Fracture					
Lower Arm	19.4%	1.4%	16.6%	-	22.2%
Wrist	28.6%	2.3%	23.9%	-	33.2%
Hand	37.8%	1.8%	34.2%	-	41.4%
Finger	14.2%	1.1%	12.0%	-	16.4%
Age					
0 to 9 Years*	0.0%				
10 to 19 Years	4.3%	1.1%	2.0%	-	6.6%
20 to 29 Years	33.9%	2.0%	30.0%	-	37.8%
30 to 39 Years	20.5%	1.1%	18.3%	-	22.7%
40 to 49 Years	18.9%	1.3%	16.3%	-	21.6%
50 to 59 Years	13.5%	1.1%	11.2%	-	15.7%
60 to 69 Years	6.7%	0.9%	4.9%	-	8.5%
70 to 79 Years	2.1%	0.6%	0.9%	-	3.3%
80 Years or Older*	0.1%				
Sex					
Male	70.9%	1.9%	67.1%	-	74.8%
Female	29.1%	1.9%	25.2%	-	32.9%
Race					
White	54.7%	4.0%	46.8%	-	62.5%
Black	7.8%	1.9%	4.0%	-	11.7%
Other*	1.2%				
Asian*	0.5%				
Native American*	0.7%				
Pacific Islander*	0.1%				
Hispanic	6.1%	1.7%	2.7%	-	9.4%
Race Not Specified	28.9%	4.1%	20.8%	-	37.0%
Disposition					
Treated and Released	35.3%	2.5%	30.3%	-	40.2%
Treated and Admitted	60.5%	3.2%	54.1%	-	66.9%
Location					
Unknown	38.3%	2.8%	32.7%	-	43.9%
Home	39.7%	2.8%	34.2%	-	45.3%
Street	7.3%	1.2%	5.0%	-	9.6%
Public	12.3%	1.3%	9.8%	-	14.7%
School*	0.6%				
Sports*	1.9%				

Legend:
† - Anatomical locations included in this analysis are as follows: Finger, Hand, Wrist, Lower Arm. Importantly, excludes all fractures/injuries at and above the elbow.



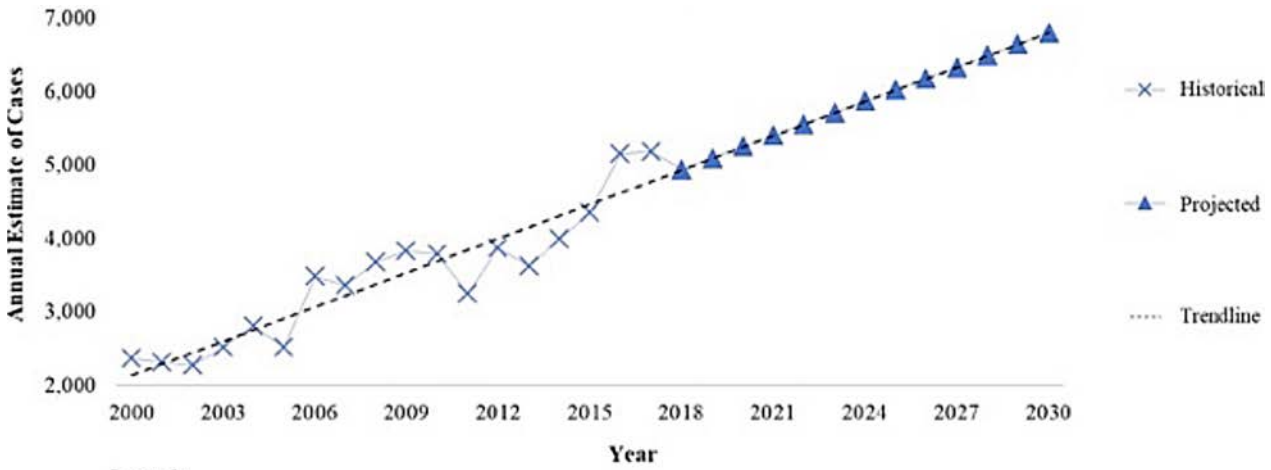
Legend: † - Anatomical locations included in this analysis: Finger, Hand, Wrist, Lower Arm. Importantly, excludes all fractures/injuries at and above the elbow.

Figure 1 demonstrates the national estimated total number of cases of traumatic hand and upper and upper extremity fractures presenting to emergency departments each corresponding year between 2000-2017. These estimates displayed a negative linear regression pattern with a $R^2 = -0.79$ and statistically significant p-value of < 0.001.



Legend: † - Anatomical locations included in this analysis: Finger, Hand, Wrist, Lower Arm. Importantly, excludes all fractures/injuries at and above the elbow.

Figure 2 demonstrates the national estimated number of cases alcohol associated traumatic hand and upper extremity fractures presenting to emergency departments each corresponding year between 2000-2017. These estimates displayed a positive linear regression pattern with a $R^2 = 0.86$ and statistically significant p-value of < 0.001.



Legend:
† - Anatomical locations included in this analysis are as follows: Finger, Hand, Wrist, Lower Arm. Importantly, excludes all fractures/injuries at and above the elbow.

Figure 3 demonstrates the historical (2000-2017) and projected (2017-2030) national estimated number of cases of alcohol associated traumatic hand and upper extremity fractures presenting to emergency departments per corresponding year using a linear regression model.

as distracted walking, which could be potentiated by alcohol use.[32] Ultimately, the linear trend we observe in our data is most likely the result of a multitude of factors as opposed to a single reason.

Our demographic data, nonetheless, is subjectively similar to that in recent literature. The prevalence of drinking, and therefore its associated consequences from risky behavior, peaks in young adults aged 18-29 and is most prevalent amongst white males, 33 who were the majority population in our patient cases.

We acknowledge several limitations of this study, which are related to the nature of the NEISS survey. Most importantly, the accuracy of our estimates depended on the accuracy of the narrative sections, which are prone to reporting and sampling biases. While the CPSC will regularly conduct internal analyses to ensure proper and comprehensive data collection processes, it cannot be ruled out that alcohol consumption was not mentioned in certain hand and upper extremity fractures. Similarly, alcohol consumption may have been underreported by patients. This, however, would suggest that our data potentially underestimates the total burden of alcohol associated hand and upper extremity fractures.

In conclusion, alcohol consumption is associated with fractures of the hand and upper extremity, and the numbers of these cases are increasing over time and this trend is predicted to continue in the future. This is new information that should motivate physicians to educate their patients regarding the risk of fracture associated with alcohol consumption. This data may also aid in the prevention of these injuries, which can be a major burden for patients in terms of cost, time off of work, and long-term function as well as a noteworthy financial burden for the healthcare system.

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A Geriatric Hip Fracture Care Pathway: An Operational Approach to Quality Improvement

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Introduction

Hand and upper extremity fractures are exceedingly common injuries in the United States population, and have been estimated to comprise 1.5% of all emergency department visits nationwide.1-3 The most common of these fractures involves the distal forearm (particularly the distal radius), though certain age groups are more likely to be afflicted with certain hand and upper extremity fractures than others.[1,4-6]

These injuries can markedly reduce quality of life. Among the elderly, wrist fractures have been associated with subsequent dependence on caregivers for activities of daily living in addition to the inherent risk for persistent pain and dysfunction.[7-8] Hand and upper extremity fractures also play a major role in disability for younger patients, as they commonly require dedicated time off work with prolonged, aggressive rehabilitation to maximize return to function.[9-10]

A principal goal in healthcare is primary prevention of conditions that result in patient morbidity. Specific to orthopaedic trauma, one critical step in prevention is the identification of associated mechanisms of injury.[11] Falls to the ground on outstretched hands have repeatedly been determined to be the leading cause of hand and upper extremity fractures.[1,6,12-13] Alcohol use and abuse is relatively common[14] and has previously been associated with fractures of the hand and upper extremity via an increased propensity for falls and risky behavior, which could lead to unintentional injury.[15-17] Not only does alcohol use contribute to postural imbalance,[15-16,18] but it also is associated with increased violence and accidents due to impaired judgment. Alcohol consumption has also been identified as a risk factor for both obesity and decreased bone mineral density; this may exacerbate injury risk due to heavier individuals sustaining more forceful impacts on fragile bones.[19-21] To the best of our knowledge, the effects of alcohol consumption on the incidence of traumatic hand and upper extremity fractures has not been reported or investigated.

The purpose of this study is to report national estimates and demographic characteristics of patients presenting to U.S. emergency departments between 2000 and 2017 with traumatic hand and upper extremity fractures associated with alcohol consumption. Our secondary aim is to project alcohol-associated fracture estimates between 2017 and 2030 as well as the annual percentage of the overall number of hand and upper extremity fractures presenting to U.S. emergency departments that are associated with alcohol consumption.

Methods

Data Sources

The Consumer Product Safety Commission's (CPSC) publicly available and deidentified National Electronic Injury Surveillance System (NEISS) was used for this cross-sectional, retrospective epidemiological study. The database is a national representative probability sample of roughly 100 hospital emergency departments that serves the purpose of observing and reliably characterizing the epidemiology of injuries in the United States. It is stratified by both hospital size and geographic location, which allows for statistically validated, weighted national estimates and sampling errors of queried injuries to be derived. The database contains a unique case record for each patient and includes date of treatment, age, sex, race, diagnosis, body part affected, patient disposition, location of injury, as well as narrative fields to provide additional comments. This data is entered into the database by providers and data coordinators and updates (i.e. recognizing and filling in any missing data) are performed daily. The NEISS has previously been utilized in hand surgery studies evaluating the epidemiology of finger amputations[22] and scaphoid fractures.[23] Specific data collection methodologies, quality control precautions, and other general information are available on the CPSC webpage.[24-26]

First, each yearly sample in the NEISS database was queried between 2000 and 2017 using the diagnosis of "fracture" and the affected body parts "finger", "hand", "wrist", and "lower arm" (excluding all injuries at and above the elbow), which were herein considered as "the hand and upper extremity". All hand and upper extremity fracture cases were subsequently identified for each year during this time period.

The narrative sections within these identified case records were then individually analyzed and queried using several keywords to help identify any relevant history of alcohol intoxication or consumption prior to admission and related to the injury event. Examples of these keywords included "alcohol", "drank", "ingested", "consumed", as well as various forms of alcoholic beverages such as "beer", "wine", "vodka", etc. Case records were also included if patients were explicitly noted to be intoxicated with alcohol and had a blood alcohol concentration above 0.08 g/dL. Following the analysis of the narrative section, unique cases of traumatic hand and upper extremity fractures associated with alcohol consumption were subsequently identified for each year during this time period.

As previously described, 27 weighted national estimates were calculated (for total and one-year interval numbers of both total and alcohol associated upper extremity fractures) using a svyset function in a statistical software which uses the NEISS data columns "PSU", "Weight", and "Stratum" as inputs for its sampling unit, sample weight, and strata fields, respectively. The software function then generates weighted national estimates for the given inputs with associated 95% confidence intervals. The incidence of alcohol associated upper extremity fractures out of total upper extremity fractures was then calculated for the total seventeen year time frame as well as one-year intervals. 95% confidence intervals for incidence were calculated using the upper and lower borders from the aforementioned weighted national estimates 95% confidence intervals.

The NEISS database allows for unique case record group analysis and will automatically calculate incidence with respect to various demographic characteristics. Specifically, anatomical location of fracture, age, sex, race, disposition, and location (of injury) were evaluated within our previously identified unique group of hand and upper extremity fractures associated with alcohol. The same svyset function was, again, used to apply standard errors and confidence intervals to the demographic incidence data.

A standard linear regression function (which generates a linear line of best fit for the inputted data and its associated equation) was then used to evaluate trends in the annual national estimate of both total and alcohol-associated hand and upper extremity fractures presenting to U.S. emergency departments over time. Projections were made by applying this regression model forward to the year 2030, by inputting future years into the function to output the predicted national number of injuries if the same linear line were extended forward in time. Significance of trends were determined using adjusted Wald tests. Two-sided p-values < 0.05 were considered significant.

Results

The NEISS database revealed a total of 394,055 cases of patients presenting to an Emergency Department in the United States with traumatic hand and upper extremity fractures between the years 2000 and 2017, which correlated to a total national estimate of 13,544,461 cases. Of these 394,055 cases, 1,541 unique cases of patients whose fracture(s) were associated with alcohol consumption were identified, which correlated to a total national estimate of 62,373 cases. These data by corresponding year, including incidence and their associated 95% CIs are provided in Table 1.

Overall demographics of the patients whose fracture(s) were associated with alcohol consumption can be observed in Table 2. The majority of fractures were located in the hand (37.8%), occurred in young adults between the ages of 20-29 (33.9%), occurred in males (70.9%), occurred in whites (54.7%), were sustained in the home (39.7%), and were also more likely to be treated and admitted to the hospital as opposed to being discharged (60.5%).

The number of total national estimated cases of any cause decreased linearly within this seventeen-year time with a statistically significant p-value of < 0.05 (0.001) and of R2 of -0.79 (Figure 1). Specifically, the number of cases decreased 13% from 788,210 cases in the year 2000 to 686,419 cases in the year 2017 (Table 1).

The number of national estimated cases that were associated with alcohol significantly increased linearly within this seventeen-year time frame with a statistically significant p-value of < 0.05 (0.001) and R2 of -0.86 (Figure 2). Specifically, the number of cases more than doubled from 2,368 cases in the year 2000 or 0.30% to 5,182 cases in the year 2017 or 0.75% (Table 1).

Projected weighted national estimates of traumatic hand and upper extremity fractures associated with alcohol consumption are provided in Figure 3. The existing, current linear trend that has been observed between 2000 and 2017 is projected to continue, with a number of total national estimate cases of 6,802 or 1.04%, by the year 2030.

Discussion

We conclude that the use of an operational management approach to address the inefficiencies in a clinical care pathway

Measure	National Avg {IGFS Member Facilities*)	Pre Pathwav Implementation (Jul 2015–Jun 2016)	Post Pathway Implementation (Jul 2016–Dec 2016)	Long Term Results (Jul 2018–Feb 2020)
Time to Surgery	36 hours	32.4 hours	17.5 hours	17.5 hours
Length of Stay	6.4 days	7.1 days	5.6 days	5.3 days
30 Day Readmission	14.5%	14.29%	8.33%	3.8%
Mortality in Hosoital	3.1%	2.79%	0%	1.3%

Figure 1. International Geriatric Fracture Society[4] averages compared to institutional averages before, immediately after, and several years after pathway implementation.

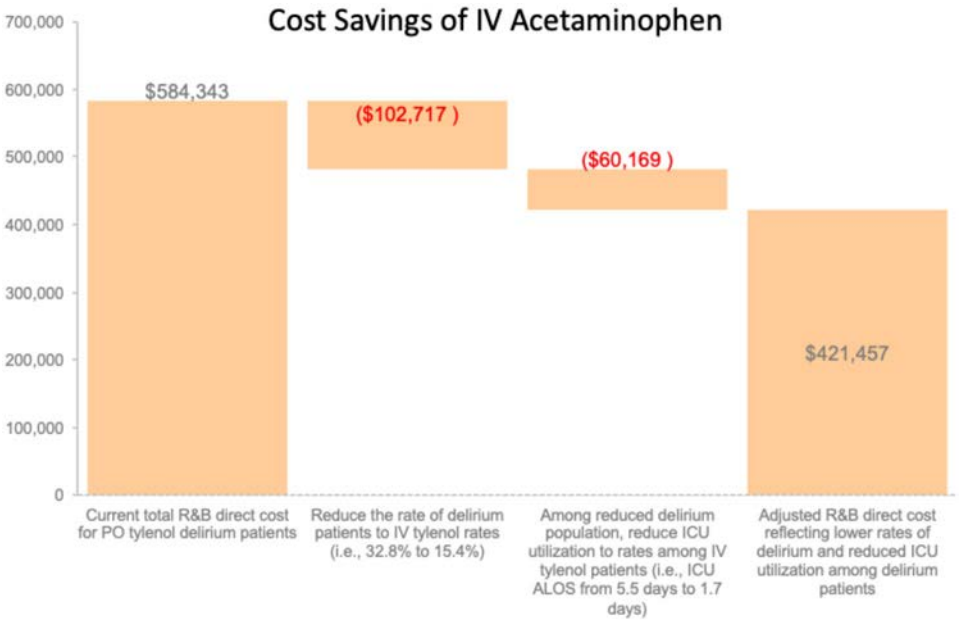

Figure 2. Cost savings of IV acetaminophen compared to oral acetaminophen.

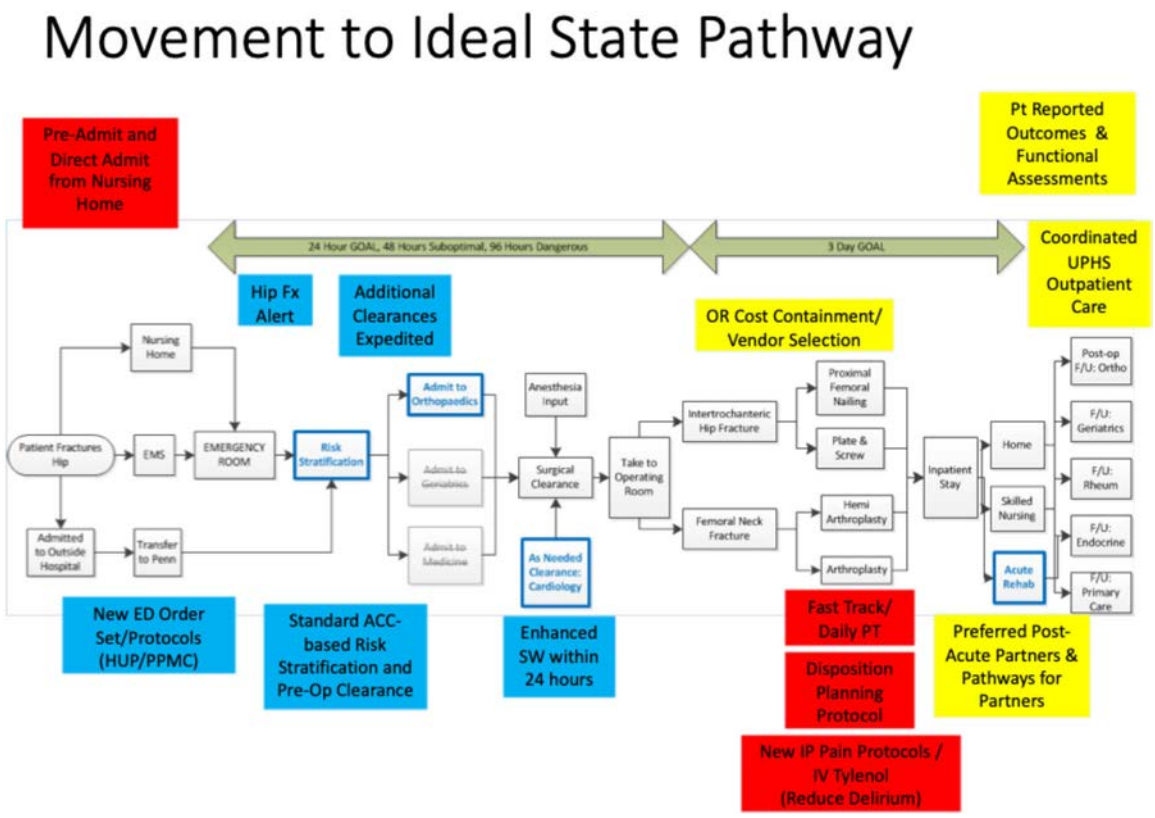

Figure 3. Process map depicting movement to an ideal state pathway with newly implemented changes in red and future directions in yellow.

resulted in a substantial and sustainable improvements in clinically relevant outcome measures in patients sustaining geriatric hip fractures. By systematically identifying the bottlenecks in the system, we have generated an ideal state pathway, which has allowed us to deliver higher quality care to our patients while simultaneously eliminating waste decreasing cost of care. Furthermore, there is a societal need to develop effective strategies of reliably improving patient care while containing costs which makes the operations approach demonstrated here particularly relevant.

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Spine

Hydroxyapatite Coating of Porous Polycaprolactone to Enhance Integration of a Tissue-Engineered Total Disc Replacement

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Introduction

Endplates form the interfaces between the intervertebral discs of the spine and the adjacent vertebral bodies. These structures consist of a thin layer of hyaline cartilage and an adjacent layer of cortical bone.[1] With aging or following injury, degeneration of the intervertebral discs and adjacent endplates is common and is frequently associated with back pain.[2] There is a significant need to develop new treatment strategies to address both the disc and vertebral endplate. Towards this end, our group developed tissue engineered total disc replacements with endplates (endplate modified disc like angle-ply structures, eDAPS) for the treatment of severe, advanced-stage disc and endplate degeneration. In contrast to other designs for tissue engineered whole discs, the porous polymer endplate analog of the eDAPS provides an interface through which integration of the engineered disc with the native vertebral body can occur.[3] However, our previous animal studies demonstrated that robust mineralization of this interface was not present after 20 weeks *in vivo*. The purpose of this study was to optimize the design of the endplate region, via the inclusion of a hydroxyapatite (HA) coating, to improve endplate mineralization and eDAPS integration following *in vivo* implantation.

Methods

Scaffold Fabrication and HA coating

Porous poly(ε-caprolactone) (PCL) scaffolds were fabricated via a salt leaching method, as previously described, to generate constructs 4mm in diameter and 1.5 mm thick.[3] To coat the PCL scaffolds in HA, foams were hydrated through a gradient of ethanol, followed by serial overnight immersions in 2M NaOH and simulated body fluid (SBF).[4]

In Vitro Studies

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. P2 bovine bone-marrow derived mesenchymal stem cells (MSCs) were seeded on the top and bottom surface of each scaffold at a density of 3,333 cells/mm^2. MSC-seeded scaffolds were cultured in either basal or osteogenic media (n=4 per group) for 5 weeks. At the end of the culture duration, construct viability (MTT assay) and alkaline phosphatase activity (ALP, Sigma Aldrich kit) were quantified. Additional samples (n=3 per group) were cryosectioned in the sagittal plane and stained for calcium deposits using a Von Kossa staining kit (Abcam).

In Vivo Studies

For *in vivo* evaluation of the HA coating, PCL scaffolds 4mm in diameter and 5mm thick were fabricated, to mimic the size of the eDAPS previously evaluated our rat tail disc replacement model. In accordance with our approved IACUC protocol at the Corporal Michael J. Crescenz VA Medical Center, the tail disc spaces of five athymic rats were implanted with acellular PCL (n=2) or HA-coated PCL scaffolds (n=3), using our previously described surgical procedure and external fixator.[3] Briefly, the native C8-C9 tail disc space was removed, and a partial corpectomy of the adjacent vertebral bodies was performed with a high-speed burr, such that the constructs could be placed in apposition with the marrow of the vertebral bodies. After 10 weeks, animals were euthanized and vertebral body-scaffold-vertebral body motion segments harvested for analysis. Motion segments were fixed in formalin and subjected to μCT scanning at 10μm resolution to visualize the three-dimensional tissue distribution within the scaffold following *in vivo* implantation. Samples were then decalcified and processed for paraffin histology. Histologic sections were stained with the Mallory-Heidenhain trichrome stain to distinguish unmineralized collagen (blue) from mineralized collagen (pink), and immunohistochemistry (IHC) was performed for osteocalcin. Significant differences ($p<0.05$) between groups were assessed via an ANOVA with Tukey's post-hoc test.

Results

In vitro studies of HA coated and PCL only scaffolds seeded with bone marrow-derived MSCs demonstrated a significant increase in

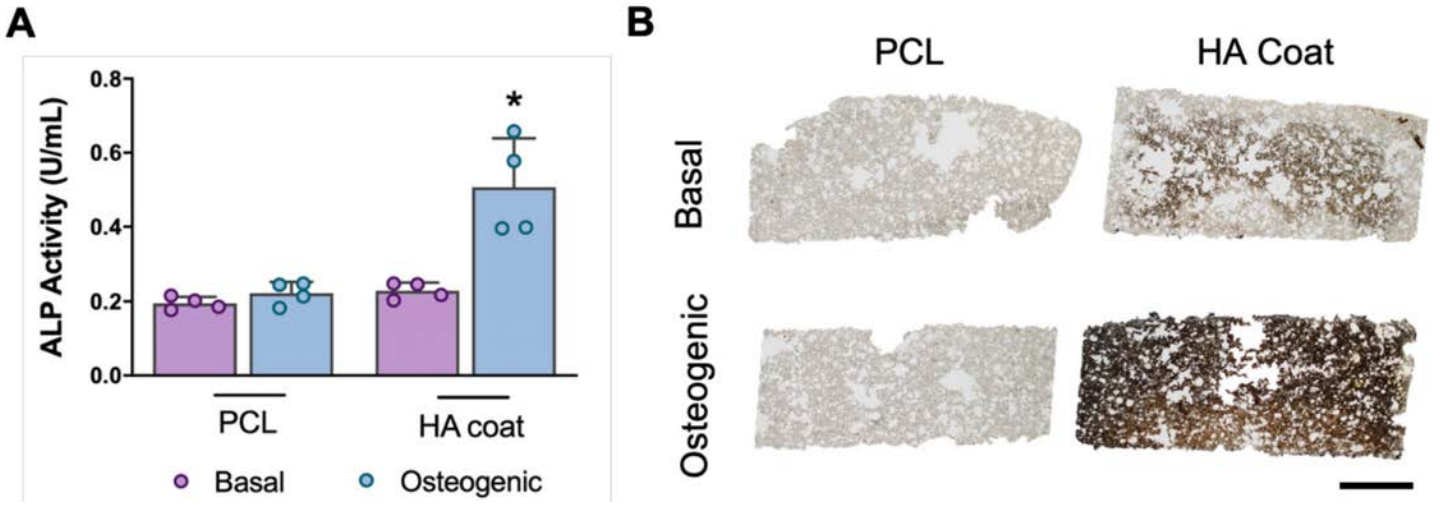

Figure 1. (A) ALP activity and **(B)** Von Kossa staining of HA coated or PCL only foams seeded with MSCs and cultured for 5 weeks. * 5 p,0.05 compared to all other groups. Scale 5 1 mm.

construct ALP activity in the HA-coated group cultured in osteogenic media (Figure 1A). There were no statistically significant differences in MTT absorbance across groups. Von Kossa staining of the constructs suggested increased calcium deposition in the HA coated group compared to the PCL only group, in both basal and osteogenic media culture conditions (Figure 1B). *In vivo*, collagenous matrix deposition occurred within the initially acellular scaffolds in both groups after 10 weeks implantation. There was increased immunohistochemical staining for osteocalcin within HA coated scaffolds compared to the PCL only controls (Figure 2, left panel). Additionally, the Mallory-Heidenhain trichrome stain revealed areas of mineralized collagen (pink staining) present in the HA coated group that were not present in the uncoated group (Figure 2, middle panels). 3D μCT reconstructions of the constructs 10 weeks post-implantation demonstrated increased mineralized tissue deposition with HA coating of PCL scaffolds (Figure 2, right panel).

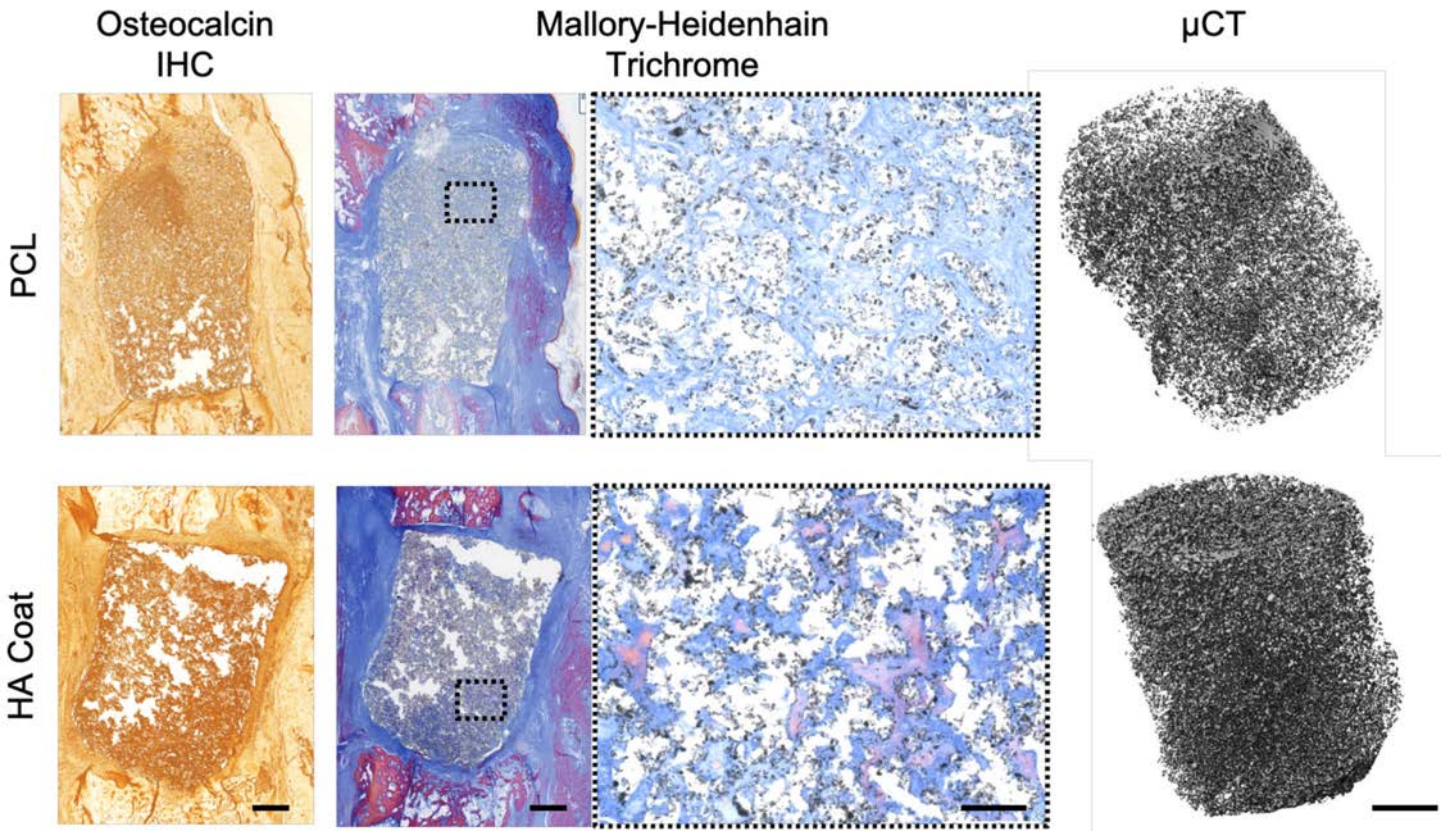

Figure 2. IHC for osteocalcin (scale 5 1mm), staining with the Mallory-Heidenhain trichrome stain (left scale 5 1mm, right scale 5 100μm), and μCT (scale 5 1mm) of acellular PCL and HA coated foams implanted in the rat caudal spine for 10 weeks.

Discussion

The results from our *in vitro* and *in vivo* experiments suggest that coating of porous PCL scaffolds with HA can increase their osteoinductive potential. In our previous work, where eDAPS with PCL only endplates were implanted in the rat caudal disc space, mineralized collagen was not observed within the endplate region until 20 weeks post-implantation.[3] Here, we observed staining for mineralized collagen within the construct at 10 weeks post-implantation in the HA coated group, suggesting that integration may be accelerated by the HA coating. Our current findings are consistent with previous work in the fracture repair field, where hydroxyapatite coating by other methods improved *in vitro* and *in vivo* osteogenesis.[5,6] Ongoing work is investigating the mechanical strength of the integration of the HA coated PCL with the native vertebral body, and the inclusion of macroscopic channels within the constructs to further promote integration. In the future, these HA coated PCL foams will be utilized for the endplate region of the engineered disc, and integration and bone formation assessed in small and large animal models.

Significance/Clinical Relevance

This design modification to our tissue engineered endplate and intervertebral disc replacement has the potential to improve and accelerate integration of the construct with the native vertebral bone, which will be critical for clinical translation.

Acknowledgments

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Risk of Ventricular Peritoneal Shunt Malfunction In Surgically Treated Early Onset Scoliosis

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Introduction

Early onset scoliosis (EOS) is commonly defined as a deformity of the spine that is present before age 10 with varying etiologies including congenital, neuromuscular, syndromic, and idiopathic[1, 2]. Patients diagnosed with EOS may go on to require surgical treatment aimed at preventing deformity progression and subsequent pulmonary decline[1, 3, 4]. Mainstays of surgical treatments for these patients emphasize growth-friendly strategies and include the vertical expandable prosthetic titanium rib (VEPTR)[5, 6], magnetic expansion control (MAGEC)[7], traditional growing rods[8], and Shilla growth guidance[9] with the goals of treatment being to control scoliosis and allow spinal growth[10].

Many patients, particularly those with neuromuscular or syndromic forms of EOS, may have hydrocephalus and undergo ventriculoperitoneal (VP) shunt placement prior to correction of spinal deformity. These shunts allow diversion of fluid from the ventricles of the brain to the peritoneum for reabsorption. Several case reports and small retrospective reviews have pointed towards the possibility of VP shunt fracture or malfunction following operative correction of scoliosis[11-15], with a potential mechanism being calcification of the shunt leading to fragility in the setting of distraction forces[16]. However, no information is available for patients treated with growth friendly strategies of scoliosis correction.

The purpose of this study was to characterize the risks of scoliosis correction in EOS patients with preexisting neurosurgical shunts and understand if the risk of shunt malfunction is higher in these patients relative to historical standards.

Methods

A retrospective chart review of all patients with ventricular peritoneal shunts who underwent growing instrumentation at a single institution over a 13-year timeframe was performed. Age and diagnosis associated with shunt placement were recorded from the medical record. Shunt related complications and complications requiring reoperation were recorded.

Observations were made between the timing of shunt malfunction and index spine procedure as well as subsequent lengthening surgeries. A minimum of 2 year follow up from the time of initial growing instrumentation insertion was required for inclusion.

Results

Nineteen patients with a VP shunt underwent implantation of Vertical Expandable Prosthetic Titanium Rib (VEPTR) for treatment of scoliosis (Figure 1). The mean age at shunt placement and growing rod instrumentation surgery was 13.7 months (1 day to 13 years old) and 6.1 years (0.5 to 15.1 years), respectively. The diagnoses requiring shunt implantation were: 12 (63.2%) spina bifida, 3 (15.8%) structural defects or obstructions, 2 (10.5%) intraventricular hemorrhage, 1 (5.3%) cerebral palsy, and 1 (5.3%) campomelic dwarfism.

During the first two years following VEPTR implantation, there was a mean of 2.5 VEPTR expansion/revision procedures (0 to 5) without any shunt related complications. The mean length of follow-up in this cohort was 7.0 years (2.6 to 13.2). A total of 3 (15.8%) patients underwent shunt revision following their VEPTR implantation at 2.4, 2.6, and 5.6 years post operatively due to a pressurized shunt, sluggish refill of the shunt, and distal shunt disconnection respectively (Figure 2). Each of these shunt revisions occurred at least 30 days following a VEPTR expansion procedure (1.9, 2.9, and 5.7 months).

Discussion

This is the largest known report of patients with EOS undergoing VEPTR implantation and subsequent lengthening procedures with pre-existing ventricular peritoneal shunts. In this study, we show that in our population there is not an increased risk of shunt malfunction relative to baseline VP shunt risk.

Despite the utility and effectiveness of VP shunts, they are associated with a high degree of complications and may require additional surgical procedures over the course of a patient's treatment. Rates of shunt complication requiring a revision procedure range between

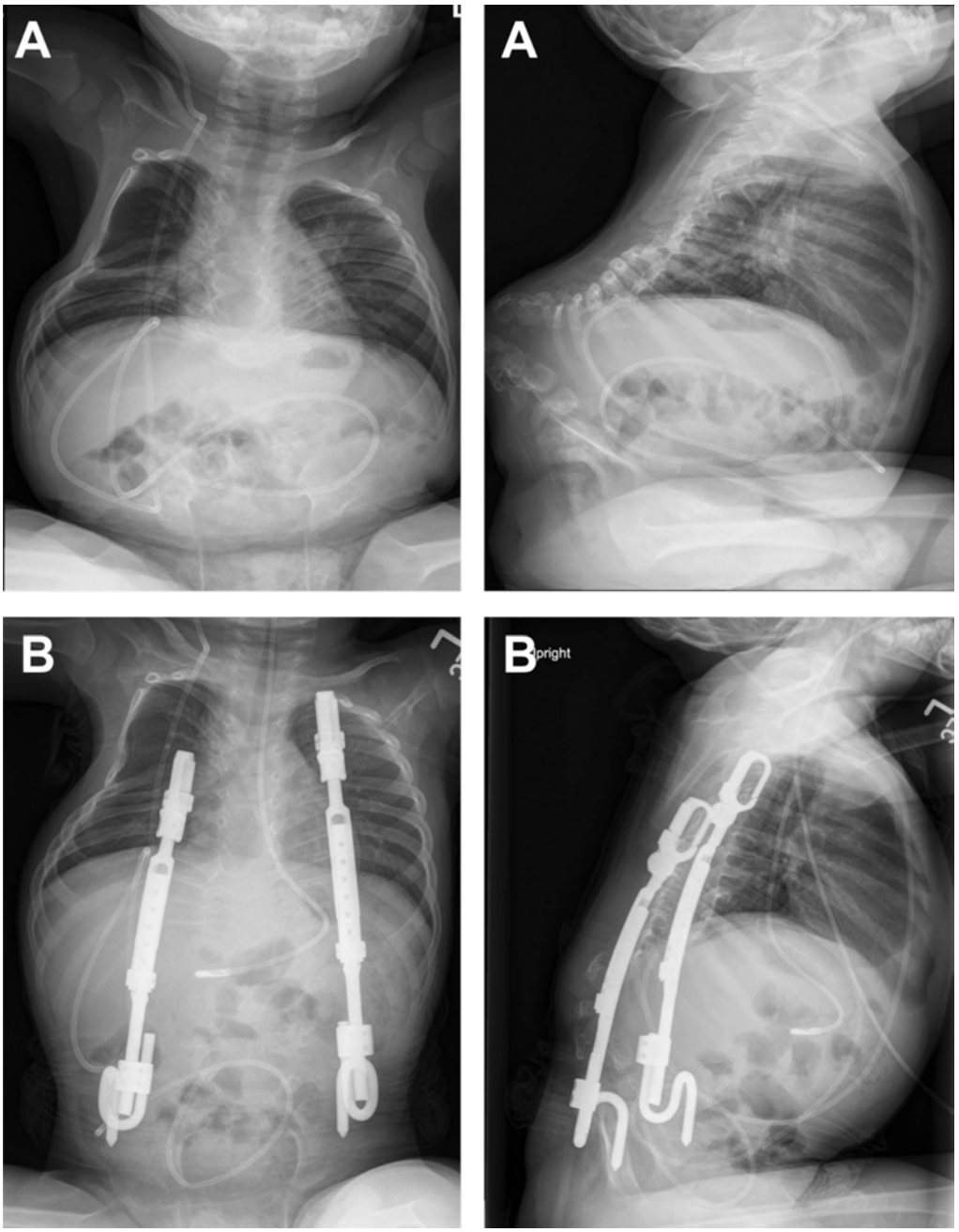

Figure 1. AP and Lateral Scoliosis Radiographs **(A)** Pre-VEPTR Insertion; **(B)** Post-VEPTR insertion in a child with a ventricular peritoneal shunt

20%-40%[17-19], with one report of 64 patients with 15 years of follow up by Stone et al[20] indicating that 84.5% of patients will require at least one VP shunt revision.

While a single center retrospective review of 35 patients with VP shunts undergoing posterior spinal fusion demonstrated a low risk of shunt complication[12], Lai et al[11] reported a series of three neuromuscular scoliosis patients with long term VP shunts experiencing shunt related complications following correction of curves by posterior spinal fusion. Additionally, Blakeney et al[21] reported a case of a 10-year-old female undergoing halo-gravity traction leading to a shunt fracture prior to planned scoliosis correction. Patel et al[22] reported a case of a 12-year-old male undergoing kyphosis deformity correction leading to shunt malfunction. However, there has been no documented cases of shunt complication following growth-friendly methods of scoliosis correction. Given the amount of distraction forces placed on the spine and the need for continued expansion of growth friendly implants[23], this poses a continued theoretical risk given the reported cases of shunt malfunction. While three patients in our cohort experienced a shunt complication during their follow up, none of these events occurred within two years of the index procedure or 30 days of a VEPTR lengthening. Additionally, none of these were a result of a broken shunt, which is the common reported complication in previous case reports[11, 21].

Potential explanations of these findings include that the population studied here, with an average age of 6 years, is

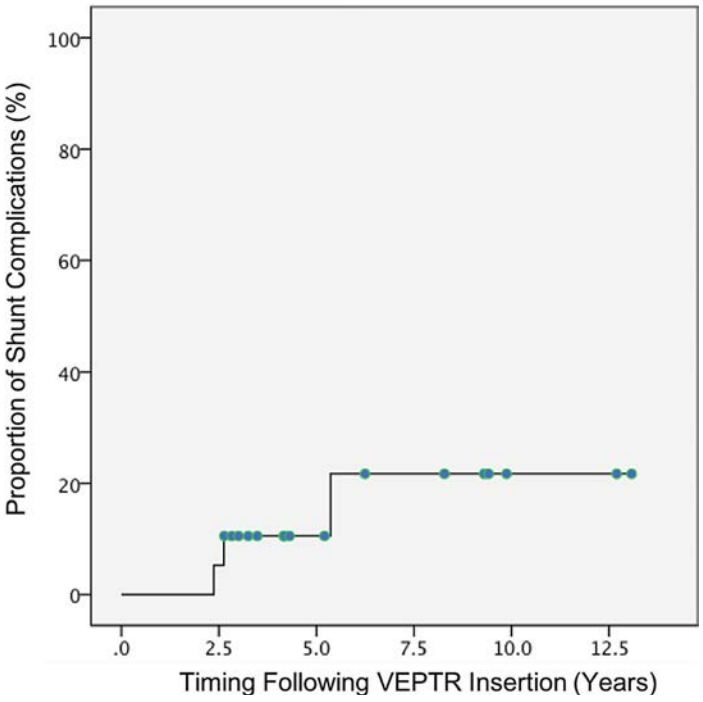

Figure 2. Burden of shunt-related complications following initial VEPTR implantation procedure

younger than the age of reported VP shunt complications and may have a lower likelihood of shunt calcification and fragility[11]. Additionally, the distraction force placed on the spine by growth friendly strategies is likely less than experienced in traditional posterior fusion techniques. Limitations of this study include its single center nature and relatively small sample size, making it difficult to detect potentially rare shunt related complications. Further multicenter analysis should be performed to determine the exact risk of ventriculoperitoneal shunt malfunction in patients with EOS.

Conclusions

EOS patients with pre-existing VP shunts undergoing deformity correction with growth friendly constructs do not have a higher risk of shunt related complication. Growing constructs can safely be employed by pediatric spine surgeons in these patients without fear of inducing immediate or short-term shunt complications. Compared to the literature, EOS patients with VP shunts are at no greater risk for long-term shunt related complications.

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U·P·O·J

Patient Undergoes Halo-Gravity Traction While Virtually Participating in School During COVID-19 Pandemic: A Case Report

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Introduction

COVID-19 was first reported in December of 2019 as a cluster outbreak in Wuhan, China[1] but quickly spread around the world reaching pandemic status according to the World Health Organization in March of 2020[2]. This has had a profound impact on everyday life for children with school closures, stay at home orders, and implementation of other social distancing policies[3, 4]. These restrictions on everyday life have led to concern that children are more likely to become depressed or develop anxiety as a result[5]. However, there is also the argument that a subset of children with social phobias or other extenuating circumstances may experience a temporary lessening of social distress associated with school closings and a shift towards virtual activities[6]. This may be the case with patients attending school while hospitalized for extended periods of time.

Prior to the COVID-19 pandemic, pediatric patients at our institution had access to educational materials provided by the hospital and the local school district. However, this is a significantly different environment compared to learning alongside fellow classmates and interacting with known teachers. Through the adoption of virtual education during the COVID pandemic, our hospitalized patients can receive the same amount of remote teaching by their own teachers as their classmates. In this study, we report on a 7-year-old male with severe early onset scoliosis who underwent staged halo-gravity traction (HGT) prior to bilateral growing rod insertion resulting in a 5-week hospitalization. We report on the patient's ability to participate fully in remote learning in the 4 weeks leading up to his operation.

Case Information

A six-month-old boy initially presented with a complex congenital rib deformity of the anterolateral chest with a left sided congenital scoliosis. The patient was treated with left sided VEPTR implantation and reconstruction of the chest followed by bilateral VEPTR placement with partial rib wedge resection. The patient's VEPTR treatment course was complicated by multiple episodes of wound dehiscence and infection leading to bilateral VEPTR removal, re-insertion, and subsequent re-removal over the 6.5 years treated with VEPTR constructs. The patient was 7-years old when presenting with progressive scoliosis following removal of bilateral VEPTR implants (Figure 1A). At this time, due to his curve stiffness, rate of scoliosis progression, and the risk of wound complications associated with rib-based anchors, traditional growing rod insertion with pre-operative halo gravity traction was recommended as the next operative step. The patient was admitted for 24 days of halo gravity traction (HGT) in August through September of 2021, in the midst of the COVID-19 pandemic. The patient's traction was increased by two pounds per day until reaching a goal weight of 30 pounds (50% of total body weight). His left thoracic curve measured 76° before HGT and decreased to 41° after. While undergoing HGT, this patient was able to participate fully in virtual schooling on a daily basis for four hours per day, the same as all of his classmates (Figure 1B).

Following insertion of bilateral growing rods, the patient was discharged after four days of inpatient recovery (Figure 1C). He was then evaluated at 1-month postoperatively via a Telemedicine visit with no complications identified.

Discussion

Significant harms with potential long-term implications are expected with school closures during the COVID-19 pandemic including a decline in child physical and mental health along with decreased future economic earning potential[4, 7-9]. However, in the same way that the medical field has adapted to the challenge posed by COVID-19 by increasing telehealth visits[10, 11], there has been a significant increase in electronic resources in a large-scale effort to apply technology in a virtual learning environment.

Although virtual learning presents unique challenges, one potential positive is that online education does not need to be limited to the home and pediatric patients who are admitted to the hospital for an extended period of time can have access to their own school's remote learning and classwork while continuing to

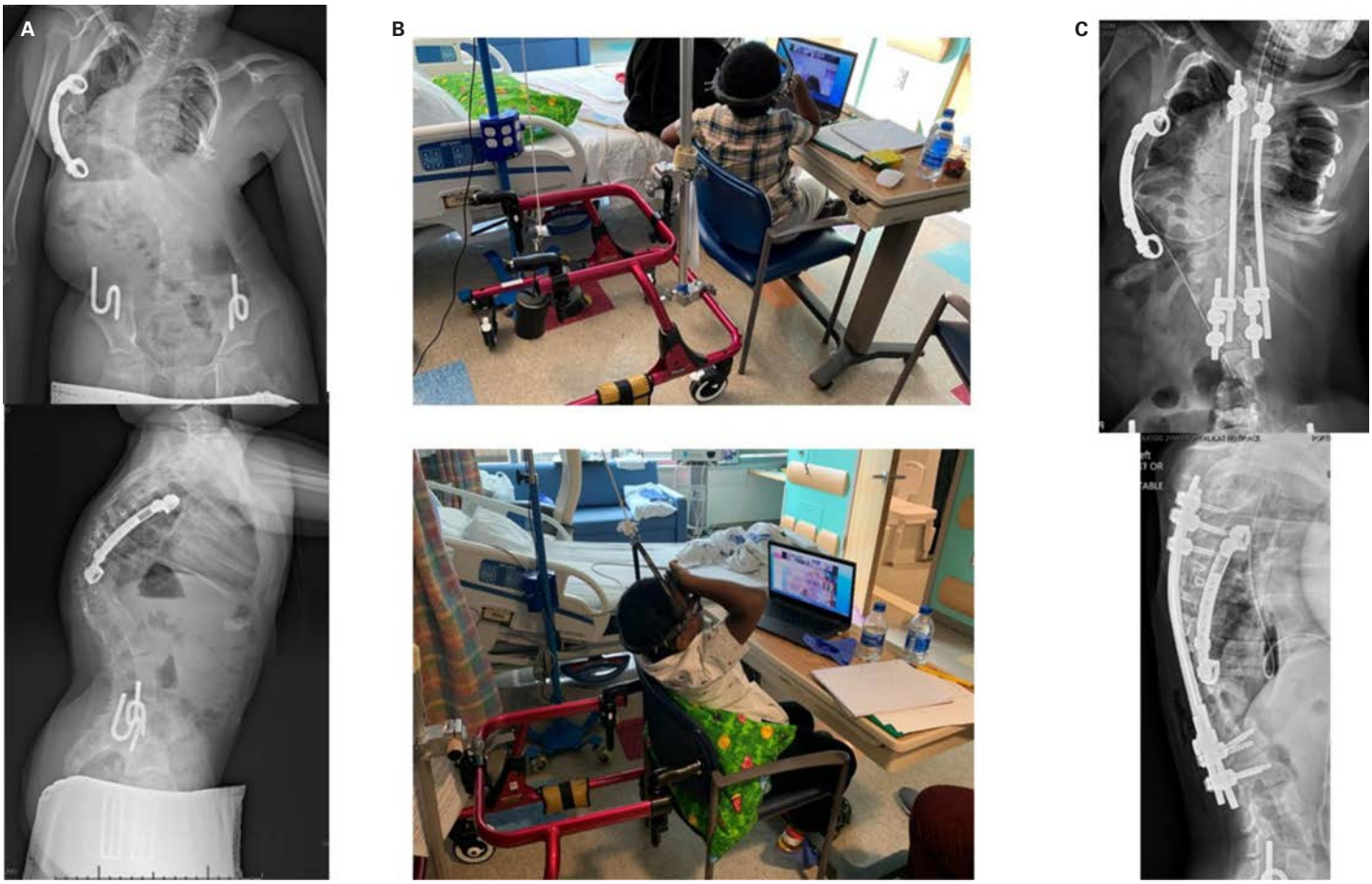

Figure 1. (A) AP and Lateral radiographs prior to halo-gravity traction; **(B)** Patient attending school virtually while in halo-gravity traction; **(C)** Post-operative AP and Lateral radiographs following growing rod insertion.

interact with their peers. While educational materials provided by the hospital and the local school district were available for hospitalized patients prior to the COVID-19 pandemic, increased adoption of virtual learning allows an increased opportunity for these patients to remain integrated with their fellow peers. Prior work has demonstrated that students with chronic illnesses are significantly more likely to repeat a year in school, have academic challenges, and report significant emotional distress. Additionally, these children tend to have lower social confidence relative to their peers[12]. Given reports that educational support for chronically ill patients varies by location and across school districts[13, 14], increased remote learning in schools may have profound benefits for chronically ill and hospitalized patients related to their education and quality of life.

While this is not the first case of a patient utilizing virtual learning materials while hospitalized, it does represent the changing learning environment for hospitalized children during the COVID-19 pandemic. Encouraging children who are hospitalized and able to continue with their schoolwork virtually alongside their peers represents an important benefit that these patients can continue to pursue.

Conclusions

This case of a 7-year-old boy with congenital scoliosis admitted to the hospital for a total of five weeks represents a potential positive side effect of the COVID-19 pandemic. Due to improvements in school's remote learning functionality, he was able to participate fully in all online school related activities alongside his classmates prior to his operation. Progress made by school districts improving access for virtual learning in a normal classroom environment should not be abandoned with the resolution of the COVID-19 pandemic.

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Sports

U·P·O·J

Multiligamentous Knee Injury in Siblings with Associated Peroneal Nerve Deficits: A Case Report

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Introduction

Multiligamentous knee injuries (MKI) are a relatively rare orthopedic injury that most commonly occur in the polytraumatized patient or in the setting of occult knee dislocation.[1,2] These injuries require careful management due to potential joint instability and/or associated neurovascular injury.[3] Multiligamentous knee injuries can be classified by the number and location of the ligaments injured, as well as by the energy of the injury mechanism (ie. high or low velocity).[4,5]

Because the literature is limited regarding treatment of MKI in children and adolescents, particularly those with neurovascular compromise, classifications and treatment algorithms from the adult literature are often used.[6] While this is necessary in order to guide safe and appropriate decision-making, it is important to consider that younger patients may have biologic and mechanical differences from adults that can lead to different injury patterns, treatment considerations, and outcomes. We present siblings who sustained MKI with associated peroneal nerve deficits as a result of low velocity, non-contact athletic injuries. The patients and their parents consented to publishing their unique cases.

Case Information

Case 1

A 17 year-old male with a history of medial meniscus bucket handle tear repaired two years prior presented with right knee pain and swelling one day after a hyperextension injury sustained while playing soccer. Examination revealed an effusion and initial ligamentous testing was limited by pain. He had strong distal pulses but was unable to dorsiflex the ankle or great toe. He had minimal firing of the peroneal muscles and decreased sensation over the dorsum of the foot. Ankle-brachial indices (ABIs) were normal and MRI demonstrated a complex medial meniscus tear, partial thickness anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) tears, and a Grade 2 lateral collateral ligament (LCL) sprain. He was initially treated with a hinged-knee brace, an ankle-foot orthosis (AFO), and physical therapy.

Six weeks later his nerve function had failed to improve and electromyography (EMG) confirmed the common peroneal nerve injury, without definitive evidence of nerve continuity. He was evaluated by a pediatric neurosurgeon and underwent peroneal exploration and neurolysis; the nerve was in continuity and did not require neuroma excision or repair. Four months after the injury he had regained full knee motion and had returned to daily activities without feelings of knee instability. He underwent arthroscopic partial medial meniscectomy for his complex meniscus tear. Continued non-operative management was chosen for his ligamentous injuries because his knee was clinically stable and MRI revealed healing ACL, PCL, and LCL tears.

At 6 months he began a slow return to sports while wearing an AFO. However, his peroneal nerve lacked clinical and EMG improvement, so internal neurolysis was performed without identification of a neuroma. He had minimal subsequent improvement in nerve function, so the option of a posterior tibial tendon transfer was discussed but the patient was eager to continue his return to sports. At 2 years after the injury, he had minimal recovery of nerve function but was satisfied with his level of activity, and played baseball and soccer with the assistance of his AFO.

Case 2

A 16-year-old female presented with right knee pain and inability to dorsiflex her right foot two days following a non-contact pivoting injury while playing soccer. On examination she had a knee effusion, instability with varus stress testing, and a 2B lachman's test. Neurologic testing revealed inability to dorsiflex or evert the foot, and diminished sensation in the peroneal distribution. MRI demonstrated a complete ACL tear, high-grade partial PCL injury, and a distal avulsion of the LCL with edema at the posterolateral corner (Figure 1). Standing lower extremity radiographs did not show mechanical malalignment.

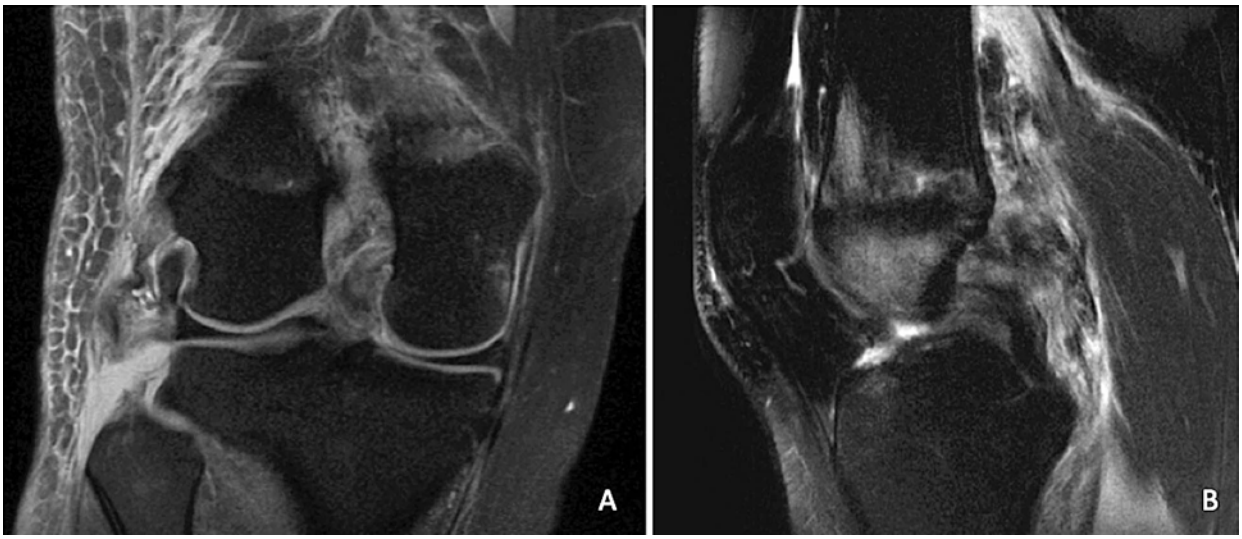

Figure 1. Selected coronal PD FS **(A)** and sagittal T2 FS **(B)** MRI images demonstrating a distal avulsion of the LCL from the fibular head, a complete ACL tear, and an incomplete PCL injury

Given her injury pattern and peroneal dysfunction, she underwent staged surgical intervention, starting with LCL stabilization and peroneal neurolysis at two weeks post-injury. Ligamentous testing under anesthesia revealed a positive dial test at 30 degrees but not 90 degrees and a negative posterior drawer test, so the PCL was treated non-operatively. The avulsed LCL was repaired to the fibular head by pulling it through a bone tunnel in the proximal fibula and securing it with a biotenodesis screw. Neurosurgery then performed a neurolysis and confirmed that the nerve was in continuity. Because the patient's brother had a similar injury, the patient underwent evaluation by genetics, which did not result in significant findings or diagnosis of underlying connective tissue disorder.

At 3 months post-injury, she did not have clinical or EMG improvement of her nerve injury. She therefore underwent repeat neurolysis and exploration, which revealed dense scar tissue around the fibular head and a small neuroma. The neuroma was resected and the nerve was primarily repaired without residual tension. Six months post-injury, the patient underwent ACL reconstruction with quadriceps autograft and had an uneventful recovery. Nine months after ACL reconstruction, her EMG showed signs of continued improvement and clinically she had improving strength and sensation in the peroneal distribution. She also passed her functional ACL testing and was cleared to progressively return to sports while wearing her ACL brace and AFO.

Discussion

MKI is far less common than isolated ACL injury in young patients, but it can be challenging to manage as there is wide variability in injury patterns, presentation, and associated pathology.[2,7-9] Recent studies found that older teens are more likely to sustain MKI, and incomplete injury patterns are more common than complete patterns.[10-11] Incomplete MKI are also more likely to go undiagnosed, and indications for reconstruction in young patients with incomplete injuries have not been established.[11] Our cases highlight the potential for neurovascular injury even in the setting of low-energy or incomplete MKI, and underscore the importance of a careful neurovascular exam in all patients with potential MKI.

Initial evaluation should include a peripheral vascular exam, with ABIs or advanced vascular imaging if asymmetry is detected, and a neurologic exam should be documented with particular attention to the peroneal nerve. Ligamentous testing should be performed with caution in the setting of a potentially self-reduced dislocation or otherwise highly unstable knee.[3] Associated fractures around the knee are common and radiographs should always be obtained.[12] This is especially important in young patients, as the physis is weaker than surrounding structures and a physeal fracture around the knee may be misinterpreted as ligamentous laxity. In the case of neurologic injury, any asymmetry or deficit should be followed with repeat examinations and EMG should be done at 6 weeks after injury if no improvement is seen. However, patients who undergo earlier reconstruction of lateral ligamentous injuries may also undergo peroneal neurolysis at that time.[13]

While principles for initial knee stabilization, ligament reconstruction, and management of neurovascular injury in pediatric MKI are typically extrapolated from the adult literature, additional factors in pediatric patients should be considered.[8] First, undiagnosed connective tissue or endocrine disorders may cause changes in tissue biology that place children at higher risk for ligamentous injury. Family history, thorough physical exam, including beighton score, and additional medical or genetic work-up should be pursued if abnormalities are suspected. Secondly, mechanical differences such as open physes, a growing skeleton, and lower extremity malalignment may lead to different injury patterns from adults. Rotational, coronal, and sagittal lower extremity alignment should be assessed on physical exam and with standing lower extremity radiographs if needed. Mechanical malalignment may be addressed at the time of ligamentous reconstruction or in a staged fashion in order to decrease the risk of recurrent injury. Finally, the psychosocial effects of MKI in children and adolescents may be under-appreciated after a low-velocity sports injury. Recent literature has demonstrated

that children and adolescents often have signs and symptoms of post-traumatic stress disorder or depression even after an isolated ACL injury, particularly those with a strong association between sports and self-identity.[14-15] Because MKI treatment can be prolonged and involve multiple surgeries, surgeons should be sensitive to the potential effects of the injury and continually re-evaluate and address the patient's psychosocial needs in a multi-disciplinary fashion.[8]

Outcome data after treatment of pediatric and adolescent MKI is mostly limited to small case series, although they have generally shown favorable function and rates of return to sport.[8,9,16,17] Multiple studies in the adult literature have shown an increased complication rate and less predictable outcomes after treatment of MKI compared to isolated ligamentous injury, but larger studies are needed to evaluate this trend in young patients.[18-24] Growth arrest, limb length discrepancy, and limb deformity are potential complications of ligament reconstruction around the knee in skeletally immature patients, but they have not yet been reported in the setting of MKI.[25] Regarding neurologic injuries, younger age is typically considered to be a favorable factor for recovery of long term nerve function, although our patients had unpredictable nerve recovery even with appropriate neurosurgical treatment.[13,26,27]

Conclusions

In this case report, we present siblings with MKI and peroneal nerve dysfunction after sports injuries. We advocate for careful neurovascular evaluation in the setting of all MKI, regardless of mechanism, as well as additional radiographic and clinical evaluation in the setting of significant family history or benign injury mechanism. Further studies are needed to evaluate the incidence, injury patterns, and patient characteristics of pediatric MKI, as well as the outcomes after treatment of pediatric MKI and associated nerve deficits, in order to better guide patient counseling and management.

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Genetic Contributions to Osteochondritis Dissecans: A Systematic Review

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Introduction

Osteochondritis Dissecans (OCD) is a focal, idiopathic alteration of subchondral bone or epiphyseal cartilage with risk for instability and disruption of adjacent articular cartilage that may result in premature osteoarthritis.[1] Prevalence has been estimated at 15 to 29 cases per 100,000 individuals and most commonly affects males between the ages of 10 to 20 years old.[2] OCD can be separated into juvenile and adult forms based on skeletal maturity. The juvenile form of OCD occurs in patients with open growth plates while the adult form refers to cases diagnosed after growth plate closure.[2,4] While originally described by König in 1887,[3] the pathogenesis of OCD has yet to be fully explained. Current theories provide support for repetitive microtraumas, focal ischemic insults to the subchondral bone, and genetics.[4]

Mechanical factors, such as repetitive microtraumas, are an intuitive theory behind the etiology of OCD as the most common lesion site, the medial femoral condyle, lends itself to impingement by the tibial eminence during internal rotation with extension.[5,6] In fact, the Wilson test, a provocative maneuver where the knee is extended from a flexed position and internally rotated, impinges the tibial eminence into the medial femoral condyle and elicits pain if medial femoral condyle OCD is present. However, other factors are likely at play given OCD lesions in other locations, the numerous cases of near identical OCD in monozygotic twins, familial cases of OCD, and reports of syndromic OCD cases associated with *ACAN* and *COL9A2* mutations.[7]

One of the last comprehensive reviews on the role of genetics in human OCD was performed in 2012.[7] The group reported on numerous twin and familial studies that established a genetic basis for OCD. However, literature describing specific gene involvement was at its infancy. They did report on the isolation of a *COL9A2* mutation[8] and identification of *ACAN* mutations, both thought to be involved in OCD pathogenesis.[9,10] The goal of this systematic review was to identify new literature published on the role of genetics in OCD pathogenesis since 2012.

Methods

Two computer databases were utilized to identify pertinent articles. Medline and EMBASE were queried for the terms "osteochondritis dissecans" AND "genetics" OR "genetic" OR "family" OR "familial" OR "twin" OR "twins" OR "triplet" OR "triplets" OR "heritable". Additionally, reference lists were cross-referenced to ensure no additional articles were missed. Only articles written or translated into English that were published from 2012 to 2021 were included. Animal studies, in-vitro studies, reviews, opinions, and editorial articles were excluded.

A total of 48 unique articles were identified by title between EMBASE and Medline. Of these, 12 met full inclusion/exclusion criteria. A manual search of references of the reviewed articles did not reveals any additional papers. Of the original 48 articles, 30 were eliminated based on title. The remaining 18 articles were all read in full. After full text analysis 12 articles remained (Figure 1) detailing 35 unique patients. Studies were predominantly level 4.

Results

Since the last systematic review in human subjects, the literature has continued to produce case series highlighting twin and familial cases of OCD. One group identified two cases of bilateral OCD of the capitellum in fraternal twins.[12] No known trauma was reported prior to the cases and the bilateral disease progression, right worse than left, was near identical in each brother. Another study identified 3 incidences of OCD occurring in the bilateral femoral heads of 3 family members.[13] The three cases occurred in a father, a nephew, and the father's son at 11, 9, and 9 years of age, respectively. There were no histories of significant trauma in these cases either. Similarly, a case series of a mother and daughter with identical, bilateral medial femoral condyle OCD lesions was published in 2015.[14] The mother's monozygotic twin sister was also found to have a unilateral medial femoral condyle OCD lesion. A separate group identified two pairs of monozygotic twins each presenting with nearly identical clinical courses.[15] Both pairs suffered from unilateral dominant knee

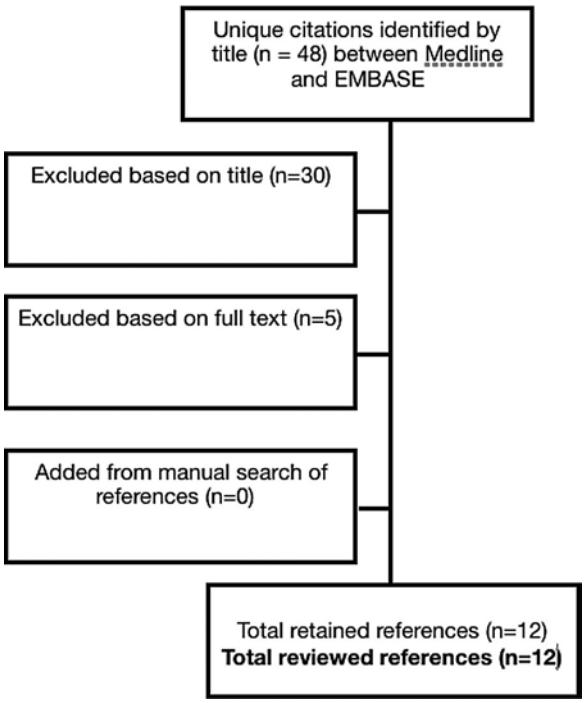

Figure 1. Flow of studies through systematic review.

OCD with overlapping time periods providing further support of a genetic component to OCD. A 2013 study identified another incidence of near identical OCD lesions occurring in monozygotic twins.[16] Again, there was no known history of trauma, their clinical courses had near identical timelines, and both lesions were located in the lateral trochlea of the same knee. Lastly, one final incidence of familial OCD in monozygotic twin brothers was published.[17] Both suffered OCD of the knee, one unilateral and the other bilateral, within 2 years of one another. Interestingly, all the patients reported in the above studies displayed no other syndromic features that normally accompany *ACAN* or *COL9A2* mutations such as short stature, brachydactyly, or other skeletal dysplasias.

Observing this trend in twin and familial OCD cases, Gornitzky and Ganley *et al.* surveyed the family history of 103 individuals treated for OCD at a tertiary children's hospital.[18] 14/103 individuals treated for OCD also had family members with a positive history. Lesion severity did not affect this relationship.

None of the above studies included genetic analyses. However, several studies have further explored the importance of *ACAN* mutations in relation to OCD. A 2019 study identified a child with a *ACAN* missense variant c.6970 T > C substitution.[11] This is located within the G3 protein domain, an area previously linked to OCD.[19] The patient exhibited extensive knee and elbow OCD, and it was determined they inherited this mutation from the mother after familial DNA sequencing was performed. A 2018 study identified a proband with a c.903G>C (p.Trp301Cys) mutation located in the nearby G1 domain of *ACAN* that resulted in short stature and familial OCD in the proband as well the father and paternal uncle.[23] In addition, 15 other probands were found with *ACAN* variants. All suffered from short stature and brachydactyly, but only the aforementioned variant was associated with OCD. Similarly, a 2017 study found early onset osteoarthritis in 12 out of 20 families with heterozygous *ACAN* mutations.[20] Three of these families exhibited mutations related specifically to OCD. The mutations included two c.7429G>A substitutions and a c.7064T>C substitution in another family. The two c.7429G>A mutations were located within the C-type lectin binding domain which is thought to be an integral component of the core protein structure.

To further elucidate the molecular and genetic etiology of OCD, a 2016 study isolated bone marrow mesenchymal stromal cells (BM-MSCs) and cartilage derived from induced pluripotent stem cells (iPSCs) from patients with known familial OCD.[21] Their work shed light on the molecular phenotype of C-type lecithin binding domain mutations in OCD patients. The mutations resulted in poor structural integrity of the induced chondrocytes, increased aggrecan protein build up within the endoplasmic reticulum opposed to the extracellular matrix, and overall cellular matrix dysregulation.

In addition to focusing on the role of the *ACAN*, a 2017 study published the first genome wide association study (GWAS) identifying candidate loci for juvenile osteochondritis dissecans.[22] While no single nucleotide polymorphism (SNP) reached the threshold for genome-wide significance, one SNP, rs1464500, lies within the coding region of a known transcription factor important for cartilage development, SOX5. This makes rs1464500 a SNP of interest for future studies.

Discussion

Significant findings regarding the role of *ACAN* mutations have been reported since the last major review on topic.[7] Most interesting are the group of mutations located within the C-terminal of the C-type lectin domain of the protein, which were also supported by earlier authors' work.[10] While the *ACAN* codes for aggrecan, a proteoglycan core protein that is ubiquitous in cartilage, the protein is also responsible for cartilage structure and growth.[24] The molecular analysis of chondrocytes derived from patients with familial OCD determined that mutations in this specific coding region, while predominantly missense mutations, have serious effects on chondrocyte integrity and extracellular matrix regulation.[21]

Lastly, the significant population of twin and familial cases of OCD without syndromic features continues to be noteworthy. While most of these studies have lacked genetic analysis, identification of rs1464500 as a SNP of interest supports the idea of alternative genetic pathways in the development of OCD.[22] Of note, a 2014 review article highlighted several GWAS studies on osteochondrosis in horse and swine populations and how identifying these candidate genes in the animal population can improve our understanding of OCD in humans.[25] In agreement with the aforementioned review, further GWAS analyses of human patients are needed.

Conclusion

Overall, the vast majority of the literature consisted of small case series, and thus, the quality of evidence remains low. This is likely due to the rarity of OCD and the difficulty of performing large genome wide studies. However, significant expansion of the literature detailing the pathogenesis of *ACAN* mutations has further solidified the role of a genetic basis in familial and syndromic cases of OCD.

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U·P·O·J

Patellar Stabilization Using a Modified Basket-Weave Allograft MPFL/MQTFL Reconstruction

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Introduction

Patellofemoral Instability (PFI) is a common disorder with an incidence ranging from 5-29 per 100,000.[1–3] The medial patellofemoral ligament (MPFL) is the primary soft tissue stabilizer to lateral displacement of the patella that along with the medial quadriceps tendon-femoral ligament (MQTFL)[4-6] provides 50-60% of the restraining force.[7–10] These structures are frequently disrupted or attenuated in patients with PFI. MPFL reconstruction is a component of treatment for the majority of patients with recurrent instability.[11]

Background

Numerous techniques have been described for MPFL reconstruction, many of which require the creation of bony tunnels in the patella.[12,13] Iatrogenic patella fracture related to tunnel drilling has been reported and is a catastrophic complication thus prompting a search for alternative patellar fixation methods.[14-19]

In this article, we present a modification of a "Basket-Weave Technique" originally described by Kodkani[19] that provides an anatomic, double-bundle MPFL/MQTFL all soft-tissue patellar reconstruction with bony femoral fixation.[5,6] This technique ensures secure graft fixation with anatomic localization whilst avoiding patellar fracture.

Preoperative Evaluation and Indications

MPFL reconstruction is a primary component of surgical intervention for any patient with recurrent PFI who has failed conservative treatments such as bracing and physical therapy. It is our practice to utilize multiple alignment measures to guide surgical decision-making including the Caton-Deschamps index (CDI) and Tibial Tubercle-Trochlear Groove (TT-TG) distance. Skeletally mature patients with significantly abnormal measurements are counseled on a tibial tubercle osteotomy (TTO) concurrent with MPFL reconstruction.[20]

Procedure

Diagnostic arthroscopy is first performed using standard anterolateral and anteromedial portals. Any retropatellar or trochlear chondral injury is addressed and the joint surveyed for loose bodies or other pathology.

Semitendinosus allograft is the preferred graft with the selected length based on patient anatomy (typically ~26mm). Each end is whipstitched with 1.3mm SutureTape* for tubularization. The middle of the graft is looped around a passing suture and an adjustable loop fixation device for optional back-up fixation. The graft is then tensioned. Next, a 3cm midline longitudinal incision is made over the patella. Dissection is carried down to the extensor mechanism with the creation of full-thickness skin flaps. Dissection is performed through the first two layers of the knee 2mm off the medial patella. A tunnel is created bluntly between layers 2 and 3. A separate counter-incision is made over the medial epicondyle and the fascia is split in line with this incision.

Next, a subperiosteal tunnel of 1cm in length and width is created at the medial patella. Two additional 1cm subperiosteal tunnels are created across the anterior surface of the patella with 1cm of prepatellar fascia left intact in between them (Figure 1). The MPFL limb of the graft is passed through the subperiosteal tunnels until the end of the graft reaches the lateral pole of the patella thus creating a basket-weave appearance. The graft is secured to the lateral retinaculum and at each weave point with 0 FiberWire using a pretzel stitch.[19] Next, two 1 cm partial thickness slits are created in the superficial layer of the quadriceps tendon just above the patella and tunneled in a similar pattern. The second MQTFL limb of the graft is then passed and secured in an identical fashion (Figure 2). One suture end from each graft limb is passed through the lateral retinaculum and tied to a suture from the other limb providing a closed loop fixation system.

Schottle's point is identified using fluoroscopic guidance and the Beath pin is advanced and angled proximally to exit along the anterolateral femur.[21] Modifications to Schottle's can be made for skeletally immature patients based on developmental anatomy.[22-24] The beath pin is overdrilled with the cannulated reamer to a depth sufficient to dock the graft (typically 30-40

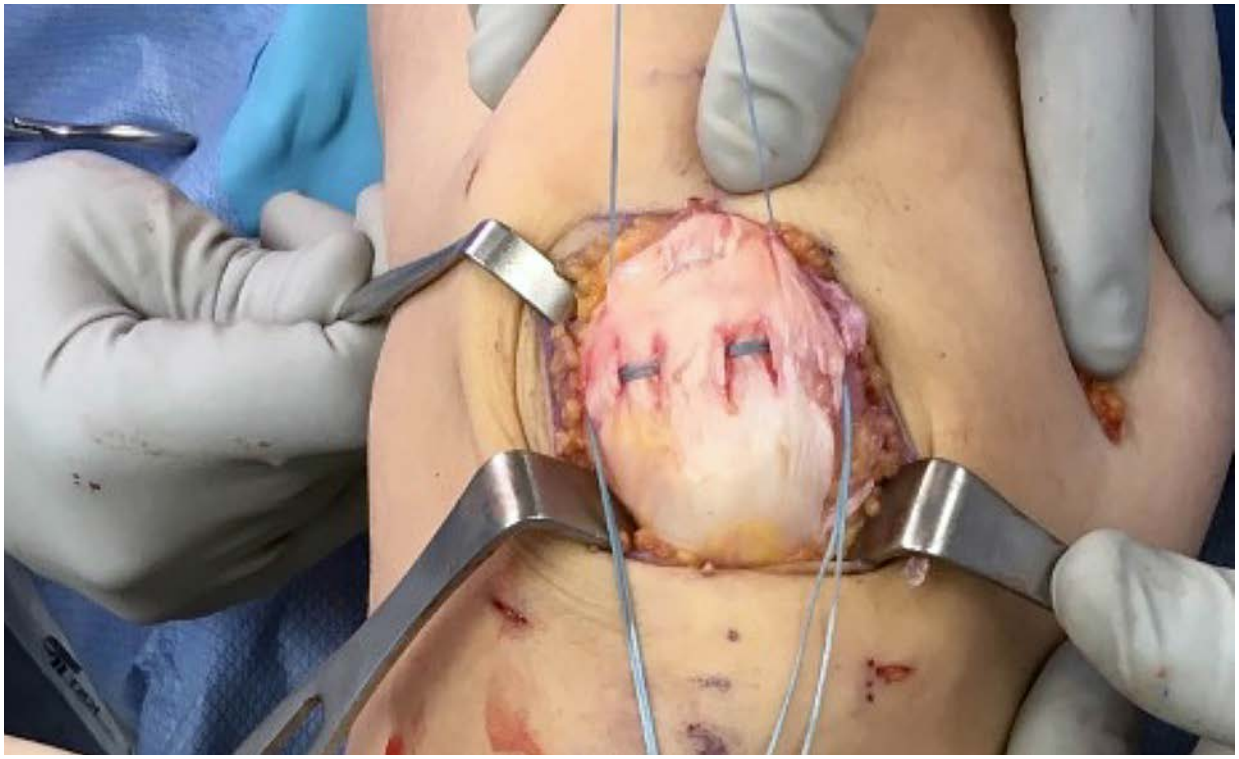

Figure 1. Basket weave preparation with passing sutures prepared for MPFL/MQTFL allograft limb passage.

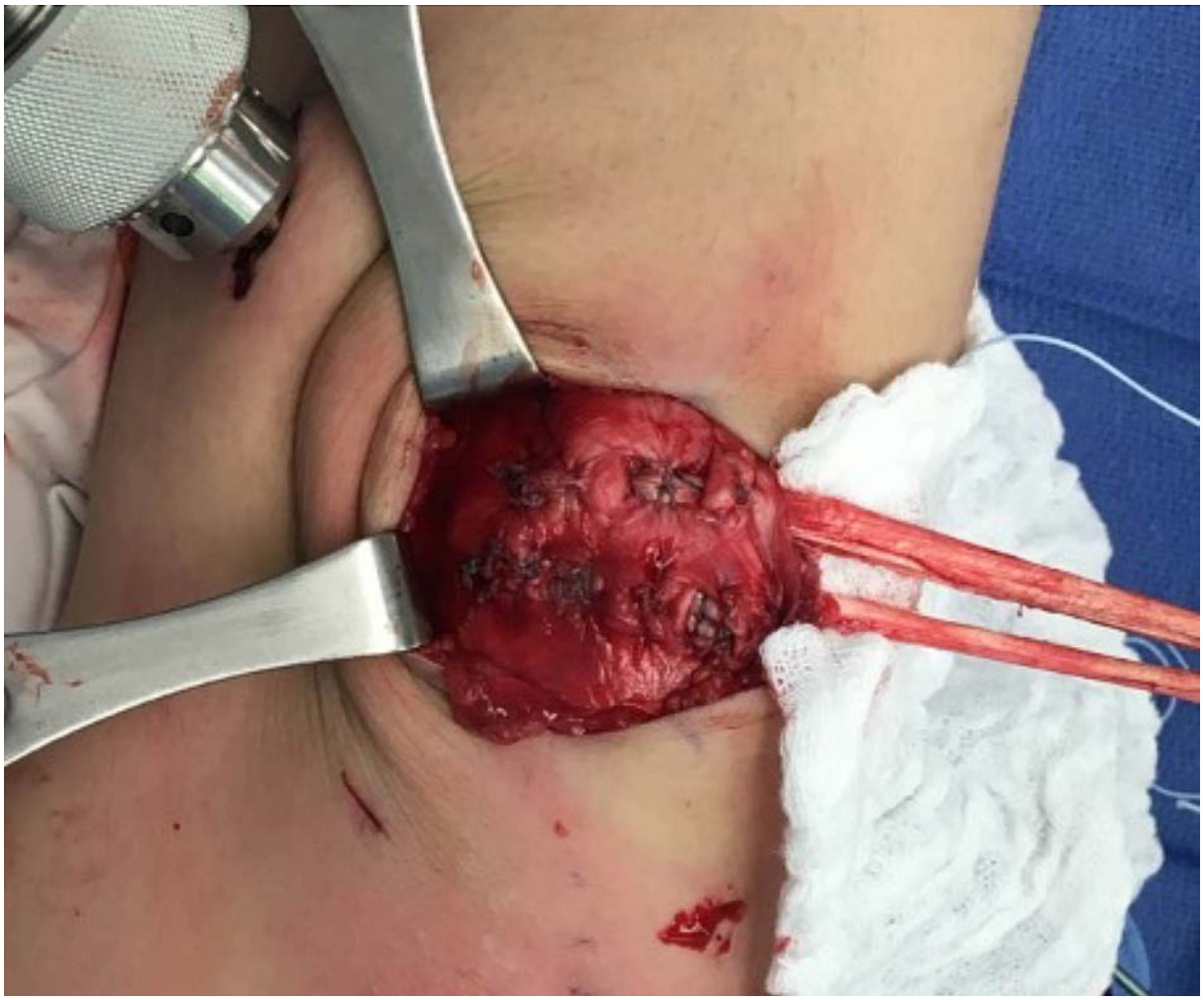

Figure 2. Basketweave double limbed MPFL graft after graft passage of whipstitched graft ends from medial to lateral and pretzel stitching at weave transition points with #0 fiberwire. Whipstiched limbs were passed subfascially through lateral patellar retinaculum and tied to provide secondary pullout fixation.

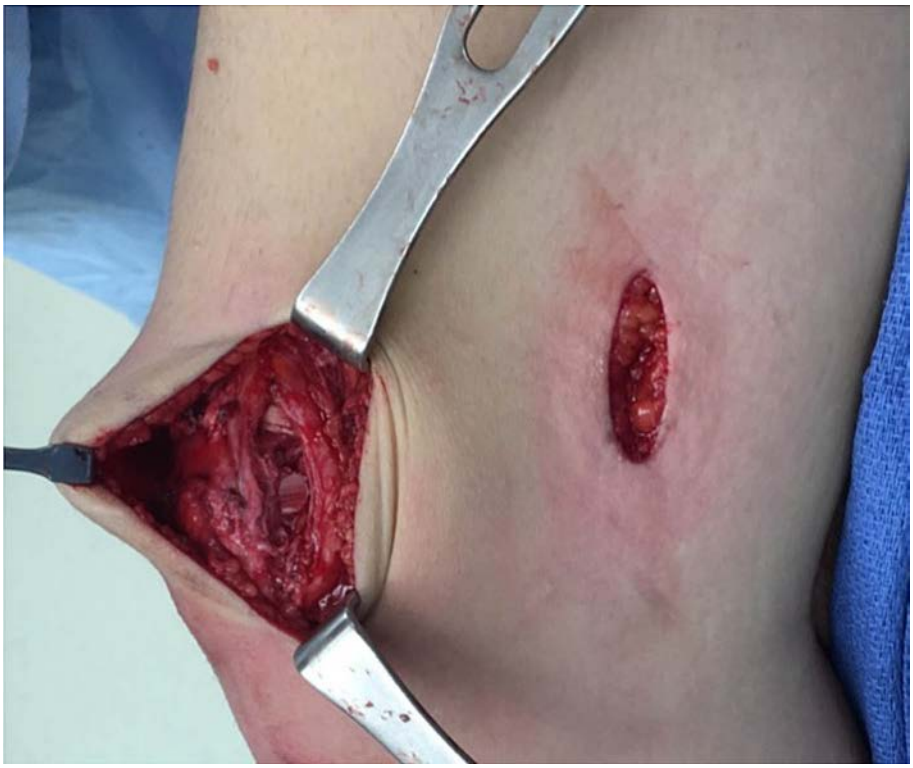

Figure 3. View from medial parapatellar incision of double limbed MPFL graft after tunneling to accessory incision (inferior) and docking into femur at Schottle's point. Fixation was performed with a bioabsorbable suture anchor backed up with an ABS tightrope fixated over a Dog Bone Button (Arthrex, Inc., Naples, FL) over lateral femur.

mm). The graft is then passed between layers 2 and 3. Isometry and patellar tracking are assessed. Once satisfactory, the Beath pin is removed and the graft seated. A nitinol wire is inserted into the femoral tunnel posteriorly. The graft is tensioned to centralize the patella within the trochlea at 45 degrees of knee flexion. An interference screw is inserted (Figure 3) and patellofemoral tracking is reassessed. If back-up femoral fixation is preferred, a DogBone cortical button* applied over an adjustable loop fixation device secured to the graft. The medial retinacular tissue can be imbricated in a pants-over-vest fashion for additional medial stabilization. The remainder of the wounds are closed in standard layered fashion.

*(Arthrex, Inc., Naples, FL)

Post-operative Protocol

Patients are discharged home on the day of surgery with a hinged knee brace permitting knee motion up to 90 degrees of flexion. They advanced to weightbearing as tolerated (WBAT) at 1 week. Straight ahead running is permitted by 3 months and return to sport is targeted at 6 months pending clearance via strength and functional testing.

Discussion

MPFL reconstruction is a popular surgical technique in the management of recurrent patellar instability that has demonstrated favorable outcomes.[25] Numerous techniques exist but Kodkani was the first to describe a Basket-weave allograft reconstruction technique that obviates the need for osseous fixation.[16-19,26]

The modification outlined in this article differs from that described by Kodkani[19] in four key ways. First, this technique provides an anatomic reconstruction of MPFL and MQTFL graft limbs. Second, our closed-loop patellar-sided design enhances the strength of the all soft-tissue fixation construct. Third, femoral fixation is via graft docking with interference screw using radiographic localization of the femoral origin whereas Kodkani describes femoral fixation with only a single soft tissue fixation point of questionable anatomic precision.[21] Lastly, in our modification, femoral fixation is performed after patellar fixation. This permits dynamic assessment of graft localization and patellar tracking allowing for adjustments prior to the final fixation. Potential disadvantages to the described technique include the reliance on soft-tissue patellar fixation, potential for graft prominence anteriorly due to suturing, and added case duration due to patellar graft suturing.

The modified technique described in this article has unique benefits that will be useful to surgeons desiring an anatomic MPFL/MQTFL reconstruction technique that avoids the risk of iatrogenic patellar injury.

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U·P·O·J

Arthroscopic Diagnosis of Occult Posterolateral Meniscocapsular Separations: Another Hidden Lesion

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Abstract

Purpose: The purpose of this study was to describe the surgical findings and clinical outcomes in a series of patients with occult posterolateral meniscocapsular separations diagnosed arthroscopically after a negative MRI.

Methods: A retrospective analysis of prospectively collected data of consecutive patients who underwent surgical arthroscopy with repair of an occult posterolateral meniscocapsular separation by two fellowship-trained orthopaedic sports medicine surgeons at a single institution was performed. All lesions were identified arthroscopically in the posterolateral aspect of the lateral compartment as a distinct pathologic separation between the posterolatreal capsule and adjacent meniscal tissue with increased excursion upon probing. Clinical examination notes, MRI and operative reports were reviewed. Patient reported outcome measures were assessed via patient questionnaire.

Results: A total of six patients were included for analysis. MRI evaluation of the lateral meniscus was unrevealing in 4 patients, suggested a possible tear of the body of the lateral meniscus in one patient and demonstrated a parameniscal cyst abutting the anterior root of the lateral meniscus in another patient. Arthroscopic examination revealed meniscocapuslar separations of the posterolateral meniscus in all six knees with two knees demonstrating concomitant bucket-handle meniscus tears. Patient reported outcomes were determined for 67% of study patients. The average reported IKDC score was 63.8, the average KOS-ADL score was reported as 63, the SF-12 Physical score averaged 46.8 with an average SF-12 Mental score of 59.9.

Conclusions: The diagnosis of occult posterolateral MCS could be missed on advanced imaging, such as MRI, so arthroscopic diagnosis may be required. This study indicates that arthroscopic diagnosis and repair of occult posterolateral MCS results in good functional and clinical outcomes.

Level of Evidence: IV, Therapeutic Case Series

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Introduction

Meniscal tears are the most commonly treated injury of the knee joint and one of the most frequently treated injuries in orthopaedic surgery with an incidence of 61/100,000 in the United States.[1] Left untreated, meniscus tears may compromise joint integrity and have been associated with degenerative changes leading to long-term dysfunction.[2,3] Due to its rigid adherence to the medial collateral ligament (MCL) and relative lack of excursion, the medial meniscus is more commonly injured as compared to the lateral meniscus with the posterior horn most often affected. Classically described tear patterns include radial, horizontal, vertical, complex, flap-type and bucket-handle.[4]

Of the various meniscus tear types, meniscocapsular separations (MCS) are uncommon injuries characterized by detachment of the meniscus from its capsular attachment. This detachment may lead to further instability of the knee with progression of meniscal tear pattern and cartilage injury.[5] Strobel et al. first introduced the term "Ramp Lesion" in 1988 to describe tears involving the meniscocapsular junction at the posterior meniscocapsular zone.[6] Since then, there has been renewed interest in these injuries and the challenges of identifying them on MRI and arthroscopy due to their position in the anatomical "blind spot" of the knee.[7] For instance, the positive predictive values of identifying MCS with MRI has been shown to be as low as 9% for the medial meniscus, and 13% for the lateral meniscus.[8] The majority of these studies have predominantly focused on MCS of the medial meniscus and often involve concomitant injuries. However, there is only one case report in the literature describing an isolated MCS involving the lateral meniscus.[9] A single case report of a lateral MCS has been described in the setting of a rare anatomic aberration known as a double-layered lateral meniscus.[10] The authors describe improvement of clinical symptoms following resection of the upper accessory meniscus and repair of the MCS. Additionally, hypermobility of the posterior horn of the lateral meniscus has been recently identified in case reports and limited case series.[11-14] Although the pathophysiology and optimal treatment have yet to be elucidated, this entity differs from a MCS as it exists in the absence of a discrete tear or traumatic capsular separation and is thought to be due to the disruption of the popliteomeniscal fascicles.

The purpose of this study was to describe the surgical findings and clinical outcomes in a series of patients with occult posterolateral meniscocapsular separations diagnosed arthroscopically after a negative MRI. We hypothesize significantly improved functional and clinical outcomes following arthroscopic repair of occult posterolateral MCS.

Methods

A retrospective analysis of prospectively collected data of consecutive patients who underwent surgical arthroscopy with repair of an occult posterolateral meniscocapsular separation by two fellowship-trained orthopaedic sports medicine surgeons at a single institution was performed between March 2016 through March 2020. All patients had an available preoperative magnetic resonance image (MRI) using a 1.5-T MRI scanner. All MRI sequences were reviewed by one of the senior orthopaedic surgeons and a fellowship-trained musculoskeletal (MSK) radiologist. All patients underwent a period of nonoperative management consisting of physical therapy and administration of non-steroidal anti-inflammatory medication. Indications for surgical intervention included objective complaints of mechanical symptoms and persistent lateral joint line (LJL) pain despite nonsurgical management for more than 3 months duration. Exclusion criteria were as follows: ligamentous instability as determined by positive Lachman, positive pivot-shift, positive anterior-posterior drawer and increased varus-valgus laxity as well as those patients undergoing surgical arthroscopy for ligamentous reconstruction and cartilage injury. Demographic information including age, sex and body mass index (BMI) were collected. Clinical examination notes were reviewed with data collected for chief complaint, laterality, mechanism of injury (MOI), time from injury to surgery and pertinent physical exam findings. MRI and operative reports were reviewed with data collected and recorded with regards to meniscus pathology, ligamentous integrity and degree and location of associated articular cartilage damage. All lesions were identified arthroscopically in the posterolateral aspect of the lateral compartment as a distinct pathologic separation between the posterolateral capsule and adjacent meniscal tissue with increased excursion upon probing (Figure 1).

Patient reported outcome measures were assessed via patient questionnaire at greater than one-month postoperatively with evaluation of the International Knee Documentation Committee score (IKDC), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), 12-Item Short Form Survey (SF-12) with inclusion of both the Mental Component Score (MCS-12) and Physical Component Score (PCS-12). Descriptive statistics were determined in an attempt to summarize the sample data.

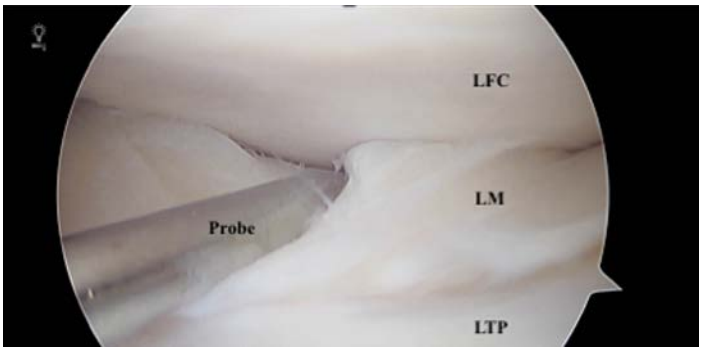

Figure 1. Pathologic Lateral MCS with Increased Meniscal Excursion. LFC = Lateral Femoral Condyle; LM = Lateral Meniscus; LTP = Lateral Tibial Plateau

Results

A total of six patients were included for analysis. Sex characteristics of the cohort are five female and one male (Table 1). The average age of the entire cohort was 44.2 years old with female age range from 31 to 63 years of age and the one male patient aged 36 years old. The average BMI for the cohort was 29.5 (range 19.1 to 39.5). There was an equal distribution of knee laterality (3 right and 3 left). All patients presented with primary complaints of intermittent mechanical locking of the knee resulting in the inability to achieve full extension with significant concomitant pain. Mechanism of injury was reported as atraumatic in 33.3% (2 of 6) of patients with the remaining patients reporting injury as the result of squatting, bus accident, exercise and getting out of bed. All patients demonstrated LJL tenderness on physical examination with an average arc of motion of 136.7° (range −5° to 135°). All other physical exam components, including ligamentous integrity, were unremarkable. The average time from onset of symptoms to arthroscopic evaluation was 45.5 months (range 3 to 144 months). MRI examination of the lateral meniscus was unrevealing in 4 patients, suggested a

Table 1. Patient Characteristics

Case	Age	Sex	BMI	Laterality	MOI	Subjective	Joint Line	ROM	Symptoms to Surgery
1	31	F	24.2	R	Atraumatic	Locking Pain	LJLT	0 to 120	8 months
2	55	F	19.1	L	Atraumatic	Locking Pain	LJLT	-5 to 135	4 years
3	39	F	37.1	L	Squatting	Locking Pain	LJLT	-5 to 135	12 years
4	36	M	23.6	L	Bus Accident	Locking Pain	LJLT	-5 to 135	10 months
5	41	F	33.5	R	Exercise	Locking Pain	LJLT	-5 to 135	5 years
6	63	F	39.5	R	Getting out of bed	Locking Pain	LJLT	-5 to 135	3 months

MOI = Mechanism of Injury; LJLT = Lateral Joint Line Tenderness; ROM = Range of Motion

possible tear of the body of the lateral meniscus in one patient and demonstrated a parameniscal cyst abutting the anterior root of the lateral meniscus in another patient (Table 2). No evidence of MCS was noted on MRI (Figure 2). However, MRI did reveal lateral compartment articular cartilage pathology in 50% of affected knees. Arthroscopic examination revealed MCS of the posterolateral meniscus in all six knees with two knees demonstrating concomitant bucket-handle meniscus tears (Table 3). All MCS lesions and both bucket handle tears were addressed via arthroscopic repair. Concomitant arthroscopic findings included International Cartilage Regeneration and Joint Preservation Society (ICRS) Grade-I pathology of the LFC in three knees, ICRS Grade-II in one knee with two knees sans articular pathology of the LFC. Similarly, diffuse Grade-I articular lesions were arthroscopically identified on the lateral tibial plateau (LTP) in two knees. One knee demonstrated a focal Grade-II articular defect, one knee revealed diffuse Grade-III articular changes and the remaining two knees were without articular abnormality.

Patient reported outcomes were determined for 67% (4 of 6) of study patients (Table 4). The average reported IKDC score was 63.8 (range 50 to 81) with 87 representing the maximum possible score. The average KOS-ADL score was reported as 63 (range 55 to 68). The SF-12 Physical score averaged 46.8 (range 42.7 to 54.2) with an average SF-12 Mental score of 59.9 (range 58.8 to 60.3).

Discussion

Six consecutive patients underwent arthroscopic repair of an occult posterolateral MCS at an average time of 45.5 months from the initial onset of symptoms. Preoperative MRI revealed varying degrees of articular cartilage damage to the LFC and tibial plateau without evidence of posterolateral MCS. Following repair, all patients reported good clinical outcomes with satisfactory IKDC, KOS-ADL, SF-12 Physical and SF-12 Mental scores. Many studies have designated medial MCS as an occult injury, citing anatomic location and limitations with MRI as the cause for missed diagnosis.[7,8,15,16] Greif et al. reviewed anatomic variants of medial MCS with associated MRI findings in an attempt to simplify and standardize the diagnosis.[17] However, the modified classification relies on mechanism of injury, associated ACL injury and associated MRI findings for diagnosis. To our knowledge there is only a single case report involving a patient with an isolated lateral MCS, which was diagnosed via ultrasound following a negative MRI.[9]

Much of the literature regarding medial MCS focuses on younger athletes sustaining a twisting injury, however, our patients were middle aged with varied mechanisms of injury.[16, 18] All six of our patients presented with lateral knee pain and locking symptoms that persisted despite months to years of conservative therapy. Additionally, our patients had normal exams aside from LJL tenderness. Persistent joint line

Table 2. MRI Findings

Case	Meniscus	Collateral Ligament	Cartilage
1	Normal	Normal	Normal
2	Normal	Normal	Chondrosis, LTP
3	Cyst abutting anterior root, LM	Normal	Normal
4	Possible small tear, LM body	Normal	Normal
5	Normal	Normal	Full thickness cartilage defect, LFC
6	Normal	Normal	Subchondral cyst formation

LTP = Lateral Tibial Plateau; LM = Lateral Meniscus; LFC = Lateral Femoral Condyle

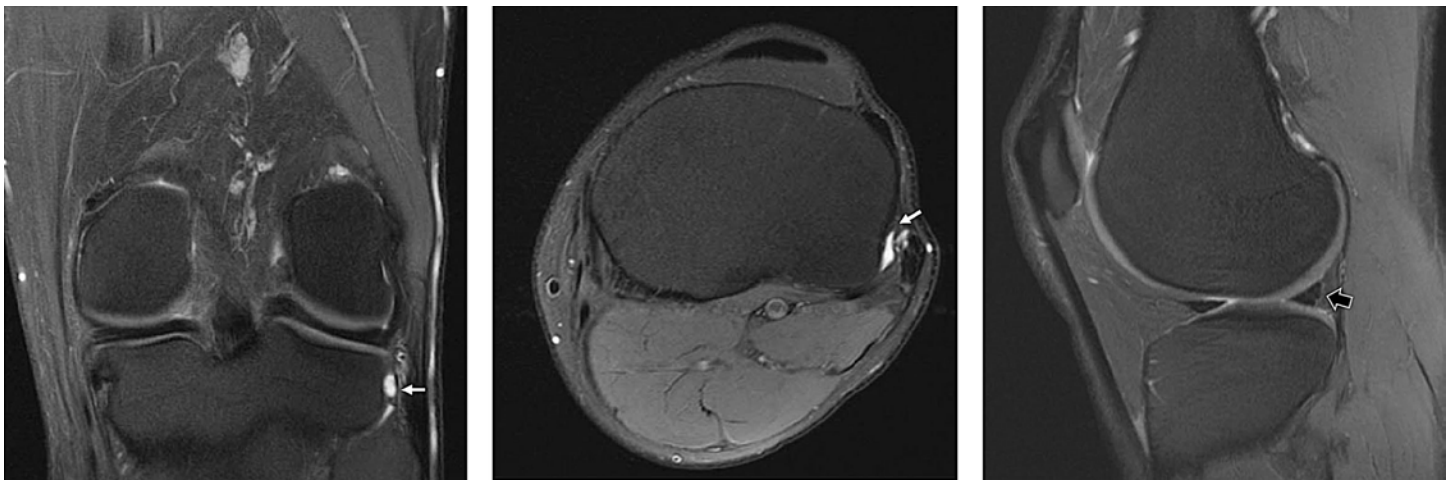

Figure 2. Coronal, Axial and Sagittal MRI Sequences Without Contrast. Images demonstrate a cystic structure along the periphery of the lateral tibial plateau (white arrow, coronal and axial images). This was called a ganglion cyst arising from the proximal tibiofibular joint on initial review. Examination of the posterior horn of the lateral meniscus does not reveal a MCS or adjacent fluid signal (black arrow, sagittal image).

Table 3. Arthroscopic Findings of Lateral Compartment

Case	Meniscus	ICRS Grade, LFC	ICRS Grade, LTP
1	MCS	Normal	Normal
2	MCS	Grade 1	Grade 3, Diffuse
3	MCS and bucket handle tear	Grade 1	Grade 2, Diffuse
4	MCS and bucket handle tear	Grade 2	Grade 2, Diffuse
5	MCS	Grade 1	Grade 2, Focal
6	MCS	Normal	Normal

MCS = Meniscocapsular Separation; ICRS = International Cartilage Regeneration and Joint Preservation Society; LFC = Lateral Femoral Condyle; LTP = Lateral Tibial Plateau

Table 4. Patient Reported Outcomes

Case	Follow-up (mos)	IKDC	KOS-ADL	SF-12 Physical	SF-12 Mental
1*	3	-	-	-	-
2	7	71/87	67/70	54.2	58.8
3	39	81/87	68/70	44.2	60.5
4*	26	-	-	-	-
5	1	50/87	55/70	45.9	60.1
6	18	53/87	62/70	42.7	60.3

IKDC = International Knee Documentation Score; KOS-ADL = Knee Outcome Survey-Activities of Daily Living; SF-12 United States Average = 50
*Patients unable to be contacted to administer questionnaires

tenderness is consistent with previous reports of medial MCS and should raise clinical concern despite the presence of unrevealing imaging.[18-19] Although subtle findings of cartilage defects and small cysts were identified on MRI in this series, no definitive lateral meniscus tears or MCS were identified on preoperative imaging. One patient's report noted a possible small tear of the body of the lateral meniscus, but there was no evidence of MCS or posterior horn involvement. Despite a fellowship trained MSK radiologist scrutinizing the images, 100% of the MCS were missed on imaging in this study. Although a 1.5T scanner was utilized for image analysis, the literature has demonstrated no benefit of 3T as compared to 1.5T scanners in the ability to diagnose MCS.[18,19]

Arthroscopy provided the definitive diagnosis of lateral MCS for all six patients in this study and should be considered the gold standard for diagnosis of this occult lesion. The lengthy average time of 45.5 months (range 3-144 months) from symptom onset to arthroscopic intervention was secondary to the absence of positive advanced MR imaging resulting in extended conservative nonoperative management. Additionally, degenerative changes to the cartilage of both the LFC and the LTP were found in 4/6 (66%) of patients. Two of those patients also had associated bucket-handle tears suggesting that a classification system similar to that for medial MCS may be warranted.[20] Understanding the intricate anatomy of the posterior horn of the lateral meniscus further explains why this pathology is persistently symptomatic and difficult to diagnose on imaging. Cadaveric analysis has demonstrated attachment of the posterolateral capsule to the superior 11% of the posterior horn of the lateral meniscus with a length of 16.7mm, which is a smaller area than the attachment of the medial meniscocapsular junction.[15]

A secondary goal of this study was to report on initial outcomes following arthroscopic repair of occult lateral MCS. Although post-operative subjective outcomes data were unavailable for two of the six patients, progress notes from their last office visits reported that one patient was improving well and the other had no residual symptoms or limitations, indicating positive response to surgical repair of the lateral MCS. Outcomes for the remaining four patients were recorded postoperatively at the time of the study. IKDC scores averaged 63.8 (range 50 to 81), which is slightly less than that reported by younger patients following repair of ramp lesions but is consistent with age and gender based normative data.[18,21,22] The SF-12 physical scores in this series were just below average, however, the mental scores were above average based on the population average of 50 by inherent design of the scoring system.[23] Additionally, the KOS-ADL scores were excellent with an average of 60.8, indicating minimal disruption in ADLs. These subjective outcomes indicate that patients with occult posterolateral MCS do very well following surgical repair, with overall above average quality of life when compared to norms.

Limitations

This study is not without limitations. As a small retrospective case series there is inherent selection bias, however, this was minimized by the consecutive nature of patient inclusion. Comparing the results of surgery at different time points

introduces bias. Also, one month follow-up may be too short a time period to fully evaluate the clinical results of surgery. The prospective collection of PRO data would have strengthened the study findings and allowed us to quantitatively analyze the degree of subjective improvement in patient outcomes. This would have also allowed for increased homogeneity in reporting, thus aiding the interpretation of these findings. However, we did not attempt to collect PRO data retrospectively at all time points as this would have contributed to significant re-call bias in patients further removed from their index arthroscopic procedure.

Conclusion

The diagnosis of occult posterolateral MCS could be missed on advanced imaging, such as MRI, so arthroscopic diagnosis may be required. This study indicates that arthroscopic diagnosis and repair of occult posterolateral MCS results in good functional and clinical outcomes.

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Hand

A Decade of Change: Levels of Evidence at the ASSH Podium from 2010-2019

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Introduction

In an effort to answer clinical questions and advance their careers[1,2], academic clinicians strive to generate research for presentation at scientific meetings. To evaluate their quality and generalizability, level of evidence (LOE) has become a nearly ubiquitous component of any manuscript.[3] Many surgical journals now require authors to report a LOE as a marker for overall quality.[4] In orthopaedics[5–10] and plastic surgery[11–13] literature, there has been a recent increase in the LOE of publications.

Abstracts at the American Society for Surgery of the Hand annual meeting (ASSH-AM) are an important way for surgeons to learn about medical advancement in the field of hand surgery.[14] Podium presentations in particular present an opportunity for authors to receive constructive criticism from experts. This may in part explain why abstracts accepted to ASSH-AMs are published at high rates.[15,16] The purpose of our study was to assess trends in the LOE and characteristics of ASSH-AM abstracts over a ten-year period.

Methods

This was an observational study of all podium presentations at ASSH-AM occurring from 2010-2019 (Figure 1). Past abstract books were obtained through the ASSH website.[17] Abstracts were reviewed by two authors independently to determine characteristics. This included determination of the number of patients, evidence of multicenter collaboration, and use of a national inpatient database. Where the patient number was not recorded, the number of cases was instead used as a proxy, with larger national database studies excluded from this analysis. The ASSH Evidence-Based Practice Committee assigns a LOE to each abstract accepted for presentation at the annual meeting, which was also recorded.

Abstracts were broken down by focus and topic. Abstract foci was characterized as either distal radius fracture (DRF), flexor tendon (FT) injury, carpal tunnel syndrome (CTS), cubital tunnel syndrome, Dupuytren's contracture, thumb carpometacarpal (CMC) arthritis, peripheral nerve injury, and congenital upper extremity deformity. In addition, each abstract was categorized based on more general topics including basic science, cost analysis, opioid and pain control, and medical education. Last, where possible, presentations were stratified based on if they focused on adult or pediatric patients.

The data was curated as totals across each year from 2010 to 2019. Subsequently, it was organized into 5-year intervals, with one set from 2010-2014 and the other from 2015-2019. Chi-squared and Fisher's exact tests were utilized to compare categorical variables, and Mann-Whitney U tests were used to compare continuous variables between time periods. All statistics were conducted assuming a significance threshold of $p<0.05$.

Figure 1. ASSH Annual Meeting Abstract Books, 2010-2019

Results

A total of 787 podium presentations were available for review: 382 (48.5%) from 2010-2014 and 405 (51.5%) from 2015-2019 (Table 1). The proportion of LOE 1 or 2 studies was significantly higher in the second half of the decade (24.0% vs 16.0%, p=0.005). Correspondingly, there was also a higher number of RCTs (9.6% vs 5.2%, p=0.019) in 2015-2019 compared to 2010-2014. The number of patients per abstract was additionally higher during the second half of the decade (median 75.5 vs 48.5) vs 2010-2014 (p<0.001).

An increased number of presentations from 2015-2019 evaluated the topics of cost analysis (5.2% vs 1.3%, p=0.002) and opioids or pain management (4.9% vs 1.3%, p=0.004). Older abstracts more frequently focused (Figure 2) on FT injuries (5.5% vs 1.5%, p=0.002) and Dupuytren's contracture (5.5% vs 2.2%, p=0.016). With the recent advent of national databanks, more abstracts from 2015-2019 (8.1% vs 2.1%, p<0.001) resulted from large national databases.

Discussion

As the fields of orthopaedic and plastic surgery observe rapid advances, so too has the LOE in published literature. Our study demonstrates increasing LOE at the ASSH-AM since 2010. Further, more podium presentations in the second half of the decade were the result of RCTs and studied a higher number of patients.

The observation of increased LOE in a surgical specialty is not new. Voleti et al reported a 19% increase in the proportion of level 1-2 studies presented at the annual meeting of the American Academy of Orthopaedic Surgeons from 2001-2010.[9] While higher LOE likely improves the generalizability of research and the power to detect true differences, it should be noted that not all such studies are created equal. Further, lower level research should not be discounted for the contributions that they have made as many foundational principles in medicine are based on lower level studies.

More than improving clinical practice, the importance of performing higher evidence research for many surgeons is the contribution of research productivity to academic rank. For hand surgeons, H-index - a measure of both publications/citations - is strongly correlated with academic rank.[2] While abstracts at national conferences are published at high rates overall[15,18–20], higher LOE abstracts tend to have higher chance of publication.[21] A similar case can be made for the increased

Table 1. Characteristics of ASSH Abstracts, 2010-2014 vs 2015-2019

	2010-2014	2015-2019	P-value
Number of Abstracts	382	405	-
Level of Evidence			
1 or 2	61 (16.0)	97 (24.0)	**0.005**
3, 4, 5, or NA	321 (84.0)	308 (76.0)	
Randomized controlled trial	20 (5.2)	39 (9.6)	**0.019**
Multicenter collaboration	26 (6.8)	32 (7.9)	0.557
Median Number of Patients*	48.5 (86)	75.5 (140)	**<0.001**
Database	8 (2.1)	33 (8.1)	**<0.001**
Focus			
Distal radius fracture or repair	51 (13.4)	39 (9.6)	0.101
Flexor tendon injury or repair	21 (5.5)	6 (1.5)	**0.002**
Carpal tunnel syndrome or release	15 (3.9)	24 (5.9)	0.197
Cubital tunnel syndrome or release	3 (0.8)	9 (2.2)	0.145
Dupuytren's contracture	21 (5.5)	9 (2.2)	**0.016**
Thumb carpometacarpal arthritis	16 (4.2)	17 (4.2)	0.738
Peripheral nerve injury or repair	45 (11.8)	64 (15.8)	0.103
Congenital upper extremity deformity	16 (4.2)	12 (3.0)	0.354
Topics			
Basic science, anatomy, or biomechanics	82 (21.5)	79 (19.5)	0.496
Cost analysis	5 (1.3)	21 (5.2)	**0.002**
Opioids and pain management	5 (1.3)	20 (4.9)	**0.004**
Medical education or publication	5 (1.3)	4 (1.0)	0.746
Age Group			
Pediatrics	42 (11.0)	48 (11.9)	0.903
Adult	194 (50.8)	207 (51.1)	
Unclassified	146 (38.2)	150 (37.0)	

Values reported as number (%) or median (IQR)
*Excluded large sample database studies

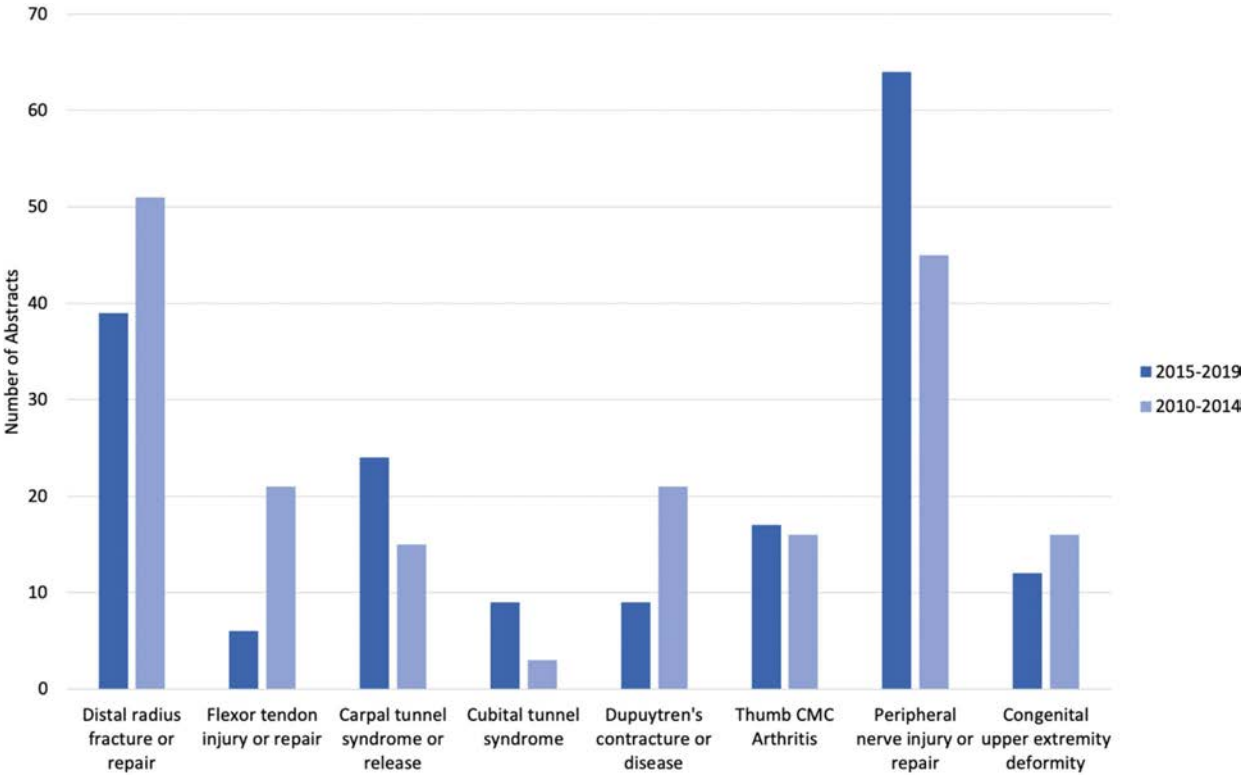

Figure 2. Comparison of Abstract Foci at ASSH Annual Meeting, 2010-14 vs 2015-19

number of abstracts resulting from national databases observed in our study, which adds to the power of any study to detect a significant result.[22]

Our study also observed a significant increase in the proportion of abstracts focused on cost analysis or opioids. This increase is in line with increasing national emphasis on cost-effective healthcare utilization[23] and appropriate opioid usage.[24] There are already many examples of such articles in the hand surgery literature, which has translated to the research presented at the ASSH annual meeting.[25-27]

Although we reviewed nearly 800 abstracts over a 10-year period, there are several limitations to our study. First, we did not assign abstract topics/focus to all presentations given the overwhelming number of possible topics. Second, because many abstracts do not report the age range of patients, it was not possible to identify the age grouping for ~40% of abstracts. Nevertheless, the simple design of our study illustrates an emerging trend across specialties of increasing LOE with an emphasis on nationally important issues, such as cost-effective care.

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U·P·O·J

A Case Report of Ecthyma Gangrenosum affecting the Thumb

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Introduction

Ecthyma gangrenosum is an atypical cutaneous vasculitis classically associated with immunocompromised or critically ill hosts. [1-2] This particular vasculitis results from bacteremia or direct inoculation of an infecting microorganism, commonly the pathogen Pseudomonas aeruginosa.[3-4] Most often lesions appear in the gluteal region, perineum, or axilla; occasionally affecting the extremities.[5-6] Appearance of the lesions on the hand and digits are particularly rare, and we present such a case diagnosed and treated at our center.

Case Information

A 33-year-old right hand dominant female presented to the emergency department with the chief complaint of a right thumb blister. The patient reported a 2-day history of an isolated right thumb lesion with accompanying erythema, swelling, and warmth. The patient noted worsening symptoms with the blister developing into an open wound at the radial border of the right thumb interphalangeal joint (Figure 1). Otherwise, she did not report systemic complaints.

Regarding pertinent past medical history, the patient did have a previous diagnosis of Sjogren's disease along with low grade B cell marginal zone lymphoma. She had recently completed her last dose of a bi-monthly rituximab maintenance regimen approximately one month prior to presentation. She was considered to be in remission by her hematologist.

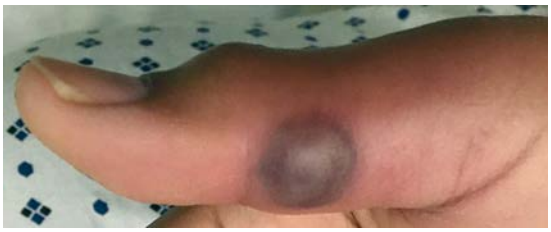

Figure 1. Lesion at time of initial presentation.

On examination her vital signs were stable. The patient was noted to have an open wound overlying the radial border of the interphalangeal joint of the right thumb measuring 1.5cm by 1.3cm surrounded by a gray border, which was necrotic in appearance. Radiographs taken of the right hand appeared within normal limits without acute or chronic osseous changes. An acute inflammatory lab panel was obtained revealing white blood cell count 5.7 K/μL, C-reactive protein 139.6 mg/L, erythrocyte sedimentation rate 87 mm/h.

Initial assessment included a differential diagnosis of abscess, interphalangeal joint septic arthritis, and flexor tenosynovitis. The patient underwent a bedside right thumb irrigation and non-excisional debridement. She was admitted to the hematology/oncology service given her history, and was started on a broad-spectrum antibiotic regimen including vancomycin, piperacillin/tazobactam, ampicillin/sulbactam, metronidazole, and cefepime. Infectious disease, dermatology, and wound care consults were also obtained.

There was a lack of improvement in the clinical appearance of the right thumb after the index procedure. Two days later the patient was taken to the operating room for more formal debridement (Figure 2a and 2b). A right thumb interphalangeal joint arthrotomy along with irrigation and excisional debridement was performed. The right thumb was incised in a mid-axial fashion along the radial border. Non-viable tissue including skin, subcutaneous fat, and fascia were excised sharply. The neurovascular

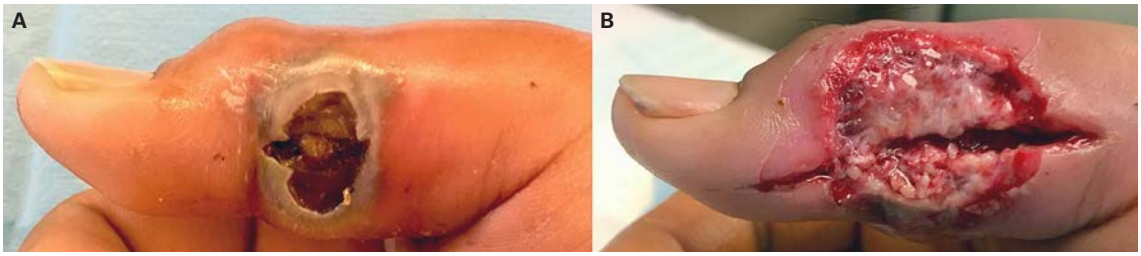

Figure 2 (A) Appearance prior to formal surgical procedure; **(B)** Appearance post-operative day 2.

bundle was isolated and protected throughout the case. Dissection was carried volarly and dorsally. In the dorsal area of the thumb a collection of murky fluid and necrotic fat was encountered. The flexor tendon sheath did not appear involved. The thumb interphalangeal joint contained murky fluid and synovitis. Four microbiology specimens and one pathology specimen were obtained. The wounds were thoroughly irrigated with normal saline. The patient tolerated the procedure well without complications.

Ultimately, the intra-operative cultures returned with growth of Pseudomonas aeruginosa. Blood cultures remained without growth. Other testing performed, which was all negative included VZV, HSV, AFV, mycobacteria, and fungal studies. At the recommendation of the infectious disease team, the patient's broad spectrum antibiotic regimen was narrowed to levofloxacin 750 mg daily for a 14-day course. Pathology analysis of the excised skin demonstrated parakeratosis, dermal necrosis, and acute inflammation of the subcutaneous adipose tissue with numerous bacilli present within dermis, consistent with ecthyma gangrenosum.

The patient's subsequent hospital course included gradual improvement in the appearance of the thumb. During the post-operative period she was noted to be neutropenic with white blood cell count 2.4 K/μL and absolute neutrophil count 266 /mm^3. The primary team began filgrastim 300 mcg to stimulate her neutrophil count**.** The total hospital course was 7 days, with the patient being discharged to home in stable condition.

In the subsequent weeks the patient was followed closely. She continued to demonstrate clinical improvement without setbacks. Her last orthopaedic hand surgery follow-up was approximately four months post-operatively at which point her thumb wound was healed (Figure 3).

Prior Reports and Relevant Literature

Ecthyma gangrenosum was first used as a diagnosis by Hitschmann and Kreibich in 1897.[5] There have since been chapters, case series, and case reports describing the condition. The association with immunocompromised patients is well known, with few reports of infections in immunocompetent individuals.[5, 7-9] The characteristic lesion begins as a macule, vesicle, or bulla; then progresses to an indurated ulcer. The ulcer sloughs to form a gangrenous ulcer with necrotic center, black eschar, and erythematous ring.[6] The maturation of the lesion is typically rapid, occurring within 12 to 18 hours.

Histologically, the lesion results from perivascular bacterial invasion of the media and adventitia layers of small vessels by gram-negative bacilli with secondary ischemic necrosis.[9] Exotoxins produced by bacteria mediate local tissue degradation. The aforementioned vasculitic changes may be seen by histologic examination of pathology specimens.[10-11] Pseudomonas aeruginosa is the most common pathogen, but Staphylococcus aureus, Citrobacter freundii, Morganella morganii, Candida species, Aeromonas hydrophila, Seratia marcescens, and other species have been reported.[12-14]

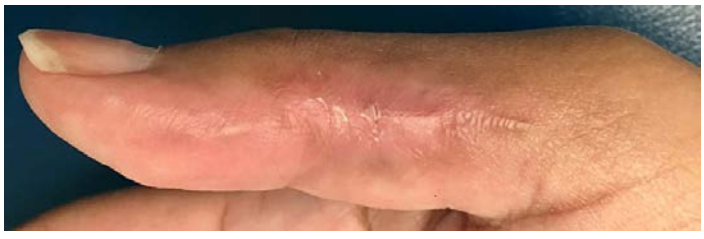

Figure 3. Appearance at four months follow-up.

Prompt recognition, diagnosis and evaluation of this process including blood cultures, wound cultures, and tissue biopsy are critical to improving prognosis and directing clinical decision making. Treatment involves the use of empiric antimicrobial therapy with anti-pseudomonal activity for a lesion suspicious for ecthyma gangrenosum. Excisional debridement may also be of benefit for more aggressive lesions.[14]

Koumaki at el. reported on a 47-year-old male diagnosed with ecthyma gangrenosum on the dorsum of the right hand.[15] The patient had been diagnosed with acute myeloid leukemia receiving first, second, and third line chemotherapy treatments. The hand lesion developed in the setting of acute bacteremia. Wound and blood cultures grew Klebsiella pneumoniae and Streptococcus vestibularis. A pathology specimen revealed vascular necrosis with many surrounding bacteria consistent with a diagnosis of ecthyma gangrenosum. The patient underwent surgical debridement and received antibiotic treatment, ultimately with complete resolution of the lesion three months after onset.[15]

Aygencel et al. reported on an 80-year-old male with a lesion on the dorsum of the left hand diagnosed as an ecthyma gangrenosum-like eruption.[16] In this case, the patient had a medical history significant for cardiovascular disease, hypertension, chronic obstructive pulmonary disease, and chronic kidney disease. He was admitted to the medical intensive care unit in critical condition with a new diagnosis of multiple myeloma. The lesion presented on the hand several weeks into the admission. Wound and blood cultures grew Burkholderia cepacian, which was antibiotic resistant according to the sensitivity testing performed. The patient ultimately died during the hospitalization from sepsis.[16]

Discussion

To our knowledge there are no other descriptions of ecthyma gangrenosum in the orthopaedic hand surgery literature. Of the available case series and case reports pertaining to this diagnosis published in other specialty journals there are two patients with ecthyma gangrenosum affecting the hand, none with digital lesions. For those two patients, both were immunocompromised, acutely ill, had an isolated dorsal hand lesion, neither grew the typical Pseudomonas aeruginosa as the infecting organism.

Our patient represents a unique instance of ecthyma gangrenosum affecting the thumb in isolation. Although our patient too was an immunocompromised host, she was not acutely ill at the time of presentation. Otherwise, the lesion presented with a history, physical examination, microbiology, and pathology characteristic for the diagnosis of ecthyma

gangrenosum. She was successfully treated with a combination of antibiotics and surgical interventions.

Conclusions

Ecthyma gangrenosum is a rare infective vasculitis that may carry a poor prognosis for immunocompromised patients. The lesions may affect the hand and digits. The consulting hand surgeon should keep ecthyma gangrenosum in the differential diagnosis during evaluation of hand lesions in immunocompromised hosts, particularly those lesions that fail to respond to conventional treatment. Biopsies are essential to target the antibiotic regimen, and histological analysis of skin and dermis specimens can help confirm the diagnosis and guide treatment.

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Anterior Interosseous Nerve Transfer for Ulnar Neuropathy: How, When and Why

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Introduction

Compressive neuropathies of the upper extremity are one of the most common diagnoses seen in orthopedic practices. A vast majority of patients are seen early in the natural history of the disease. In this state, patient complaints may vary but it is unlikely that any permanent damage has taken place. In the latter stages, prolonged nerve damage of motor fascicles and resultant lack of neural input to motor units can produce progressive muscle wasting.

Secondary muscle atrophy and weakness due to compressive neuropathy can be managed in a variety of ways. Tendon transfers are often the treatment of choice particularly for advanced carpal tunnel syndrome with loss of thumb opposition. For longstanding compression of the ulnar nerve and loss of a majority of the intrinsic muscles, tendon transfers remain a common and viable option. Alternatively, in cases where motor recovery is still possible, nerve transfers can aid in restoring lost function.

The terminal extent of the anterior interosseous nerve (AIN) is a very popular and widely utilized donor nerve for transfer. Similar to tendon transfers, certain principles must be followed in order to have a successful outcome. The aim of this paper is to detail the surgical steps of the procedure using a case report and identify the indications for its use.

Case Report

A 53-year-old male presented with a nearly one-year history of numbness and tingling in the ulnar nerve distribution on the right side. He had recently noticed weakness and was beginning to drop objects. He reported that his hand seemed smaller compared to the contralateral side. On presentation to his hand surgeon, he had already undergone an electromyography and nerve conduction study which demonstrated cubital tunnel syndrome with evidence of denervation to the first dorsal interosseous muscle. On exam, the patient had a positive Tinel sign over his cubital tunnel and had weakness and atrophy of his ulnarly innervated hand muscles. Due to his advanced symptoms, it was suggested that he undergo a cubital tunnel release. In addition, an AIN transfer was proposed to augment his recovery.

Within a few weeks of his consultation, the patient was taken to the operating room for a cubital tunnel release and AIN transfer. The ulnar nerve was released throughout its course at the elbow utilizing a standard open incision technique. To perform the nerve transfer, an extensile, curvilinear incision was placed over the distal ulnar forearm. The ulnar neurovascular bundle was identified deep to the flexor carpi ulnaris on the radial side. The ulnar artery and nerve were separated carefully, and the takeoff of the dorsal sensory branch of the ulnar nerve was identified. This was found about 9 centimeters proximal to the ulnar styloid. This landmark is important due to the intrinsic topography of the ulnar nerve. At the level of the distal forearm, distal to the takeoff of the dorsal sensory branch, the motor fascicles occupy the ulnar most portion of the continuation of the ulnar nerve.

Next, identification and dissection of the anterior interosseous nerve was performed. This was completed by retracting the flexor carpi ulnaris and the ulnar neurovascular bundle ulnarly while sweeping the remaining tendons and muscles radially. Placing a large Deaver retractor on the radial side helped facilitate exposure. At the base, the pronator quadratus was easily identified. At the proximal most portion of the muscle, the anterior interosseous artery, vena comitantes, and nerve were encountered entering the muscle. The nerve was the most radial structure lying just superficial to the interosseous membrane. Intramuscular dissection of the AIN was then performed until it began to branch in to several smaller branches. The nerve was then freed proximally to ensure an adequate arc of rotation and tensionless neurorrhaphy.

With the AIN free and transposed near the ulnar nerve, the area of nerve coaptation was identified. This location was distal to the dorsal sensory branch, and again, was on the ulnar side of the proper ulnar nerve. Under loupe magnification and utilizing micro instruments, careful dissection of the nerve took place. A small area of epineurium was removed from the ulnar nerve at the neurorrhaphy site. A total of three 9-0 nylon suture were then used to connect

the AIN to the ulnar nerve in the area of motor fascicles. Fibrin glue was used to reinforce the coaptation. The transfer was noted to have a smooth course to the ulnar nerve and there was no tension.

Discussion

AIN transfer to the ulnar nerve has been performed for more than 20 years.[1] Since that time, it has become a popular adjunctive procedure for people with ulnar nerve compression and evidence of intrinsic hand muscle wasting. A large body of evidence supports its utility and reinnervation of the intrinsic hand muscles.[1-4] This is perhaps best demonstrated in cases of high ulnar nerve injury when one would not expect any motor recovery from the ulnar nerve itself .[1] The transfer is utilized to solely provide or "supercharge" the neural input of the native nerve.

There are variations in technique that have been described. The two main differences that exist are in the extent of nerve decompression and identification of motor fascicles. Some surgeons advocate for release of the cubital tunnel as well as Guyon's canal in order to ensure there are no sites of impingement. This also allows for identification of the motor branch which can be traced proximally to the site of transfer. Alternatively, or in addition, nerve stimulators can be used to better identify the appropriate fascicles.

The indications for AIN transfer in compressive neuropathy of the ulnar nerve are widely inclusive if muscle atrophy is present. A recent study by Dengler et. al found that only advanced age was predictive of treatment failure.[2] This study included assessment of electromyography and nerve conduction studies and found that there were no values from those studies which predicted an unsuccessful nerve transfer.

Historically, nerve deficits of the upper extremity were treated with bracing and tendon transfers. However, as our understanding of nerve pathology and healing has improved, the use of nerve transfers has become a common treatment approach. There is even some evidence to suggest patients fare better with nerve transfers than tendon transfers .[5] The AIN is a popular choice for both radial and ulnar nerve deficits due to its relatively long course with terminal innervation to a redundant muscle (pronator quadratus). [5,6] As we gain more experience and knowledge of how these transfers can be utilized, this procedure and others like it will be used even more frequently.

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Thumb CMC Arthroplasty. Is it Time to Move Away from LRTI?

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Hypothesis

Thumb carpometacarpal osteoarthritis (CMC-OA) is present on 21% of hand x-rays in patients over 40 years old, with symptoms reported in 1.9% of adults over 60 and 4.1% by age 70.[1,2] Numerous surgical methods have been developed to treat symptomatic CMC-OA, with no clear advantage to any one procedure.[3,4] We hypothesized that newer surgical techniques would confer improvements in both surgical outcomes and patient-reported outcomes, compared to traditional ligament reconstruction tendon interposition (LRTI).

Methods

A retrospective review was performed of all primary thumb CMC arthroplasties performed by the University of Pennsylvania's Hand Surgery Section from 2015 to 2019. Demographic data included age, sex, and hand dominance (Table 1). Disease and surgical data included duration of symptoms, Eaton stage, operative time, and complications. X-rays were assessed for trapezial space height. Patient-reported outcomes included visual analog scale pain scores and PROMIS scores, for up to six months post-operatively (Table 2). Statistical analysis was performed using ANOVA and Tukey-Kramer Honest Significant Difference tests for continuous variables and Chi-square and Fisher's exact tests for categorical variables.

Results

172 thumb CMC arthroplasties were performed: 100 LRTI, 49 suture suspensionplasty (SS), 15 Arthrex suspensionplasty with InternalBrace (IB), and 8 Arthrex Mini TightRope (MTR) arthroplasties. 75% of patients were female. Surgery was performed at a mean age of 62 years of age, 50% involved the dominant hand, and Eaton stage III arthritis was most frequent with symptoms present for a mean of 36.6 months. There were no significant differences in these characteristics or preop VAS pain scores (mean 6.4) between groups.

Operative time was significantly shorter for MTR (65 min) and SS (81 min) compared to LRTI (102 min) and IB (109 min). There was no difference in postoperative subsidence between groups (−6.4mm). MTR was associated with a 50% complication rate including one failure, one postoperative fracture, and one symptomatic hardware removal. Complications were lower for other methods (LRTI 8%; SS 18%; IB 20%). Pain consistent with complex regional pain syndrome was more frequent with SS. Two MTR and two SS patients required revision arthroplasty.

Table 1. Demographics (all continuous variables are reported as mean values except where noted; median values are italicized in parentheses where appropriate).

	LRTI	Suture Suspensionplasty	Swivel Lock	Mini Tightrope
N	100	49	15	8
Age	63	62	63	57
Female	71 (71%)	39 (81%)	11 (73%)	7 (88%)
Dominant hand	44 (44%)	26 (53%)	9 (60%)	6 (75%)
Duration of symptoms (months)	36.3	31.7	50.2	34.0
Eaton Stage	3 (*3*)	2.8 (*3*)	2.9 (*3*)	2.9 (*3*)
Preop Trapezial Space Height (mm)	11.3	11.5	12.3	11.1
Preop Pain	6.1 (*6*)	6.9 (8)	6.1 (*7*)	8.3 (*8.5*)
Preop PROMIS Physical Score	13.7 (*14*)	12.1 (*12*)	12.9 (*13*)	12.0 (*13*)
Preop PROMIS Mental Score	14.2 (*15*)	13.2 (*13*)	14.2 (*15*)	14.0 (*14*)

Table 2: Outcomes (all continuous variables are reported as mean values except where noted; median values are italicized in parentheses where appropriate).

	LRTI	Suture Suspensionplasty	Swivel Lock	Mini Tightrope
Operative time (minutes)	102	81*	109	65*
Complications	8 (8%)	9 (18%)	3 (20%)	4 (50%)**
Complications requiring reintervention	2 (2%)	2 (4%)	0 (0%)	3 (38%)#
Number of follow up visits	4 (*4*)	4 (*4*)	5 (*5*)	7 (*5.5*)##
Postop Pain – final visit	1.9	3.3§	1.7	3.3
Postop Trapezial space height (mm)	5.0	5.5	4.2	5.0
Subsidence (mm)	6.3	5.6	7.8	6.0
Postop PROMIS Physical Score – final visit	14.4	13.1 ¥	15.5	11.0 €
Postop PROMIS Mental Score – final visit	15.0	13.7	15.3	12.3

*Suture Suspensionplasty and Mini Tightrope significantly shorter operative times than other two methods ($p < 0.01$).

**Mini Tightrope with significantly higher complication rate than LRTI ($p = 0.005$).

Significant difference between Mini Tightrope and all other methods ($p < 0.005$).

Significantly more follow ups for Mini Tightrope versus LRTI and Suture Suspensionplasty ($p < 0.01$ for both).

§ Significant difference between LRTI and Suture Suspensionplasty ($p < 0.001$).

€ Significant difference between Mini Tightrope and LRTI and Swivel Lock ($p < 0.005$ for both).

¥ Significant difference between Suture Suspensionplasty and Swivel Lock ($p < 0.005$).

Patients undergoing LRTI and IB reported lower pain scores at the final visit (1.9, 1.7) although there was no significant difference in pain improvement from the preoperative to final visit (−4.0). Preoperative PROMIS physical (13.0) and mental (13.9) health scores were similar between groups with no significant difference in the change in PROMIS scores from pre to postoperatively.

Trends in arthroplasty technique changed over the 5 year period (Figure 1). LRTI made up 70% or more of thumb CMC arthroplasties performed during the first three years declining

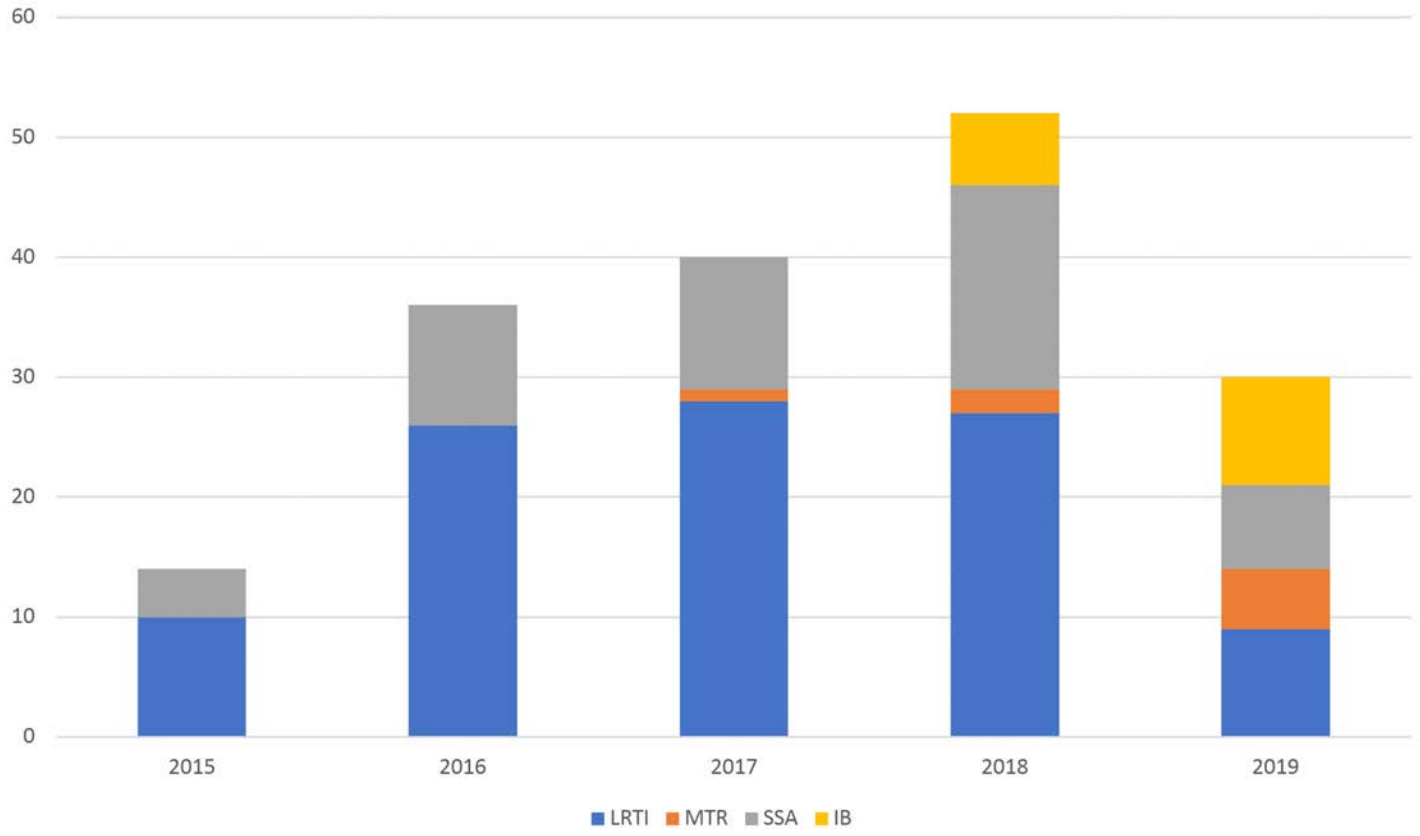

Figure 1. Annual Trend in Thumb CMC Arthroplasty Technique. LRTI = ligament reconstruction tendon interposition; MTR = Mini Tight Rope; SSA = suture suspension arthroplasty; IB = Internal Brace.

to 30% by 2019. Frequency of SS stayed relatively stable throughout the 5 year period. The use of newer, implant-based techniques were the main influence on frequency of LRTI.

Conclusions

There was no superior method of arthroplasty for CMC-OA in regards to subsidence or patient-reported outcomes. SS and MTR arthroplasty required less operative time than other methods. MTR, however, was associated with a higher complication and reoperation rate. The use of LRTI was also shown to decrease in frequency over the 5 year study period. When one considers these findings in conjunction with practice patterns more frequently utilizing removable splints instead of casting for shorter periods of postoperative immobilization and a quicker return to normal activities, there is the suggestion of continued evolution in the surgical management of thumb CMC OA.

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Pediatrics

Juvenile Osteochondritis Dissecans of the Knee Shows Early Evidence of Radiologic Irregularity

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Introduction

The etiology and development of juvenile osteochondritis dissecans (JOCD) of the knee remain heavily debated[1]. Since the initial description by Franz König suggesting an inflammatory process[2], the definition of OCD has evolved into our current understanding of the disease as "a focal idiopathic alteration of subchondral bone with risk for instability and disruption of overlying articular cartilage that may result in premature osteoarthritis" [1,3,4]. The precise underlying pathophysiology for the development of JOCD remain unknown and is likely multifactorial, including genetic predisposition, vascular insufficiency, trauma, and bone fragility with non-specific histologic findings showing changes that resemble fracture non-healing. Nonetheless, providers should ideally be able to identify early disease with the goal of intervening before a lesion becomes unstable. While it is common for providers to look at old imaging studies in the clinic, to the authors' knowledge there are no reports investigating the timeline of lesion development in those patients later confirmed to have diagnosis of JOCD. This study aimed to determine the radiologic presence of JOCD lesions up to a decade prior to diagnosis.

Methods

Records at a single pediatric orthopaedic hospital between 2012-2020 were retrospectively reviewed for patients diagnosed with JOCD of the knee who also had imaging studies of the lower extremity performed >1 year prior to the establishment of a JOCD diagnosis. Only patients with both MRI and radiographic studies of the lower extremity at the time of diagnosis of JOCD of the affected knee were included. The search resulted in 24 patients that were included in the present study. 8 patients were excluded for poor visualization on early imaging of the affected knee and 2 patients were excluded for carrying a diagnosis other than JOCD upon further review[5]. Investigators carefully examined the early studies for any irregularities in the anatomic area of the later JOCD lesion, including lucency or sclerotic margin on plain radiographs and hypointense signal in subchondral bone on T1-weighted MRI sequences or subchondral bone edema on fluid-sensitive MRI sequences. Mann-Whitney U tests were performed to evaluate the difference in time to presentation and age at early imaging between patients with early images that showed irregularity and patients with early images that were normal.

Results

18 lesions in 14 patients (5 female) were included. Lesion location and imaging details are presented in Table 1.

All 18 lesions had early plain radiographs and 5 also had early MRI. 2 patients had multiple plain radiographs. The mean age at diagnosis was 12.5 years (range 6.4-17.7) and the mean interval between early imaging and diagnosis was 4.4 years (range 2.3-7.8). 36% (5/14) of all patients had early radiologic irregularities in the area of a later diagnosed JOCD lesion. 5/20 early radiographs and 1/5 early MRIs (Figure 1) had radiographic irregularities in the area of the later diagnosed lesion. All irregularities visible on plain radiographs were subtle lucency in a similar location and geometric pattern to the later diagnosed lesion (Figure 2). No difference was observed in time from imaging to diagnosis ($p=0.156$) or age at early imaging ($p=0.069$) between patients with images that showed irregularity and patients with normal images.

Discussion

Multiple classification schemes have attempted to radiologically stage knee OCD lesion progression [6–10]. Suggestions for the earliest possible imaging findings of OCD include focal subchondral lucency with sclerotic margins using radiographs or subchondral bone bruise, edema, and thickened articular cartilage with low signal changes using MRI [6,10,11].

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Table 1: Lesion location and early imaging

ID	Sex	Age (diagnosis)	OCD Location	Side	Imaging Type	Indication	Age (imaging)	Early Evidence?	Description
1	M	15.0	MFC	L	XR	limp, heel pain	12.3	Y	lucency
			MFC	R	XR	limp, heel pain	12.3	N	
2	F	13.3	LFC	R	XR	pain, swelling	7.4	N	
3	M	12.0	MFC	R	XR	limp	4.2	N	
4	F	12.4	LFC	R	XR	pain	7.0	N	
					XR	distal femur fracture	9.9	Y	lucency
5	F	9.0	Tibial Plateau	R	XR	pain, swelling	5.7	N	
			Tibial Plateau	L	XR	pain, swelling	5.7	N	
6	M	17.7	LFC	R	XR	pain, swelling	12.9	N	
					MR	pain, swelling	12.9	N	
7	F	10.4	LFC	R	XR	unknown	4.4	N	
					XR	postop meniscectomy	8.2	N	
					MR	meniscal tear	7.7	N	
8	F	12.3	MFC	L	XR	pain, buckling	6.2	N	
					MR	pain, buckling	6.2	N	
9	M	13.3	LFC	R	XR	osteochondroma	10.5	N	
			MFC	R	XR	osteochondroma	10.5	Y	lucency
10	M	12.9	LFC	R	XR	postop meniscectomy	7.4	Y	lucency, sclerosis
					MR	meniscal tear	5.7	N	
11	M	6.4	MFC	R	XR	tibia/fibula fractures	1.2	N	
12	M	14.6	LFC	L	XR	skeletal survey	9.8	N	
13	M	9.1	LFC	R	XR	pain, limp	5.5	N	
			LFC	L	XR	pain, limp	5.5	N	
14	M	12.5	LFC	R	XR	postop meniscectomy	8.9	Y	lucency
					MR	postop meniscectomy	8.5	Y	hypointense T1 signal

MFC denotes medial femoral condyle, LFC denotes lateral femoral condyle, XR denotes radiograph, MR denotes MRI.

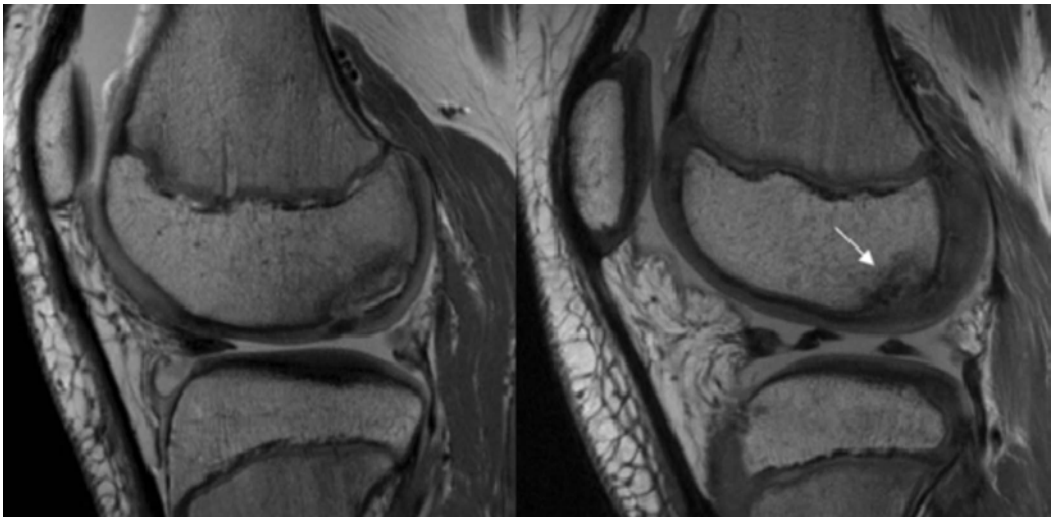

Figure 1. Sagittal PD images of the right knee of patient 14 diagnosed with OCD of the lateral femoral condyle at age 12 (left). Early images performed at age 8 (right) showing hypointense signal (arrow) in the area of the later diagnosed OCD lesion.

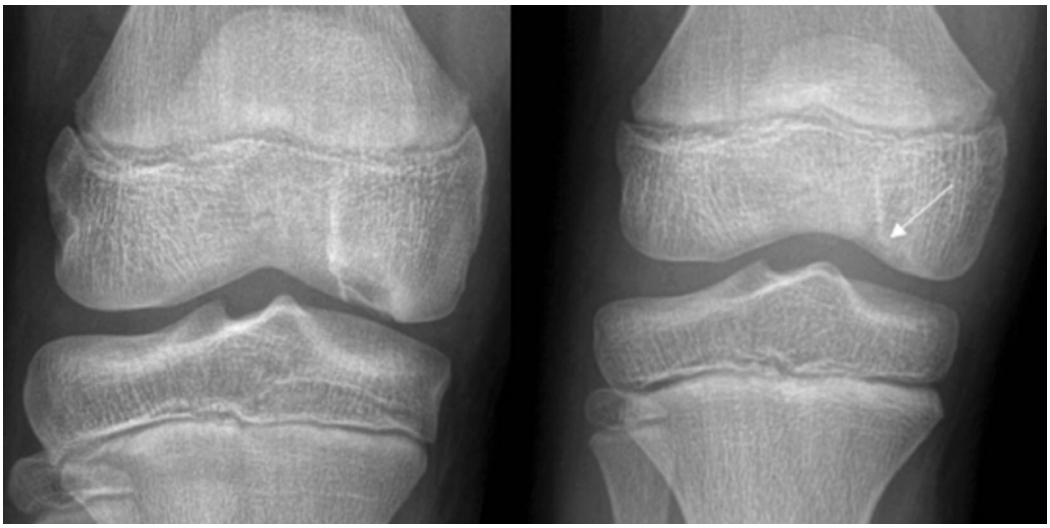

Figure 2. AP views of the right knee of a patient diagnosed with OCD of the medial femoral condyle at age 15 (left). Radiographs performed at age 12 (right) for a limp and heel pain show a subtle lucecny (arrow) in the area of the later diagnosed OCD lesion.

However, many of these studies examine patients at the time of diagnosis who likely went on to be treated. Thus, providing little insight into the radiologic development and evolution of untreated lesions. Here, we found that 36% of patients had radiologic irregularities in the location of the later diagnosed JOCD of the knee. Given these findings, and keeping in mind that JOCD has been partially attributed to prior trauma[12], providers evaluating post-traumatic radiographs of a pediatric patient should pay close attention to the subchondral bone of the knee to look for radiologic irregularities and early signs of JOCD. The most common finding was a subtle lucency on plain radiographs in the exact area of the future JOCD lesion. These incidental irregularities may then be followed with the aim of initiating early nonoperative treatment, when appropriate, and preventing lesion instability if JOCD develops[13,14]. We found no difference in time to diagnosis or age at early imaging between patients with imaging that showed irregularity and patients with normal imaging. Together, this data suggests that the rate of progression from irregularity to diagnosis of JOCD may vary between patients, rather than follow a predictable timeline.

While we show that radiologic irregularities can be visible for years prior to diagnosis, we could not provide evidence to support a JOCD tissue of origin. Studies using advanced imaging with 9.4-T MRI and histologic specimens provide some evidence for vascular insufficiency of the epiphyseal cartilage[15–17]. Other studies support the hypothesis that JOCD of the knee results from dysfunction of endochondral ossification in the maturing femoral condyles[18–20].

This study was limited by the small sample size and the potential for confirmation bias as early images were reviewed. We attempted to mitigate this bias by confirming evidence of early lesions with the senior author. Further studies are needed to fully map the early radiologic development of OCD of the knee.

Conclusion

More than one in three patients diagnosed with OCD of the knee may show early incidental radiologic irregularities in the location of the later diagnosed JOCD. Careful attention should be awarded to the subchondral bone as providers evaluate knee imaging of children who present with a lower extremity complaint.

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Increases in Pediatric Sports Injuries Late in the COVID-19 Pandemic

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Introduction

Since reaching a pandemic status in March 2020, COVID-19 has caused many public health policies to be put in place including social distancing, self-quarantining, and a variety of public closures.[1,2] Importantly, this included schools, extracurricular activities, and organized sports. As sporting organizations attempt to ensure an adequate season, variations in weekly games and more condensed schedules could be contributing to increased risk of injuries.

This study aimed to examine the impact COVID-19 had on the incidence of pediatric sports related musculoskeletal injuries as public health measures changed. Our hypothesis was that sports injuries would increase in rates over the summer months as athletes began to train for their fall sports seasons following months of rest or unorganized training.

Materials and Methods

This is a retrospective cohort study of pediatric patients presenting for musculoskeletal injuries during the COVID-19 pandemic compared to previous years. The patients were sorted by date of initial presentation for care. The "Early" cohort consisted of patients presenting between March 15th and April 15th. The "Middle" cohort consisted of patients arriving between June 15th and July 15th, while the "Late" cohort consisted of patients arriving between August 15th and September 15th. Control groups consisted of patients presenting in similar time frames in the two previous years, 2018 and 2019,

Patients were included if they were between the ages of 5 and 18 when presenting to an orthopedic clinic office or the emergency room for one of the following acute injuries occurring as a result of sports: ACL injury, meniscus injury, patellar dislocation, shoulder dislocation, ankle ligament sprain, clavicle fracture, medial epicondyle fracture, tibial spine fracture, and stress fracture.

Variables were compared between the 2018-2019 and 2020 cohorts and the "Early", "Middle", and "Late" cohorts. Statistical significance was defined in this study with a threshold of $p < 0.05$. Chi squared and Fisher's exact tests were used to compare categorical variables. Mann-Whitney U tests were used for continuous variables. Statistical analysis was performed using IBM SPSS Statistics for Macintosh, Version 24.0 (IBM Corp., Armonk, NY).

Results

A total of 1384 patients with the injuries of interest were reviewed with 643 (46.5%) occurring as a result of a sport-related injury. 506 of these patients presented in between 2018 and 2019, while 137 presented in 2020. Ankle sprains were the most common injury and accounted for 54.2% of all injuries, while tibial spine fractures represented 0.5% of injuries. Basketball was the single sport that contributed the most number of injuries with 126 (24.9%) in 2018-2019 and 40 (29.2%) in 2020 ($p = 0.506$). ACL injuries, meniscal injuries, patellar dislocations, medial epicondyle fractures, and stress fractures saw an increase in relative proportion of injuries in 2020 ($p = 0.002$).

A total of 227 patients were seen in the Early cohort (March 15th-April 15th) with 217 being seen between 2018-2019 and 15 being seen in 2020. 170 patients were seen in the Middle cohort (June 15th-July 15th) with 132 in 2018-2019 and 38 in 2020 and finally, 246 in the Late cohort (August 15th-September 15th) with 162 in 2018-2019 and 84 in 2020. 31 (14.6%) patients in the Early cohort required surgical intervention in 2018-2019, while only 2 (13.3%) underwent surgery in 2020 ($p = 0.891$). In the Middle cohort, surgical treatment was seen in 27 (20.5%) patients in 2018-2019 and 8 (21.1%) in 2020 ($p = 0.936$). Yet, in the Late cohort, 18 (11.1%) patients underwent surgery in 2018-2019, while 20 (23.8%) were treated surgically in 2020 ($p = 0.009$).

Discussion

As the world continues to adapt to the COVID-19 pandemic, schools, extracurriculars, and sports have all made various attempts to provide children with safe environments. This study examined sport-related injury trends presenting to a pediatric hospital during the COVID-19 pandemic and demonstrated significant changes in injury type. Previous studies have shown the effects of prolonged

Table 2: Injury Characteristics and Management of Early (March, April), Middle (June-July), and Late (August-September) Patients in 2018-2019 versus 2020

Variable	March/April 2018-2019	March/ April 2020	P-value	June/July 2018-2019	June/July 2020	P-value	August/September 2018-2019	August/ September 2020	P-value
Injury Type									
ACL Injury	20 (9.4)	2 (13.3)		17 (12.9)	5 (13.2)		16 (9.9)	13 (15.5)	
Meniscus	4 (1.9)	3 (20)		8 (6.1)	1 (2.6)		4 (2.5)	4 (4.8)	
Injury	17 (8.0)	2 (13.3)		11 (8.3)	4 (10.5)		11 (6.8)	9 (10.7)	
Patellar	11 (5.2)	0 (0)		2 (1.5)	0 (0)		6 (3.7)	1 (1.2)	
Dislocation	21 (9.9)	2 (13.3)		11 (8.3)	1 (2.6)		25 (15.4)	6 (7.1)	
Shoulder	10 (4.7)	0 (0)		5 (3.8)	4 (10.5)		2 (1.2)	4 (4.8)	
Dislocation	1 (0.5)	0 (0)		0 (0)	0 (0)		1 (0.6)	1 (1.2)	
Clavicle	123 (58)	6 (40)		75 (56.8)	15 (39.5)		89 (54.9)	41 (48.8)	
Fracture	5 (2.4)	0 (0)	**0.018**	3 (2.3)	8 (21.1)	**0.002**	8 (4.9)	5 (6.0)	0.190
Medial Epicondyle Fracture									
Tibial Spine Fracture									
Ankle Sprain									
Stress Fracture									
Injury Laterality	105 (49.8)	8 (53.3)		66 (50)	22 (59.5)		81 (50.6)	44 (52.4)	
Right	104 (49.3)	7 (46.7)	0.906	66 (50)	15 (40.5)	0.309	77 (48.1)	39 (46.4)	0.848
Left	2 (0.9)	0 (0)		0 (0)	0 (0)		2 (1.2)	1 (1.2)	
Bilateral									
Seen at Previous Institution	42 (19.8)	5 (33.3)		25 (18.9)	10 (26.3)		20 (12.3)	19 (22.6)	
OSH Urgent Care	52 (24.5)	1 (6.7)		22 (16.7)	2 (5.3)		29 (17.9)	12 (14.3)	
OSH ED	17 (8.0)	2 (13.3)		20 (15.2)	9 (23.7)		12 (7.4)	16 (19)	
OSH Clinic	93 (43.9)	5 (33.3)		59 (44.7)	17 (44.7)		99 (61.1)	32 (38.1)	
Not Previously Seen	8 (3.8)	2 (13.3)	0.179	6 (4.5)	0 (0)	0.262	2 (1.2)	5 (6.0)	<**0.001**
Not Recorded									
Delay to Presentation (days) †	7.23 ± 12.3	18.3 ± 26.7	0.140	9.26 ± 15.3	10.7 ± 25.7	0.730	8.14 ± 27.7	11.3 ± 31.5	**0.023**
Initial Visit Type									
ED	71 (33.5)	2 (13.3)		45 (34.1)	8 (21.1)		71 (43.8)	17 (20.2)	
Clinic	141 (66.5)	11 (73.3)	<**0.001**	87 (65.9)	30 (78.9)	0.126	91 (56.2)	67 (79.8)	<**0.001**
Virtual	0 (0)	2 (13.3)		0 (0)	0 (0)		0 (0)	0 (0)	
Treatment									
Surgical	31 (14.6)	2 (13.3)	0.891	27 (20.5)	8 (21.1)	0.936	18 (11.1)	20 (23.8)	**0.009**
Non-Surgical	181 (85.4)	13 (86.7)		105 (79.5)	30 (78.9)		144 (88.9)	64 (76.2)	

†Mann-Whitney U

rest on sports injuries, but this study set out to understand sports injury progression during the COVID-19 pandemic, specifically.[3-6] Understanding how this pandemic has already affected sports injuries in the pediatric population will be paramount in further understanding future sources of musculoskeletal injury for children.

Bram et al. demonstrated how pediatric fracture volume presenting to a single pediatric health system decreased by 2.5-fold during the peak of the COVID pandemic in March and April 2020.[7] When looking specifically at sports injuries, this study found a 1.8-fold decrease in monthly sports injury volume during this time. In the early fall however, the relative proportion of sport injuries in 2020 increase and surpasses the proportion seen in previous years (Figure 1). COVID precautions during the early part of the pandemic led to many organized youth sports leagues being suspended causing our reported decrease in volume during the early spring and early summer.[8,9]

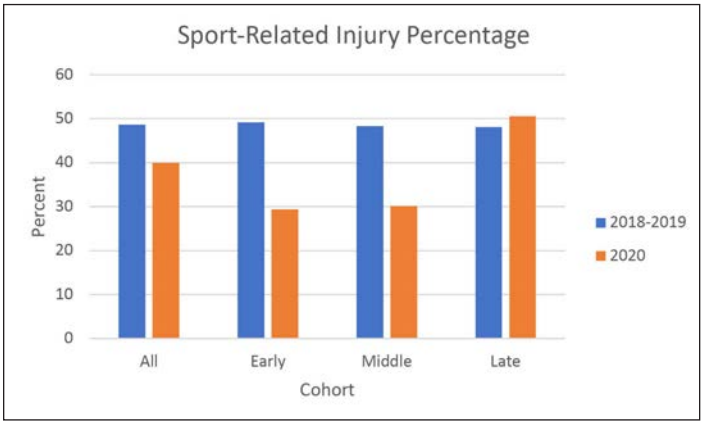

Figure 1. Percent of all injuries occurring during sport represented by cohort. All represents all data collected. Early represents data from March 15th-April 15th. Middle represents June 15th-July 15th. Late represents August 15th-September 15th.

In the summer and fall of the pandemic, many fall sports including football and soccer were resuming in a variety of different capacities.[10,11] As a result, we were able to show an increase of almost 13% in the rate of injuries requiring surgical intervention during the late summer and early fall of the pandemic relative to non-pandemic timeframe (Figure 2). With organized sports returning for a fall season in late August to early September, the statistically significant increase in surgical interventions during this interval suggest injuries during COVID may be more severe. Instituting training programs could help reduce the risk of knee injuries and prevent significant injuries necessitating surgical treatments as the COVID pandemic progresses.[21–23]

Several limitations to this study should be noted. This study only analyzed injuries occurring while playing sports and therefore does not take into account other injuries that may be due to deconditioning but did not occur during the act of playing sports. Additionally, due to the concern for COVID transmission, while several different injuries were evaluated, we cannot definitely state whether sports related injuries are changing due to altered behaviors and staying away from sports or due to failure to present. Relative rates of injuries may be skewed due to failure of less severe injuries to present

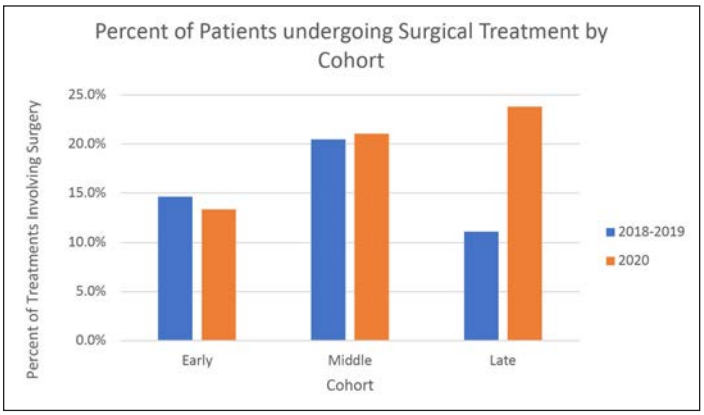

Figure 2. Percent of Injuries necessitating surgical intervention broken down by cohort and year. Early Cohort is defined as those presenting between March 15th-April 15th. Middle Cohort represents June 15th-July 15th and Late Cohort represents August 15th-September 15th.

in 2020. Additionally, with a lack of data on patients training schedules during 2020, it is difficult to assess if the COVID pandemic has changed how many hours of exercise patients are doing per week. Finally, as social distancing rules continue to evolve, some sports are not played in the same way as they were previously and therefore may change the risk of injury for patients.

Conclusion

The COVID-19 pandemic has led to several changes in sporting events and extracurricular activities for the pediatric population. This retrospective study demonstrated an overall decrease in sport-related injuries during three different time intervals throughout the evolving COVID-19 pandemic. Furthermore, the proportion of injuries requiring surgical treatment between August 15th and September 15th 2020 increased compared to previous years suggesting a greater risk for significant injuries as patients are returning to organized sports. As the COVID-19 pandemic continues, providers should be aware of the increased risk of significant injuries to their patients and counsel patients on gradual return to sport.

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Psychosocial factors impacting the mental health of the orthopaedic workforce

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Introduction

Since the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), healthcare workers have been at the forefront of the pandemic[1]. The United States has witnessed over 30,085,827 cases with over half a million fatalities[2]. Physicians and nurses have been the frontline workers involved heavily with the treatment, diagnosis, and screening of the infected individuals. However, while managing the ever-increasing crisis during the pandemic, psychosocial impact on the mental health and welfare of healthcare professionals cannot be ignored. Some of the most common concerns include increased professional workload, work-life balance due to shutdowns, increased risk of cross-contamination, and fluctuating availability of personal protective equipment[3].

Previous reports have cited lower epidemiological rates among pediatric patients undergoing orthopaedic surgeries compared to adult patients[4]. However, most of the infected patients were asymptomatic. Treating such patients pose challenges to healthcare workers by possibly increasing the risk of infections along with an increased psychosocial impact with unknown consequences. Currently, no studies have been conducted to identify possible factors that contribute to the psychosocial impact of COVID-19 on pediatric orthopaedic healthcare workers. The purpose of this study is to assess the psychosocial factors associated with the mental health status of pediatric orthopaedic clinicians at an academic tertiary care center during the COVID-19 pandemic.

Methods

An electronic survey via RedCap [6,7] was sent to the pediatric orthopaedics healthcare team members including surgeons and advanced practice providers. All surveys responses were collected during September 2020. The participants were recruited from an academic tertiary care pediatric orthopaedic department.

The psychometric item scales in the survey were selected based on Bandura's Social Cognitive Theory and Theory of Planned Behavior – based on an integrated framework to identify the psychosocial factors that may impact providers negatively or positively. Six validated surveys were chosen, namely, Obsession with COVID Scale (OCS), Coronavirus Anxiety Scale (CAS), Emotional Exhaustion inventory (EE), Insomnia Severity Index (ISI), PROMIS Emotional Support, Grit-S survey, and Trauma Coping Self-Efficacy Scale (C-SET). The survey instruments were chosen to evaluate the provider's attitude, provider's behavior, provider's social support, and provider's "state of mind". A detailed breakdown of survey instruments can be found in Table 1. We also collected demographic variables such as gender, professional experience, marital status, race, ethnicity, and number of children. Based on the normality of data, correlations, Mann Whitney U-test and Chi[2] and Fisher's Exact tests were conducted.

Results

In total, 39 providers participated in the study (surgeons: n = 22; 56.4%; nurses: n = 17; 43.6%) with a response rate of 71% (39/55). Our participant demographics were white (84.6%); a mean age of 44.9 years (range: 28 – 72); female (59.0%); married (79.5%), had two children (35.9%) and mean professional experience of 16.6 years (range: 1 – 41). The mean score of survey items were as follows: "Obsession with COVID-19" – 3.39 (± 2.3) indicating mild dysfunctional thinking and obsession with COVID-19; "coronavirus anxiety" – 1.18 (± 2.7) indicating mild anxiety; no insomnia symptoms: 5.76 (± 4.2); emotional support: 56.2 (± 6.9) indicating slightly above acceptable threshold; grit: 3.9 (± 49) meaning robust resolve and lastly, trauma coping self-efficacy was 43.3 (± 9.4) meaning medium coping style from traumatic situations. About 36% had one or more symptoms of burnout.

No significant differences were seen based on provider role. Grit and emotional support had significant and protective effects on trauma coping self-efficacy. However, the provider's coping ability with trauma was significantly and negatively impacted by insomnia. In addition, provider burnout was significantly correlated with insomnia and sleep quality ($p < 0.001$).

Table 1: Survey instruments and interpretation

Item Scale	Scale interpretation	No. of items	Scoring	Score interpretation
Obsession with COVID Scale (OCS)[7]	Constant thoughts about COVID-19	4	5-point Likert scale	Score of ≥ 7 is interpreted as probable problematic and constant thinking about COVID-19 pandemic.
Coronavirus Anxiety Scale (CAS)[8]	Anxiety due to COVID-19	5	4-point Likert scale	Score of ≥ 9 indicates problematic and constant anxiety towards COVID-19 pandemic.
Maslach Burnout Inventory: Emotional Exhaustion inventory[9]	Physician burnout	1	7-point Likert scale	Score of ≤ 2 is interpreted as no symptoms of burnout). Score of ≥ 3 indicate that participant has one or more symptoms of emotional exhaustion.
Insomnia Severity Index (ISI)[10]	Sleep difficulty	7	Score range: 0-28	0−7 = No clinically significant insomnia; 8−14 = Subthreshold insomnia; 15−21 = Clinical insomnia (moderate severity); 22−28 = Clinical
PROMIS Emotional Support[11]	Emotional support from family and friends	4	T scores; Computer Adaptive Test	Raw score is converted standardized score with a mean and a standard deviation
Grit-S[12]	Tenacity to persevere through difficult situations	8	5-point Likert scale	Score of 1 represents "not gritty at all" while score of 5 indicates "extremely gritty"
Trauma Coping Self-Efficacy Scale (C-SET)[13]	Self-ability to cope with trauma	9	7-point Likert scale: Range: 9 - 63	Lower score indicates lower coping self-efficacy for trauma

Table 2: Correlation of item scales within the sample

Variables	Professional Experience (in years)	Obsession with COVID	Anxiety due to COVID-19	Physician Burnout	Insomnia	Emotional Support	Grit	Trauma coping self-efficacy
Professional Experience	1							
Obsession with COVID-19	0.1212	1						
Anxiety due to COVID-19	0.1319	0.4525**	1					
Physician Burnout	0.1236	0.2631	0.3800**	1				
Insomnia	0.0197	0.2617	0.2331	0.4949***	1			
Emotional Support	0.0419	−0.0616	0.0994	−0.2700	−0.2212	1		
Grit	−0.0703	−0.1152	0.1549	−0.2613	−0.2865	0.1728	1	
Trauma coping self-efficacy	−0.0610	−0.2866	−0.1468	−06922*	−0.6839***	0.5761***	0.4765**	1

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 2 summarizes our findings. More than three-quarters of the participants felt their scholarly activities decreased or remained the same (n = 30; 76.9%).

Discussion

After COVID-19 was declared a pandemic in early 2020, major disruptions were witnessed on all aspects of life globally. This included cancellation of elective surgeries as concerns arose for limited personal protective equipment (PPE) and blood products along with increasing COVID-19 cases.[14] Additionally, the orthopaedic workforce weathered major concerns of imparting infections on families along with their colleagues while treating their patients. Various changes were made overnight to incorporate changing practice patterns such as the incorporation of telemedicine, online education and trainings, and reallocation of staff members. Our study

aimed to quantify the impact of COVID-19 on the orthopaedic workforce in a tertiary care hospital.

While mental health indicators fluctuated substantially among our pediatric orthopaedics care team, most of the indicators revealed above-threshold results, which is concerning. We observed mild dysfunctional thinking and obsession, as well as mild anxiety about COVID-19, which indicate preoccupation with the disease among our responders. Furthermore, we found that more than a third of our responders are in a state of burnout. Anxiety and burnout are codependent and may lead to a vicious cycle that makes it impossible for the person to function well, both at their job and in the personal life. Orthopaedic providers in our sample exhibited grit, i.e., perseverance to withstand challenges. Grit and emotional support of providers were strongly correlated with coping with traumatic situations such as COVID in this situation.

Conclusion

Healthcare providers are under considerable pressure during the COVID-19 pandemic. While the rate of infection and complications are lower in children, COVID-19 has had a significant impact on the psychosocial health of nurses and provider working at children's hospitals.

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U·P·O·J

SutureBridge Transosseous Fixation of Complete Radial Tears: A Philosophical Approach

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Introduction

While increased participation in organized sports has caused a rise in pediatric anterior cruciate ligament (ACL) injury, the rate of meniscal tears in children is also increasing.[1] Meniscal tears are one of the most common injuries in pediatric athletes, frequently occurring in the setting of ACL injury, with concomitance rates as high as 66% reported.[2] The role that the intact menisci play in knee biomechanics, and the significance of meniscus injuries in the development of knee osteoarthritis (OA) is well documented; thus it is imperative to ensure functioning menisci to prevent long-term morbidity.[3,4] Specifically, radial and root tears pose a greater risk to the function and integrity of the meniscus by disrupting the circumferential fibers that provide resistance to hoop stress. This results in a diminished ability to absorb shock from the tibiofemoral load.[5] Previous studies have shown that a complete radial tear, such as the case below, is functionally equivalent to a total meniscectomy and increases the risk of OA by concentrating high stress on a focal area of the cartilage.[6,7,8]

Controversy exists regarding the best treatment of radial tears, as they are often not amenable to common meniscus repair techniques. Historically, radial tears were treated with partial meniscectomies due to their poor healing capacity. However, it is now known that partial meniscectomies are associated with impaired function and accelerated degenerative changes.[5,9,10] Therefore, it is imperative to determine the optimal techniques which will maintain meniscal integrity and function, and prevent long term degeneration of cartilage. While various techniques have been described in the literature, they have focused on the adult population.[11,12,13] The purpose of this article is to present a complete radial tear of the lateral meniscus in a pediatric patient which was treated with a SutureBridge Single-Tunnel Transosseous Fixation (Arthrex).

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Case report

A 14-year-old female visited our pediatric sports clinic, 18 months post right ACL reconstruction with medial and lateral menisci repairs, due medial right knee pain after playing basketball. On the clinical exam, McMurray's Test elicited trace discomfort at the medial hemijoint and the patient had diffuse tenderness at the medial hemijoint. Given the persistent pain and swelling in the setting of previous ACL reconstruction and meniscus repairs, an magnetic resonance imaging (MRI) study was ordered. The MRI indicated postsurgical changes versus tear of the medial meniscus with an intact lateral meniscus. The patient was reexamined in the office and continued to complain of right knee pain. The decision was made to proceed with surgical arthroscopy of the right knee.

The patient was placed supine on a standard operating table, with the knee flexed to 90 degrees. After evaluation under general anesthesia, the procedure began with a diagnostic arthroscopy with a standard 30 degree arthroscope. The standard anteromedial and anterolateral portals were placed in the usual fashion. We also opted to use an accessory midlateral portal to allow for ease of instrument passage, using three portals instead of two. Diagnostic arthroscopy revealed a lateral meniscus tear not appreciated on the patient's preoperative MRI from an outside institution, in addition to the medial meniscus tear. A full thickness radial tear at the 9 o'clock position of the lateral meniscus was visualized, with friable edges with a poor quality (Figure 1). Due to the chronic, degenerative tear, and the low probability of healing with direct repair, the decision was made to use a SutureBridge Transosseous fixation.

A meniscal Scorpion (Arthrex) was placed to secure the meniscus ends with sutures, and a single tunnel was then drilled slightly anteromedial to the footprint of the meniscus tear. A small amount of exposed bleeding bone was created using a small curette at the precise point where the guidepin was drilled. A retrieving suture was then passed into the joint and was used to bring the meniscus sutures down through the tibial drilling site (Figure 2). The meniscus was then appropriately reduced and probed to confirm stability. Once stable, it was secured using a PushLock anchor (Arthrex) on the medial tibia, drilled and placed as per the manufacturer's protocol. The meniscus was probed again for stability and a shaver was used to remove loose debris (Figure 3).

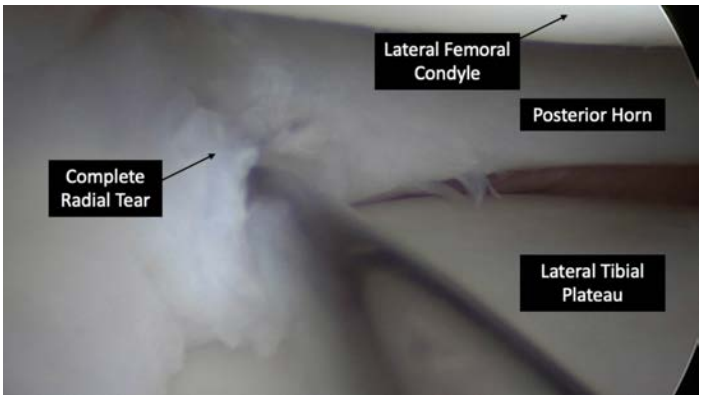

Figure 1. Arthroscopic image of right knee from anterolateral portal demonstrating a full-thickness radial tear of the midbody of the lateral meniscus.

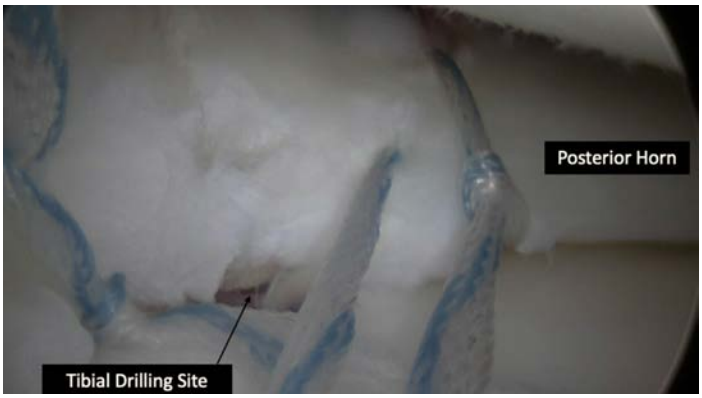

Figure 2: Sutures anchoring lateral meniscus through tibial drilling site.

Postoperative Management

Following surgery, the patient was placed into a range of motion control brace locked in extension and restricted to toe-touch weightbearing. Knee flexion was restricted to 90 degrees until week 2 and 110 degrees until week 4. After 3 weeks, the patient weaned out of the brace as appropriate quadriceps strength was noted by physical therapy. Toe-touch weight bearing was maintained until 6 weeks postoperative. At 3 months, the patient was given clearance to initiate straight line running and plyometric exercises, given the acceptable isokinetic strength and functional testing results. Gradual return to unrestricted activity was allowed at 6 months postoperative when she met all goals outlined by our meniscus repair protocol. Progressive return to sports was allowed at 4 months postoperative.

Discussion

Meniscus injuries are increasing in children and adolescents, especially with the rise in their activity level, year-round sports participation, and early specialization. Due to the significance of the menisci in maintaining the normal biomechanics of the knee, diagnosis and management of these injuries are of utmost importance.[3]

Physical examination of the meniscus is difficult in children and is less reliable in lateral meniscus tears. In fact, physical examination only has a 50% sensitivity in the diagnosis of

Figure 3: Stable SutureBridge transseous repair of lateral meniscus.

lateral meniscus tears in the pediatric population. MRI is the preferred imaging modality in the diagnosis of meniscal tears, which can also characterize the tear and also provide details on associated injuries. However, MRI has lower diagnostic performance in the evaluation of meniscus in skeletally immature patients. Additionally, radial tears can be especially difficult to detect.[14,15,16] As with the case presented here, the initial radiology report failed to appreciate the meniscus tear, although in retrospect, the tear was visualized by the fellowship-trained radiologist at our institution.

Given the importance and vascularity of the immature skeleton's menisci, repair of the torn meniscus is usually the preferred treatment in children. Whereas degenerative tears are common in adults and might not be amenable to repair, most tears in children are of sufficient quality to undergo a repair.

The most common meniscus tear in children is a longitudinal tear in the red-red zone, and thus is the best candidate for surgical repair. The outcomes of arthroscopic repair of meniscus tears in children are generally excellent and will most commonly result in normal or near-normal knee biomechanics.[1,4,17] All techniques used in adults can be applied to the pediatric population, including inside-out, outside-in, and all-inside repairs, depending on the location of the tear, quality of the tissue, and surgeon's preferences. In the less-common lateral meniscus root tears, fixation of the detached root to the tibial cortex through an intra-osseous tunnel provides a rigid, stable fixation with excellent results.[18]

When incomplete, radial tears can successfully be debrided to normal tissue. However, complete radial tears disrupt the normal meniscus function through the circumferential fibers and are challenging to treat. Even with repair, the fibrous tissue replacing the normal meniscus might not be of the same biomechanical properties, and therefore, might not be able to convert the longitudinal forces into circumferential hoop stresses as well.[19] The situation is even worse when facing a degenerative radial tear, as in the case presented here. In such cases, considering the poor results of a partial meniscectomy, the treating surgeon might opt to perform a total meniscectomy, followed by a meniscal allograft transplant in a second surgical stage, with favorable results.

However, in this case, the patient had an otherwise healthy meniscus despite the poor quality of the tear edges. Therefore, we decided against a meniscectomy. Instead, the SutureBridge transosseous technique was used to fix the tear ends to the tibia through an intraosseous tunnel. While this technique is commonly utilized in root tears, we have found it applicable to complete radial tears and is currently our treatment of choice in similar cases. With this technique, the meniscus is practically divided into two functioning segments, each acting as one full meniscus and withstanding longitudinal forces applied to the knee. However, due to the trimmed edges being brought through the same tunnel, the potential for the primary healing of the tear edges is also present. While the biomechanical properties of this technique have not been evaluated, our preliminary clinical results are promising and show excellent function and return to sports.

Conclusion

In conclusion, we have presented the case of a 14-year-old female who presented with a degenerative radial tear of the lateral meniscus which we treated with a transosseous bridge technique. The patient has regained knee motion and has returned to sports with no pain. We believe that this technique is a viable option in cases where the only other option would be a total meniscectomy and meniscal allograft transplant.

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Shoulder and Elbow

Poly-N-Acetyl Glucosamine (sNAG) is Dose Dependent for Healing of a Rat Rotator Cuff

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Introduction

Rotator cuff injuries are a common musculoskeletal problem and frequently require surgical intervention, with repair failure remaining a frequent problem.[1] Many biologic therapies have been utilized in an effort to improve tendon repair.[2] Our previous work demonstrated that 0.2 mg (one 4 mm round) of Talymed (Marine Polymer Technologies, Inc.) material improved tendon-to-bone healing, with treated supraspinatus tendons demonstrating increased maximum load and maximum stress at 4 weeks post-injury compared to saline-treated controls.[3] However, whether an increased dose of this nanofiber material could further improve tendon-to-bone healing after supraspinatus injury is unknown. Therefore, the purpose of this study was to continue to investigate the healing properties of sNAG polymer in a rat rotator cuff repair model, increasing the dose of Talymed (sNAG) delivered at the site of injury and repair. We hypothesized that this increased dose sNAG would improve supraspinatus tendon-to-bone healing compared to saline-treated controls.

Methods

Study Design

36 adult male Sprague-Dawley rats (400-450g) were used in this IACUC-approved study. All animals underwent bilateral, full thickness transection and repair of the supraspinatus tendon as described.[4-5] Animals were randomized into one of two groups receiving either sNAG or a saline injection (n = 18/group). For sNAG treated animals, immediately prior to repairing the supraspinatus, a 0.8 mg dose of the thin sNAG membrane (4 stacked pieces, 4mm diameter) was placed on the "foot print" of the supraspinatus tendon to bone attachment site. All animals were allowed normal cage activity after surgery. Animals were sacrificed either 2 (n = 6/group) or 4 weeks (n = 12/group) post-injury and repair. Animals sacrificed at 4 weeks underwent longitudinal in vivo ambulatory assessment with measurements pre-injury and 1, 2, and 4 weeks post-injury and repair.[6] *Ex-Vivo*: The right supraspinatus tendons of animals sacrificed at 2 weeks were immediately harvested and processed for histological analysis including quantitative collagen fiber organization analysis.[5,8-9] Animals sacrificed at 4 weeks had their right supraspinatus immediately dissected and processed for histology (n = 6/group) and were frozen at −20°C and later thawed for dissection at the time of quasistatic mechanical testing (n = 12/group).[7-8]

Statistics

Mechanical testing and collagen fiber organization data were evaluated using one-tailed t-tests after confirming data normality. Semi-quantitative histological comparisons were made using Mann-Whitney U tests. Ambulatory assessment comparisons were made using a 2-way ANOVA with repeated measures on time with follow-up t-tests between groups at each time point. Significance was set at $p < 0.05$ for all comparisons.

Results

Mechanical Properties

At 4 weeks after injury, there were no differences between saline-treated control and sNAG-treated tendons for cross-sectional area, maximum load, modulus, or stiffness (Figure 1).

Histologic Observations

Semi-quantitative grading indicated that cellularity was increased with sNAG treatment at the insertion at 4 weeks post-injury (Figure 2A) and in the midsubstance at 2 weeks post-injury (Figure 2B). There were no differences between groups for cell shape in the tendon insertion or midsubstance (Figure 2 C,D).

Ambulatory Measurements

sNAG had no effect at any time point on animal stride width, stride length, stance time, rate of loading, propulsion force, or peak vertical force (Figure 3).

Discussion

The purpose of this study was to further investigate the healing properties of an increased dose of sNAG polymer in a rat rotator cuff repair model. Surprisingly, a higher dose did not

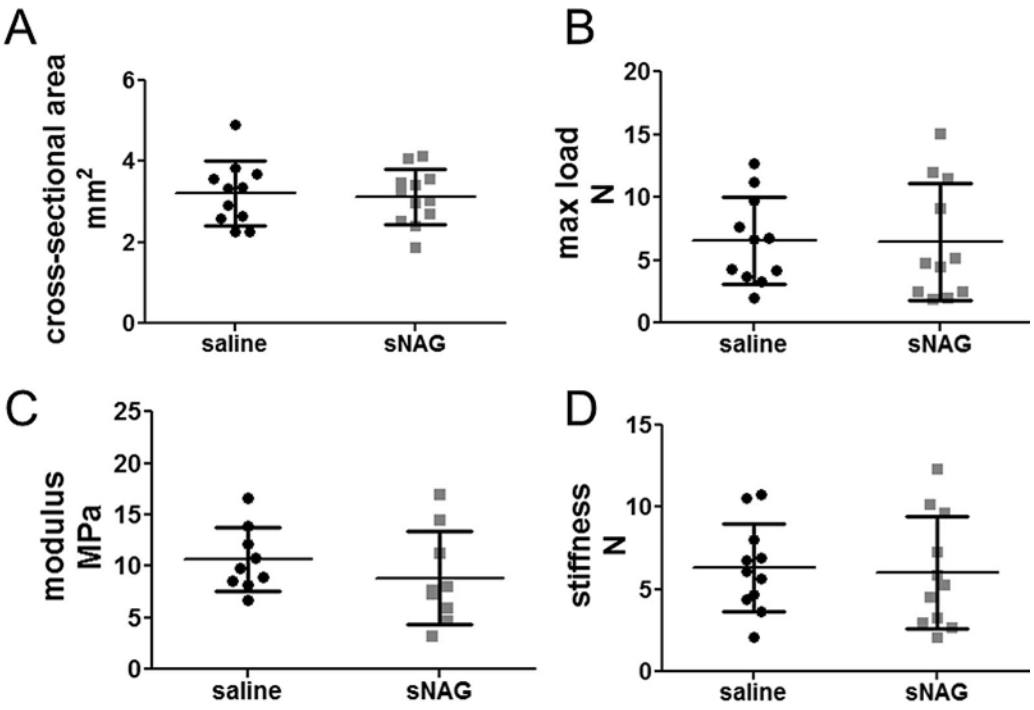

Figure 1. Mechanical Properties. Four weeks after injury, there were no differences between saline-treated controls and sNAG-treated tendons for **(A)** cross-sectional area; **(B)** maximum load; **(C)** modulus; or **(D)** stiffness. Data shown as mean ± SD.

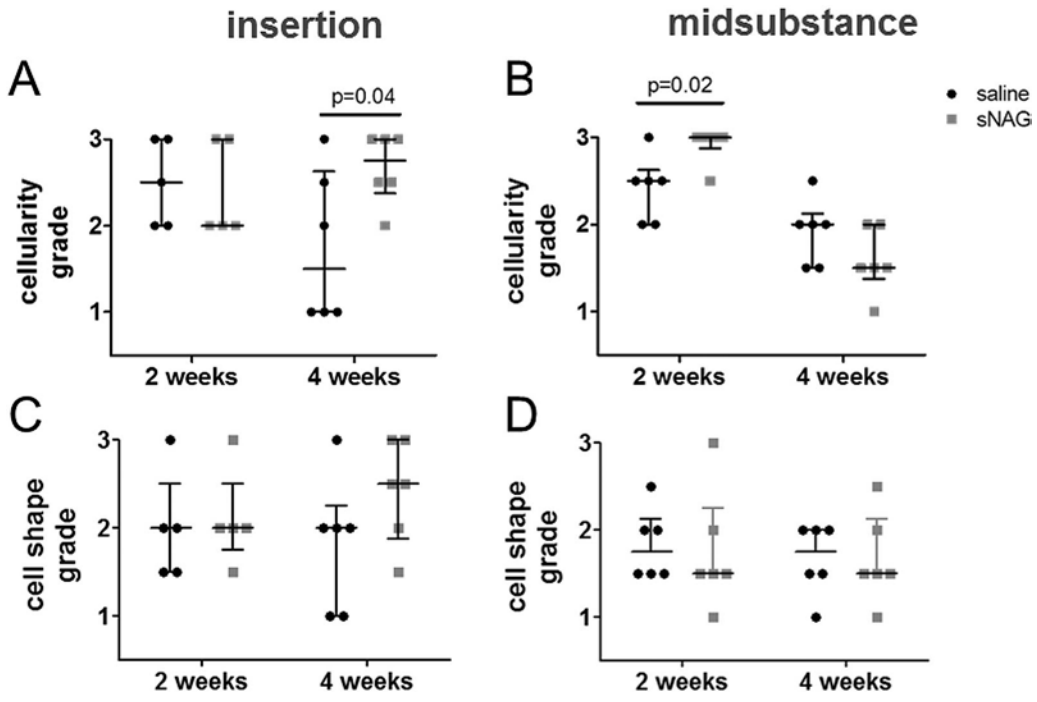

Figure 2. Histological Properties. In the tendon insertion, **(A)** cellularity was increased with sNAG treatment at 4 weeks post-injury. Similarly, in the midsubstance, **(B)** sNAG increased cellularity at 2 weeks. There were no differences between groups for cell shape **(C)** in the tendon insertion or **(D)** midsubstance. Data represented as median ± IQR.

produce significant improvements in rotator cuff healing as was seen with a previously studied "standard dose".[3] Although many parameters did not show differences between groups, there were no negative effects with an increased dose of sNAG. Treated tendons did demonstrate increased tendon cellularity, but this did not translate to improved mechanical properties. Another previous study utilizing repeated injections of 0.2 mg of a liquid-formulation of sNAG led to improved Achilles tendon healing 3 weeks after a full thickness, partial width tear.[10] This study suggests that sNAG may be dose-dependent. Early histological changes with this dose could lead to later improvements in tendon strength; further studies are needed to investigate this possibility, as well as to explain the mechanism of action for the changes identified.

Significance

The effects that sNAG has on rotator cuff tendon healing may be dose-dependent, as the higher dose tested in this study (4x original) did not improve tendon properties.

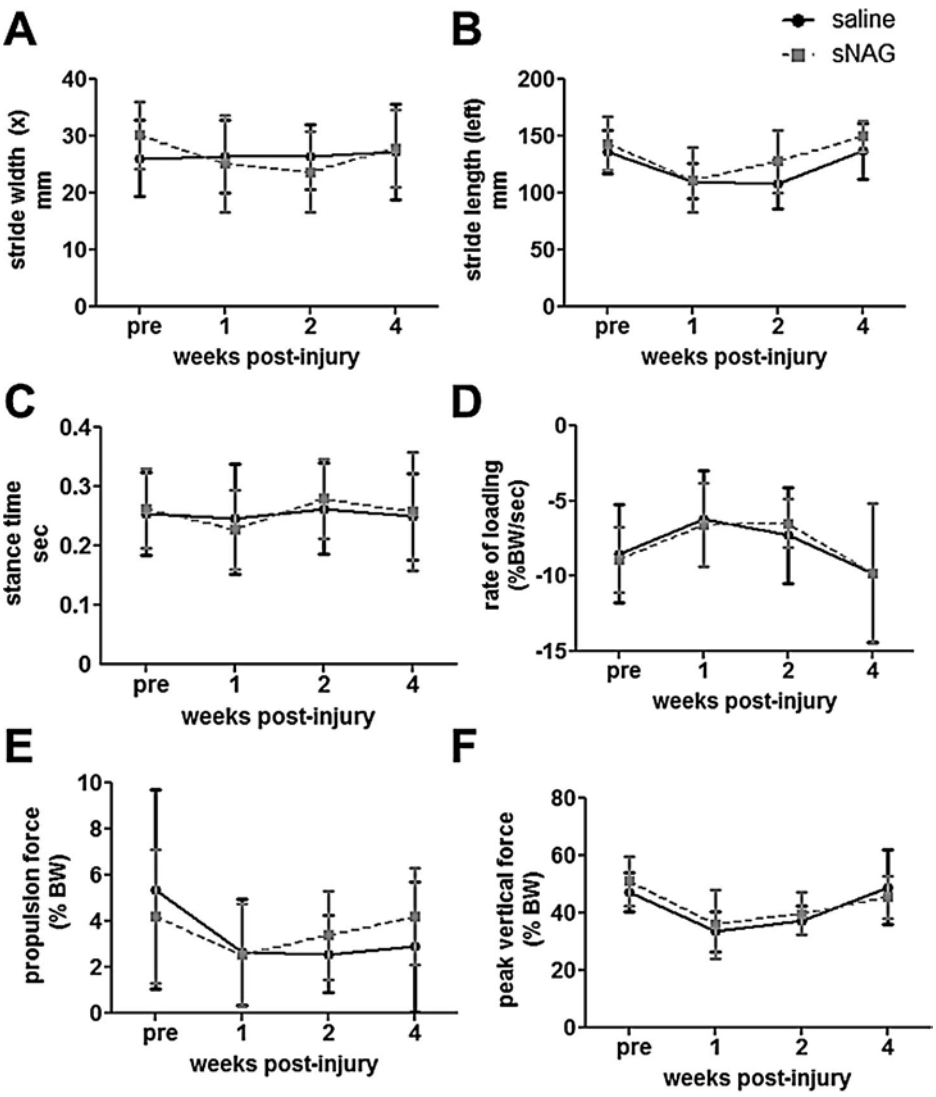

Figure 3. Gait Properties. sNAG treatment had no effect at any time point on animal **(A)** stride width between paws; **(B)** stride length; **(C)** stance time; **(D)** rate of loading; **(E)** propulsion force; or **(F)** peak vertical force. Data shown as mean ± SD.

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Disclosures

Nuss CA (N), Huegel J (N), Finkielsztein S (3A- Marine Polymer Technologies, Inc.), Kuntz AF (N), Soslowsky LJ (5)

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State of the Field: Proposed Suture Anchor Design for Rotator Cuff Repair in Osteoporotic Bone

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Introduction

Rotator cuff tears (RCT) are a common cause of shoulder pain and disability. In the United States (US) alone, RCT account for 4.5 million office visits and 250,000 surgeries per year, resulting in over $3 billion in total healthcare costs.[1, 2] RCT are especially prevalent among older populations, affecting up to 25% of patients 60 years old and up to 50% of patients 80 years and older.[3] Given the aging US population and increasing labor force participation among older populations, the burden of RCT is expected to rise in the future.

Surgical repair of RCT in individuals with osteoporosis remains a challenge due to systemic low bone mineral density (BMD) and lower rates of bone-tendon healing following repair.[4] Moreover, the proximal humerus is a region that is especially susceptible to osteoporotic bone loss, resulting in a higher rate of complications due to suture anchor loosening, migration, and pullout before adequate bone-tendon healing can take place.[4, 5] Chung et al. reported RC repair failure rates as high as 42% in patients with osteoporosis as compared to 9% for patients with normal BMD.[4] Furthermore, in a study of 80 patients with RC repair failure, Djurasovic et al. found that 10% of RC repair failures were due to suture anchor-bone interface.[6] Given the significance of the suture anchor as an important cause of RC repair failure in osteoporotic patients, suture anchor design represents an important field of research driving improvements in rotator cuff repair outcomes.[7]

Suture Anchor Design: Mechanical Design

Mechanical design, anchor material, and reinforcement represent three important aspects of suture anchor design. The mechanical design of the suture anchor, which refers to the interface between the suture anchor and the bone, contributes to the pullout strength of the anchor. There are three primary interfaces—the threaded anchor, the wedge fit anchor, and the all-suture anchor. In a biomechanical study, Tingart et al. showed that threaded, screw-in anchors provided superior pullout strength in osteoporotic bone compared to wedge-type anchors.[8] Threaded suture anchors themselves vary by pitch, flight depth, thread depth, and length. A biomechanical investigation of threaded anchors by Chae et al. found that pullout strength was positively correlated with the contact surface area between the anchor threads and surrounding bone, as well as the overall length, number of threads, and depth of the thread of the suture anchor.[7] The authors also noted that the relative effect of these design factors upon pullout strength varied with the direction of applied force. Specifically, the contact surface area was the most important design factor when tension was applied at 0° and 45° relative to the long-axis of the screw, while screw length was the predominant design factor at a direction 75° from the long-axis of the screw.[7] In contrast, the pullout strength of all-suture anchors, which are reliant deformation of the suture within the drill hole, is positively correlated with the number of sutures anchored together.[9] For example, triple-loaded anchors have been shown to be stronger than double-loaded anchors, and double-loaded anchors have been shown to be stronger than single-loaded anchors.[9]

Suture Anchor Design: Suture Material

Suture anchor material affects the physiologic response from the body and dictates how well the suture anchor will perform over time. Non-biodegradable anchors are typically made of metal (e.g., steel or titanium alloys) or polymers (e.g., polyethylene), while biodegradable anchors are typically made of poly-L-lactic acid and polyglycolic acid copolymers.[10, 11] Generally speaking, non-biodegradable anchors have the short-term advantage of greater mechanical stability while biodegradable anchors have the long-term advantage of replacement by bone over time.[10] However, the etiology of this osteogenic effect is unclear, and some patients experience a lack of bone regrowth with biodegradable anchors. The lack of bone regrowth can lead to tunnel widening, effusion, and cyst formation at the implantation site which may ultimately lead to anchor pullout.[12-15] In a recent biomechanical study comparing the titanium TwinFix anchor (Smith and Nephew, Memphis, Tenn), the

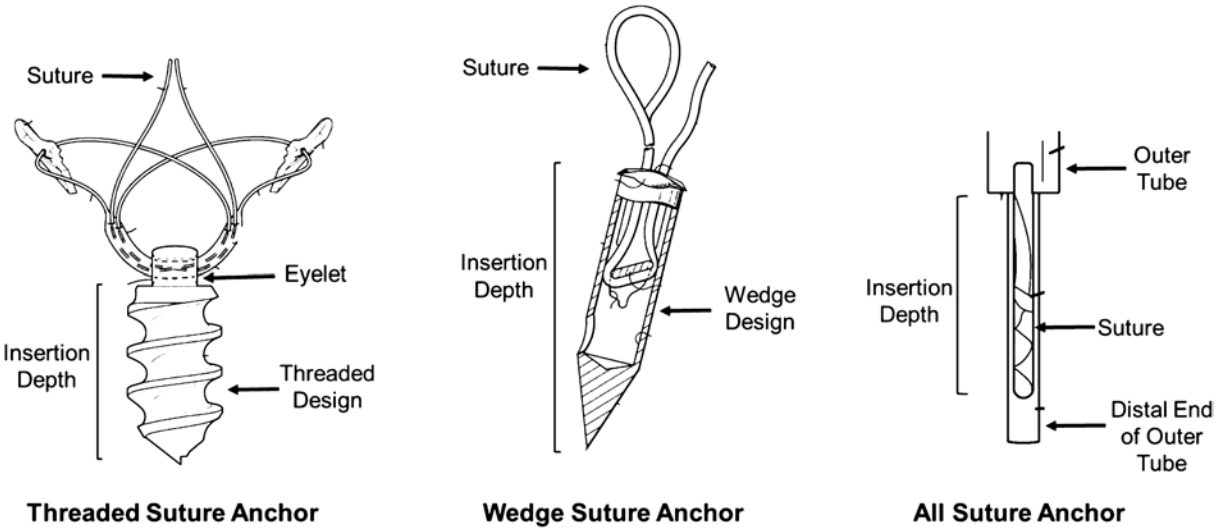

Figure 1. The three primary mechanical designs of suture anchor.

bioresorbable Healix anchor (DePuy Mitek, Raynham Mass.), and the all-suture Iconix anchor (Stryker, Kalamazoo, MI) in an osteoporotic bone model, Rosso et al. found that all three anchors could withstand physiologic loads of 250 N. However, the bioabsorbable suture underwent greater deformation following cyclic loading than the titanium suture anchor (0.40 mm vs 0.22 mm), suggesting that metal anchors have greater RC repair stability in osteoporotic bone.[16]

Suture Anchor Design: Reinforcement

Metallic suture anchors placed into osteoporotic bone are frequently reinforced with either polymethylmethacrylate (PMMA) or bioabsorbable tricalcium phosphate (TCP) cement.[17, 18] In a biomechanical study of corkscrew suture anchors, Er et al. found that TCP augmentation improved pullout strength by 86% in simulated osteopenic bone and by 364% in simulated severely osteoporotic bone. Similarly, PMMA augmentation increased pullout strength by 148% and 524%, respectively.[19] The use of bone cement augmentation with biodegradable anchors and all-suture anchors has not been reported in the literature. Despite the mechanical advantages of anchor augmentation with bone cement, arthroscopic injection of cement into the anchor hole is technically demanding due to the risk of spillage into the joint space.[19] While the Jamshidi needle has been successfully repurposed for the injection of TCP cement, the development of new tools for the arthroscopic injection of bone cement are needed.[19]

Proposed Suture Anchor Design for Osteoporotic Bone

Given the existing literature, the authors of this study see a need to develop an improved suture anchor design for increased RC repair stability in osteoporotic bone. We suggest using a conical, threaded suture anchor to increase anchor-bone surface area for increased pull-out strength. We also suggest using a bioresorbable design using PLLA and B tricalcium phosphate, which will afford increased resistance to deformation following cyclic loading and not induce cavitary lesions in the greater tuberosity. Given the evidence supporting the use of TCP augmentation, we also suggest using TCP to reinforce suture anchors in osteoporotic bone. A new supporting device can be developed that assists the surgeon in precise injection of TCP into the anchor hole, which will give a near immediate increase in fixation upon bone 'cement' curing. A paucity of user friendly designs may be one reason that TCP is not frequently used for arthroscopic suture anchor augmentation. Our design will facilitate injection of TCP immediately upon anchor insertion and obviate the need for PMMA or the usage of a larger anchor.

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Arthroplasty

Tertiary Care Centers Provide Successful Revision TKA to External Referrals, Despite Increased Patient Complexity

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Introduction

The incidence of both primary and revision total knee arthroplasty (rTKA) continues to grow in the United States. Tertiary referral centers absorb a large share of the rTKA healthcare burden. This study characterizes the referral patterns and outcomes of rTKA cases performed at a tertiary referral center. We hypothesize that 1) external referrals have higher rates of prior TKA revision, and 2) referral status does not impact post-operative outcomes following rTKA.

Methods

We retrospectively reviewed 243 consecutive rTKAs between 2013-2018 performed at a tertiary referral center by a single surgeon. Patient demographic information was recorded, and referrals were characterized as: external, internal within hospital system, or internal within surgeon's practice. Post-operative outcomes included 90-day, 1-year, and 2-year all-cause reoperation rates. Univariate and multivariate regression analyses evaluated the impacts of demographic variables, prior revision and referral status on post-operative outcomes.

Results

Of the 243 rTKA cases, 51.0% (124) were external referrals, 33.7% (82) internal within hospital system, and 15.2% (37) internal within the surgeon's practice. External referrals had significantly higher rates of prior TKA revision (45.3%), compared to patients internal within surgeon's practice (25.0%; $p = 0.029$). Multivariate logistic regression revealed prior revision TKA as an independent risk factor for reoperation at 90-days (OR: 3.1; $p = 0.017$), 1-year (OR: 2.4, $p = 0.032$), and 2-years (OR: 3.4, $p < 0.001$). However, on univariate and multivariate analyses, referral status had no association with reoperation rates.

Conclusion

External referrals were more likely to have had undergone prior revision, increasing their risk of rTKA failure at 90-days, 1-year and 2-years. However, no differences in rTKA outcomes were observed between referral groups. Tertiary care centers provide successful rTKA for external referrals, despite increased inherent patient complexity. Designation of specialty revision centers will help to ensure access to care for patients in need of complex revision total knee arthroplasty.

U·P·O·J

Pre-operative Complexity Scoring Accurately Predicts Total Knee Arthroplasty Operative Time

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Introduction

Primary total knee arthroplasty (TKA) is projected to grow to 935,000 procedures in the United States by 2030.[1] Medicare reimbursement rates for TKA have decreased by approximately 1.7% per year since 2000 after adjusting for inflation.[2] The total cost of providing quality care in total joint arthroplasty continues to rise at a rate that is not commensurate with Medicare reimbursement rates.[3] Decreasing TKA profit margins, when compared to operating room (OR) costs which are estimated to be as high as $80/min, highlight the need for increasing OR efficiency.[4]

Proper surgical scheduling may decrease the risk of unexpectedly long OR days and result in enhanced OR efficiency. Surgical schedulers generate OR schedules, despite unfamiliarity with specific considerations inherent to the procedures that are being scheduled. Schedulers rely on institution metrics, such as the average surgical time for the last ten cases of a specific common procedural terminology (CPT) code, when predicting case duration and number of cases to be performed on a given OR day. However, schedulers are often unaware of patient complexity variations that may impact actual surgical duration.[5] All TKA procedures, regardless of complexity, share a single CPT code. Conversion TKA, which does not have a separate CPT code, has an increased mean operative time when compared to standard TKA (102.1 minutes versus 71.7 minutes); this time discrepancy must be considered when scheduling procedures.[6] Streamlined communication between surgeon and scheduler can more accurately reflect the OR time needed for a case, and potentially result in more cases being performed on a given OR day.

Delays in surgical execution have been associated with increased costs by up to 39%, and the mismatch between reimbursement and case complexity further requires enhanced OR efficiency.[7] Multiple patient factors have been associated with increased OR time in primary TKA, including younger age, male gender, increased ASA score, smoking, general anesthesia, and obesity.[8–10] However, previous studies have not evaluated surgery specific factors that influence surgical time, such as degree of knee deformity or presence of hardware, that may be accurately assessed by the operating surgeon but cannot be estimated by a large database. We anticipate that subjective surgeon assessment, influenced by multiple technical and anatomic patient factors, will accurately estimate increased OR time and subsequently promote efficient scheduling of both complex and routine surgical cases. This study evaluated the correlation between a single surgeon's pre-operative complexity scoring system and the resulting TKA procedure time, and secondarily the effect of the primary surgical assistant training level on surgical time. We hypothesized that a subjective orthopedic severity score will predict the intra-operative time required for performing a TKA. As a secondary endpoint, we hypothesized that surgery performed with a more inexperienced surgical trainee/assistant will increase surgical time.

Methods

This study qualified as a quality improvement initiative that did not meet the definition of human subjects' research and was exempt by the institutional review board. This was a retrospective review of one attending surgeon's patients at a single hospital within a large academic health system. All patients who underwent primary, unilateral TKA between February 2014 and November 2019 with an assigned, subjective pre-operative complexity score were included in this study.

A total of 674 patients were identified. A final cohort of 551 patients were included in the study. Patients were excluded due to: absence of a pre-operative complexity score (n = 99), inadequate anesthesia documentation (n = 1) and lack of tourniquet use during TKA (n = 23). All TKAs were performed through either the medial parapatellar or midvastus approach. The patient's age, gender, pre-operative body mass index (BMI), American Society of Anesthesiologists (ASA) status, and co-morbidities were documented in the pre-operative anesthesia note. The patient's type of anesthesia, spinal versus general endotracheal, was recorded in the operative anesthesia procedure note. The tourniquet time for each

procedure was recorded at the end of each procedure. At the time of TKA, the average patient age was 62.3 years (range, 17.2-86.3 years) and the average BMI was 31.9 (range, 15.6-53.3). Patient demographics are summarized in Table 1.

Tourniquet time, defined as the procedure time from incision to start of arthrotomy closure, was the primary dependent variable and was recorded for all TKAs by the operative surgeon in the final operative report. The criteria used for the pre-operative complexity score (Table 2) was determined and documented in the patient progress note by the operative surgeon at the pre-operative outpatient visit. Scores recorded as "1+" or "2+" in the pre-operative progress note were analyzed as scores of 2 and 3, respectively.

Descriptive statistics were calculated for all variables (frequencies, ranges, means, confidence intervals). Spearman's correlation was used to determine the correlation between complexity score and tourniquet time. Shapiro-Wilk normality test was used to determine whether parametric or non-parametric tests of hypothesis were appropriate for analysis of complexity score, surgical specific variables, and patient specific variables as a function of tourniquet time. For variables with two groups, either *t*-test or Mann-Whitney U test were used as appropriate depending on the normality test. For variables with more than two groups, either ANOVA or Kruskal-Wallis test were used as appropriate depending on the normality test. All data analysis was performed using STATA 16 software (StataCorp LLC, College Station, TX). The level of significance was set to $p \leq 0.05$.

Table 1. Summary of Patient Demographics

		n	%
Age (<65)		320	58
Gender (Male)		166	30
BMI			
	<30	223	40
	30-35	164	29
	35-40	86	15
	>40	78	14
Current Tobacco Use			
	no	443	80
ASA			
	1 or 2	318	57
	3 or 4	233	42
Spinal Anesthesia		411	74
General Anesthesia		140	26
DMII		92	16
Bleeding Disorder		7	1.2
HTN		343	62
COPD		27	4.9

BMI: Body mass index. *ASA:* American Society of Anesthesiology Physical Status. *DMII:* Diabetes mellitus type II. *HTN:* Hypertension. *COPD:* Chronic obstructive pulmonary disease.

Results

Pre-operative complexity score was positively correlated with tourniquet time ($p < 0.001$, rho = 0.196) (Figure 1). A complexity score of 1 had a mean tourniquet time of 59 minutes (CI, 56.8 to 61.2); a score of 2 had a mean time of 64.2 minutes (CI, 62.2 to 66.3); and a score 3 had a mean time of 76 minutes (CI, 66.6 to 85.4) ($p < 0.001$) (Figure 2). Other factors associated with increased tourniquet time were age ($p < 0.001$), male gender ($p < 0.001$), positive smoking status ($p = 0.004$), general anesthesia ($p = 0.021$), conversion TKA ($p = 0.011$), and obesity ($p = 0.048$) (Table 3).

Patient specific factors not associated with increased tourniquet time included: ASA status ($p = 0.352$), type 2 diabetes mellitus ($p = 0.573$), hypertension ($p = 0.477$), bleeding disorder ($p = 0.929$), and chronic obstructive pulmonary disease (COPD) ($p = 0.819$). The training level of the assistant during the surgical case also did not correlate with a longer tourniquet time ($p = 0.492$).

Discussion

Pre-operative, subjective surgical scoring can help predict surgical case duration in TKA. We found that pre-operative subjective complexity scoring by the operative surgeon correlated with primary TKA operative time. Surgeons incorporate patient and technical factors into OR time estimates, which are not readily recognized by surgical schedulers. Our study highlights the utility of a pre-operative complexity score as a method to streamline communication between the surgeon and surgical scheduler, accurately predict and communicate case length, and enhance OR efficiency.

Appropriate scheduling and accurate case length prediction optimize OR time utilization and minimize the number of long operative days. Surgeons have been shown to endure an average 51 minutes of wait time between cases (turn-over time) and up to 29.5 hours of turn-over time per month.[11] The evolution in OR scheduling from a first-come first-serve basis to historical averaging has maximized OR throughput and minimized resource underutilization.[12,13] Bartek et al. used machine learning to predict case-time duration and found increased accuracy with machine learning; prediction within 10% of actual case duration was seen in 39% of cases.[14] Wu et al. developed a predictive model for determining surgical time in revision total hip arthroplasty and found that that the operative surgeon's predicted surgical time improved the accuracy of the model to a greater extent than historical averages.[15] Additionally, Eijkeman's et al. performed a similar study in general surgery and showed that surgeons' estimates provided the most important predictors of total OR time.[16] However, there is evidence that historical averages of primary TKA are stronger predictors of surgical time than surgeon prediction.[17] Another issue is that CPT codes for a specific procedure are not all inclusive; CPT codes do not distinguish between the unequivocally more challenging conversion TKA from a standard TKA, but instead rely on complexity qualifiers

Table 2. Criteria for Patient Complexity Score

Score	Description
1	Anticipated operative time <60 minutes
2	Anticipated operative time 60-120 minutes due to technical challenges (obesity, deformity, prior hardware) or patient disease
3	Anticipated operative time >120 minutes due to severe technical challenges (deformity, prior hardware)

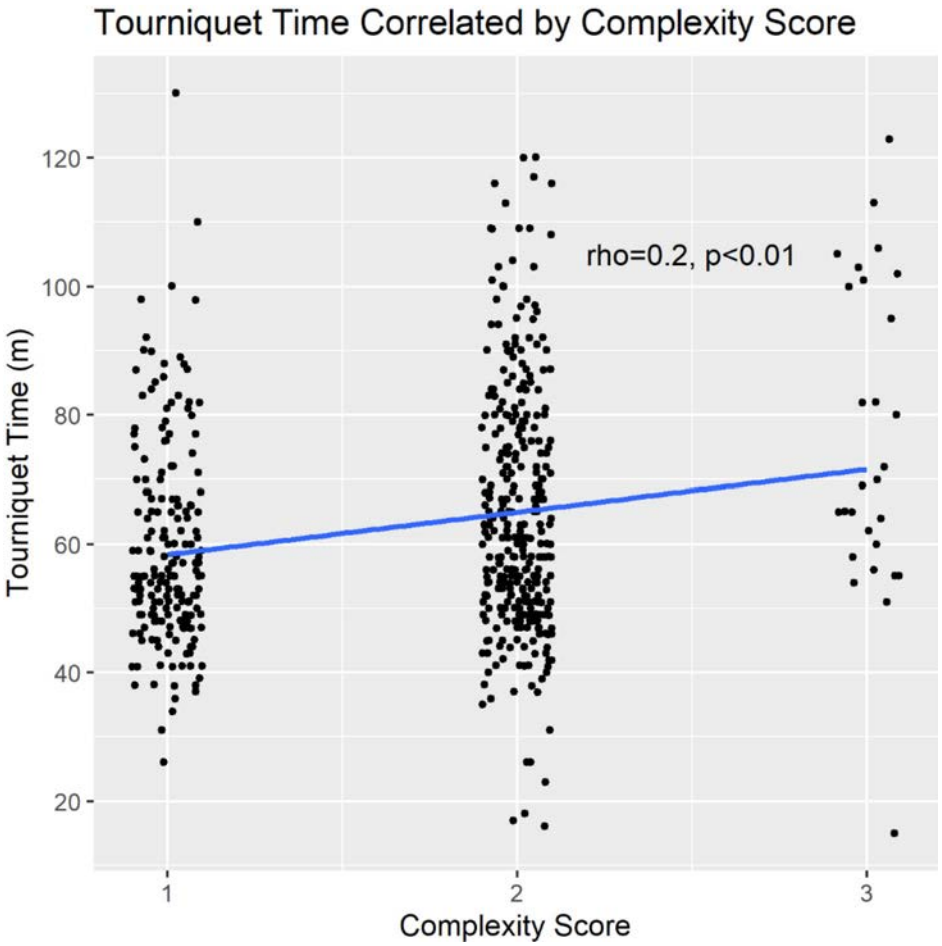

Figure 1. Tourniquet time in minutes as a function of complexity score. All individual patients are represented as an individual point. Spearman's coefficient (ρ, rho) and p value are displayed. Linear regression line displayed in blue.

that are non-specific.[18] Our study demonstrates that variation exists among patients undergoing the same procedure and may be anticipated by the operative surgeon. A pre-operative subjective score does not predict exact surgical times, but rather classifies surgeries into a relative time range based on specific case complexity.

The assigned complexity score and conversion TKA were the most significant predictors of operative duration when compared with other patient and operation-derived metrics. Additional predictors of operative duration were gender, age, smoking status, obesity, and anesthesia type, although these factors demonstrated a small effect size and did not account for surgery specific differences. Several studies have identified similar patient specific factors associated with OR time. These patient specific factors included younger age, male gender, smoking status, and obesity.[8–10] While the literature describes the relationship of these associated predictors of OR time, OR efficiency has been based on peri-operative and intra-operative improvements. Attarian et al. used inter and intra-operative workflow analysis to invoke peri-operative changes that led to a 29% increase in total joint arthroplasties per OR per day.[19] The standardized OR setup and parallel task completion were found to decrease total OR time per case.[20] Decreasing OR time per case continues to be at the focal point of improving OR efficiency, but accurately anticipating surgical case length may impact OR efficiency to a greater extent.

In academic hospitals, the training level of the assistant may result in greater OR time variation, as fellows, physician sssistants, and senior or junior residents regularly act as the primary assistant for a single surgeon. We anticipated that training level of the assistant would be a significant predictor of OR time, however, this did not hold true. Contrary to our

Table 3. Patient factors in relation to tourniquet time

		Tourniquet time (m)	95% CI min	95% CI max	p-value
Age					<0.001
	<65	66.2	64.1	68.4	
	>65	58.3	56.2	60.4	
Gender					<0.001
	Male	68.6	65.5	71.8	
	Female	60.5	58.8	62.2	
Complexity Score					<0.001
	1	59	56.8	61.2	
	2	64.2	62.2	66.3	
	3	76	66.6	85.4	
BMI					0.0479
	<30	61	58.5	63.5	
	30-35	62.3	59.7	64.8	
	35-40	65.5	61.6	69.5	
	>40	67.2	62.5	71.9	
Current Tobacco Use					0.004
	Yes	66.5	63.2	69.7	
	No	62.1	60.3	63.8	
ASA					0.352
	1 or 2	62.6	60.5	64.7	
	3 or 4	63.5	61.2	65.8	
Anesthesia					0.021
	Spinal	62	60.2	63.7	
	General	65.8	62.6	69	
DMII					0.573
	Yes	63.6	59.9	67.3	
	No	62.8	61.1	64.5	
Bleeding Disorder					0.929
	Yes	61.4	49.4	73.4	
	No	63	61.4	64.5	
HTN					0.477
	Yes	63.2	61.3	65.1	
	No	62.5	60	65.1	
COPD					0.819
	Yes	62.8	55.8	69.8	
	No	63	61.4	64.6	
Assistant					0.492
	Physician's Assistant	61.7	53.6	69.7	
	Resident	61.9	59.9	63.9	
	Fellow	64.4	61.9	66.9	
Conversion TKA					0.03
	Yes	74	63	85	
	No	62.6	61.1	64.2	

CI: Confidence interval. *BMI:* Body mass index. *ASA:* American Society of Anesthesiology Physical Status. *DMII:* Diabetes mellitus type II. *HTN:* Hypertension. *COPD:* Chronic obstructive pulmonary disease. *Conversion TKA:* Conversion total knee arthroplasty.

findings, the literature supports training level of the assistant as having a significant impact on OR time. In general surgery, seniority of surgical resident has been found to significantly reduce surgical time.[21,22] Yamaguchi et al. performed a NSQIP database study of lumbar spinal fusions and found that not only was orthopaedic resident involvement significantly associated with increased OR time, but also with length of stay and development of surgical site infection.[23] Orthopaedic surgical procedures with orthopaedic resident involvement are consistently associated with increased OR time throughout the literature.[24–26] An explanation of our finding is that the single surgeon in this study pre-operatively defined the role of the assistant based on their experience level preventing an excessive increase in procedure time. Pre-operatively setting expectations and having consistent help over a six-week clinical resident rotation allows for gradual independence and minimal variation in case length. If our study was expanded to include all arthroplasty surgeons within our institution, a positive correlation between resident involvement and OR time would most likely have been observed.

This study represents initial data derived from a novel method for estimating OR length and has inherent limitations. The criteria underlying the three-point scoring system, which relies on the experience of a single, arthroplasty fellowship trained attending, is not exact and limits the reproducibility of the score. However, the subjective nature of the score allows the operative surgeon to consider an array of unmeasurable factors that influence OR time, both intrinsic and extrinsic to the patient, as contributors to the score. A subjective score may be an all-encompassing and potentially most useful predictor of OR time. This may be even more apparent in revision TKA where surgical complexity is significantly greater. Further study of the complexity score in both primary and revision TKA may demonstrate more significance.

Furthermore, this scoring system has not been validated in the literature. We present this scoring system, utilized in practice to coordinate OR schedules, as a proof of concept with potential for more ubiquitous utilization. A subjective scoring system would necessitate individualization at the surgeon level; a single system may not be conducive to validation and widespread use. We allow a surgeon's experience to drive predicted surgical time, theoretically incorporating several patient factors that general assessment tools cannot.

Our findings demonstrate that a subjective complexity scoring system assigned by the operative surgeon is correlated with OR time. The results of this work suggest exploring OR utilization and efficiency by implementing the pre-operative complexity scoring system in the scheduling algorithm. Additionally, studies involving multiple arthroplasty attendings may determine if this system can be ubiquitously adopted. While initial implementation among other surgeons may be met with tepid enthusiasm, constant use, personalization of the scoring system, and working with a consistent team would improve the ability to estimate case duration. This study demonstrates that the operative surgeon can anticipate which cases will take longer, a resource that can be used to streamline pre-operative scheduling and enhance OR efficiency.

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Evaluating Dental Clearance Prior to Total Joint Replacement at the Philadelphia Veterans Affairs Medical Center: One Answer, Ten More Questions

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Introduction

Periprosthetic infection is a dreaded complication of total joint replacement, and surgeons should take all reasonable steps to avoid it. One possible source of infection is periodontal bacteria. Because of this possible association, some surgeons maintain that all patients should be evaluated and treated for periodontal disease and tooth decay before undergoing arthroplasty—so-called "dental clearance."

The practice of dental clearance is somewhat controversial, as the prevalence of periodontal disease and significant tooth decay might be too low to justify it. As noted in a recent review, "dental disease has long been anecdotally associated with increased periprosthetic joint infections, although case-control studies do not support this relationship."[1]

At the Philadelphia Veterans Affairs (VA) Medical Center, dental clearance has traditionally been part of the routine preoperative checklist. Still, requiring dental clearance has been complicated by the fact that many veterans are not eligible for full dental services. As such, clearance is performed on an *ad hoc* basis and surgery is not scheduled until clearance can be obtained.

We therefore sought to determine whether a more formal system is needed, by measuring the yield of these examinations: namely, the rate of discovering pathology. Our working hypothesis was that the yield from such examinations would be sufficiently high to justify their continuance.

Methods

A list of patients who underwent total knee or total hip arthroplasty in the calendar year 2019 was generated. The patient record for all such patients was then examined to determine the outcome of the dental clearance examination.

Notably, patients who had a dentist outside of the VA health system ("private dentists") were allowed to obtain clearance from their outside practitioner.

Patients were thus characterized as follows:

- Edentulous (those with no teeth were not subject to further screening)
- Cleared by VA dentist
- Periodontal disease/significant tooth decay discovered by VA dentist
- Non-periodontal disease discovered by VA dentist
- Ultimately cleared by private dentist (this includes both "no disease" and "disease treated by private dentist")

Results

There were 151 patients who underwent total knee or total hip arthroplasty in 2019. There were 43 patients ultimately cleared by their private dentist and 25 who had no teeth, leaving 83 patients to be locally evaluated by VA dentists.

Of these, 44 were cleared and 39 failed—38 with periodontal disease or significant tooth decay and one with leukoplakia.

Discussion

We discovered a staggeringly high rate of periodontal disease within our VA cohort. Excluding those who went to a private dentist or who were exempt from clearance because they had no teeth, 47% of patients failed their dental clearance examination. By contrast, a study conducted by Tokarski et al. in our same city and using similar methodology found that only 35 out of 300 patients (11.6%) failed.[2] (The chi-square statistic for this 35/300 vs. 39/83 discrepancy is 52.03; the associated p-value is <0.00001.)

Even if the 43 patients examined by their private dentist were folded back into our calculations (contributing an additional 5 positives and 38 negatives, as implied by the 11.6% prevalence rate found by the Tokarski et al. study), the resulting failure rate, 35%, is still higher than the failure rate reported by any study of the general population.

As a practical matter, the results of our pilot study confirm the need for continued dental clearance at our medical center. If nothing else, requiring dental clearance prior to total joint replacement and addressing dental problems preoperatively should reduce the need for dental procedures in the immediate aftermath of surgery. Given that transient bacteremia is associated with dental procedures and that there is persistent localized hyperemia around replaced joints, avoiding dental procedures in the first few years after surgery should minimize the risk of periprosthetic infection.

Further, while the results of a single year's cohort at a single institution are hardly definitive, they do serve as a springboard to further investigation. We propose that there are at least ten questions still unanswered by the results presented here:

1. Is there a more efficient way to screen for dental clearance outside of requiring all patients to see a dentist preoperatively?

It may be possible to identify low-risk patients through a series of questions, such that not all patients are required to see a dentist prior to surgery. For example, patients who avoid tobacco, visit their dentist regularly, and report no pain or sensitivity when chewing are less likely to have clinically significant periodontal disease and tooth decay. However, the specific questions needed to reliably identify low-risk patients (akin to the Ottawa Ankle Rules to obviate the need for radiographs in the Emergency Room) are yet to be defined.

2. Are the risks of periodontal disease and tooth decay fully mitigated by screening and treatment?

It is reasonable to assume that dental clearance reduces the risk of periprosthetic infection caused by oral disease. However, it is not known whether the overall infection rate (or more broadly, the overall complication rate) is markedly lower. For one, periodontal disease and tooth decay may reflect medical comorbidities, such as diabetes, that themselves pose significant postoperative risk. For another, longstanding periodontal disease may induce chronic low grade inflammation whose harmful effects are not mitigated completely by cleaning the mouth. Moreover, if any teeth are retained, the very processes that led to periodontal disease and tooth decay in the first place may affect these remaining teeth in the future. Finally, the presence of periodontal disease and tooth decay may reflect poor hygiene habits that will affect a total joint replacement. As such, we would be hesitant to operate on a patient who will not "take care" of his or her prosthesis, and periodontal disease and tooth decay may be a marker for this issue.

3. How do edentulous patients compare to the others?

The standard protocol, by which edentulous patients are *per se* cleared, assumes that "no teeth = no periodontal disease or tooth decay." The logic is simple: missing teeth cannot be diseased. However, if oral disease does indeed reflect comorbidities or behavioral/socioeconomic confounders, then removing teeth will no more reduce the risks of oral disease than abdominal liposuction will reduce the cardiac risks of belly fat.[3] In both cases, only the marker, not the underlying process, is being addressed. Whether edentulous patients should be considered in the "cleared" category or more aptly in the "treated periodontal disease and tooth decay" category is not known. A study of edentulous patients' outcomes might elucidate the role of active versus prior oral disease as a risk factor.

4. If the rate of periodontal disease is so much higher among veterans, does this suggest that veterans are so different from the general population that veteran outcome studies cannot inform general policies?

In 2002, a now classic paper by Moseley et al. studied the use of arthroscopy for arthritis and found that "sham surgery" was equally effective.[4] The pushback from orthopaedic surgeons was harsh.[5] A common form of rebuttal can be paraphrased as "well, that study was done at the VA." While that comment is factually accurate, what might be questioned is the implication. Namely, "well, that study was done at the VA and the patients there are so different that VA results have no meaning outside of the VA system." It is known that the veterans who seek care at the VA are more likely to be male, with greater comorbid conditions, a higher prevalence of smoking, and a lower socioeconomic status.[6] Outcomes studies explicitly account for these known confounders. At the very least, if the prevalence of periodontal disease is much higher among veterans, future VA outcomes studies (on any topic) might have to control for this variable as well.

5. What are the true costs of dental evaluation and treatment?

As noted, dental clearance at our medical center is performed on an *ad hoc* basis. Patients are sent out for clearance and treatment [see below] without formal budgetary authority. In order to obtain the formal authority to continue dental clearance officially, it would be necessary to document the costs and benefits. We know that nearly half of our patient cohort needs local clearance, and that within that cohort, nearly half fail their examination. What we do not know is the cost of getting those failed patients ready for surgery and the benefits of complications avoided. Although it would be ethically impermissible to conduct a randomized controlled trial in which some patients are not sent for clearance—a method that would define costs and benefits precisely—simple models can be created to estimate the number of periprosthetic infections that can be avoided with each clearance. With that, some estimate of the dollars saved by a clearance program can be estimated.

6. Is it possible to reduce the prevalence of periodontal disease and tooth decay by implementing an "upstream" intervention?

In the realm of cost-benefit analysis, one can further consider not only the two possible treatment paths (clearance versus no clearance), but also the costs and benefits of an option that includes an intervention. Ideally, periodontal disease would be

prevented from happening in the first place and not merely mitigated by late treatment. It is therefore reasonable to wonder what early interventions could be implemented. For example, if veterans, who are ordinarily not eligible for dental care, were allowed to undergo semi-annual cleanings as part of their benefit, would there be a measurable reduction in disease rate? The alternative hypothesis is also possible: patients' lack of participation in regular hygiene or continuation of at-risk behaviors such as smoking may overwhelm whatever benefit a periodic cleaning could offer. This question needs further investigation.

7. Should there be a national VA policy?

Currently, there is no national policy that provides dental coverage for most veterans. How the (approximately 170) VA Medical Centers in the United States (US) work around this is unknown. A national policy for determining who needs clearance, where that clearance is done, and what needed treatments are to be covered is essential, and advocating for such a policy requires robust data. At the bare minimum, a replication of the study here should be completed. Data collection on the various local discretionary policies—either providing clearance/treatment or denying surgery as well as associated outcomes—may provide additional helpful insight.

8. Is it proper to screen for periodontal disease if full treatment is not covered?

Under the current arrangement, all patients with clinically significant periodontal disease and tooth decay are offered extraction as the only option. Patients with dental coverage—or those willing and able to pay out of pocket—may avail themselves of restorative surgery, including fillings, crowns, and implants. In other words, the dental care currently offered to patients who fail dental clearance is not the gold standard. It bears repeating that Congress has not authorized the VA to provide gold standard dental care; this is not a local decision. At the same time, one could argue that because total joint replacement is authorized, and because giving state-of-the-art total joint replacement care requires state-of-the-art dental care, there is an implicit mandate for better dental coverage, at least for total joint replacement patients. This argument can be fleshed out with more refined cost-benefit analyses.

9. Will dental clearance or a similar rule cause disparate access to care by race or socioeconomic status?

Wang, Wong, and Humbyrd have shown that "clinical decision-making algorithms that set inflexible cutoffs with respect to BMI, HbA1c, and smoking status disproportionately discourage

performing lower extremity arthroplasty for non-Hispanic blacks and individuals of lower socioeconomic status."[7] It is not hard to imagine that applying such algorithms to dental status might have a similar effect, as the underlying prevalence of disease in those groups is likely to be higher. Thus, the question above is raised.

A few points must be kept in mind. A rule that disproportionately restricts access to care by certain groups is not necessarily discriminatory and not necessarily worthy of being discarded. Specifically, if the patients restricted are those at excessively high risk, then a restrictive rule can help ensure a lower rate of complications in those groups. Such a rule is "anti-discriminatory," one might say. Intent and optics matter less; what matters most is outcome. A rule that lowers complications is beneficent. Thus, the outcome of any rule of exclusion must be carefully examined, especially at the level of patient preferences (not system economics).

Of course, if there is a disparate impact caused by a rule, then there is an accompanying moral imperative to do everything that can be done to minimize risk in a healthy way. If HbA1c levels predict outcome, as they do, and if an HbA1c rule disproportionately affects certain populations, as it does as well, the best response is not to ignore the rule (for that puts patients at risk) and not to impose it blindly either, but to make every effort to normalize the HbA1c level in all patients.

10. Does the US, the richest country in the history of the world, offer its citizens (veterans and non-veterans alike) reasonable access to dental care?

This final question is asked rhetorically, as the data collected here do not speak directly to this point. Still, it is worth noting that the lack of routine dental care for veterans is consistent with what is found on the civilian side as well. Dental coverage is decidedly lacking in the US. Medicare does not cover routine dental care at all, and the majority of people on Medicare have no supplemental (private) dental coverage.[8] Medicaid covers dental care for children, but fewer than half of the states in the US elect to include dental services for adults. When Medicaid provides benefits, reimbursement and access are, by definition, at (low) Medicaid levels and this low payment hinders access. By contrast, other Western countries offer quite a bit more. For example, the British National Health Service includes (with a copay) preventative dental care as well as X-rays, fillings, and crowns.[9] In Canada, preventative dental care is not covered under Canadian Medicare, although dental surgery is; and 67% of Canadians have supplemental (private) insurance to cover dental care.[10] The French National Health Insurance (NHI) covers 70% of dental costs, though 95% of French patients have private insurance to cover the remaining balance.[11] And finally, under the German Statutory Health Insurance (SHI), preventative and basic dental care are fully covered.[12]

For historical reasons, in the US "a dentist is not just a special kind of doctor, but another profession entirely."[13,14] For better or worse, that's unlikely to change. Nonetheless, the findings here make it clear that oral health impacts overall health in general and musculoskeletal health in particular. As such, the divide must be bridged if we are to maximize overall wellbeing and human flourishing.

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Foot and Ankle

U·P·O·J

Prospective Evaluation of Opioid Consumption in Multimodal Analgesia following Isolated Hallux Valgus Correction or First MTP Joint Arthrodesis

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Introduction

Postoperative pain management following orthopaedic surgery is critical as the amount of pain is the most important element of patient satisfaction after surgery.[1] Prescription opioids are commonly used to manage postoperative pain. The number of opioid prescriptions has been increasing dramatically over the past few decades in the United States[2-4] approximately tripling from 76 million in 1991 to 207 million in 2013.[5]

The consequences of increased opioid prescriptions in the United States includes deaths due to opioid-related overdoses tripling, increasing from approximately 17,500 in 2006 to 42,200 in 2016.[6] Furthermore, the US Department of Health and Human Services declared the opioid crisis a national public health emergency in October 2017.[7] Orthopaedic surgeons are the fourth-highest group of opioid prescribers (7.7% of total prescriptions) among physicians based on private pharmacy prescription data in 2009 behind primary care physicians with 28.8%, followed by internists (14.6%), and dentists (8.0%). Multiple previous studies demonstrated that opioids were overprescribed after outpatient foot and ankle surgery.[5,8,9] However, it is difficult to establish a guideline prescribing opioids because of wide variability in both prescription and consumption of opioids based on procedure type and location. A multimodal pain protocol proposed by Michelson et al.[10] seems to have favorable outcomes including less adverse effects of opioid in patients undergoing ankle and hindfoot fusion. However, there is still limited evidence in foot and ankle surgery regarding the use of multimodal pain regimens. With a lack of evidence, the appropriate amount of opioid to prescribe following foot and ankle procedures is still controversial and unclear.

Hallux valgus is one of the most common forefoot deformities with a prevalence of 15.0% among people younger than 18 years and 26.3% for ages 18 to 65 years in a recent meta-analysis.[11] Operative correction of hallux valgus is one of the most common elective operative procedures in the field of foot and ankle. Hallux rigidus is another common forefoot disorder with an estimated incidence of one in 40 in patients aged over 50 years.[12] Though there are many different operative techniques, first metatarsophalangeal (MTP) joint arthrodesis is a well-established procedure in the treatment of severe hallux rigidus. As these two most common forefoot operative procedures can reflect a pattern of opioid consumption following elective forefoot surgery, we chose them for this study.

The purpose of this study was to prospectively investigate opioid consumption using a multimodal analgesia regimen after two common forefoot surgeries: isolated hallux valgus correction or first MTP joint arthrodesis.

Methods

This is a prospective cohort study conducted at a single academic institution. Approval from our institutional review board was obtained prior to the initiation of this study and written informed consent was obtained from all patients before the study. We prospectively enrolled 21 patients who underwent isolated hallux valgus correction or first MTP joint arthrodesis with three foot and ankle fellowship-trained orthopaedic foot and ankle surgeons between January 2019 and December 2019. Patients were included if their age was between 18 and 80 years old and underwent an outpatient operative procedure for hallux valgus correction with distal soft tissue procedure and proximal first metatarsal crescentic osteotomy or first MTP joint arthrodesis in isolation. Exclusion criteria were (1) Individuals outside of age range (2) current or chronic opioid therapy (3) Inability to take ibuprofen or acetaminophen (4) Patients underwent any additional operative procedures (5) Inpatient procedures, and (6) Revision surgery. Patients were instructed to take 5mg of oxycodone every 4 hours as needed for pain, and 600 mg of ibuprofen as well as 1,000 mg of acetaminophen every 8 hours regularly. As a part of multimodal analgesia, all patients had the same type of regional ankle block with 20 ml of 0.5% bupivacaine and 20 ml of 2% lidocaine under monitored anesthesia care (MAC). In this study,

only one type of opioid, 5mg of oxycodone, was prescribed to patients. The number of oxycodone pills that the patient consumed was recorded at postoperative followup at 1 week, 2 weeks, 4 weeks, 8 weeks, and 12 weeks. This was performed in person or through a phone interview by a member of the research team. Any medication including Aspirin for deep vein thrombosis prophylaxis was not considered as patients were allowed to ambulate in the postoperative shoe immediately after the surgery.

A chart review was performed to investigate patient demographic and operative data from the electronic medical record. Demographics included age, sex, body mass index (BMI), smoking, diabetes mellitus, rheumatoid arthritis, and other comorbidities. Operative data review confirmed anesthesia type, type of procedure, prescription type and amount written at the time of surgery, and perioperative nerve block type. Only those who underwent hallux valgus correction or first MTP joint arthrodesis in isolation without any concomitant procedures were included to evaluate opioid consumption following these two most common forefoot surgeries. Three subgroup analysis were performed in this study. The first subgroup analysis was to evaluate opioid consumption according to the prescription type: Only oxycodone was prescribed in group A (n = 10) while oxycodone as well as prescription strength ibuprofen and acetaminophen were prescribed in group B (n = 11). The prescription type between prescription strength and OTC was determined by patients' preferences. However, the same dosages of ibuprofen and acetaminophen were utilized for all patients in this study. The second subgroup analysis was performed based on the quantity of opioid prescription. Patients were stratified into two subgroups: $\leq$ 30 pills in group C (n = 10) while $>$ 30 pills in group D (n = 11). The third subgroup analysis was based upon the procedure type: Hallux valgus correction group (n = 10) vs first MTP joint arthrodesis group (n = 11).

A total of 21 patients were included in the final analysis. The mean age of the cohort was 55.8 $\pm$ 13.8 (range, 25 to 74) years. Most patients were female (85.7%). The proportion of hallux valgus correction and first MTP joint arthrodesis in this study was 38.1 % (8/21) and 61.9 % (13/21), respectively. Patient demographics data is shown in Table 1.

All statistical analyses were performed with SPSS software (version 21.0; IBM, Armonk, NY, USA). The Mann-Whitney test was used to compare continuous or continuously ranked data, including the amount of oxycodone consumption between subgroups. The chi-square test or Fisher exact test was used to access categorical values between the subgroups. Statistical significance was set as $p < 0.05$.

Results

The overall mean opioid consumption following isolated hallux valgus correction with distal soft tissue procedure and proximal first metatarsal crescentic osteotomy or first MTP joint arthrodesis at 12 weeks postoperatively was 16.2 $\pm$ 14.7 (median, 9; range, 0 to 51) pills while 37.3 $\pm$ 9.4 (median, 40; range, 28 to 60) pills were prescribed on the average. The amount of opioid consumption at each followup was shown in Table 2. Five out of 21 patients required oxycodone at 2 weeks postoperative followup, and two patients consumed oxycodone at 4 weeks postoperative followup. Only one patient consumed oxycodone at 12 weeks postoperative followup.

Patients were asked to complete a survey at each postoperative followup, which included pain score during activity and pain control satisfaction with our multimodal analgesia protocol. The average VAS pain score during activity including walking, climbing stairs, or housework at each postoperative followup is shown in Table 3. Regarding patients' satisfaction with pain control, 10 out of 21 patients were extremely satisfied, six patients were satisfied, three patients were neutral, and one patient was unsatisfied at 1 week postoperative followup. Beyond the postoperative 2 weeks followup, 100 % of patients were satisfied or extremely satisfied in pain control: 62.5 % were extremely satisfied, and 37.5 % were satisfied at 2 weeks; 60 % were extremely satisfied,

Table 1. Patient demographics

Characteristic	
Age, yr, mean $\pm$ SD (range)	55.8 $\pm$ 13.8 (25 to 74)
Sex, n, male/female	3/18
Body mass index (BMI), kg/m^2, mean $\pm$ SD (range)	26.6 $\pm$ 4.8 (20.7 to 36.8)
Active smoker, n, yes/no	1/20
Diabetes Mellitus, n, yes/no	0/21
Rheumatoid arthritis, n, yes/no	0/21

Table 2. The amount of opioid consumption at each postoperative followup

	1 week	2 weeks	4 weeks	8 weeks	12 weeks
Opioid consumption (Pills, mean $\pm$ SD (median, range))	12.8 $\pm$ 11.2 (median, 7; range: 0 to 32)	2.9 $\pm$ 6.6 (median, 0; range: 0 to 26)	0.7 $\pm$ 1.6 (median, 0; range: 0 to 5)	1.3 $\pm$ 3.6 (median, 0; range; 0 to 12)	0.7 $\pm$ 2.4 (median, 0; range: 0 to 8)

Table 3. The average VAS pain score at each postoperative followup

	1 week	2 weeks	4 weeks	8 weeks	12 weeks
VAS pain score (mean ± SD (median, range))	3.7 ± 2.5 (median, 2.8; range: 0 to 9.1)	2.8 ± 2.2 (median, 2.8; range: 0 to 7.4)	0.5 ± 0.6 (median, 0.5; range: 0 to 1.6)	0.7 ± 0.7 (median, 0.5; range; 0 to 2)	1.0 ± 1.1 (median, 0.5; range: 0 to 3.3)

and 40 % were satisfied at 4 weeks; 90.9 % were extremely satisfied, and 9.1 % were satisfied at 8 weeks; 76.9 % were extremely satisfied, and 23.1 % were satisfied at 12 weeks.

In our first subgroup analysis, significant lower opioid consumption was noted in group B when prescription-strength ibuprofen and acetaminophen were prescribed compared to group A when patients took over-the-counter (OTC) ibuprofen and acetaminophen: 24.1 ± 15.9 (median, 24.5; range, 0 to 51) pills in group A vs 9.0 ± 9.4 (median, 6; range, 0 to 31) pills in group B ($p = 0.036$) (Table 4). The second subgroup analysis was performed to evaluate the opioid consumption based on the amount of opioid prescription. Group C, which was given less than or equal to 30 pills, consumed 9.8 ± 9.4 (median, 7; range, 0 to 28) and group D, which was given greater than 30 pills, consumed 22.0 ± 16.6 (median, 21; range, 0 to 51). There was a trend showing higher opioid consumption in group D prescribed more oxycodone. However, it did not reach a significant difference between the two subgroups ($p = 0.099$) (Table 5). The group of hallux valgus correction consumed 15.8 ± 17.0 (median, 7; range, 0 to 51) while the group of first MTP joint arthrodesis consumed 16.5 ± 13.9 (median, 16; range, 0 to 40) . There was no significant difference in opioid consumption between the two subgroups ($p = 0.750$) (Table 6).

Discussion

Our findings in this study demonstrated that the average use of 5mg oxycodone was 16.2 pills while the average number of opioid prescribed was 37.3 pills after isolated hallux valgus correction or first MTP joint arthrodesis using our multimodal analgesia regimen. Only 43.4 % of the opioids that were prescribed were actually used, which is comparable with previous studies. Saini et al.[5] assessed opioid consumption patterns following outpatient orthopaedic foot and ankle procedures. They found that the utilization rate of opioid was only 50%: a median amount of opioid consumption was 20 pills whereas the median number of pills prescribed was 40. A similar opioid consumption pattern was noted following outpatient foot and ankle procedures in a prospective cohort study of Bhashyam et al.[13]. In their study, 37.4 pills were prescribed, and 18.9 pills were used on average representing 47.6% utilization. Recently, Rogero and colleagues[14] investigated postoperative opioid consumption in patients undergoing operative correction of hallux valgus, including chevron osteotomy, proximal osteotomy, soft tissue/proximal phalanx osteotomy, and first MTP joint arthrodesis. They included only patients who underwent hallux valgus correction and demonstrated that patients consumed a median of 27 pills. Compared with their study which included only forefoot surgeries, our result in opioid consumption was lower. This could be explained with the multimodal analgesia in the current study.

One of the main goals of multimodal postoperative analgesia is to improve patient recovery while reducing the need for opioids and decreasing side effects related to opioids. The multimodal protocol provides more effective pain control than a single intervention by blocking pain generation and perception through multiple pathways.[15-17] Inhibition of the perception of pain is provided by acetaminophen,

Table 4. Opioid consumption according to the prescription type of ibuprofen and acetaminophen

	Group A (n = 10)	Group B (n = 11)	P value
Opioid consumption (Pills, mean ± SD (median, range))	24.1 ± 15.9 (median, 24.5; range, 0 to 51)	9.0 ± 9.4 (median, 6; range, 0 to 31)	**0.036**

Table 5. Opioid consumption according to the amount of opioid prescribed

	Group C (n = 10)	Group D (n = 11)	P value
Opioid consumption (Pills, mean ± SD (median, range))	9.8 ± 9.4 (median, 7; range, 0 to 28)	22.0 ± 16.6 (median, 21; range, 0 to 51)	0.099

Table 6. Opioid consumption according to the procedure type

	Hallux valgus correction (n = 10)	First MTP joint arthrodesis (n = 11)	P value
Opioid consumption (Pills, mean ± SD (median, range))	15.8 ± 17.0 (median, 7; range, 0 to 51)	16.5 ± 13.9 (median, 16; range, 0 to 40)	0.750

opioids, and possibly COX-2 inhibitors within the central pathway including the brain. Inhibition of inflammation and pain generation is achieved through nonsteroidal anti-inflammatories, specifically the COX-2 inhibitors through the peripheral pathway.[10] Previous studies have demonstrated an opioid sparing effect of multimodal analgesia therapy following total hip replacement, total knee replacement, spine surgery, and shoulder rotator cuff repair.[18-21] However, there is limited literature regarding multimodal analgesia regimens in the field of foot and ankle. Michelson and colleagues[10] provided evidence that multimodal therapy reduced the length of stay for patients undergoing major hindfoot or ankle fusion surgery in their retrospective study. Further, a systematic review demonstrated that the use of multimodal analgesia in foot and ankle surgery provided superior pain relief, reduction in dependence on opioids, and decreased opioid-related side effects.[22] To our knowledge, there is no study investigating the effect of multimodal analgesia focusing on forefoot surgeries. We used a multimodal analgesia regimen as a part of the effort to decrease the amount of opioid that patients consume. With the regimen in the present study, patients were 100% satisfied or extremely satisfied in pain control beyond the postoperative 2 weeks followup representing that pain was controlled adequately in the postoperative period. Furthermore, the consumption of opioid was lower compared with previous studies.[5,13,14]

Nonsteroidal anti-inflammatory (NSAID) was used as a part of the multimodal analgesia regimen in this study although we acknowledge the concern that it can delay bony healing and possibly increase the risk of nonunion. NSAIDs may affect bony healing by inhibiting cyclooxygenase (COX) enzymes. Previous animal studies provided evidence that COX inhibition slows fracture healing.[23-25] However, the data on the effect of NSAIDs on human fracture healing are still controversial.[26-28] A systematic review investigating the effect of NSAID on acute phase fracture-healing reported that there was not enough clinical evidence to demonstrate patient detriment resulting from the short-term use of NSAIDs following fracture.[29] Recently, Hassan and Karlock[30] demonstrated that short-term use of oral ibuprofen and ketorolac in the postoperative period following elective foot and ankle surgeries was not associated with nonunion. Opioids are another option to manage postoperative pain, and emerging basic science has been showing that opioids may also inhibit bone formation.[31] Moreover, they are associated with adverse effects such as nausea, vomiting, respiratory depression, constipation, rising tolerance, and overdose related deaths. Drug overdoses resulted in 70,237 deaths in 2017. Among these, 47,600 (67.8%) involved opioids (14.9 per 100,000 population), representing a 12.0% rate increase from 2016.[32] In light of the opioid crisis in the United States, more alternative pain management is required and multimodal analgesia protocols including NSAIDs can contribute in reducing opioid consumption. Several studies reported that the use of NSAIDs reduced the side effects related to opioids as well as the need for higher opioid doses in postoperative pain management.[33,34]

One of the important findings in this study was the difference in opioid consumption according to the prescription type of ibuprofen and acetaminophen. Oxycodone was prescribed to all of the patients while prescription ibuprofen and acetaminophen were prescribed to 11 out of 21 patients. The remaining 10 patients took OTC ibuprofen and acetaminophen. All patients in this study were instructed to take oxycodone, ibuprofen and acetaminophen as our multimodal analgesia protocol. Significant lower opioid consumption was found when prescription ibuprofen and acetaminophen were prescribed ($P = 0.036$). This finding suggests that patients are more compliant when taking prescription medication rather than taking OTC medication.

The appropriate number of opioids required after various orthopedic operative procedures is unknown. Several previous reports demonstrated that the quantity of opioid prescribed is associated with higher patient-reported opioid consumption for postoperative pain management.[35-37] Howard and colleagues[36] demonstrated that one of the strongest predictors of opioid consumption was the amount of opioids prescribed to the patient. They estimated that 5.3 more pills were consumed for every 10 additional pills prescribed. Similarly, a trend showing higher opioid consumption in patients who had more opioid prescribed was noted in this study. However, there was no significant difference statistically in opioid consumption according to the amount of opioid prescription in a subgroup analysis in this study ($P = 0.099$). Moreover, no difference was found in opioid consumption based on the type of procedures in this study despite the general preconception that postoperative pain is worse in hallux valgus correction than in first MTP joint arthrodesis.

This study has several limitations. First, the sample size of the subgroup is small, thereby limiting the ability to demonstrate significant differences in postoperative opioid consumption between subgroups. Second, there is a possibility that patients may be taking another pain medication in addition to our multimodal analgesia regimen, which could affect the results of the opioid consumption. Third, we only investigated the amount of opioid consumption for one type of hallux valgus correction, distal soft tissue procedure and proximal first metatarsal crescentic osteotomy. However, Rogero et al.[14] reported that there was no significant difference in postoperative opioid consumption among four different hallux valgus correction procedures.

Despite these limitations, our findings provide beneficial information regarding opioid consumption following foot and ankle surgery, particularly forefoot procedures. One of the strengths in this study is that we only included isolated hallux valgus correction and first MTP joint arthrodesis without any additional procedures. Second, only one type of opioid, 5mg oxycodone, was used for the multimodal analgesia regimen, which allows us to evaluate the opioid consumption after these two procedures without distraction by the influences of different type and dose of opioid. Third, all of the patients in this study received the same type of anesthesia, regional ankle block under MAC. Given the lack of a specific guideline for opioid prescriptions in the field of foot and ankle, the results

in the current study may offer guidance on opioid prescribing for forefoot surgery using multimodal analgesia protocol.

Conclusion

Our cohort consumed 16.2 pills of 5mg oxycodone out of 37.3 pills prescribed after isolated hallux valgus correction or first MTP joint arthrodesis using our multimodal analgesia regimen, representing only 43.4% utilization. In addition, this study demonstrated the lower amount of opioid consumption in patients given alternative pain medication prescriptions (ibuprofen and acetaminophen) than in those who took the same medications over the counter. We recommend a multimodal analgesia protocol after forefoot surgeries to manage postoperative pain and decrease the amount of opioid prescribed and taken.

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Comparison of Four Different Fixation Strategies for Midfoot Arthrodesis: A Retrospective Comparative Study

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Introduction

The midfoot joints transfer load from the hindfoot to the forefoot. This transfer occurs in every step and is particularly important during the push-off phase of the gait cycle making stability of the midfoot critical for daily of activity.[10] Any pathology affecting these joints such as degenerative arthritis, inflammatory arthritis, or trauma can lead to midfoot arch collapse, planovalgus deformity, and medial instability.[21] Further, dysfunction of the midfoot is associated with chronic pain, affects mechanics and results in decreased quality of life.

Nonoperative treatment for midfoot arthritis includes shoe modification, activity modification, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroid injections, and orthotics and bracing, such as the University of California Berkeley Lab (UCBL) brace.[15,21] Operative intervention is considered if these conservative management fail. Arthrodesis of the arthritic midfoot joints is the mainstay of operative treatments. The primary goal of arthrodesis is achieving stable osseous union with correction of deformity if present. There have been several reports delineating the risk factors for nonunion, which include smoking, diabetes mellitus, poor compliance with weightbearing instructions, and osteoporosis.[5,25] Besides these risk factors associated with patients, meticulous operative technique with proper implant selection for adequate stability is critical for the success of midfoot arthrodesis. Various implant constructs exist for midfoot arthrodesis including compression plates and screws, crossed screws, and staples. Although previous studies have tried to determine the superiority of one fixation construct over another, there is no consensus regarding the optimal implant fixation strategy for midfoot arthrodesis.[3,4,9,14,22,23]

The purpose of this study was to compare the union rate of midfoot arthrodesis and the complication rate using four different fixation implant constructs: staple fixation, compression plate fixation, compression plate with lag screw fixation, and compression screw fixation. Risk factors for nonunion were also investigated.

Methods

Institutional review board approval was obtained prior to the initiation of this study. The Current Procedural Terminology (CPT) codes 28730 and 28740 were used to identify patients who underwent single or multiple midfoot joint arthrodesis between January 2014 and May 2019 at a single academic institution. The midfoot joints included tarsometatarsal (TMT), medial naviculocuneiform (NC), middle NC, lateral NC, and intercuneiform joints. The inclusion criteria were (1) age older than 18 years, (2) arthrodesis of a single or multiple midfoot joints arthrodesis using one of the fixation constructs among the following: a staple fixation, compression plate fixation, compression plate with lag screw fixation, and compression screw fixation, and (3) followup until union or nonunion could be determined. Exclusion criteria were (1) revision surgery, (2) Charcot arthropathy, (3) lack of complete records, and (4) arthrodesis via a different fixation method than the inclusion criteria.

A retrospective chart review was performed. Characteristics that were investigated included age, sex, body mass index (BMI), smoking, comorbidities such as diabetes mellitus and rheumatoid arthritis, history of steroid injection prior to surgery, etiology of arthritis, number of joints fixed, type of fixation implant, use of bone graft, time to union, time to full weightbearing, and any complication including nonunion, wound infection, and hardware irritation.

Postoperative radiographs were used to assess the bony healing of the operative midfoot joints. Delayed union was defined as an absence of fusion by 12 weeks postoperative followup, which has been previously described.[18] Although the definition of nonunion for midfoot arthrodesis is poorly defined in the literature, lack of radiographic union by 6 months without progression on sequential radiographs was used in this study.[4,22] The first postoperative weightbearing radiographs taken between 6 weeks and 12 weeks postoperative followup were utilized to evaluate the alignment of the operatively corrected foot[17,19] The following criteria were used to assess alignment: (1) Anteroposterior (AP) Radiograph: the alignment

between the medial edge of the second metatarsal and the medial edge of the middle cuneiform bone, (2) Internal Oblique Radiograph: the alignment between the medial border of the third metatarsal and the medial border of lateral cuneiform and between the medial border of the fourth metatarsal and the medial border of the cuboid bone, (3) Lateral Radiograph: the talo-first metatarsal angle (Meary's angle) was measured as the angle formed by a line originating from the center of the body of the talus, bisecting the talar neck and head, and the line through the longitudinal axis of the first metatarsal. Lateral foot alignment was considered as anatomic if the Meary's angle was between 4 degrees and -4 degrees. If any view of postoperative weightbearing radiographic parameters was not anatomic, it was considered to be nonanatomic alignment.

The primary outcomes in this study were radiographic evidence of complete union in patients who underwent midfoot joint arthrodesis and any postoperative complication including wound problem, hardware irritation, and infection. All of these outcomes were compared among four different types of fixation constructs. The secondary outcome was identifying risk factors of nonunion.

A total of 95 patients (99 feet) were included in the final analysis. The mean age of the cohort was 60.5 ± 10.0 (range, 25 to 80) years. Overall BMI was 30.0 ± 6.1 (range, 19.8 to 48.7) on the average. There were 17 (17.2%) males and 82 (82.8%) females. A total of 240 midfoot joints were treated: 25 (10.4%) joints with a staple fixation, 19 (7.9%) joints with compression plate fixation, 90 (37.5%) joints with compression plate with lag screw fixation, and 106 (44.2%) joints with compression screw fixation. Patient demographics data are shown in Table 1. The mean followup period was 78.4 ± 62.9 weeks (range, 6.0 to 269.4). The average time to complete union for the operative sites was 10.8 ± 3.8 weeks (range, 6.0 to 40.0). Patients were initially managed in a splint and then cast followed by a CAM boot. On average, patients were allowed to wean out of the boot and initiate full weight bearing at 11.4 ± 2.8 weeks (range, 6.0 to 19.57).

All procedures were performed by one of three foot and ankle fellowship trained surgeons at a single academic institution. They were completed in the supine position and under tourniquet control. The midfoot arthrodesis was performed with a single or dual incision depending on the affected joints. If arthrodesis involved 1st TMT joint or medial NC joint, a medial incision in the interval between the anterior tibialis tendon and the posterior tibialis tendon was used. If arthrodesis involved 2nd TMT joint, 3rd TMT joint, or middle/lateral NC joint, a dorsal incision was made. For all joints, sharp dissection was carried down through the joint capsule. Any osteophyte or bony spur was excised using a rongeur. Meticulous articular surfaces preparation was performed using osteotomes, curettes, and sometimes resurfacing burs. Each joint was irrigated and drilled using multiple

Table 1. Patient demographic data

Characteristic	Value
Patients, n	95
Feet, n	99
Sex, n (%)	
Male	17 (17.2)
Female	82 (82.8)
Age, years	60.5 ± 10.0 (25–80)
Body Mass Index (BMI), kg/m^2	
Overall	30.0 ± 6.1 (19.8–48.7)
≥ 30, n (%)	38 (38.4)
< 30, n (%)	61 (61.6)
Diabetes Mellitus, n (%)	13 (13.1)
Smoking, n (%)	
Current	6 (6.1)
Never	68 (68.7)
Former	25 (25.3)
Rheumatoid Arthritis, n (%)	5 (5.1)
Steroid injection prior to Surgery, n (%)	12 (12.1)
Etiology of arthritis, n (%)	
Degenerative	75 (75.8)
Posttraumatic	22 (22.2)
Inflammatory	2 (2.0)
Bone graft, n (%)	68 (68.7)
Postoperative midfoot anatomic alignment, n (%)	
Yes	88 (88.9)
No	11(11.1)
Mean followup, weeks	78.4 ± 62.9 (6.0–269.4)

passes of a drill bit. The decision to use bone graft was at the operating surgeon's discretion. However, it was used if defects or gaps were observed intraoperatively. The choice in types of bone graft was based on the surgeon's preference. Recombinant human platelet derived growth factor-BB with beta-tricalcium phosphate (rhPDGF-BB/β -TCP) (Augment; Wright medical, Memphis, Tennessee) or highly porous β -TCP (Vitoss; Stryker, Kalamazoo, Michigan) with bone marrow aspirate concentrate (BMAC) (Harvest Technologies, Plymouth, MA) were used in this study for bone graft. The joints were manipulated to achieve plantigrade alignment of the foot. Then, one of four fixation constructs were utilized with the choice of implant based on the surgeon's preference: staple fixation, compression plate fixation, compression plate with lag screw fixation, and compression screw fixation. The data associated with fixation implants are shown in Table 2. Postoperatively, a well-padded short leg splint was applied. It was converted to a short leg non-weightbearing cast at 2 weeks postoperatively. Nonweightbearing immobilization was maintained for 6 weeks from the day of surgery. The cast was removed, and a controlled ankle movement (CAM) boot was applied at 6 weeks postoperative followup visit. The patients were advised to bear weight in the CAM boot as tolerated. Radiographic evaluation of the union was performed between 6 weeks and 12 weeks postoperative followup visit. If there were any clinical symptoms such as pain or swelling, or radiological evidence of nonunion, then a further period of non-weightbearing was recommended.

All statistical analyses were performed with SPSS software (version 21.0; IBM, Armonk, NY, USA). Data are presented as the mean and standard deviation. Continuous variables such as age and overall BMI were compared using one-way analysis of variance (ANOVA), and categorical variables were compared using chi-square test or Fisher exact test. Bonferroni correction method post hoc analysis was performed after chi-square test to investigate which fixation construct had a statistical significance in terms of the nonunion rate (Table 3); a significant difference was found only in compression screw alone fixation group regarding the nonunion rate. All variables which can affect the nonunion rate was

Table 2. Data associated with four different fixation constructs

Characteristic	Staple	Compression plate	Compression plate with lag screw	Compression screw	P Value
Joints, n (%),					
Overall	25 (10.4)	19 (7.9)	90 (37.5)	106 (44.2)	-
1st TMT	3	1	36	12	
2nd TMT	9	10	26	43	
3rd TMT	8	7	22	39	
Medial NC	2	1	6	9	
Middle NC	1	0	0	0	
Lateral NC	2	0	0	0	
Intercuneiform	0	0	0	3	
Female, n (%)	21 (84.0)	15 (78.9)	78 (86.7)	86 (81.1)	0.715
Age, years, mean ± SD (range)	59.5 ± 15.3 (25–76)	59.6 ± 11.8 (28–80)	62.1 ± 9.6 (30-80)	59.8 ± 9.5 (25–78)	0.415
BMI, kg/m^2, mean ± SD (range)	27.1 ± 4.6 (20.5-35.3)	30.0 ± 7.0 (21–40.9)	29.3 ± 5.2 (19.8–48.7)	30.3 ± 6.8 (19.8–48.7)	0.108
Overall					
≥ 30, n (%)	5 (20.0)	10 (52.6)	28 (31.1)	39 (36.8)	
< 30, n (%)	20 (80.0)	9 (47.4)	62 (68.9)	67 (63.2)	0.121
Laterality, n (%)					0.967
Right	13 (52.0)	9 (47.4)	42 (46.7)	52 (49.1)	
Left	12 (48.0)	10 (52.6)	48 (53.3)	54 (50.9)	
Diabetes Mellitus, n (%)	0 (0.0)	6 (31.6)	8 (8.9)	12 (11.3)	**0.008**
Smoking, n (%)					0.218
Current	0 (0.0)	0 (0.0)	4 (4.4)	10 (9.4)	
Never	16 (64.0)	16 (84.2)	65 (72.3)	69 (65.1)	
Former	9 (36.0)	3 (15.8)	21 (23.3)	27 (25.5)	
Rheumatoid Arthritis, n (%)	0 (0.0)	0 (0.0)	4 (4.4)	10 (9.4)	0.136
Steroid injection prior to Surgery, n (%)	2 (8.0)	8 (42.1)	6 (6.7)	8 (7.5)	**< 0.001**
Etiology of arthritis, n (%)					0.404
Degenerative	16 (64.0)	17 (89.5)	68 (75.6)	80 (75.5)	
Posttraumatic	9 (36.0)	2 (10.5)	20 (22.2)	22 (20.8)	
Inflammatory	0 (0.0)	0 (0.0)	2 (2.2)	4 (3.8)	
Bone graft, n (%)	19 (76.0)	5 (26.3)	82 (91.1)	64 (60.4)	**< 0.001**
Postoperative midfoot anatomic alignment, n (%)	0 (0.0)	6 (31.6)	5 (5.6)	16 (15.1)	**0.001**

investigated and were reported with Odds Ratio (OR) with 95% Confidence Interval (CI). Only variables with $p < 0.05$ were included in a multivariable logistic regression analysis to identify independent predictors of nonunion following midfoot arthrodesis. The level of statistical significance was set as $p < 0.05$.

Results

Overall bony union was achieved in 86 out of 99 (86.9%) patients in this study, which included 218 out of 240 (90.8%) midfoot joints. Among 22 midfoot joints which developed nonunion, five cases (22.7%) developed in 1st TMT joint; eight cases (36.4%) in 2nd TMT joint; seven cases (31.8%) in 3rd TMT joint; two cases (9.1%) in medial NC joint, respectively. In terms of the type of fixation construct, 15.8% of nonunion (3/19) with compression plate fixation; 3.3% (3/90) with compression plate with lag screw fixation; 15.1% (16/106) with compression screw fixation; 0.0% (0/25) with staple fixation was shown, respectively. We found a significant difference in the nonunion rate according to the type of fixation construct ($p = 0.011$) (Table 3). Five patients with eight midfoot joints required revision surgery due to symptomatic nonunion while the remaining patients were asymptomatic, and no further procedure was required.

Besides the complication of nonunion, another 21 postoperative complications were reported: six patients developed superficial wound infection with dehiscence, two patients had deep wound infection, 11 patients had hardware irritation, and two patients developed hardware backing out or breakage without irritation. There was no significant difference in the complication rate according to the type of fixation construct ($p = 0.237$) (Table 3). All patients with superficial wound infections were managed with oral antibiotics without need for further procedures while two patients with deep wound infections underwent irrigation and debridement with hardware removal. One of the deep infection cases was managed with vacuum assisted wound closure therapy. All 11 patients who had hardware irritation symptoms underwent a hardware removal procedure.

We also investigated risk factors of nonunion following midfoot arthrodesis. They were classified into patient-related factors and surgeon-related factors. Patient-related factors included sex, age, BMI, smoking, comorbidities such as diabetes mellitus and rheumatoid arthritis, history of steroid injection prior to surgery in the affected midfoot joints, and etiology of arthritis. We stratified patients into subgroups for several variables: ≥ 65 years and < 65 years in age; ≥ 30 and < 30 in BMI. Surgeon-related factors included the type of fixation construct, the use of bone graft, and the postoperative anatomic alignment of the foot. Variables in each category were investigated with OR with 95% CI. Variables which had a significant difference with $p < 0.05$ in the nonunion rate were included in the multivariable logistic regression analysis: Diabetic Mellitus ($p = 0.001$; OR: 4.888 [95% CI: 1.775, 13.461]), history of steroid injection prior to surgery ($p = 0.037$; OR: 3.080 [95% CI: 1.023, 9.278]), bone graft ($p = 0.006$; OR: 0.032 [95% CI: 0.124, 0.737]), postoperative midfoot anatomic alignment ($p = 0.013$; OR: 0.284 [95% CI: 0.100, 0.805]), and type of fixation construct ($p = 0.009$). Post hoc analysis (Bonferroni correction method) was completed to investigate which fixation construct showed a statistically significant difference regarding the nonunion rate among four different types of fixation constructs. The compression screw alone fixation construct was noted as the only group which reached a statistical significance in the nonunion rate. Our multivariable logistic regression analysis identified diabetes mellitus, the type of fixation construct (compression screw alone), lack of adjuvant bone graft, and the postoperative nonanatomic alignment as independent predictors of nonunion following midfoot arthrodesis (Table 4).

Discussion

Our results demonstrated that overall union rate of midfoot arthrodesis was 86.9% (86/99) of patients and 90.8% (218/240) of joints, which are comparable with previous studies.[9,10,15,18] Among four different fixation constructs for midfoot arthrodesis, the compression screw alone construct showed a significantly higher nonunion rate than other fixation constructs. It was identified as one of independent risk factors of nonunion through our multivariable logistic regression analysis. In addition to the fixation construct using compression screws alone, diabetes mellitus, lack of adjuvant bone graft, and postoperative nonanatomic alignment played a role as independent predictors of nonunion following midfoot arthrodesis.

Nonunion is one of the major complications of foot and ankle arthrodesis and occurs in approximately 12% (range, 3

Table 3. The rates of nonunion and postoperative complication in each fixation construct group

Characteristic	Staple	Compression plate	Compression plate with lag screw	Compression screw	P Value
Nonunion, n (%)	0/25 (0.0)	3/19 (15.8)	3/90 (3.3)	16/106 (15.1)	0.011
Complication, n (%)					
Overall	2 (8.0)	4 (21.1)	8 (8.9)	7 (6.6)	0.237
Hardware irritation	0 (0.0)	2 (50.0)	6 (75.0)	3 (42.9)	
Hardware loosening or breakage	1 (50.0)	1 (25.0)	0 (0.0)	0 (0.0)	
Superficial wound Infection w/ dehiscence	1 (50.0)	1 (25.0)	1 (12.5)	3 (42.9)	
Deep wound infection	0 (0.0)	0 (0.0)	1 (12.5)	1 (14.2)	

Table 4. Multivariable logistic regression analysis for risk factors of nonunion following midfoot arthrodesis

Characteristic	P Value	OR* (95% CI*)
Patients related risk factors		
Diabetes Mellitus (reference: yes)	0.002	0.179 (.059, .542)
Steroid injection prior to surgery	0.718	1.314 (.298, 5.799)
Surgeon related risk factors		
Type of fixation construct (Compression screw alone) (reference: other fixation constructs)	0.026	1.789 (1.071, 2.978)
Bone graft (reference: use)	0.034	2.803 (1.081, 7.268)
Postoperative midfoot nonanatomic alignment (reference: anatomic)	0.017	3.937 (1.278, 12.126)

OR*: Odds Ratio, CI*: Confidence Interval

to 23%) of foot and ankle fusions.[7,8,11,24,27] Specifically, the rate of nonunion following midfoot arthrodesis has been reported variously from 2.0% to 12%.[9,13,15,18,22] As nonunion of midfoot arthrodesis may not result in satisfactory outcomes in the long term, every effort should be made to mitigate or avoid risk factors for nonunion.[18] A recent current concepts review of nonunion risk factors in foot and ankle arthrodesis surgery found fair evidence to support smoking, diabetes mellitus, and soft tissue injury as risk factors.[26] Variables such as higher BMI, rheumatoid arthritis, etiology of arthritis, or steroid injection prior to surgery may affect the rate of nonunion after midfoot arthrodesis. However, there is currently not sufficient evidence to support their association with nonunion. There have been just a few clinical studies reporting the predictors of nonunion.[15,18,24,25,28] Nemec et al.[18] investigated outcomes following midfoot arthrodesis for 95 cases of primary arthritis. One of their findings suggested that a higher BMI was associated with inferior clinical results leading to more complications and less improvement in AOFAS scores. In this study, we stratified patients into two subgroups based on their BMI ($\geq$ 30 vs $<$ 30) but the result did not reach statistical significance in the rate of nonunion: 12.2% (10/82) in $\geq$ 30 group vs 7.6% (12/158) in $<$ 30 group, $p = 0.241$. Patients who had a steroid injection prior to the index surgery had a significantly higher nonunion rate ($p = 0.037$, OR: 3.080, [95% CI: 1.023, 9.278]). However, it was not identified as an independent predictor of nonunion when it was included in the multivariable regression analysis.

There is currently insufficient data in the literature to show difference in outcomes following midfoot arthrodesis according to the etiology of arthritis. Several studies only reported outcomes of midfoot arthrodesis in patients of primary degenerative arthritis. Therefore, the association between the etiology of midfoot arthritis and outcomes following arthrodesis procedure were not determined.[13,18] On the other hand, Mann and his colleagues included all types of arthritis in their study and investigated clinical outcomes of mid-tarsal and TMT arthrodesis surgery. They included 17 patients of posttraumatic arthritis, 21 patients of primary degenerative arthritis, and two patients of inflammatory arthritis. During the followup period, a total of three nonunion occurred: two cases with posttraumatic arthritis and the other case with primary degenerative arthritis.[15] Similar to Mann's study, we classified the etiology of arthritis into three categories. Although our study showed a trend indicating a higher nonunion rate in posttraumatic arthritis than other etiologies, it did not reach statistical significance ($p = 0.069$).

There is a paucity of information regarding surgeon-related risk factors for nonunion in the literature. The type of fixation implant, the use of bone graft, and the postoperative midfoot alignment can be considered as surgeon or operation-related risk factors of nonunion. Many biomechanical studies have tried to determine the most stable fixation implant strategy for midfoot arthrodesis in an effort to decrease the nonunion rate. The stability of different fixation implants and different fixation configurations for midfoot arthrodesis have been compared in previous studies including compression screws, compression plates with or without screws, H-locking plates, staples, or even external fixators.[3,14,16,20,23,29] Besides biomechanical studies, several clinical studies also examined the nonunion rate according to the fixation methods for midfoot arthrodesis.[2,10,22] However, there is still little evidence in terms of the superiority of one fixation device over the others. Buda et al.[2] compared the nonunion rate among three different hardware configurations: Cross-screw fixation, isolated plate fixation, and plate with compression screw fixation. The authors reported that the use of isolated plate fixation was significantly associated with delayed wound healing as well as with nonunion in their study. Gougoulias and Lampridis[10] reported that plates provided better initial stability allowing earlier mobilization, and compression screw fixation might be problematic in osteoporotic bone. The rates of nonunion were similar between screws alone and plate with screws without a significant difference. However, total sample size was only 30 patients in their study, and the authors stated that their study was underpowered to detect differences in outcomes. Additionally, they did not advocate the use of staples as they failed to have adequate control of compression and stability. On the contrary, Schipper and his colleagues[22] advocated the use of staples for midfoot and hindfoot arthrodesis. A high union rate of 95.3% (142/149) of joints was shown in their study. They also reported no significant difference in the union rate between a staple construct and a staple with a compression screw: 95.1% (98/103) and 95.7% (44/46), respectively.

In our study, compression screw fixation alone showed a significantly higher nonunion rate than the other three fixation constructs. In addition, this study revealed that staple fixation

construct had 100% union rate with a low complication rate. This finding failed to reach statistical significance due to the small sample size as our institution started using staples for midfoot arthrodesis in 2017. Despite this, staple fixation has many advantages such as shorter operation time and lower cost than anatomic locked plate and screw implant.[22] Previous biomechanical studies showed nitinol staples created a larger contact area and more contact force, and maintain time zero contact force and contact area after mechanical loading, unlike a compression plate and screw construct.[1,12] Staples can be considered as a viable alternative to the traditional fixation configuration such as plates or screws.

Various types of bone graft have been used to maximize the union rate in foot and ankle arthrodesis procedures. DiGiovanni and his colleagues[6] demonstrated the substantial value of using bone graft in hindfoot and ankle arthrodesis: Autograft or rhPDGF-BB/β -TCP was used in their study. About 80% of joints with adequate graft fill, which was defined as ≥ 50% of the cross-sectional area of the fusion site on computed tomography (CT), achieved successful fusion. No significant difference was noted based on type of graft material, graft harvest site, joint type, and number of joints fused in their study. Buda et al.[2] evaluated the effect of autologous bone grafting on TMT joint fusion and reported significant reduction in nonunion rate when they used bone graft. The result in our study also confirmed the positive effect of bone graft on the union rate in midfoot arthrodesis: Highly porous β -TCP with BMAC or rhPDGF-BB/β -TCP bone graft was used in our study. The nonunion rate was significantly reduced when bone graft was used for midfoot arthrodesis.

Plantigrade foot position and anatomic alignment following midfoot arthrodesis are essential to transfer the loading properly from hindfoot to forefoot. Mann et al.[15] demonstrated that realignment of the foot in midfoot arthrodesis can lead to a satisfactory result for posttraumatic arthritis as well as primary degenerative arthritis. Buda et al.[2] showed that nonanatomic alignment following TMT arthrodesis was a significant predictor of nonunion in their multivariable logistic regression analysis. Furthermore, several studies reported sesamoid problems after midfoot arthrodesis procedure due to nonanatomic alignment.[13,15] Sesamoid pain following midfoot arthrodesis may come from the loss of flexibility of the first ray. It also can be explained by inappropriate plantarflexion of the first ray following the surgery. Thus, anatomic realignment of the foot should be considered as a critical factor to achieve better outcomes following midfoot arthrodesis. In this study, postoperative nonanatomic alignment was identified as an independent risk factor of nonunion. Nonanatomic alignment had about 4-fold increase in nonunion. (OR: 3.937, [95% CI: 1.278, 12.126]).

There are several limitations to our study. First, there is an inherent risk of bias as it was a retrospective study. The completeness and validity of the data relied on the content of the medical record. Second, the determination of nonunion was based on plain radiograph and chart review rather than CT imaging which has been considered to be the gold standard for assessing nonunion. Third, our study did not investigate clinical functional scores. Fourth, we did not exclude patients with additional procedures at the same time of midfoot arthrodesis procedure. This may have changed the period of non-weightbearing postoperatively which could affect the outcome of nonunion. Lastly, the choice of implant fixation construct was decided by the surgeon's preference and was not randomized.

Conclusion

To the best of our knowledge, this study is the largest single-center report on midfoot arthrodesis. The rate of nonunion following midfoot arthrodesis among four different commonly used fixation constructs was compared and risk factors for nonunion were investigated revealing that diabetes mellitus, compression screw fixation alone, lack of adjuvant bone graft, and postoperative nonanatomic alignment are independent predictors of nonunion following midfoot arthrodesis. Identification of these independent predictors for nonunion provides guidance for orthopaedic surgeons to improve fusion rates in midfoot arthrodesis.

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Oncology

MALPs Promote Osteoclastogenesis in Bone Remodeling and Pathologic Bone Loss

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Disclosures

None

Introduction

Bone is maintained by coupled activities of bone-forming osteoblasts/osteocytes and bone-resorbing osteoclasts. Osteoclast differentiation predominantly depends on the signal from RANKL (encoded by *Tnfsf11* gene) and is modulated by other cytokines and growth factors. It is well known that osteogenic cells, particularly osteocytes, support osteoclastogenesis. Osteogenic cells are derived from mesenchymal stem cells (MSCs), which also give rise to marrow adipocytes. Using single cell RNA-sequencing (scRNA-seq), we recently discovered a new bone marrow cell population, marrow adipogenic lineage precursors (MALPs), which functions to maintain vessel structure and inhibit bone formation[1]. Our scRNA-seq datasets also contained many hematopoietic cells, including osteoclasts. To our surprise, our in-silico data indicated that MALPs, but not osteoblasts or osteocytes, are the most supportive cells for osteoclast formation. To validate this finding, we constructed adipocyte-specific *Tnfsf11 CKO* mice to investigate the role of MALP-derived RANKL in regulating bone remodeling under physiological and pathological conditions.

Methods

Animals

All procedures were approved by our institution's Animal Care and Use Committee. *Col2-Cre Tomato* (*Col2/Td*) mice, *Adipoq-Cre Rosa-tdTomato 2.3kbCol1-GFP* (*Adipoq/Td/Col1-GFP*) mice, *Adipoq-Cre* $Tnfsf11^{flox/flox}$ (*RANKL* CKO^{Adipoq}) mice and their *WT* siblings ($Tnfsf11^{flox/flox}$) were generated. Mice received a PBS or Lipopolysaccharides (LPS, 25mg/kg) injection above calvariae at 1.5 month of age and were harvested 7 days later. Female mice at 3 months of age received ovariectomy surgery and vertebrates were harvested 1.5 month later.

ScRNA-seq analysis

Td^+ cells sorted from bone marrow of 1-month-old (2 batches, n = 5) and 3-month-old (1 batch, n = 3) male *Col2/Td* mice were subjected to 10X Genomics library construction and sequencing. Unsupervised clustering was conducted by Seurat and trajectory analysis was conducted by Monocle.

μCT

Bones were scanned by vivaCT 35 (Scanco Medical AG) at a resolution of 6 and 15 μm for trabecular/cortical bone and calvaria analysis, respectively.

Histology and bone histomorphometry

Bones were processed for paraffin and frozen sections for immunostaining, TRAP staining, and dynamic histomorphometry.

Statistics

Data are expressed as means±SD and analyzed by Student's t-test or two-way ANOVA.

Results

We obtained a total of 9952 mesenchymal cells and 6977 hematopoietic cells, clustered in 18 groups, in our scRNA-seq dataset (Fig. 1A). Computational analysis of monocyte-macrophage lineage cells generated one monocyte cluster (Mono) at one end of the pseudotime trajectory, one macrophage cluster (Mϕα) at the branch point, one macrophage cluster (Mϕβ) at the 2nd end, one early osteoclast cluster (OC) and one late osteoclast cluster at the 3rd end (Fig. 1B), suggesting that monocytes undergo bi-lineage differentiation into mature Mϕβ cells and osteoclasts via Mϕα as the intermediate cell type. Ligand-receptor pair analysis suggested that MALPs, but not osteoblasts nor osteocytes, have the most signal interactions with macrophage lineage cells (Fig. 1C) due to their high expression of osteoclast regulatory factors, including RANKL (Fig. 1D). *Adipoq-Cre* has been used to label mature adipocytes in peripheral fat tissues. In bone marrow, Td^+ cells in 3-monthold *Adipoq/Td/Col1-GFP* mice labeled stromal cells, pericytes, lipid-laden adipocytes (LiLAs, which are hundred times less than MALPs[1]) but not osteoblasts, or osteocytes (Fig. 1E a-d), indicating that *Adipoq-Cre* is specific for MALPs in adult mouse bone.

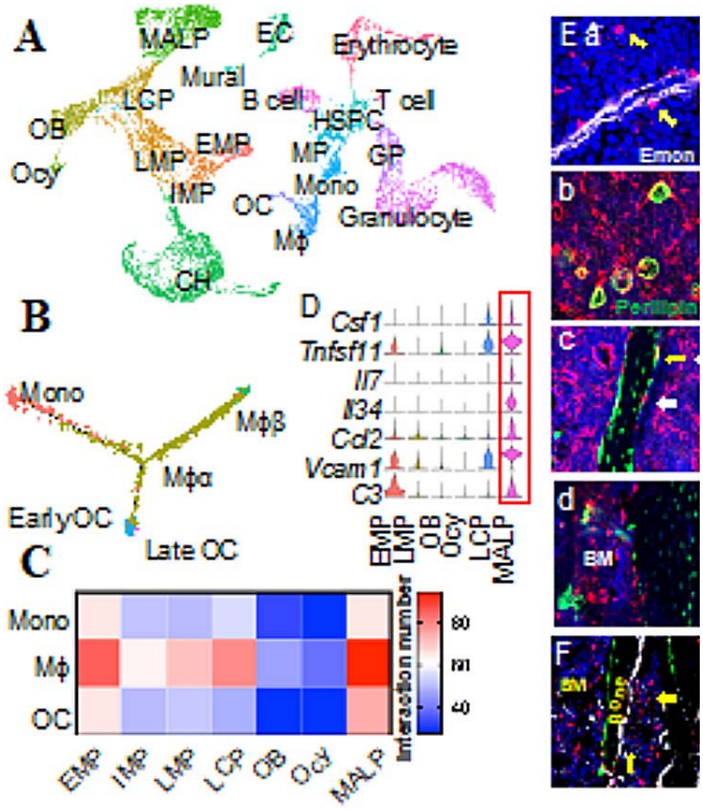

Figure 1. MALPs are the major source of RANKL that regulate osteoclastogenesis in vivo. (A) The UMAP plot of cells isolated from bone marrow of 1-3-month-old Col2/Td mice. EMP: early mesenchymal progenitor; LMP: late mesenchymal progenitor; OB: osteoblast; Ocy: osteocyte; LCP: lineage committed progenitor; CH: chondrocyte; EC: endothelial cells; HSPC: hematopoietic stem and progenitor cells; MP: monocyte progenitor; GP: granulocyte progenitor **(B)** Monocle trajectory plot of monocyte-macrophage lineage cells. **(C)** Ligand-receptor pair analysis of mesenchymal subpopulations with monocytes, macrophages, and osteoclasts. **(D)** Violin plots of osteoclast regulatory factors in mesenchymal subpopulations. **(E)** Representative fluorescent images of 3-month-old Adipoq/Td/Col1-GFP mouse bone reveal that Td labels stromal cells, pericytes (a), and Perilipin$^+$ adipocytes (b), but not osteoblasts or osteocytes (c, d). c: a yellow arrow points to a Td$^+$GFP- cell on bone surface and a white arrow points to a Td$^+$GFP$^+$ cell, which only accounts for 4% of GFP$^+$ osteoblasts/osteocytes. **(F)** Representative fluorescent TRAP staining image reveals that Td$^+$ MALPs touch nearby osteoclasts (white).

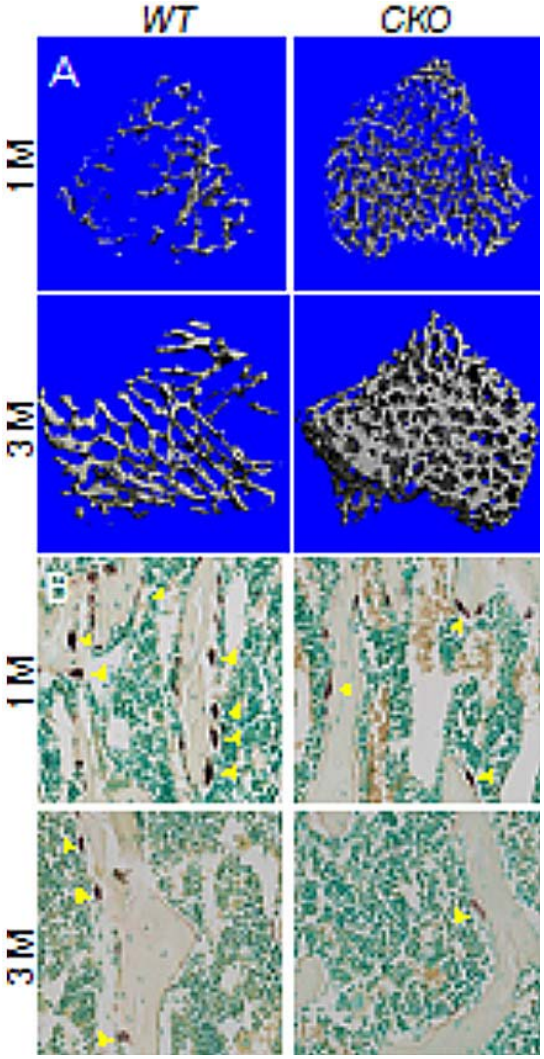

Figure 2. *RANKL CKO^{Adipoq}* mice have high trabecular bone mass. (A) 3D μCT images of tibial trabecular bone from *WT* and *RANKL CKO^{Adipoq}* mice at 1 and 3 months of age. **(B)** TRAP staining shows that osteoclasts are reduced at secondary spongiosa area in *RANKL CKO^{Adipoq}* mice.

Interestingly, we observed that bone attaching osteoclasts are often contacted by cell processes of neighboring Td$^+$ MALPs but rarely by osteoblasts (Fig. 1F). Strikingly, both male and female *RANKL CKO^{Adipoq}* mice (n = 5-6/group) displayed a drastic increase of trabecular bone mass (BV/TV) in long bones (1.6- and 2.9-fold, at 1 and 3 months of age, respectively, Fig. 2A) and vertebrates, due to a remarkable decrease of osteoclast number and activity (65% and 60%, Fig. 2B). Osteoblast number and activity was also reduced, implying a crosstalk between osteoclasts and osteoblasts. Growth plate and cortical bone were not affected. MALPs also exist in calvarial bone marrow. Osteolytic lesion in calvaria induced by LPS injections was completely abolished in *RANKL CKO^{Adipoq}* mice (n = 6/group) due to reduced osteoclast number (Fig. 3A, C). Furthermore, in ovariectomized mice (n = 5-6/group), elevated bone resorption in vertebrates was partially attenuated by RANKL deficiency in MALPs (Fig. 3B, D).

Discussion

In our study, we delineate the in vivo differentiation routes of osteoclasts and macrophages from bone marrow monocytes. MALPs, which form a multi-dimensional cell network in bone, are the most interactive mesenchymal subpopulation with monocyte-macrophage lineage cells in the bone marrow. We propose that osteoclast formation is controlled by a variety of mesenchymal cells in skeletal site-specific and disease-dependent manners. While osteocytes play a major role in promoting cortical bone resorption, MALPs predominately contribute to trabecular bone osteoclast formation, especially in young mice, because mice with osteocyte-specific deficiency of RANKL showed no or minor bone changes at 1 month of age[2].

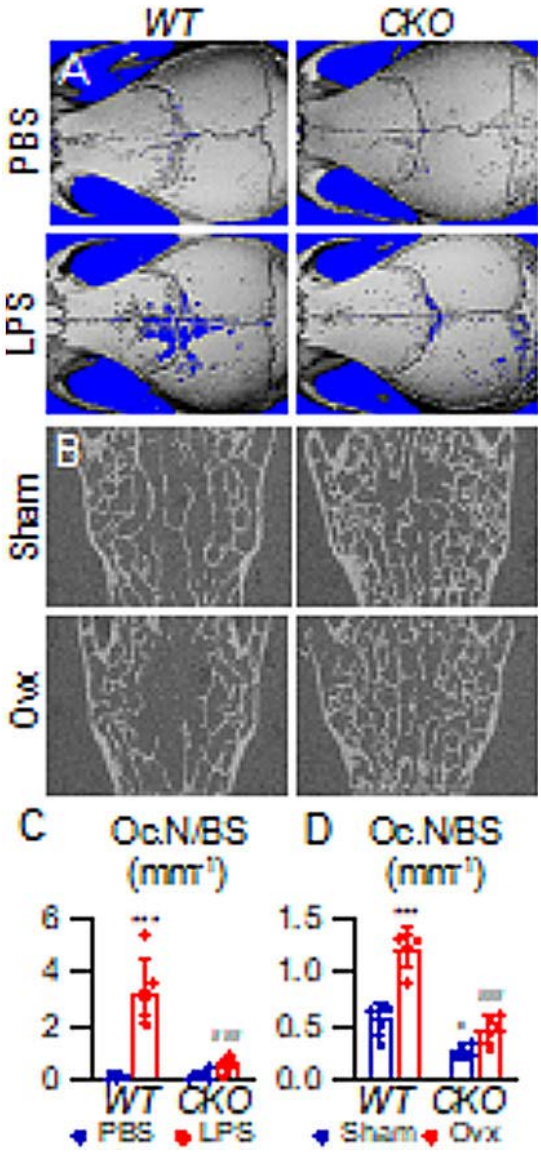

Figure 3. *RANKL CKO*^{Adipoq} mice are protected from pathologic bone loss. (A) Representative 3D μCT reconstruction of mouse calvaria at 1 week after vehicle (PBS) or LPS injections. **(B)** 2D μCT reconstruction of *WT* and *RANKL CKO*^{Adipoq} mouse vertebrate at 1.5 months after sham or ovx surgery. **(C)** Quantification of osteoclast number (Oc.N) in calvaria after injection. **(D)** Quantification of osteoclast number (Oc.N) in vertebrate after surgery.

Significance

MALPs are a critical player in controlling bone remodeling during normal bone metabolism and pathological bone loss in a RANKL-dependent fashion.

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Transient Expansion and Myofibroblast Conversion of Marrow Adipogenic Lineage Precursors (MALPs) Mediate Bone Marrow Repair after Radiation

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Disclosures

None

Introduction

Radiotherapy treats malignant tumors effectively but also damages surrounding tissues, such as bone marrow. It is well known that radiation causes a collapse of bone marrow cells and elimination of microvasculature. At a less severe level, radiation damage can be reversed, indicating that bone marrow has a regenerative ability. However, the mechanism governing such recovery is still largely unknown. Apart from hematopoietic cells and endothelial cells, mesenchymal lineage cells are also a major component of bone marrow providing supportive microenvironment for hematopoiesis and angiogenesis. Using single cell RNA-sequencing (scRNA-seq) technique, we recently discovered a novel subpopulation of mesenchymal cells that express most adipogenic markers but with no lipid accumulation and named them marrow adipogenic lineage precursors (MALPs)[1]. In this study, we utilized a modest focal radiation dosage to generate a bone marrow repair model and investigate the underlying mechanism.

Methods

Animals

All animal work was approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pennsylvania. *Col2-Cre Rosa-Tomato (Col2/Td)* mice and *Adipoq-Cre Rosa-Tomato (Adipoq/Td)* mice were generated. For focal radiation, mouse right femur received a clinically relevant radiation dose of 5 Gy using small animal radiation research platform (SARRP).

scRNA-seq analysis

Sorted Td^+ cells from the endosteal bone marrow of 1-month-old *Col2/Td* male mice with no radiation (NR, 2 batches, n = 5) or at 3 days after radiation (R, 1 batch, n = 3) were subjected to library construction and sequencing. Unsupervised clustering was conducted by UMAP to generate cell clusters of the overall cell populations. Pseudotime trajectory analysis was conducted using Monocle 3.

Whole mount immunofluorescence

Bones were processed for 50 μm-thick whole mount cryosections and stained with indicated antibodies.

Statistics

All analyses were conducted using t-tests or one-way ANOVA with Tukey post test.

Results

5 Gy focal radiation to femurs of 1-month-old mice caused acute damage on bone marrow cellularity and vasculature at day 3, which was recovered at day 14. Using *Col2-Cre* that labels the entire mesenchymal lineage cells in bone[2,3], we unexpectedly observed a 5.5-fold increase of bone marrow Td^+ cells at day 3 after radiation, which later gradually disappeared. ScRNA-seq on Td^+ cells sorted from NR or R bones at day 3 generated the same clustering pattern consisting of early mesenchymal progenitors (EMPs), late mesenchymal progenitors (LMPs), lineage committed progenitors (LCPs), osteoblasts, osteocytes and MALPs and the same pseudotime trajectory pattern (Fig.1 A, B). After integration of 2 datasets, we found that the mesenchymal progenitor pool including EMPs and LMPs was drastically shrunk while MALPs were greatly expanded after radiation (Fig.1 C). Interestingly, cell cycle analysis revealed that MALPs, a non-proliferative cell type, became highly proliferative after radiation (Fig1.D). Analyzing differentially expressed genes (DEGs) found that radiation upregulates many myofibroblast (*Acta2, Tagln, Myl9* etc) and extracellular matrix (*Col9a1, Col10a1, Col1a1* etc) genes in MALPs, indicating a myofibroblast transformation. Using *Adipoq-Cre* to label MALPs *in vivo*, we observed that radiation significantly increased the number of MALPs and its proliferation (EdU^+Td^+ cells) at day 3 post radiation (Fig.2). qRT-PCR of sorted Td^+ cells from *Adipoq/Td* mice confirmed that myofibroblast markers are indeed increased

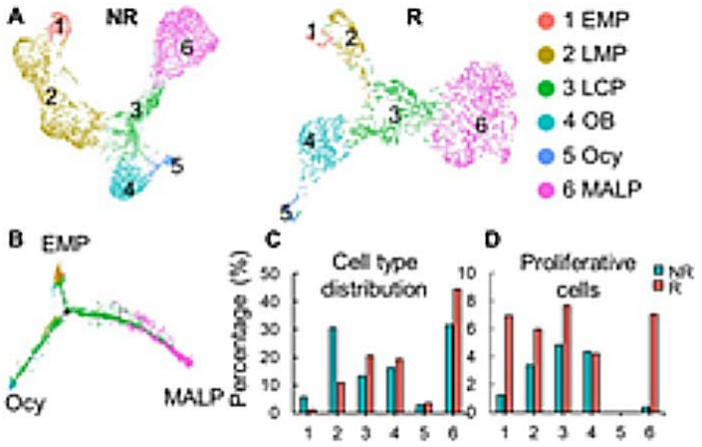

Figure 1. ScRNA- seq analysis predicts MALPs expansion and cell cycle entry after radiation. **(A)** The UMAP plot of Td$^+$ mesenchymal lineage cells isolated from 1 month-old Col2/Td mice with no radiation (NR) or at 3 days after radiation (R). **(B)** Monocle trajectory plot from R dataset. **(C)** The distribution of cells from NR and R datasets in each cluster. **(D)** The percentage of proliferative cells (S/G2/M phase) among each cluster in NR or R conditions was quantified.

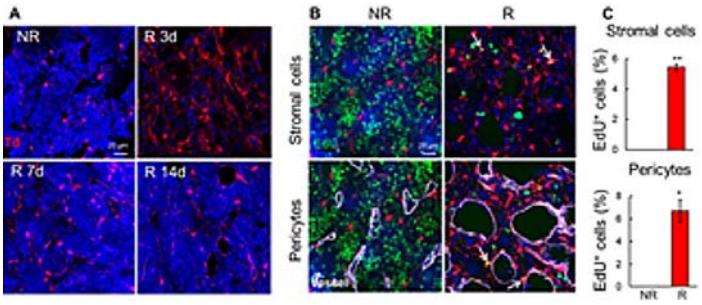

Figure 2. Radiation transiently expands MALP pool via stimulating its proliferation. **(A)** Fluorescent images of Td$^+$ cells in the endosteal bone marrow of 1-month-old *Adipoq/Td* femur before and after focal radiation. **(B)** Fluorescent images of EdU incorporation in bone marrow cells of *Adipoq/Td* femurs at 3 days post radiation. Arrows point to EdU$^+$Td$^+$ cells. **(C)** Quantification of EdU$^+$ cells in both stromal and pericytes from *Adipoq/Td* mice.

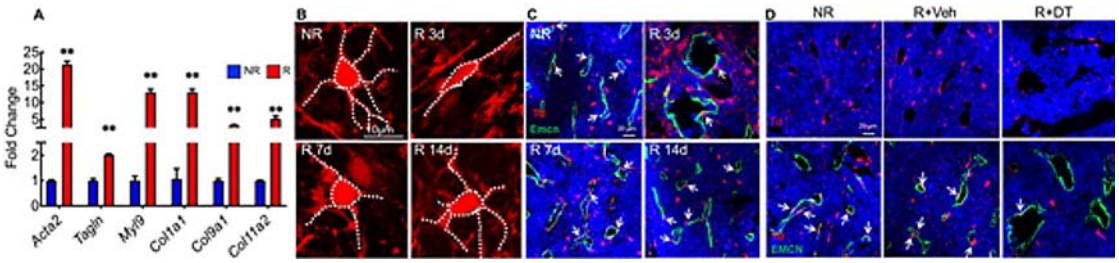

Figure 3. MALPs acquire myofibroblastic features and are indispensable for bone marrow repair after radiation. (A) qRT-PCR of sorted bone marrow Td$^+$ cells from *Adipoq/Td* mice. **(B)** Cell processes in 3D image of MALPs. **(C)** Fluorescent images of vessel and Td$^+$ pericytes on vessel post radiation. **(D)** Fluorescent images of vessel and Td$^+$ pericytes on vessel after radiation and DT treatment.

(Fig.3 A). MALP is composed of a cell body with several cell processes. Strikingly, radiation diminished the number of its cell processes and changed its shape to more spindle-like (Fig.4 B). Many MALPs exist as pericytes. Td$^+$ pericytes in *Adipoq/Td* mice decreased by 76% along with vessel dilation at day 3 post radiation but returned to normal numbers with relatively normal vessel structure at day 14 (Fig.3 C). Ablation of MALPs in *Adipoq/Td/DTR* mice after radiation almost completely abolished the recovery of bone marrow cellularity (decreased by 85%) and vessel structure at day 14 (Fig3. D).

Discussion

In the adipogenic differentiation route of bone marrow mesenchymal stem cells, MALPs are situated after mesenchymal progenitors and before lipid-laden adipocytes (LiLAs). They normally do not proliferate. Our study on radiation effects on bone discovered that MALPs start to proliferate and acquire myofibroblastic features after radiation, which are essential for subsequent bone marrow repair. Our data revealed the plasticity of MALPs and shed light on seeking new target for alleviating radiation damage on bone.

Significance

MALPs play a crucial role in bone marrow regeneration after radiation injury.

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Orthoplastics

Correction of Congenital Upper Extremity Contracture with Flexor Origin Slide

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Abstract

The clinical features seen in patients with chromosome 16p13.11 duplications are poorly described and reports of successful treatment modalities for their musculoskeletal issues are limited. Existing literature has highlighted a clinical picture consistent with a general hypermobility syndrome. We report a 9-year-old male with a 16p13.11 microduplication who presented with worsening contractures of his hands which were present since birth but had gradually worsened and caused dysfunction. He was surgically treated with a flexor origin slide procedure and z-lengthening of the hypothenar skin on his right hand, successfully restoring full motion and function of his fingers.

Introduction

Chromosome 16p13.11 microduplication is a rare disorder with uncertain clinical significance. It has been linked to patients with cognitive impairment, developmental delay, autism, and schizophrenia[3,4,8] . Affected populations have been described as being phenotypically normal to having a diverse set of physical characteristics. In a series of 10 patients with 16p13.11 microduplications, Nagamani et al identified different phenotypic manifestations[4]. They described dysmorphic facial features such as epicanthic folds, low set ears, posterior rotated ears, and nasal abnormalities. Musculoskeletal manifestations included craniosynostosis, hypermobility, polydactyly, syndactyly, arachnodactyly, and pes planus.

We present a case of a 9 year-old male who was referred to our orthopaedic surgery upper extremity clinic for contractures of bilateral hands, right worse than left, with associated pain and difficulties with daily activities. Rather than hypermobility, which is more commonly reported in patients with 16p13.11 microduplications, our patient had stiffness of his fingers. He failed nonsurgical measures including a year of occupational therapy with stretching and nighttime splinting. We performed a flexor origin slide procedure to improve his contractures. At the 1 year follow-up, the patient had full extension of his fingers, resolution of contractures, and improved function.

Case Report

Our patient is a 9-year-old right hand dominant male who presented to our clinic with his mother, a phenotypically normal woman, with worsening flexion contractures of both hands over the past two years. His right hand was more affected than the left. He was found to have mildly abnormal facial findings, including a low, narrowed anterior hairline, synophyrs, flattened cheekbones, and midface hypoplasia. The unusual constellation of findings prompted a referral to a geneticist, who ordered a chromosomal microarray. This exhibited an approximately 819 kb gain of 16p13.11. He lacked other findings consistent with this microduplication, such as intellectual delay, autism, or schizophrenia.

Musculoskeletal examination of his right upper extremity revealed ulnar deviation of the index, long, ring and small fingers at the metacarpophalangeal joints (MCPJs), as well as contractures of the MCPJs, and distal interphalangeal joints (DIPJs) of digits 2-5. The ring and small finger active MCPJ motion was limited to an arc of 70-90° (normal 0-100°), and the DIPJs to 45-90° (normal 0-85°). With wrist extension, the patient was unable to extend his fingers actively or passively. However, he was able to extend them fully with the wrist in neutral, signifying an extrinsic etiology of his contractures (Figure 1). Initial treatment of his contractures consisted of a stretching and splinting therapy program supervised by an occupational therapist. Unfortunately, he had minimal symptomatic improvement, so he and his family elected to proceed with surgical correction.

He underwent a flexor origin slide of the right upper extremity and a z-plasty (local soft tissue rearrangement) of the hypothenar aspect of the palm. The purpose of the flexor origin slide was to move the origin of the wrist and finger flexors distally without affecting resting muscle length. An incision was made along the ulnar aspect of his forearm, starting posterior to the medial epicondyle and extending distally down the forearm to the ulnar wrist flexion crease. The entire flexor-pronator mass was elevated from the humerus, ulna, and interosseous

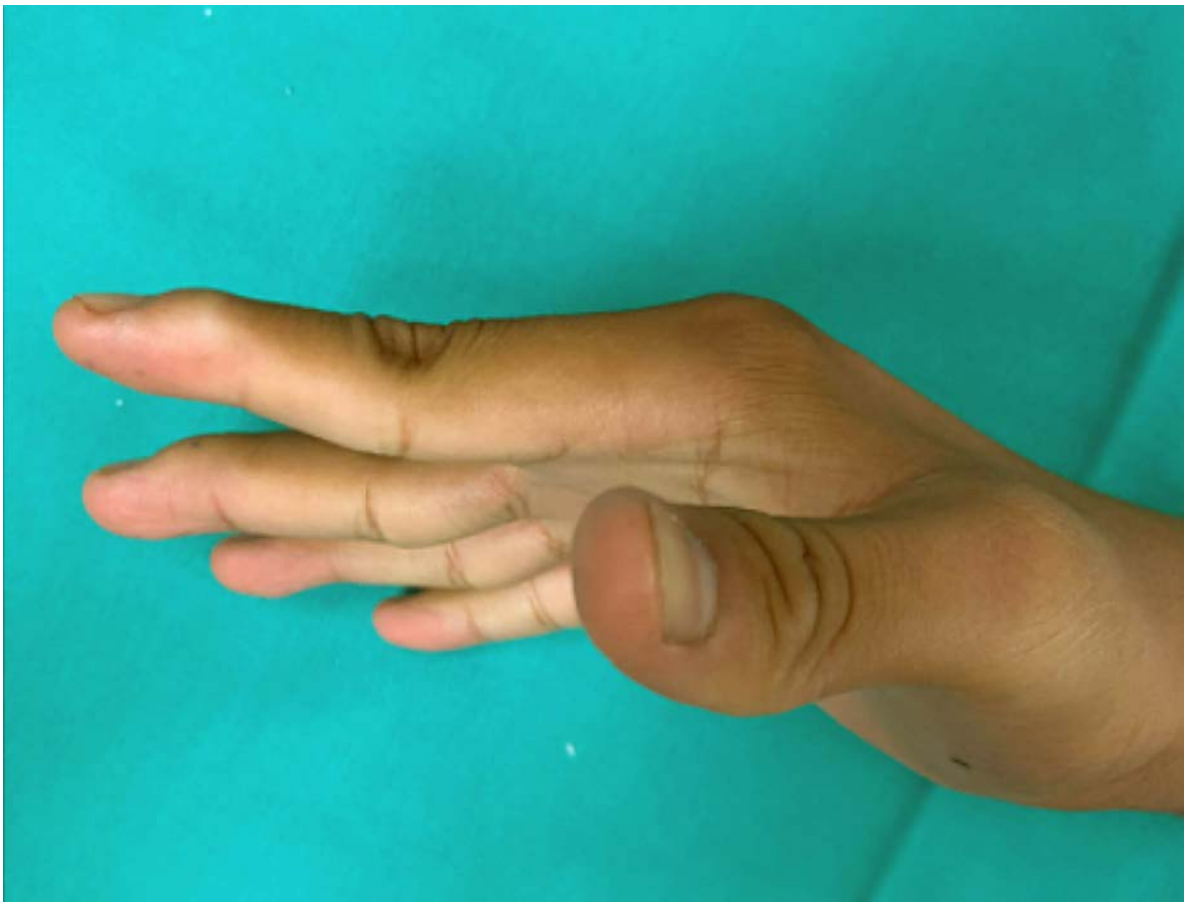

Figure 1. Clinical photograph of hand deformity prior to surgery.

membrane in a subperiosteal fashion, taking care to protect the neurovascular structures. After the release was performed, full passive extension of the wrist and fingers was observed in the operating room (Figure 2).

Postoperatively, the patient was casted with the wrist and fingers in full extension for 6 weeks. He was then referred to an occupational therapist for stretching, ROM, and night splinting. At his 1 year follow-up visit, he had full active and passive ROM of all digits and resolution of his pain and discomfort (Figure 3). He was able to perform all of his desired activities including playing basketball.

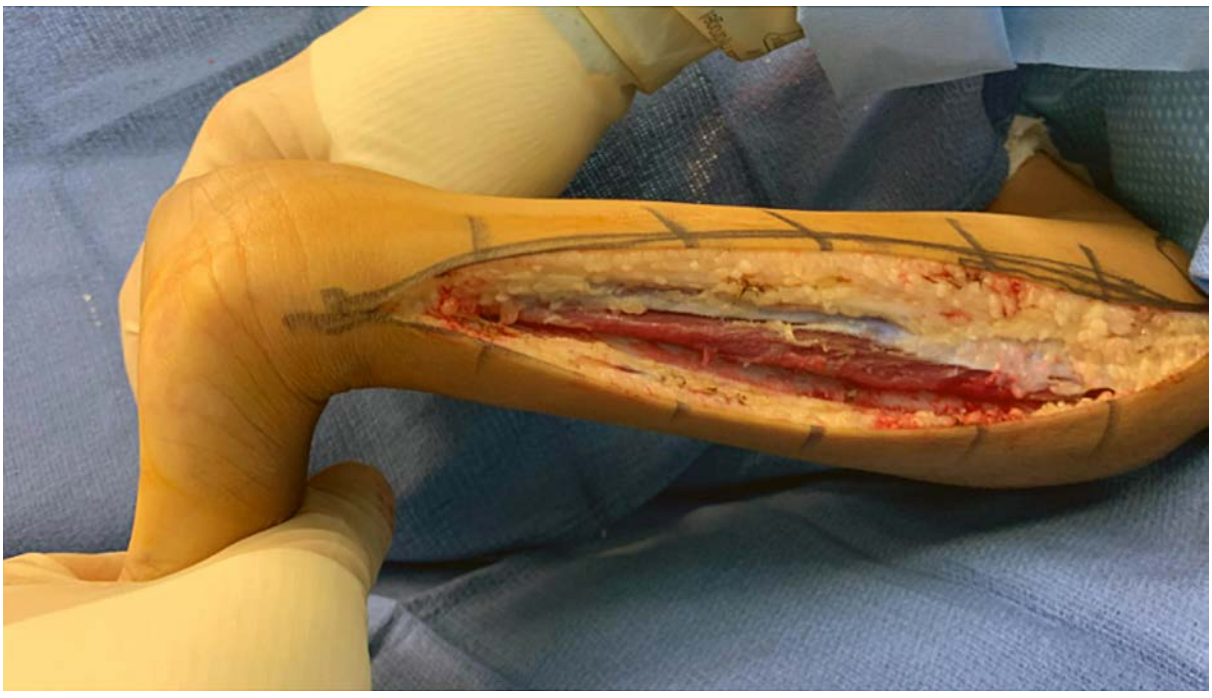

Figure 2. Clinical photograph intraoperatively demonstrating full passive extension of wrist and fingers after flexor origin slide procedure.

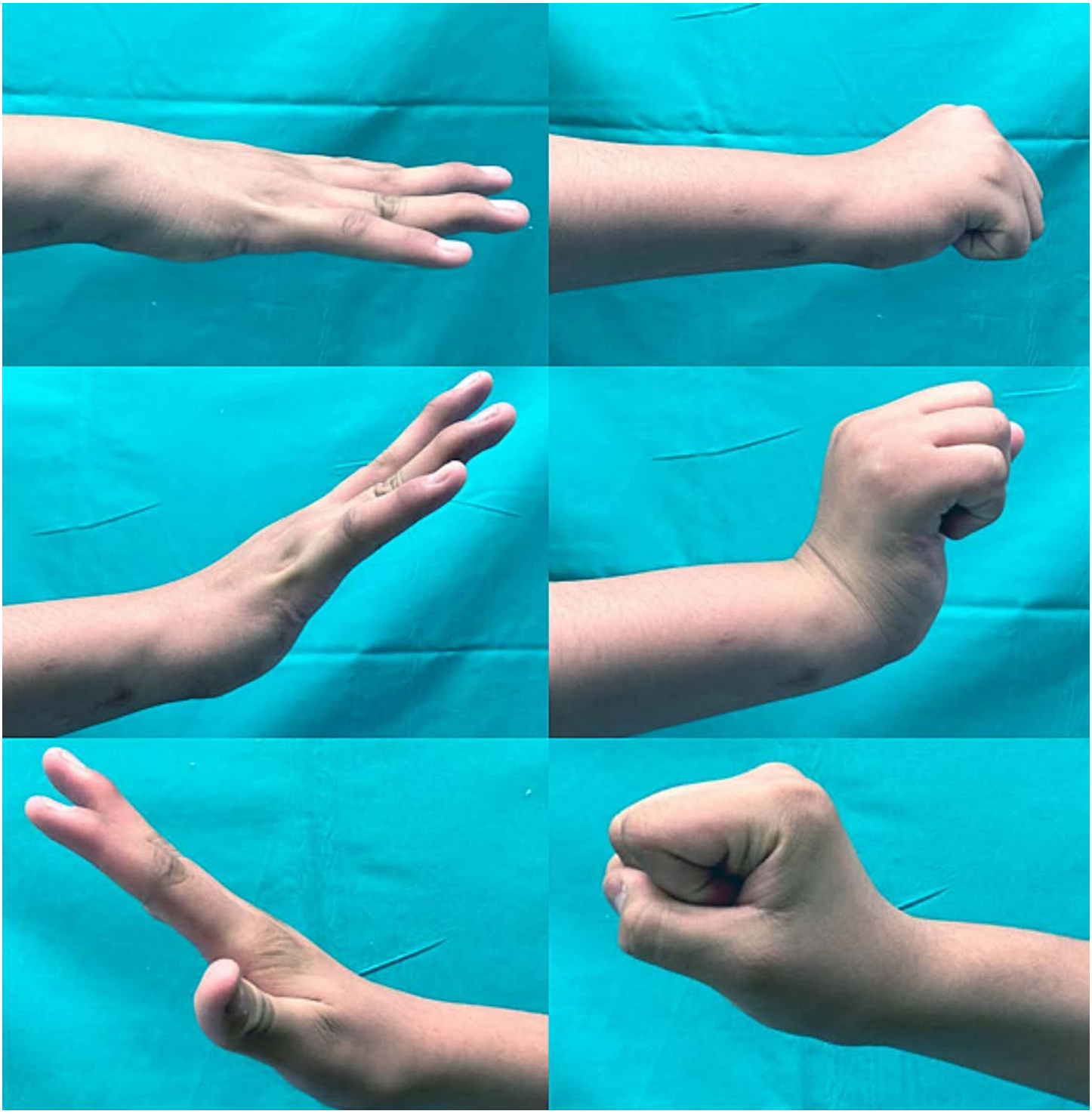

Figure 3. Clinical photos 1 year postoperatively demonstrating full active ROM.

Discussion

We present a patient with a rare genetic disorder, a microduplication of chromosome 16p13.11, with clinical manifestations not previously reported. Specifically, our patient was found to have contractures of his hands and fingers, with the right side being more involved than the left, which led to significant functional impairment. Recent literature have highlighted clinical findings including schizophrenia, intellectual disability, and urinary tract problems in this patient population, but have not reported on specific musculoskeletal manifestations[2,3]. To our knowledge, successful surgical treatment of a patient with musculoskeletal pathology due to a chromosome 16p13.11 microduplication has yet to be published.

Hand and finger contractures in children are often a complication of compartment syndrome, referred to as

Volkmann's contracture. The etiology is a reduction in tissue perfusion caused by increased intracompartmental pressures, leading to muscle ischemia and eventual necrosis. The volar forearm muscles (which include the wrist and finger flexors) contract, leading to dysfunction of the hand[6]. While nonsurgical treatment options such as stretching and bracing play an important role, surgical intervention is often required for meaningful recovery.

First described by Page in 1923, the flexor origin slide is a surgical procedure in which the extrinsic flexor and pronator muscle origins are subperiosteally released from the forearm and allowed to heal in a more distal origin to permit increased finger and wrist extension[5]. It has been shown to be effective in both congenital and ischemic contractures[7]. Geissler et al also reported good results for 3 patients with entrapment and adhesions of the flexor tendons after a forearm fracture, or so-called Pseudo-Volkmann contracture[1].

The relationship between chromosome 16p13.11 microduplication and the development of the contractures remains unclear. Our patient was unique in that the onset of his hand contractures did not correlate with a traumatic injury and were not present at birth. It is difficult to draw conclusions on the etiology because of the rarity of this syndrome and lack of other reports in the literature due to the wide phenotypic variations seen. Further research and case series may illuminate this relationship.

In summary, we present a 9-year-old male with bilateral hand and finger contractures found to have a chromosome 16p13.11 microduplication. He underwent a flexor origin slide with local soft tissue arrangement of his right hand with excellent results. To our knowledge, this is the first report of this specific pathology in this population, and the first documentation of successful treatment.

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Bone

Targeting Cartilage EGFR Pathway for Osteoarthritis Treatment

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Disclosures

A.T. is a founder of and owns equity in AlphaThera, Inc.

Introduction

Osteoarthritis (OA) is a widespread chronic joint disease characterized by cartilage degeneration. We previously discovered that EGFR signaling is critical for maintaining the superficial layer of articular cartilage and found that mice with cartilage-specific (*Col2-Cre*) EGFR deficiency develop spontaneous OA[1]. Here, we designed a two-pronged approach to investigate the effects of positively targeting the EGFR pathway on articular cartilage. First, we genetically enhanced EGFR activity by adopting a *Rosa-DTR* model. Originally identified as a receptor for bacterial diphtheria toxin (DT), DTR was later discovered to be human full-length HBEGF[2], a ligand for EGFR. Thus, it allows us to study the effect of cartilage-specific EGFR over-activation on OA progression. Second, we synthesized and characterized nanoparticles (NPs) conjugated with TGFα, another EGFR ligand, and tested their therapeutic efficacy in OA mice.

Methods

Animals

All animal work was approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pennsylvania. *Col2-Cre Rosa-DTR* (*HBEGF Over^{Col2}*) and *Aggrecan-CreER Rosa-DTR* (*HBEGF Over^{AgcER}*) mice, and their *WT* (*DTR* or *Cre* only) siblings were generated. *HBEGF Over^{AgcER}* mice and *WT* received Tamoxifen (Tam, 75 mg/kg/day) injections for 5 days before surgery. Male mice at 3 months of age were subjected to destabilization of medial meniscus (DMM) or sham surgery at right knee. For treatment, *WT* mice received 10 µl of PBS, TGFα-DBCO (10 µM TGFα content), Ctrl-NP (no TGFα) and TGFα-NPs (10 µM TGFα content) intra-articularly once every 3 weeks starting from right after DMM surgery for 3 months.

TGFα-NP Synthesis

Bacteria-expressed human TGFα were labeled at the C-terminus with a constrained alkyne, dibenzocyclooctyne (DBCO), via sortase-tag expressed protein ligation (STEPL). TGFα-NPs were then prepared via copper-free click chemistry, by mixing TGFα-DBCO with azide-functionalized NPs made from 55mol% poly(ethylene glycol)-polycaprolactone (PEG-PCL)/20mol% poly(L-lysine-block-poly(α-caprolactone) (PLL-PCL)/25mol% 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[azido(polyethylene glycol)-5000] (DSPE-PEG5K-N3) using the film hydration method.

Histology

Knee joints were processed for paraffin sections followed by HE, Safranin-O/fast green (SO/FG), p-EGFR, Ki67, TUNEL, and PRG4 staining.

µCT

Femurs were scanned from the epiphyseal end at a 6-µm resolution by µCT 35. The 3D images of the femoral distal end were reconstructed to generate a 3-D color map of thickness for the entire subchondral bone plate (SBP).

Cell Culture

Chondroprogenitors were harvested from articular cartilage of 5-month-old mouse knee joints by enzymatic digestion. Cells were then used for Western blots and CFU-F assays.

Statistics

Data are expressed as means±SEM and analyzed by one- or two-way ANOVA and unpaired, two-tailed Student's t-test.

Results

HBEGF Over^{Col2} mice displayed normal knee joints. No gross abnormality was detected. Long bone structure, including subchondral trabecular bone, subchondral bone plate (SBP), and metaphyseal trabecular bone, was also not affected. The most obvious change was cartilage. *HBEGF Over^{Col2}* mice displayed expanded growth plate and articular cartilage at

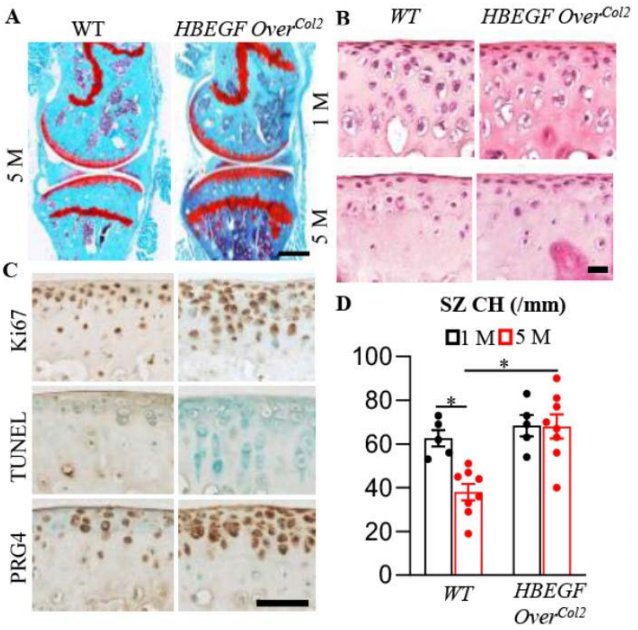

Figure 1. HBEGF overexpression in chondrocytes enlarges cartilage thickness and expands the chondroprogenitor pool. (A) SO/FG staining of *WT* and *HBEGF Over*^{Col2} knee joints at 5 months of age. Scale bar, 1 mm; **(B)** HE staining of *WT* and *HBEGF Over*^{Col2} knee joints at 1- and 5-month-old mice. Scale bar, 50 μm; **(C)** Ki67, TUNEL, and Prg4 staining in articular cartilage. Scale bar, 100 μm. **(D)** Quantification of superficial layer chondrocytes of (B). n = 8 mice/group. *: $p < 0.05$.

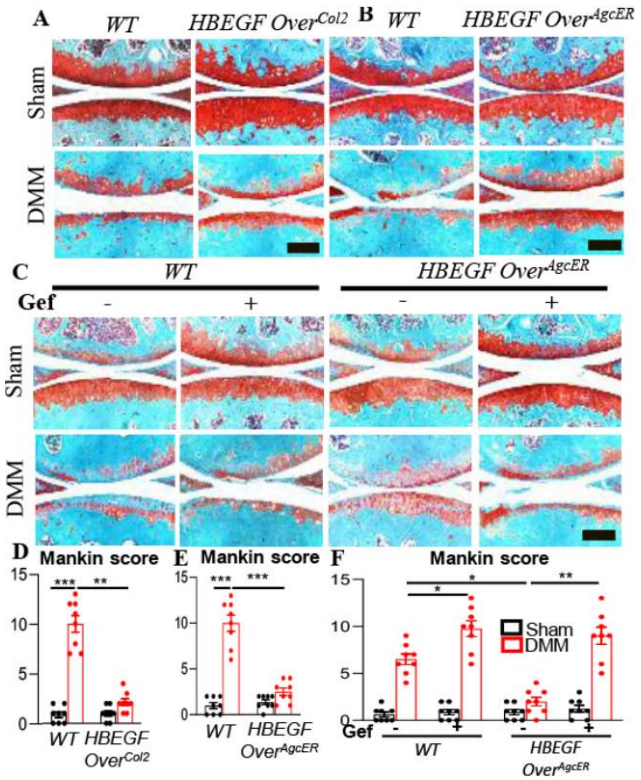

Figure 2. Cartilage-specific EGFR overactivation attenuates OA progression. A: *WT* and *HBEGF Over*^{Col2} joints at 4 months post sham or DMM surgery were stained with SO/FG. **B:** *WT* and *HBEGF Over*^{AgcER} mice received Tam injections right before DMM and their joints were harvest at 4 months post-surgery for SO/FG staining. **C:** *WT* and *HBEGF Over*^{AgcER} mice were subjected to sham or DMM surgery followed by vehicle or Gefinitib (100 mg/kg, once every other day) treatment for 3 months. Joints were harvested for histology analysis. Scale bars, 200 μm. **D:** The OA severity of (A) was measured by Mankin score, n = 8 mice/group. **E:** Mankin score of (B). n=8 mice/group. **F:** Mankin score of (C). n = 8 mice/group. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

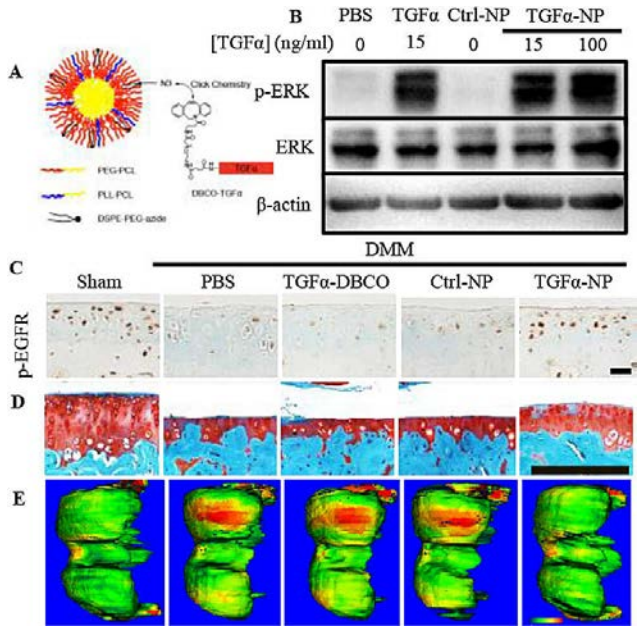

Figure 3. TGFα-NPs maintain EGFR signaling in chondrocyte and prevents cartilage damage after DMM surgery. A: Schematic diagram of TGFα-NPs. **B:** Western blots of EGFR activity (p-ERK) in primary chondrocytes with indicated treatment. **C:** EGFR activity (p-EGFR) staining in the articular cartilage of mice received intra-articular injections of PBS, free TGFα, Ctrl-NPs, and TGFα-NPs for 3 months after sham or DMM surgery. Scale bar, 100 μm. **D:** SO/FG staining. Scale bar, 200 μm. Mankin score: 0.63 ± 0.26 (Sham); 8.88 ± 0.74 (DMM PBS); 8.13 ± 0.81 (DMM TGFα-DBCO); 8.38 ± 0.82 (DMM Ctrl-NP); 3.25 ± 0.59 (DMM TGFα-NP). (TGFa-NP vs PBS: $p < 0.001$) **E:** Representative 3D color maps showing SBP thickness. Color ranges from 0 (blue) to 320 μm (red).

1 and 5 months of age (23.27% and 34.28% thicker than *WT* cartilage, respectively) (Fig. 1A). The superficial layer contains chondroprogenitors for articular cartilage. *HBEGF Over*^{Col2} articular cartilage had 1.79-fold more superficial chondrocytes (Fig. 1B, D) and formed 1.96-fold more CFU-F colonies than *WT* mice at 5 months of age, which was accompanied by enhanced Ki67 and Prg4 staining and reduced TUNEL staining (Fig. 1C). Interestingly, after DMM injury, articular cartilage degeneration was remarkably attenuated in *HBEGF Over*^{Col2} mice (Fig. 2A, D) and *Over*^{AgcER} mice (with Tam injections before the surgery, Fig. 2D, E). This cartilage protective action is mediated by EGFR signaling because it was completely abolished by co-treatment of EGFR inhibitor, Gefinitib (Fig. 2C, F). TGFα-NPs (Fig. 3A) were approximately spherical in shape with a hydrodynamic diameter of 25.93 nm. They activated EGFR signaling in primary chondrocytes as potent as free TGFα (Fig. 3B). Due to a positive charge, TGFα-NPs had superior cartilage uptake, penetration, and joint retention abilities compared to free TGFα. Strikingly, intra-articular delivery of TGFα-NPs effectively maintained EGFR activity (p-EGFR) in cartilage (Fig. 3C) and attenuated DMM-induced OA cartilage degeneration (Fig. 3D), SBP sclerosis (Fig 3E) and joint pain measured by von Frey assay. Free TGFα or NPs alone did not alter OA progression.

Discussion

Our study provides genetic evidence demonstrating that overactivation of EGFR signaling modestly thickens the

articular cartilage and completely blocks OA progression after DMM surgery. Other joint tissues, such as bone, synovium, and meniscus, as well as major vital organs, appeared normal in mice up to 12 months of age, suggesting that EGFR signaling could be precisely regulated in vivo to fulfill its anabolic actions without inciting catabolic, damaging effects. We also provided proof-of-principle evidence that administration of TGFα into mouse joints using an advanced nanoparticle delivery system is effective in preventing DMM-induced OA initiation and development.

Significance

Our studies uncover the critical role of EGFR signaling in cartilage homeostasis and demonstrate the feasibility of targeting EGFR signaling for OA treatment as a novel therapeutic approach using nanotechnology.

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Marked Differences in Local Bone Remodeling Based on Marrow Stimulation Technique in a Large Animal

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Introduction

Marrow stimulation is commonly performed to promote cell-mediated cartilage repair. Traditionally, a conical-tipped awl is used to perforate the underlying subchondral bone to enable the upward migration of marrow cells. However, awl-based microfracture results in irregular holes, inconsistent marrow effusion, and compacted bone[1]. In animal models, microfracture has also been shown to cause significant bone resorption[2], confounding the translation of augmented microfracture strategies. However, recent nanofracture approaches show promise[3]. In an effort to better understand the bony changes that occur post-microfracture, and improve upon the clinical gold standard of cartilage repair, we compared awl-based microfracture (Mfx) to other techniques—subchondral drilling (K-wire), and needle puncture (small SmartShot, large SmartShot)[4]—in a large animal cartilage defect repair model. We hypothesized that needle puncture would reduce bone resorption, and stimulate local bone formation at the puncture site, as assessed 4-weeks post-surgery.

Methods

Surgical Model

Six 1-year old castrated male Yucatan minipigs were used for this study. Six unilateral full thickness chondral defects (5 mm diameter) were created in the trochlear groove of the right hindlimb of each animal (Figure 1). Treatment conditions (1: empty defect, 2: Mfx (1.2 mm diameter, 2 mm depth, 3 holes), 3: K-wire drilling (1.25 mm diameter, 6 mm depth, 3 holes), 4: large SmartShot (1.2 mm diameter, 6 mm depth, 2 holes), 5: small SmartShot (0.9 mm diameter, 6 mm depth, 3 holes)) were randomized to defect location (n = 6-8 defects/treatment). Healthy cartilage, distal to the defects was used as a control for each animal. In conjunction with the knee procedure, an indwelling central venous catheter was implanted to facilitate fluorochrome labeling (xylenol orange (90 mg/kg) at the time of surgery and calcein (15 mg/kg) 2 weeks post-surgery). All animals were euthanized 4 weeks post-surgery.

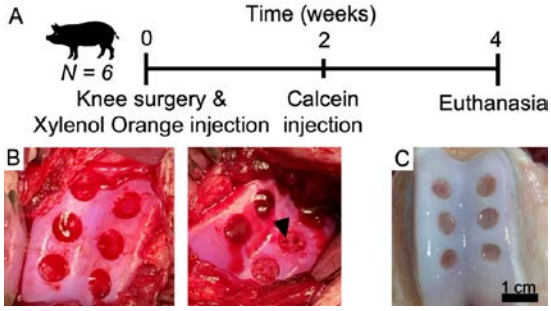

Figure 1. Study outline and macroscopic photos. **(A)** Study outline. **(B)** Six full thickness chondral defects in the trochlea, and treatment holes (arrowhead). **(C)** Gross view of cartilage healing at 4 weeks.

Micro-Computed Tomography & Analysis

Samples were scanned using a high resolution μCT (4.4 μm voxel size, SCANCO μCT50). 2D images were captured at the midplane of each sample, and FIJI was used to quantify the bone resorption area. Three blinded reviewers separately analyzed the images.

Mineralized Cryohistology & Analysis

All samples were formalin-fixed, infiltrated with a sucrose-polyvinylpyrrolidone solution, embedded, sectioned undecalcified with cryofilm, and imaged. After imaging fluorochrome labels, slides were stained for tartrate resistant acid phosphatase (TRAP), and imaged again[5].

Statistics

Figure 2: One-way ANOVA with Tukey's post-hoc test. Figure 3: Mann-Whitney test. Significance $p < 0.05$. Data shown: mean ± std dev.

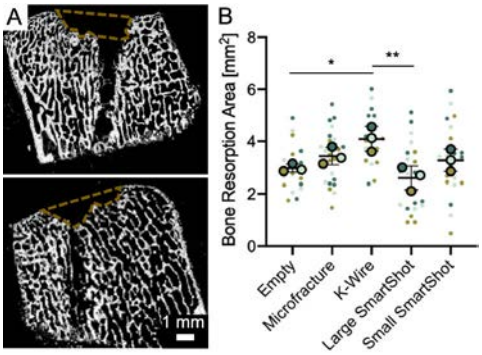

Figure 2. Bone resorption area decreases with SmartShot (needle puncture) device. **(A)** Representative μCT K-wire (top) and large SmartShot (bottom) images with quantified regions outlined. **(B)** Quantification of bone resorption area (n = 6-8 samples/treatment). Colors represent 3 separate blinded reviewers. ** $p < 0.01$, * $p < 0.05$.

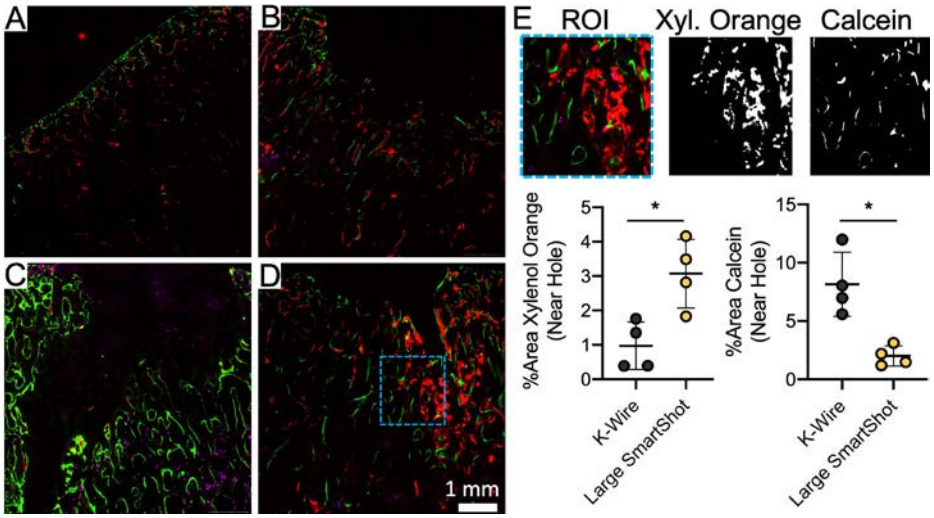

Figure 3. Dynamic bone remodeling in minipigs post-marrow stimulation. **(A-D)** Fluorochrome mineral labels (Xylenol Orange—red, Calcein—green) and tartrate resistant acid phosphatase staining (purple; osteoclasts). Images shown for intact cartilage, microfracture, K-wire, and large SmartShot, respectively. **(E)** Image analysis pipeline and quantification of the %Area of each mineral label proximal to the marrow stimulation hole (1.5 mm x 1.5 mm area). * $p < 0.05$. $n = 4$ defects/treatment quantified.

Results

While macroscopically the cartilage repair tissue looked similar across treatments at the 4-week sacrifice (Figure 1C), the subchondral bone showed marked differences. Defects treated with the K-wire underwent significant bone resorption in comparison to the empty (untreated) defects ($p < 0.01$), and defects treated with the large SmartShot ($p < 0.05$) (Figure 2). μCT images showed bony bridging/nascent bone formation across many of the SmartShot holes. In agreement with the bone resorption data, more osteoclasts (purple TRAP stain) were observed in the K-wire treated defects (Figure 3). Additionally, there was significantly less xylenol orange (1st injected mineral label) incorporation near K-wire holes, in comparison to SmartShot holes ($p < 0.05$). However, there was increased calcein (2nd injected mineral label) incorporation near the K-wire holes, suggesting a delayed subchondral remodeling in these defects.

Discussion

The health and strength of the subchondral bone likely plays a role in the downstream success or failure of a cartilage repair strategy. In this large animal study, drilling had the most deleterious impact on the underlying bone. Both μCT and bone fluorochrome labeling support the use of a more controlled, consistent needle puncture device for marrow stimulation. Further work will explore whether one or more of these bone metrics correlates with cartilage repair quality.

Significance

This is the first large animal study to utilize bone fluorochrome labeling to elucidate the dynamic bony changes that occur post-marrow stimulation. These results may directly guide clinical care and the development of improved micro/nanofracture devices.

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Cartilage

High Dose Enzyme Replacement Therapy Attenuates Joint Disease Progression and Preserves Mobility in Mucopolysaccharidosis VII Dogs

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Introduction

Mucopolysaccharidosis VII (MPS VII) is a lysosomal storage disorder characterized by impaired activity of the enzyme β-glucuronidase (GUSB), leading to aberrant accumulation of incompletely degraded chondroitin, dermatan and heparan sulfate glycosaminoglycans (GAGs).[1,2] Synovial joint disease is common in MPS VII patients, and manifests as joint stiffness and limited range of motion, thought to result from abnormalities in the ligaments, joint capsules, and underlying epiphyseal bone.[1,2] Intravenous enzyme replacement therapy (ERT) for MPS VII using recombinant human GUSB (rhGUS, Mepsevii®) has shown promising results in clinical trials.[3,4] While previous studies have evaluated rhGUS ERT in MPS VII mice,[5] there have been no such evaluations in large animal models of MPS VII. The naturally occurring canine model of MPS VII presents advantages over mouse models, including more closely recapitulating the nature and progression of skeletal disease manifestations that occur in human patients. The objective of this study was to investigate the effects of intravenous ERT using Mepsevii®, administered at two dose levels: the standard clinical dose (4 mg/kg, SD) and a high dose (20mg/kg, HD), on synovial joint disease progression in MPS VII dogs.

Methods

With IACUC approval, MPS VII affected dogs were treated from birth with intravenous Mepsevii® at either the standard clinical dose (ERT SD, 4mg/kg, n = 5) or a high dose (ERT HD, 20mg/kg, n = 3). Bolus administrations were given at 2 and 9 days-of-age, the first 2-hour infusion performed at 23 days-of-age, and subsequent 2-hour infusions were every 14 days. For ERT HD animals, prophylactic dexamethasone was required to prevent adverse reactions (nausea, vomiting and rash). Control animals included MPS VII affected untreated dogs (n = 6) and untreated heterozygous controls (n = 6). An additional control group of MPS VII dogs (n = 3) received dexamethasone without ERT. Monthly physical examinations were performed to assess ability to ambulate and joint swelling. All animals were euthanized at 6 months-of-age. Synovial fluid was collected for measurement of inflammatory biomarkers using a multiplex enzyme immunoassay. Synovial membrane and articular cartilage were harvested for assessment of enzyme (GUSB and hexosaminidase (HEX)) and GAG content. Excised stifle joints were imaged using 3T MRI, and pathological changes in major joint tissues, including cartilage, synovial fluid, meniscus, fat pad and subchondral bone assessed using a custom grading scheme.

Results

All MPS VII untreated animals exhibited a profound decline in mobility over the study duration. By 6 months-of-age, these animals were no longer ambulatory, and had severe joint effusions in all limbs and marked loss of muscle mass. MPS VII ERT SD animals exhibited somewhat attenuated progression of joint disease and decline in mobility, but by 6 months-of-age, all were no longer ambulatory, and all but one exhibited joint effusions similar to untreated. In contrast, MPS VII ERT HD animals exhibited more marked attenuation of joint disease and less decline in mobility. By 6 months-of-age, all three animals were still ambulatory, bright, alert and responsive. MPS VII steroid control animals were no longer ambulatory by 6 months-of-age and clinically indistinguishable from untreated. MPS VII dogs treated with Mepsevii® exhibited elevated rhGUS activity, and corresponding lower HEX activity and GAG content in synovial membrane (Figure 1). Results were dose-dependent, with ERT HD animals exhibiting higher rhGUS, and lower HEX and GAG compared to ERT SD animals. ERT HD animals exhibited significant attenuation of joint pathology assessed by MR imaging in the synovium, patella, meniscus, and fat pad (Figure 2) and reduced expression of inflammatory biomarkers in synovial fluid (Figure 3). Clinical and imaging findings (Figure 2A) from animals administered steroid alone suggests improvements in joint disease are attributable to ERT and not the steroid.

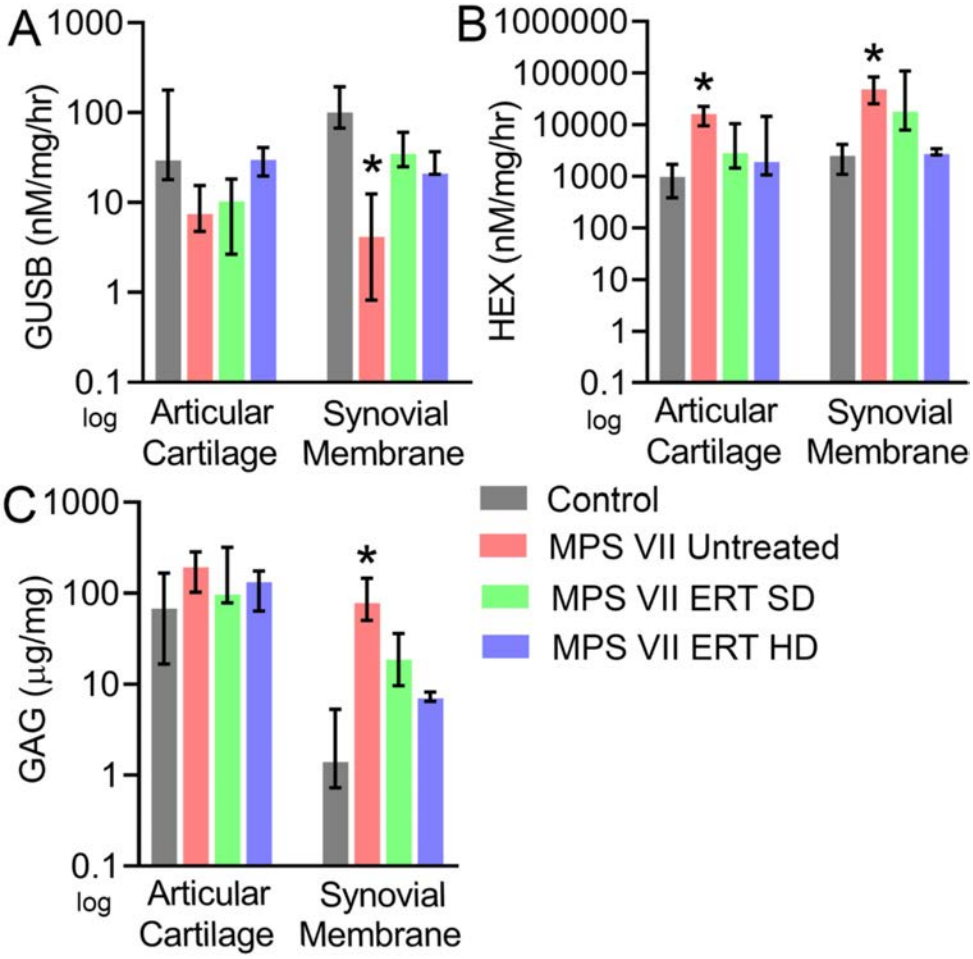

Figure 1. (A) GUSB. **(B)** HEX and **(C)** GAG content in articular cartilage and synovial membrane. N=3-6; *p<0.05 vs Control.

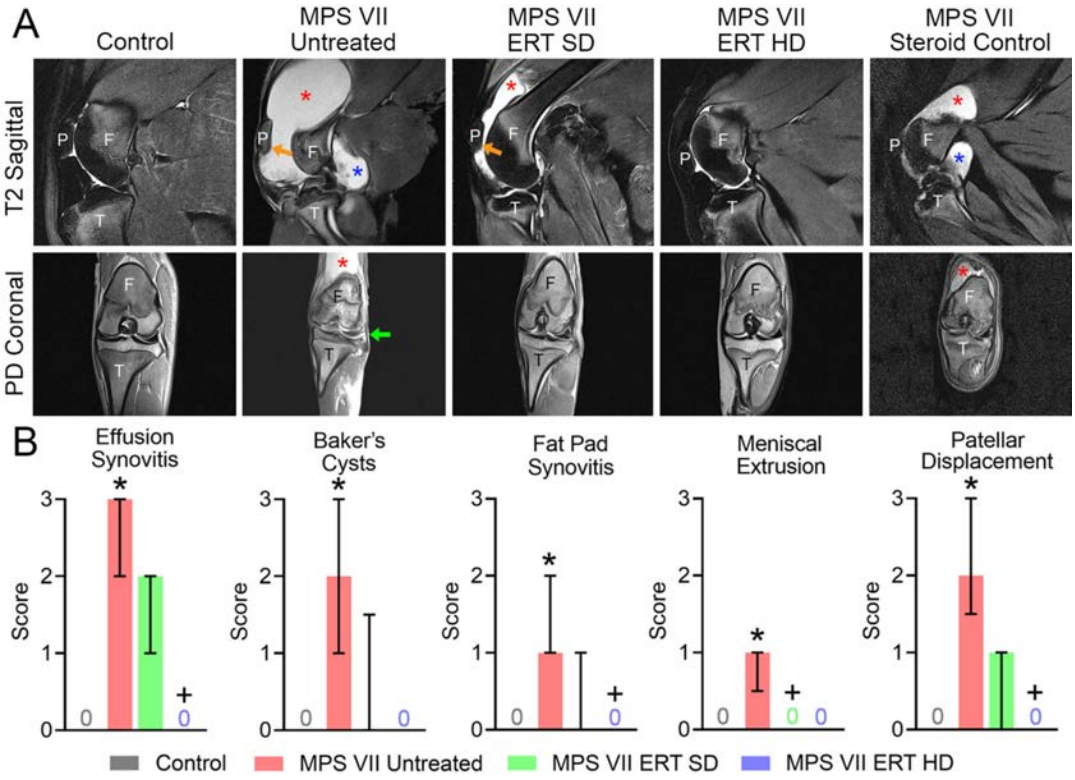

Figure 2. (A) MRI images of canine stifle joints showing synovial effusions (red *), Baker's cysts (blue *), patellar displacement (orange arrows) and meniscal extrusion (green arrow). **(B)** Semi-quantitative grading of pathological features. N=3-6; *p<0.05 vs Control; +p<0.05 vs Untreated MPS VII.

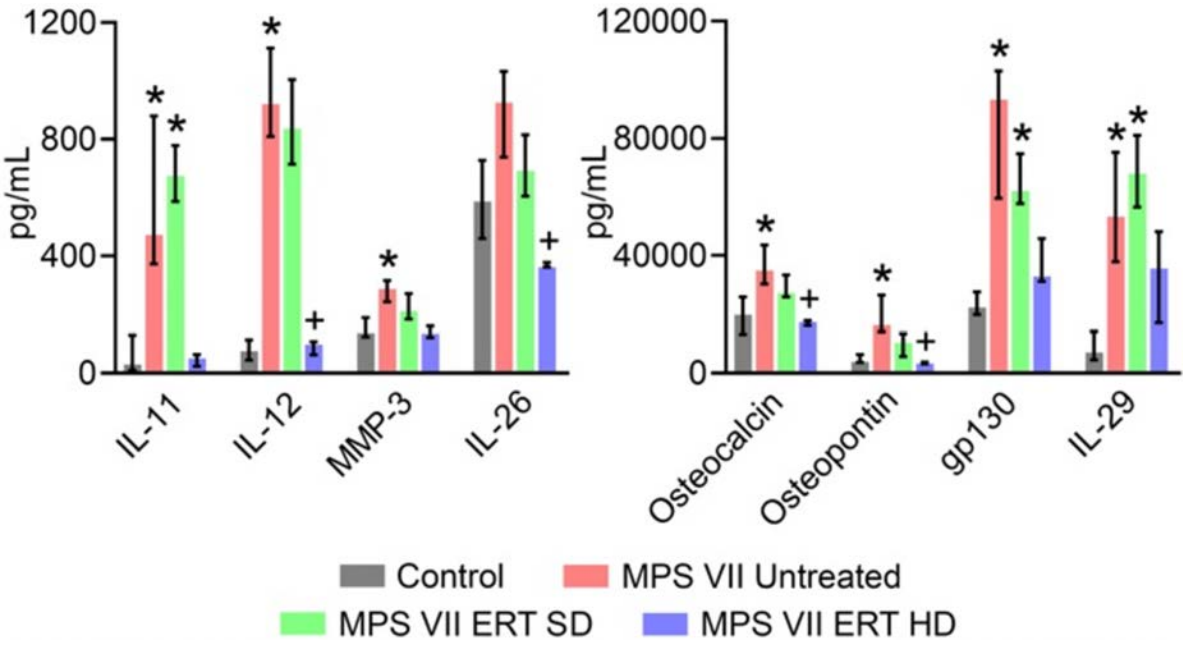

Figure 3. Inflammatory biomarker expression in stifle joint synovial fluid. N=3-6. *p<0.05 vs Control; +p<0.05 vs Untreated MPS VII.

Conclusions

Overall, our findings indicate that Mepsevii® administered shortly after birth at the higher dose of 20mg/kg compared to the standard clinical dose of 4mg/kg results in improved clinical outcomes with respect to joint pathology and mobility in MPS VII dogs. Should these findings be replicated in the clinic, attenuation of synovial joint disease and preservation of mobility has the potential to significantly improve patient quality of life.

Significance

MPS VII patients exhibit severe synovial joint disease resulting in chronic pain and impaired mobility, negatively impacting quality of life. Here we demonstrate that high dose ERT results in a significant improvement in joint disease and mobility in a clinically relevant large animal model.

Acknowledgments

Funding was received from Ultragenyx Pharmaceuticals, Inc, and the NIH. Animal care provided by staff from the Resource Center for Animal Models at UPenn is gratefully acknowledged.

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Fate of Mechano-Sensitive Microcapsules after Intra-Articular Onjection in a Large Animal

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Introduction

Intra-articular injections are commonly administered to relieve joint pain, dampen inflammation, and ultimately slow the progression of joint disease. However, within the synovial joint environment most drugs and drug delivery systems are rapidly cleared, limiting their efficacy. To extend the joint residence time of injected agents, a number of drug delivery vehicles are under development, including nanoparticles[1] and microcapsule-based carriers.[2] Microcapsules are particularly appealing for their efficient encapsulation of biologics that are contained within an aqueous core. The physical dimensions of theses microcapsules, which we term mechanically activated microcapsules (MAMCs), can be tuned to release their contents based on hydrolytic degradation of the (lactic-co-glycolic-acid) (PLGA) shell or via direct mechanical rupture.[3] In this study, we sought to assess the fate of MAMCs and determine their retention, localization, and integrity after intra-articular injection into a large animal knee. We hypothesized that the MAMCs would be retained in the joint space and progressively rupture over time *in vivo*.

Methods

MAMC fabrication

Microcapsules were fabricated using a glass capillary device as previously described (Figure 1A, B).[4]

Animal model

Six 1-year old castrated male Yucatan minipigs were used for this study. Each animal received a single intra-articular knee injection (1mL, 500,000 microcapsules/mL) in the left hind limb, either 2 weeks (N = 3) or 1 day (N = 3) before euthanasia (Figure 1C). For each knee injection, an anterolateral approach was taken whereby a 21 gauge 1 1/2 inch needle was positioned perpendicular to the skin with the tip of the needle directed at a 45-degree angle into the center of the knee (Figure 1D). Sterile saline was first injected to ensure proper placement of the needle. Post-injection, the animals were weight-bearing and walking within an hour.

Limb preparation & In Vivo Imaging System (IVIS®) (microcapsule retention).

After sacrifice, both the left (injected) and right (control) limbs were removed, skinned, and segmented to remove the proximal femur and distal tibia. The hind limbs were then imaged (Perkin Elmer IVIS Spectrum) to assess the retention of injected microcapsules. The excitation and emission wavelengths were set in accordance with Nile Red (Ex. 549/Em. 628), marking the microcapsule shells. Each knee was imaged in four positions—anterior, posterior, lateral, and medial, to determine the viewpoint with the maximum radiant efficiency. Images were analyzed using the Living Image Software and FIJI.

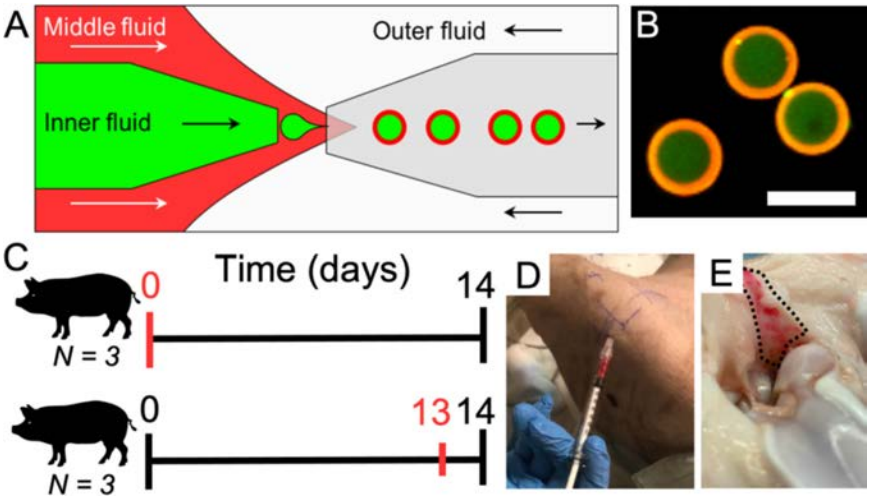

Figure 1. *Microcapsule fabrication and injection.* **(A)** Capillary device forms the microcapsules. **(B)** Injected capsules. Scale bar = 40 μm. **(C)** Study timeline. Red lines depict injection time point. **(D)** Anterolateral injection. **(E)** Microcapsules adhered to and within the adipose tissue (outlined).

Microcapsule localization & integrity

Following IVIS imaging, the left (injected) limbs were finely dissected in order to assess microcapsule localization (Figure 1E) and integrity (% intact). A Zeiss Axio Zoom.V16 was used to acquire images, with n = 100 + microcapsules/animal quantified using the FIJI cell counter.

Statistics.

Figure 2B, C: n.s. Fig. 3: One-tailed Mann-Whitney test. Significance $p \leq 0.05$. Data shown are the mean ± standard deviation.

Results

IVIS imaging showed the presence of the MAMCs within the knee joint both 1 and 14 days post-injection (Figure 2). There was no signal from the control limbs. On average, both the maximum radiant efficiency and the total signal area decreased with increasing time *in vivo*, as expected. After opening joint capsule, MAMCs were observed to be dispersed throughout the synovial and adipose tissues (Figure 3A, B). Most excitingly, intact MAMCs were identified after both 1 (average: 76.1% intact, std dev: 17.1) and 14 days (average: 26.6% intact, std dev: 9.2) (Figure 3C-E). There was a significant

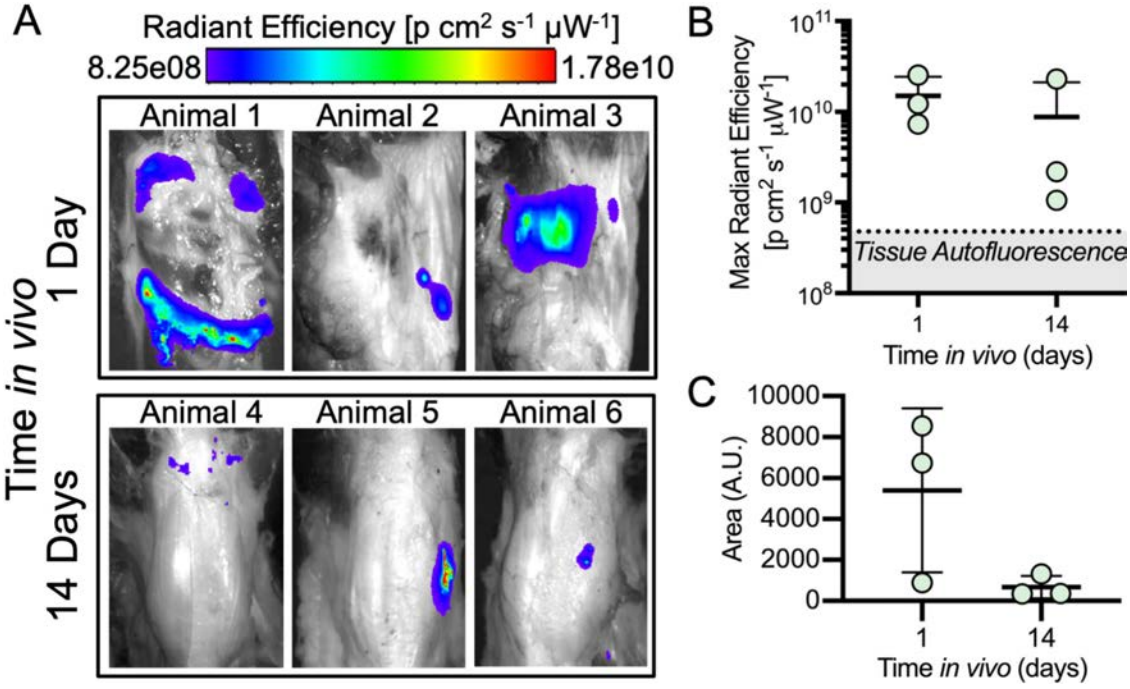

Figure 2. Contact pressure maps (top) and quantification of peak contact pressure. *Microcapsule retention in knee joint.* **(A)** IVIS images at the viewpoint of the maximum signal. **(B)** Quantification of the maximum radiant efficiency. **(C)** Quantification of the total signal area, in arbitrary units (A.U.).

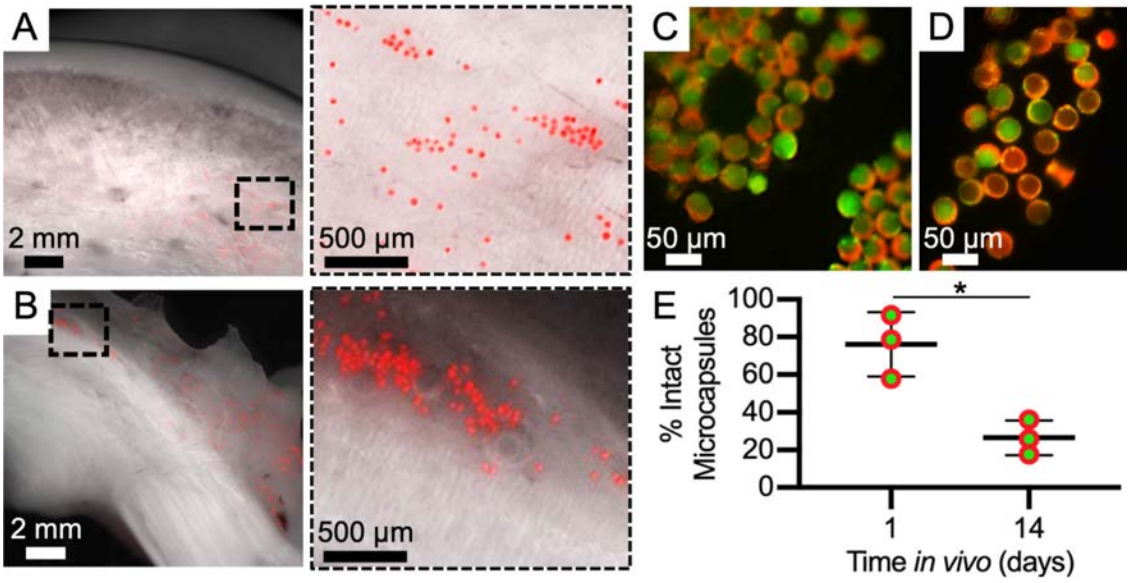

Figure 3. *Microcapsule localization and integrity in knee joint.* **(A, B)** Microcapsules were adherent to the boundaries of the trochlea, and meniscus, respectively. **(C, D)** Microcapsules after 1 and 14 days *in vivo*, respectively. **(E)** Quantification of % of microcapsules that remained intact (with green interior).

decrease in the percentage of intact MAMCs from 1 to 14 days ($p = 0.05$).

Discussion

The variability in the IVIS signal area and location motivates local, directed delivery of the MAMCs for the treatment of specific tissues. However, a simple injection may be advantageous for non-specific delivery of anti-inflammatory molecules, disease modifying agents, or corticosteroids throughout the entire joint. To further modulate the sustained release of an aqueous therapeutic using these microcapsules, a mixture of microcapsule sizes (diameter and shell thickness) with unique rupture profiles and degradation rates could be injected. Future work will also tune the adhesivity of the microcapsules to improve retention at specific locations (e.g., to direct mechano-activation), as well as explore the incorporation of MAMCs within regenerating tissues.

Significance

This work establishes that MAMCS can be injected into the joint space as a potential delivery vehicle for therapeutics and demonstrates a pipeline for assessing their retention, localization, and integrity in a large animal model. Additionally, these results show promise for hydrolytically and mechanically activated sustained delivery of therapeutics to the knee joint.

Acknowledgments

This worked was supported by the Department of Veterans' Affairs, the NSF (CMMI: 15-48571), and the NIH/NIAMS (R01 AR071340, T32 AR007132, and P30 AR069619). The authors would also like to acknowledge Dr. Ching-Hui Huang, IVIS director, at the Small Animal Imaging Facility.

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Muscle, Tendon, and Biomechanics

Collagen V Haploinsufficiency Results in Delayed Healing and Altered Wound Matrix Post-Injury in Murine Tendons

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Disclosures

None

Introduction

Patients with Classic Ehlers-Danlos syndrome (*c*EDS), a disorder characterized most commonly by *COL5A1* haploinsufficiency, suffer from tissue hyperelasticity, skin hyperextensibility, tendon/ligament fragility and abnormal wound healing[1,2]. Collagen V (ColV) haploinsufficiency leads to abnormal tissue development and altered collagen assembly, and mechanical loading of the mouse patellar tendon shows a delay in healing[3] and alterations in stiffness and dynamic modulus post-injury[4]. Furthermore, human studies have shown that females have decreased collagen synthesis[5] and altered gene expression during repair[6], likely influencing the healing potential of *c*EDS tendons.

The objective of this study was to determine the effect of ColV deficiency in female mice on wound matrix formation and the resultant structure-function relationships when mechanical load is applied post-injury. We hypothesized that ColV deficiency will have effects post-injury, resulting in increased fibril diameter and cellularity and decreased mechanical properties, leading to a delayed healing response when compared to wild-type tendons.

Methods

Adult female wild-type (WT) C57/BL6 and heterozygous *Col5a1*$^{+/-}$ mice, a model for *c*EDS, at 120 days of age (n = 84) were used (IACUC approved). Mice were randomly divided into uninjured and injured groups, with injured mice undergoing bilateral patellar tendon injury surgery as previously described[7]. Injured mice were sacrificed early in the proliferative phase at 1-week (1w), early in the remodeling phase at 3-weeks (3w) or later in the remodeling phase at 6 weeks (6w). Uninjured age-matched mice were also sacrificed. Uninjured and injured patellar tendons of both genotypes were assessed.

Gene Expression and Transmission Electron Microscopy (TEM)

Real-time PCR was done as previously described[8]. Each sample (n = 4) was run in duplicate and data was analyzed using StepOne software v2.0. Samples for TEM analysis of fibril structure (n = 4) were fixed *in situ* and processed as described[9].

Mechanics and Histology:

The patella-patellar tendon-tibia complexes were dissected and prepared for mechanical testing (n = 12)[10]. Tendons were subjected to a viscoelastic testing protocol containing three stress relaxations cycles followed by frequency sweeps, culminating in a ramp-to-failure. Dynamic collagen fiber realignment was quantified using cross-polarization imaging during the ramp-to-failure[10]. Histological sections of the patellar tendon-bone complex (n = 4) were prepared using standard techniques. Cellularity was calculated using a standard grading scale.

Statistics

Two-way ANOVAs with post-hoc Bonferroni tests were used to assess the effects of genotype and time on gene expression. Two-way repeated measures ANOVAs with post-hoc Bonferroni tests were used to assess the changes in realignment for increasing strain levels. Kruskal-Wallis non-parametric one-way ANOVA followed by post-hoc Dunn's test for multiple comparisons were used for histologic data. Significance was set at $p \leq 0.05$.

Results

Col5a1 expression was significantly increased in WT tendons at 1w and 3w post-injury (PI) compared to uninjured controls. However, no significant changes in *Col5a1* expression were seen following injury in *Col5a1*$^{+/-}$ tendons (Figure 1). Genotypic differences in *Col5a1* expression were seen at 1w and 3w PI (Figure 1). Fibrils from the mid-substance of WT and *Col5a1*$^{+/-}$ tendons are shown in Figure 2A, with injured tendons having a dominant population of smaller diameter fibrils. Uninjured WT and *Col5a1*$^{+/-}$ distributions were comparable (data not shown), however, distinctly different distributions for WT and *Col5a1*$^{+/-}$ fibrils PI were seen, with *Col5a1*$^{+/-}$ fibrils being larger and more broadly distributed (Figure 2B). Further, WT and *Col5a1*$^{+/-}$ tendons realigned through 5% strain, with *Col5a1*$^{+/-}$ tendons continuing

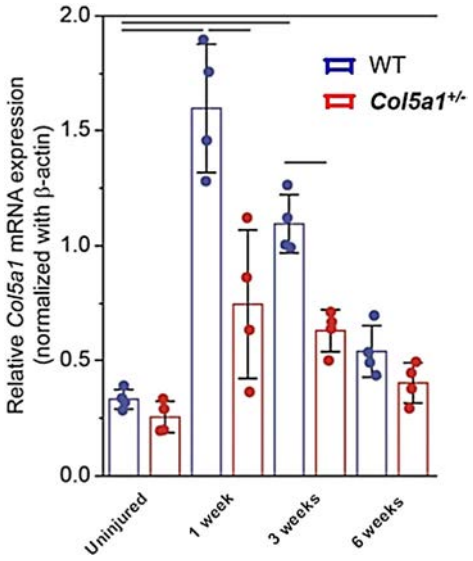

Figure 1. *Col5a1* expression increases 1w and 3w PI in WT but not in *Col5a1*$^{+/-}$ tendons. Solid lines denote significance.

to realign through 6% strain (Figure 3A). Lastly, significant differences in cellularity (Figure 3B) were seen between uninjured and both 1w and 3w samples in both genotypes, and between 1w and both 3 and 6w samples, with no difference between genotypes at any time-point. *Col5a1*$^{+/-}$ tendons had a significant increase in cellularity persisting to 6w PI when compared to uninjured tendons (Figure 3B).

Discussion

ColV plays a key role in fibrillogenesis, matrix remodeling and response to injury, affecting the structure and function of healing tendon. The lack of an increase in *Col5a1* expression 1w PI in *Col5a1*$^{+/-}$ tendons would affect all stages of later healing and indicates a reduction in regulation of fibrillogenesis throughout healing. WT *Col5a1* expression returns to uninjured and *Col5a1*$^{+/-}$ levels by 6w PI injury, indicating that the early increase affects fibril diameter, mechanical properties and cellularity throughout healing. Without the initial increase in ColV following injury, fibrillogenesis is less regulated, resulting in a broader distribution of fibril diameter and a shift to larger fibrils of *Col5a1*$^{+/-}$ tendons PI, which explains the delayed realignment and is supported by previous work[11]. Following injury, a shift towards smaller fibrils was expected as these are new fibrils from collagen secreting myofibroblasts to fill the injury void. Additionally, increased cellularity in *Col5a1*$^{+/-}$ tendons would alter the matrix alignment and architecture, weakening the tissue and affecting mechanical properties. The persistence of increased cellularity in *Col5a1*$^{+/-}$ tendons at 6w PI is consistent with viscoelastic[3] and fatigue data[4], which indicates a delayed healing response

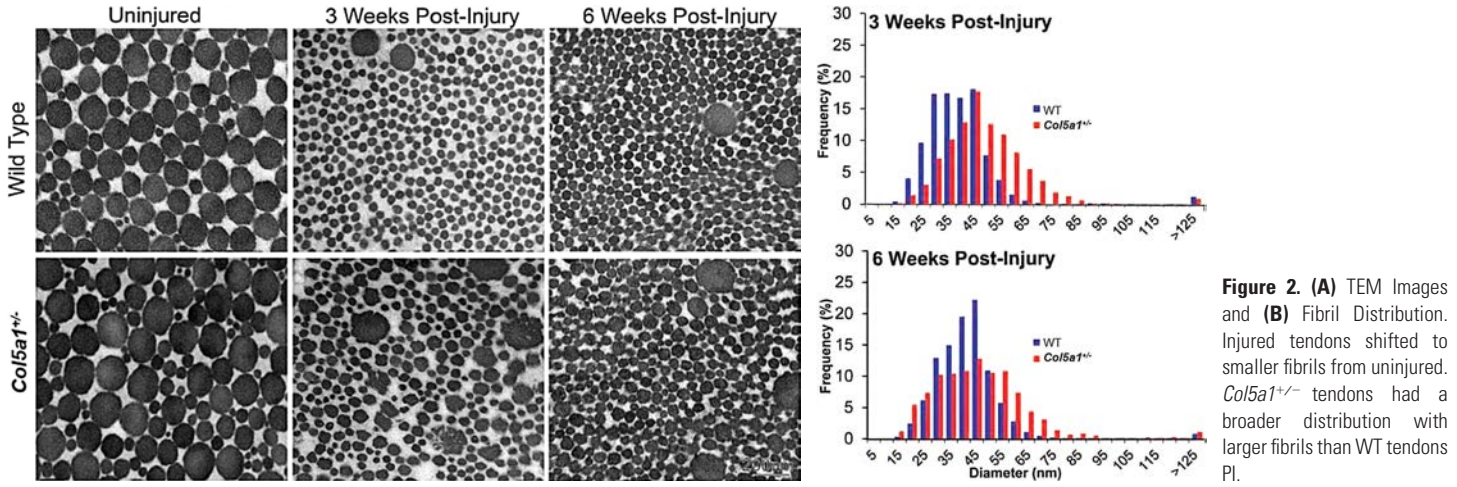

Figure 2. (A) TEM Images and **(B)** Fibril Distribution. Injured tendons shifted to smaller fibrils from uninjured. *Col5a1*$^{+/-}$ tendons had a broader distribution with larger fibrils than WT tendons PI.

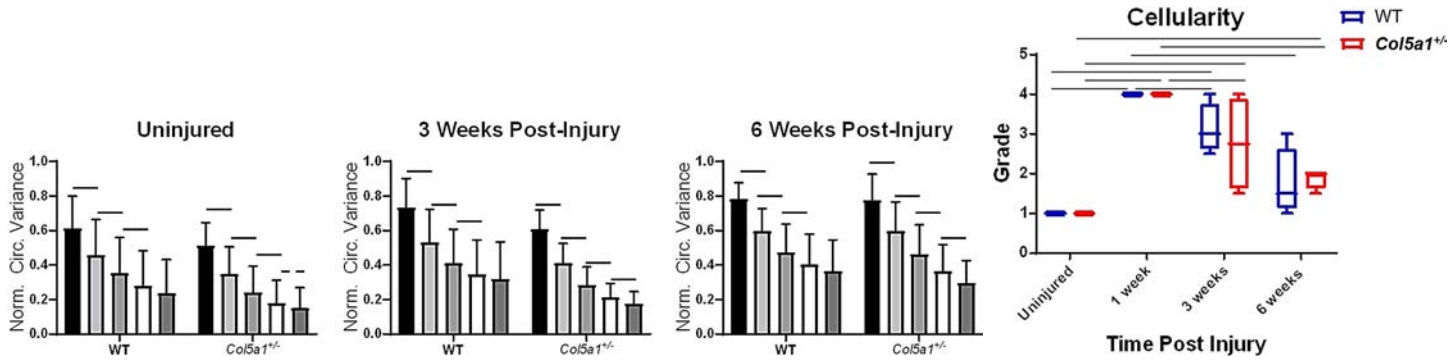

Figure 3. (**A**) Midsubstance Fiber Realignment. *Col5a1*$^{+/-}$ uninjured and injured tendons realign through 6% strain, while WT realign through 5% strain. **(B)** Tendons of both genotypes increased significantly in cellularity 1 and 3w PI when compared to uninjured, this increase persisted to 6w PI in *Col5a1*$^{+/-}$ tendons. Differences in cellularity were also seen between 1w and both 3 and 6w PI in both genotypes. Solid lines denote significance.

in *Col5a1*$^{+/-}$ tendons. Qualitative comparisons to male data show *Col5a1*$^{+/-}$ fibril distribution was similar to WT and cellularity returned to uninjured levels by 6w PI, unlike the data shown, indicating that sex affects outcomes of reduction in ColV[12]. Future directions may include later healing time points to better understand the extent of the delayed healing.

Significance

This study indicates that the lack of an early increase in *Col5a1* expression PI in *Col5a1*$^{+/-}$ tendons influences matrix architecture, alignment, and cellularity throughout tendon healing, demonstrating altered and delayed healing compared to WT tendons.

Acknowledgements

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Scaffold-free 3D Tendon Cell Culture Using Mouse Tendon Cells

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Disclosures

None

Introduction

Standard two-dimensional (2D) cell culture has been widely used for *in vitro* studies to understand molecular mechanisms. However, tenocyte phenotype is not well-maintained in monolayer culture and it is difficult to study extracellular matrix (ECM) organization and morphological maturation of cells without a 3-dimensional (3D) environment. To overcome this limitation, several 3D tendon cell cultures were developed by suture model[1] and Flexcell tissue culture plate system[2]. Based on these 3D tendon culture studies, we developed a scaffold-free 3D tendon culture system using mouse tenocytes, which can be used for genetic manipulation of specific target genes.

Methods

All procedures were approved by the University of Pennsylvania's Institutional Animal Care and Use Committee. Tendon cells were isolated from mouse tail after one hour digestion with type I collagenase. Isolated tendon cells were grown in 20% FBS and 2mM L-glutamine in a-MEM medium. We generated growth channels with 3D-printed mold and the 2% agar in 6-well plate (Figure 1A). To enhance the attachment of the tendon cells to anchor, the anchors were surrounded by hydrophilized PCL-scaffolds. Growth area and PCL-scaffolds were coated with fibronectin. To generate the 3D tendon cell structure, tendon cells were seeded on the fibronectin-coated growth area at 2.5 x 10^6 cells/well with 20% FBS in a-MEM medium. To differentiate 3D tendon cells, TGF-β was treated every two days after seeding. Histological analysis was conducted on the 3D tendon structure at various time points (days 0, 3, 7, 14, and 21 after TGF-b treatment). qRT-PCR analysis examined tendon-related gene markers in 3D tendon structures at various time points (days 0, 3 and 7 after TGF-b treatment). To test the genetic gene manipulation by adenovirus, 3D tendon structures generated using cells from Rosa26-Ai9 mouse and $Tsc1^{f/f}$ mouse. Then, 3D tendons were infected with Ad-CMV-Cre-eGFP. All quantitative data were analyzed using student's t-test.

Results

We can generate six 3D tendons (7-8 mm length and 0.5-0.8 mm thickness) using tendon cells from one mouse tail (Figure 1B). The thickness of the 3D tendon structure was dramatically decreased without TGF-b 3D tendon cell (Figure 1C). This data suggests that TGF-b treatment is essential to maintain 3D tendon structure. Interestingly, we found that the outer layer of the 3D tendon became a tendon-like structure (Figure 1D, blue Box). This tendon-like structure also showed a maturation process similar to the one found during postnatal mouse tendon development, including decreased cell density, increased thickness, and flat cells between highly aligned extracellular matrix (Figure 1D). Consistent with histological changes, the expression of tenogenic genes are increased through time (Figure 2). These results suggest that our 3D tendon culture is a reliable *in vitro* system to study the underlying molecular and cellular mechanism regulating tendon maturation. To test the feasibility of the gene manipulation in 3D tendon culture, we infected 3D tendon with Adenovirus. We generated 3D tendon using tendon cells from R26-Ai9 mice which can express mTomato genes upon CRE recombinase expression. Adenovirus can express CRE recombinase and eGFP (Ad-CMV-Cre-eGFP). We confirmed the infection of virus by the expression of eGFP in outer layer of 3D tendon (Figure 3A, Green color). We also confirmed the CRE recombinase activity by the expression of mTomato (Figure 3A, Red color). We then used the adenovirus to activate mTORC1 signaling in 3D tendon culture by deleting Tsc1, a negative regulator of mTOC1. We generated 3D tendon using tendon cells from conditional *Tsc1* mouse line (*$Tsc1^{f/f}$*). We treated Ad-CMV-eGFP (control) or Ad-CMV-Cre-eGFP (gain-of-function) in 3D tendon generated by *$Tsc1^{f/f}$* tendon cells. Interestingly, our histologic analysis showed that the activation of mTORC1 caused increased thickness and disorganized matrix with bigger and round cells in the tendon-

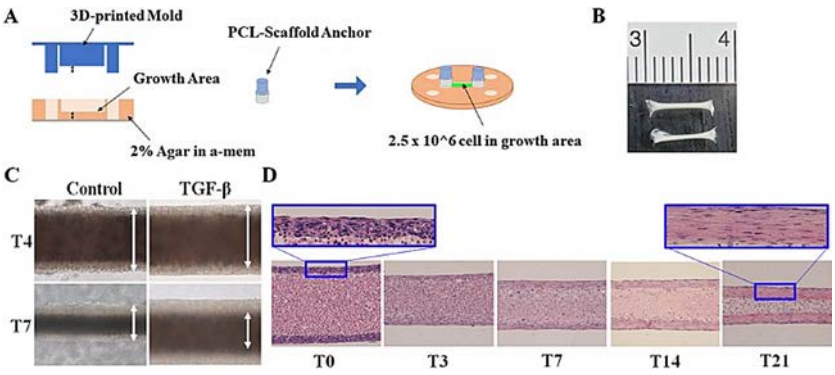

Figure 1. Method of 3D tendon cell culture system and Histology analysis of 3D tendon differentiation. The base of the 3D tendon cell culture was consisted growth area with 2% agaroses with 3D-printed-mold and hydrophilized PCL-scaffold anchor. 3D tendon cell structure was generated tendon cells at 0.5 x 10^6 in fibronectin coated growth area between PCL-scaffold anchor **(A)**. The length of 3D tendon structure is 7 to 8 mm and the thickness is 0.5 to 1 mm **(B).** 3Dtendon structure with or without TGF-b on days 4 and 7 **(C).** H&E stained 3Dtendon structure during tendon cell differentiation **(D).**

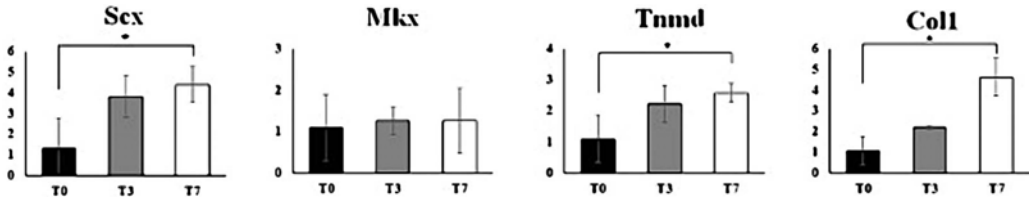

Figure 2. Transcription analysis of 3D tendon. Scleraxis, Mohawk, Tenomodulin, and Collagen type I, of tendon related genes were increased in 3D tendon differentiation.(*indicate P , 0.05 between T0 3D tendon (n 5 4).

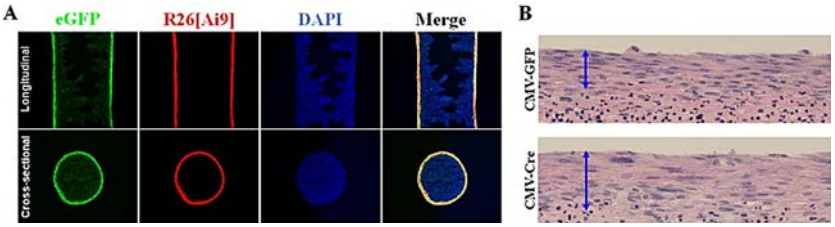

Figure 3. Infection of Adeno-virus in 3D tendon structure. CMV-eGFP and CMV-Cre-eGFP were infected 3D tendon structure from Tsc1fl/fl;R26:Ai9 mice. Green fluorescence shows the expression o feGFP and red fluorescence shows the expression of ROSA26-tdTomato, and DAPI at T7 **(A)**. H&E stained 3D tendon structure from Tsc1fl/fl mice infected CMV-GFP or CMV-Cre-eGFP at T7 **(B)**.

like structure, which is similar to the tendon phenotypes of mTORC1 gain-of-function mouse model (Figure 3B)[3].

Discussion

Our results suggest that the 3D tendon culture system using mouse tendon cells is feasible to manipulate gene expression and effective tools to investigate the molecular mechanism underlying cell maturation and ECM organization. Although 3D tendon showed tendon-like structure, the result may not fully represent an *in vivo* mechanism. The thorough comparison between *In vivo* and *in vitro* result will be necessary to increase the scientific rigor of future research using our 3D tendon culture. We also expect that this system can also be used for pharmacological screening study for tendon diseases.

Significance

This study will contribute to the understanding of cellular and molecular mechanism underlying tendon maturation in vitro using genetic manipulation.

Acknowledgements

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Stat3 Mediates the Function of mTORC1 in Fibrovascular Scar Formation During Postnatal Tendon Development

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Introduction

Tendon injuries are challenging clinical problems due to slow, incomplete healing with fibrovascular scar formation, which reduces tendon function and causes chronic complications such as pain and tendon ruptures. The limited understanding of the regulatory mechanisms underlying fibrovascular scar formation hinders the development of effective treatment modalities for tendon diseases. Our recent study showed that constitutive activation of mTORC1 signaling during postnatal tendon development caused fibrovascular scar-like phenotypes in tendons, including disorganized extracellular matrix (ECM), high cellularity, and neovascularization[1]. However, the downstream mechanism mediating mTORC1 function in fibrovascular scar formation is not clear.

Stat3 is a transcription factor and plays a crucial role in fibrosis and inflammation via the regulation of cell proliferation and ECM organization[2]. Interestingly, a previous study showed that Stat3 can be activated by mTORC1 signaling[3]. This study aims to determine if Stat3 is a mediator of mTORC1 function in fibrovascular scar formation in tendons.

Methods

All procedures were approved by the University of Pennsylvania's Institutional Animal Care and Use Committee. To genetically determine Stat3 as a mediator of mTORC1 function in fibrovascular scar formation in tendons, we performed a genetic rescue experiment by generating three types of the tendon-specific deficient mouse: 1) *Scx-Cre; Tsc1$^{fl/fl}$* (tendon-specific mTORC1 gain-of-function mouse model), 2) *Scx-Cre; Stat3$^{fl/fl}$* (tendon-specific Stat3 knockout mouse model), and 3) *Scx-Cre; Tsc1$^{fl/fl}$; Stat3$^{fl/fl}$* (tendon-specific Tsc1 and Stat3 double knockout mouse model for rescue experiment). Histological analyses were conducted on patellar and Achilles tendons at one month of age. RNA sequencing analysis was used to examine gene expression changes in Achilles tendons of wildtype and *Scx-Cre; Tsc1$^{fl/fl}$* mice. Primary tenocytes were isolated from tail tendon to perform *in vitro* molecular studies using monolayer cell culture. A western blotting experiment was performed to examine the alteration in phosphorylated protein *in vitro*. All quantitative data were analyzed using student's t-test.

Results

Fibrovascular scar-like phenotypes in *Scx-Cre; Tsc1$^{fl/fl}$* (mTORC1 gain-of-function mouse model) prompted us to examine the transcriptional changes of fibrotic markers and metalloproteinases (*Mmps*). Consistent with histological data, *Scx-Cre;Tsc1$^{fl/fl}$* mouse exhibited an increased expression of *Col3a1*, *Fibronectin1* (*Fn1*), *Tenascin C* (*Tnc*), and *Metalloproteinases* (*Mmps*) in tendon, which are highly expressed in pathogenic tendon conditions such as tendon repair and tendinopathy (Figure 1). These data suggest the involvement of mTORC1 in the transcriptional gene regulation during fibrovascular scar formation.

Stat3 is involved in transcriptional gene regulation, and mTORC1 can activate Stat3 via phosphorylation of serine-727 (S727). We performed western blot analysis using primary tendon cells from wildtype and *Scx-Cre; Tsc1$^{fl/fl}$* to determine if mTORC1 can activate Stat3 in tendons. The serine-727 phosphorylation of Stat3 (Stat3 S727), which is mTOR dependent, was significantly increased in tendon cells from *Scx-Cre; Tsc1$^{fl/fl}$* mouse. The mTORC1 independent tyrosine-705 phosphorylation of Ststs3 (Stat3 Y705) tended to increase in *Scx-Cre; Tsc1$^{fl/fl}$* cells (Figure 2). These results suggest that Stat3 can be a downstream target of mTORC1 in tendons.

To genetically confirm that Stat3 is a downstream mediator of mTORC1 function in fibrovascular scar formation, we performed a genetic rescue experiment in which we tested if the deletion of Stat3 can rescue fibrovascular scar-like phenotypes caused by constitutive activation of mTORC1 signaling. We first generated the Stat3 loss-of-function mouse model (*Scx-Cre; Stat3$^{fl/fl}$*) to determine the function of Stat3 in tendon development. *ScxCre; Stat3$^{f/f}$* mouse showed normal growth in tendons (Figures 3A and 3B, second panel). We then generated a conditional double knockout mouse (*Scx-Cre; Tsc1$^{fl/fl}$; Stat3$^{fl/fl}$*) model to perform a

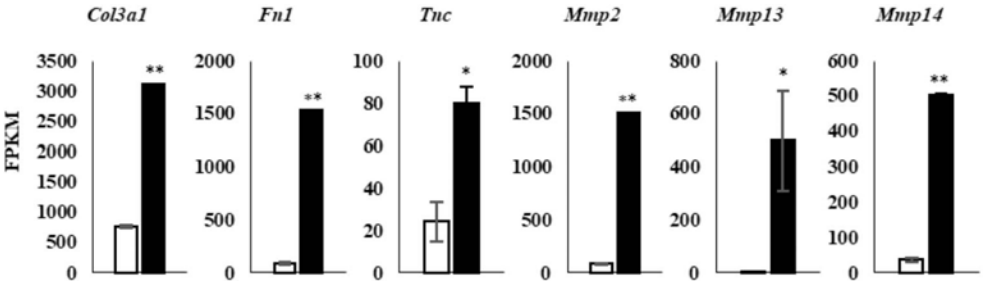
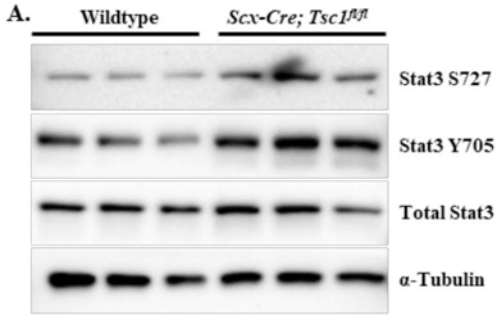


Figure 1. Transcriptome analysis of tendon from Gain-of-mTOR (*Scx-Cre; Tsc1$^{fl/fl}$*) mouse. FPKM (Fragment Per Kilobase of transcript per Million mapped reads) values of RNA-seq data from Achilles tendon of wildtype and *Scx-Cre;Tsc1$^{fl/fl}$* mice in *Co3a1*, *Fibronectin1 (Fn1)*, T*enascin C (Tnc)*, and *Metalloproteinases (Mmps)*. (White bar indicates wildtype mice, Black bar indicates *ScxCre; Tsc1$^{fl/fl}$* mice, *indicate $P < 0.05$ and **indicate $P < 0.001$ between genotypes,n = 3).



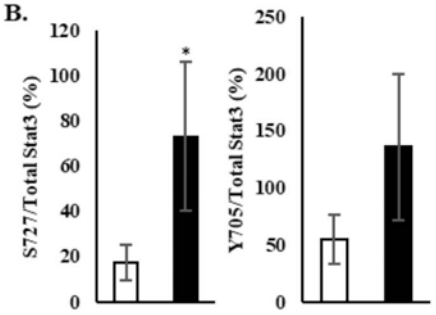


Figure 2. Gain-of-mTOR activated Stat3 signaling in primary tendon cells. Western blots to assess Stat3 signaling, phosphorylation of S727 is mTOR dependent and phosphorylation of Y705 is mTOR independent, activation in *Scx-Cre; Tsc1$^{fl/fl}$* cells **(A)**. Quantification of the western blot bands **(B)**. (White bar indicates wildtype cells, Black bar indicates *Scx-Cre; Tsc1$^{fl/fl}$* Cells,*indicate $P < 0.05$ between genotypes, n = 3).

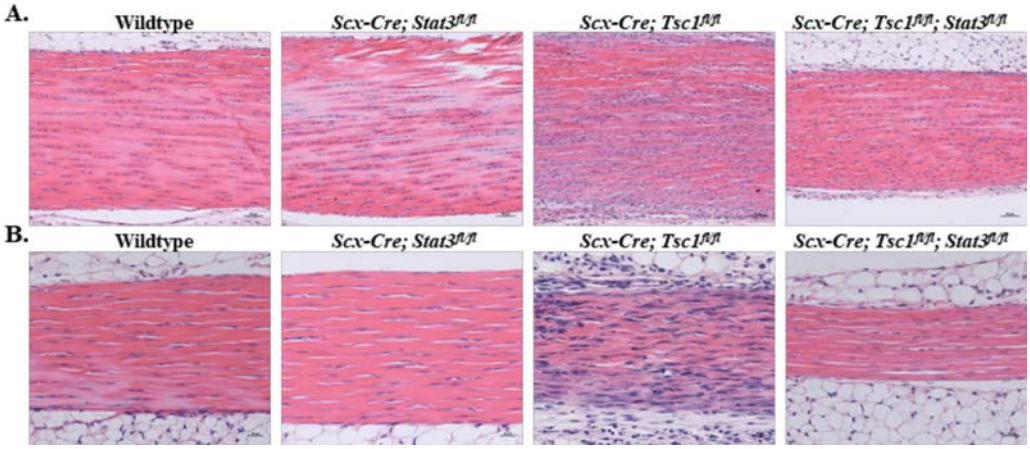


Figure 3. Tendon phenotype of wildtype, *Scx-Cre; Stat3$^{fl/fl}$*, *Scx-Cre; Tsc1$^{fl/fl}$*, and *Scx-Cre; Tsc1$^{fl/fl}$; Stat3$^{fl/fl}$* mouse at 1 mouth old. H&E stained Achilles tendon section **(A)** and patellar tendon section **(B)**.

genetic rescue experiment. Very interestingly, our histological analysis showed that the deletion of Stat3 noticeably rescued the fibrovascular scar-like phenotypes in the mTORC1 gain-of-function mouse (Figures 3A and 3B, third and fourth panel). This data strongly supports our hypothesis that Stat3 mediates mTORC1 function in tendon fibrovascular scar formation.

Discussion

Our study suggests that mTORC1 can be a major biological mechanism regulating fibrovascular scar formation in pathogenic tendon conditions. Our cell and mouse genetic data strongly support that Stat3 is a mediator of mTORC1 function in fibrovascular scar formation. Further molecular study will be required to confirm that the direct molecular interaction between mTORC1 and Stat3. We only tested our hypothesis using the developmental model. Further investigations with healing or repair models will be necessary to confirm the precise function of mTOR/Stat3 signaling in fibrovascular scar formation during tendon healing.

Significance

This study will contribute to the understanding of regulatory mechanisms for fibrovascular scar formation, which may provide the basis and therapeutic approach for pathogenic tendon conditions such as tendon injury repair and tendinopathy.

Acknowledgements

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Adverse Mechanical Consequences from Abnormal Activation and Deactivation of the mTORC1 Pathway in Tendons

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Disclosures

None

Introduction

Tendon, a collagen-rich tissue, is the primary component that transmits loads from muscle to bone. It is relatively avascular and hypocellular, and thus can be afflicted with tendinopathy or ruptures without a clear solution towards complete recovery. Thus, recent efforts have strived to understand the mechanistic basis of tendon development and maturation, which might help guide better treatment options. The mechanistic target of rapamycin complex 1 (mTORC1) regulates multiple cellular biological processes such as metabolism, growth, proliferation, and survival. Recently, we showed that both deactivation and activation of mTORC1 in tendon caused impaired postnatal tendon development with immature collagen fibrillogenesis, which suggest that fine-tune regulation of mTORC1 signaling is essential for normal postnatal tendon development. While these data highlight the molecular effects of deactivation and activation of the mTORC1 pathways, downstream macroscale effects on tendon mechanical function remain unclear. Therefore, the objective of this study was to examine the mechanical response of mouse Achilles tendons after activation or deactivation of mTORC1, via tendon-specific deletion of *Tsc1* (gain-of-function) or *Raptor* (loss-of-function), respectively. We hypothesized that any deviations from physiological levels of mTORC1 signaling will adversely affect the structural and material properties of tendons, with a pronounced effect due to impaired collagen fibrillogenesis.

Methods

All procedures were approved by the University of Pennsylvania's Institutional Animal Care and Use Committee. Mouse hindlimbs (n = 10/group) were collected from the *ScxCre; Raptor$^{f/f}$* mice at P60 for loss-of-function study. Mouse hindlimbs (n 5 7/group) were collected from the *ScxCre;Tsc1$^{f/f}$* mice for gain-of-function study at P30. All mice assigned for mechanical testing were frozen at −20° C until the day of testing. Mice were thawed at room temperature and calcaneal bone-Achilles tendon-muscle complexes were grossly dissected. All extraneous soft tissues and muscles were finely dissected, and a custom laser device was used to measure the cross-sectional area (CSA) of the Achilles tendon. The myotendinous junction was sandwiched between two sandpaper tabs with cyanoacrylate glue to prevent any slippage. The calcaneal bone was gripped with a custom fixture and the construct was mounted onto a material testing machine (Instron 5542, Instron Inc., Norwood, MA). All testing was conducted in phosphate buffered saline bath at room temperature. Each sample was preloaded to 0.02 N followed by 10 cycles of preconditioning between 0.02 to 0.04 N. After a resting period of 60 seconds at 0 N, the sample was quasi-statically ramped to failure at a strain rate of 0.03 %/s. All data were collected at 100 Hz. Ensuing force-displacement curves were analyzed to obtain failure load (N) and tissue stiffness (N/mm, defined as the slope of the linear region). Cross-sectional areas (mm^2) and gauge length (mm) values were used to obtain stress-strain curves for each sample. Modulus (MPa) was calculated as the slope of the linear region of the stress-strain curve and failure stress (N/mm^2) as the maximum stress value observed.

Results

Consistent with previous histological studies, Achilles tendons from *ScxCre;Raptor$^{f/f}$* mice had structural deficits with a significantly reduced CSA (Figure 1A). This further resulted in a significantly reduced failure load (Figure 1B) and significantly lower tendon stiffness (Figure 1C). *ScxCre; Raptor$^{f/f}$* tendons did not show material deficits with no significant differences observed in tendon modulus (Figure 1D) and failure stress (data not shown). Consistent with previous histological study, Achilles tendons from *ScxCre;Tsc1$^{f/f}$* did not have any macroscale structural changes with no significant difference in tendon CSA (Figure 2A). Unexpectedly, structural properties including failure load (Figure 2B) and tendon stiffness (Figure 2C) were significantly lower. Further, material effects were evident in *ScxCre;Tsc1$^{f/f}$* tendons

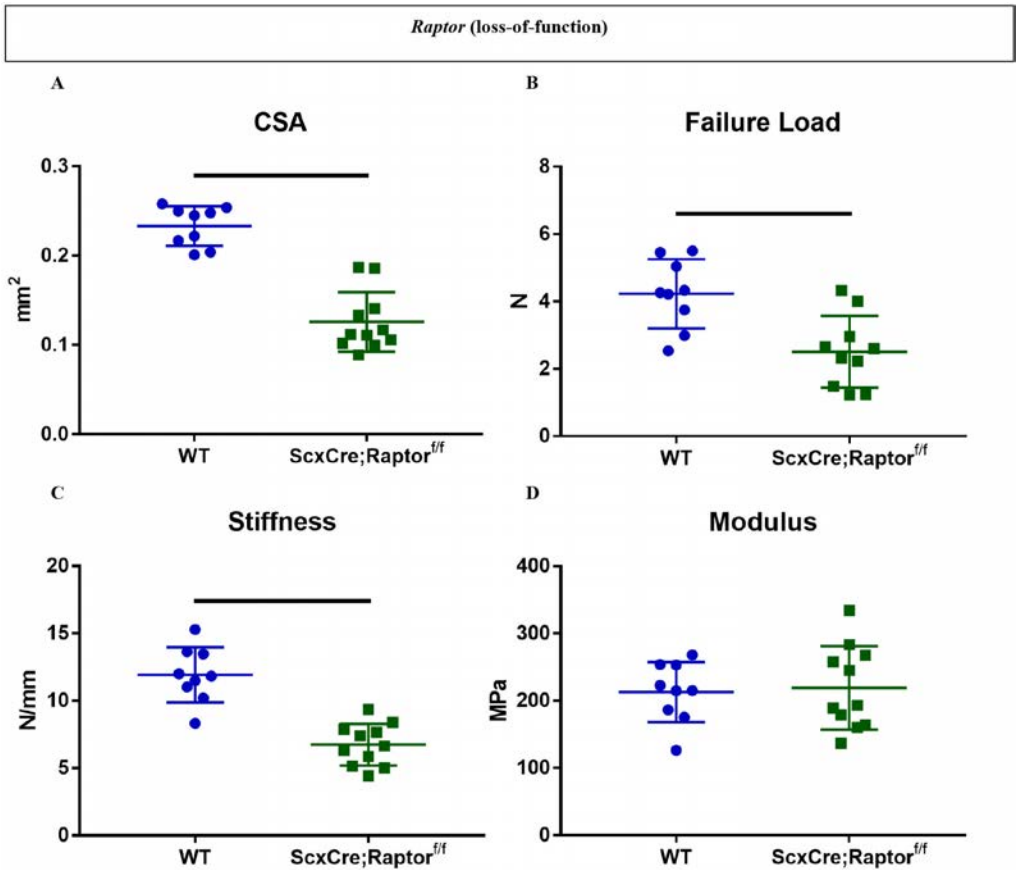

Figure 1. Comparison of mechanical properties of control and *ScxCre;Raptor*$^{f/f}$ mouse Achilles tendons **(A)** Cross-sectional area; **(B)** Failure load; **(C)** Stiffness; **(D)** Modulus. Bars indicate a significant difference at $p < 0.05$ after unpaired two-tailed t-tests.

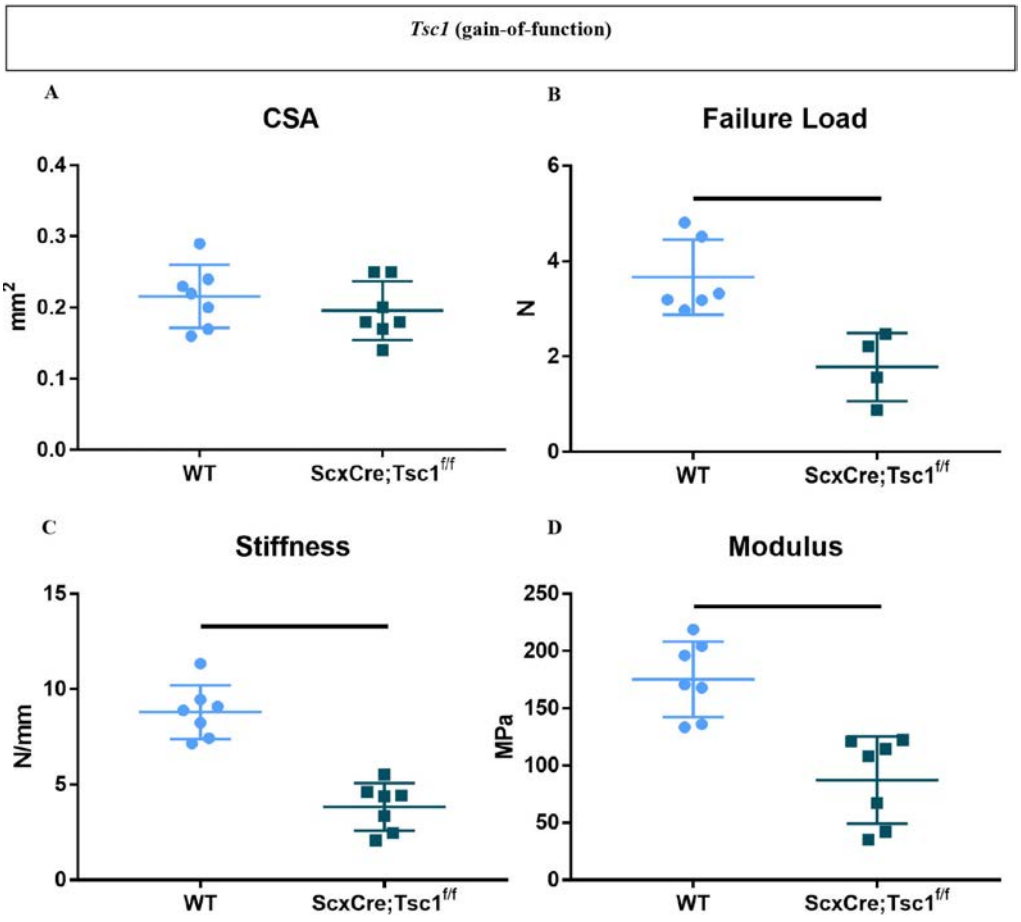

Figure 2. Comparison of mechanical properties of control and *ScxCre;Tsc1*$^{f/f}$ mouse Achilles tendons: **(A)** Cross-sectional area; **(B)** Failure load; **(C)** Stiffness; ***(D)*** Modulus. Bars indicate a significant difference at $p < 0.05$ after unpaired two-tailed t-tests.

with a significantly reduced tendon modulus (Figure 2C) and a trending difference ($p < 0.1$) in failure stress (data not shown).

Discussion

This study investigated the macroscale mechanical sequelae from abnormal activation and deactivation of the mTORC1 pathway in murine Achilles tendons. Each of these perturbations resulted in substantial, but interestingly divergent disruption of tendon mechanical response. Our previous work with *ScxCre;Raptor$^{f/f}$* tendons showed the loss of the typical bimodal fibril diameter distribution with abrogation of all large diameter fibrils. Surprisingly, this resulting unimodal distribution of smaller diameter fibrils did not affect the material properties of these tendons with not differences observed in tendon modulus or failure stress. Transmission electron microscopy of *ScxCre;Tsc1$^{f/f}$* tendons showed a more severe effect on collagen fibrils with most diameters in the 40-50 nm range. Further, histological analysis depicted a very disorganized matrix and increased neovascularization. These structural and extracellular matrix (ECM) disruptions may explain the significant material property effects seen here in *ScxCre;Tsc1$^{f/f}$* tendons. However, it was surprising that even with these ECM deficiencies, macroscale structure *i.e.,* cross-sectional area was not affected. Future studies will explore microscale structural changes in tendon ECM via second harmonic generation imaging of collagen fibrils, and atomic force microscopy imaging to measure fibril sliding and deformation, which might explain the macroscale mechanical response reported here.

Significance

The findings reported here suggest that *optimal* mTORC1 signaling is crucial for postnatal tendon development and abnormal activation or deactivation has deleterious effects on tendon mechanics. Clinically, temporal control of this pathway might allow for improved tendon healing outcomes.

Tendon Resident Macrophages Internalize Type 1 Collagen and Express Trophic Signaling Factors

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Disclosures

None

Introduction

While the majority of cells within the growing tendon are tendon fibroblasts that express the common tendon reporters Scx-GFP and Col1a1-CFP, we recently identified a population of cells that are positive for the macrophage marker F4/80 and negative for the Col1a1-CFP and ScxCre;R26R-tdTomato fluorescent reporters in the mouse[1]. It is unknown at what stage these resident macrophages begin to populate the tendon and what their role is in tendon growth and development. Therefore, the objective of this study was to determine the distribution of tendon resident macrophages throughout development and elucidate potential mechanisms by which these cells may support extracellular matrix (ECM) regulation and tenogenic differentiation.

Methods

Transgenic mice

All procedures were approved by the University of Pennsylvania's Institutional Animal Care and Use Committee. Col1a1(3.6kb)CFP (Col1CFP) mice containing 3.6kb of the Col1a1 promoter driving CFP expression were used in this study[2].

Experimental design

Knees from Col1CFP mice at E15.5, P4, P28, and P56 were used for patellar tendon (PT) immunofluorescence (n = 2-3/time point). Tail tendons (TTs) were isolated from 4-6-week-old Col1CFP mice for explant culture (n = 4). TTs from P28 mice were used for cell sorting and gene expression analysis (2 mice per biological replicate; n = 3). Knee sections were stained with rat anti-F4/80, stained with Hoechst, and imaged.

TT explant and protease substrate culture

TTs were cultured in individual channels of 6-channel slides (Ibidi μ-Slide VI) in media supplemented with 200 nM MMPSense 645 FAST MMP-activated fluorescent dye and 10 μg/ml DQ Collagen (Type 1, fluorescein conjugate) collagenase-activated fluorescent substrate (5 TTs/mouse); explants were imaged after 2 days in culture.

Cell isolation and qPCR

TTs were serially digested to discard surface cells and obtain internal cells. Isolated cells were labeled with anti-F4/80 magnetic particles and sorted to obtain F4/80-enriched and F4/80-depleted populations. RNA was isolated and expression was measured via qPCR for *18S*, *Col1a1, Adgre1, Csf1, Csf1r, Tgfb1, Tgfb2, Tgfb3,* and *Tgfbr2.* qPCR results were compared via Kruskal-Wallis followed by Mann Whitney U tests adjusted for multiple comparisons. Publicly available single-cell RNA sequencing (scRNA-seq) datasets were obtained from the NCBI GEO (GSE139558[3] and PRJNA506218[4]). Count matrices were filtered, normalized, scaled, cell cycle regressed, reduced, and clustered using Seurat v3.1[5].

Results

Resident macrophages are present throughout tendon development.

To investigate the presence of resident macrophages during tendon development, we performed immunofluorescence for the macrophage marker F4/80 on PT sections. We found that Col1CFP(−);F4/80(+) resident macrophages were present in the linear arrays of the PT at E15.5, P4, P28 and P56, ranging from 4% to 9% of total cells within the midsubstance (Figure 1; magenta).

Tendon resident macrophages internalize cleaved DQ Collagen and MMPSense

Because macrophages are present throughout tendon growth and development, we hypothesized that they may play a role in ECM assembly. Upon culturing P28 TT explants with media supplemented with DQ Collagen and MMPSense, we found that the unquenched cleaved fluorescent substrates were localized almost exclusively within the Col1CFP(−) cells (Figure 2; yellow arrows). Given this finding and the fact that virtually all Col1CFP(−);MMPSense(+) are F4/80(+) [1], we concluded that resident macrophages are capable of internalizing excess proteolytically cleaved collagen

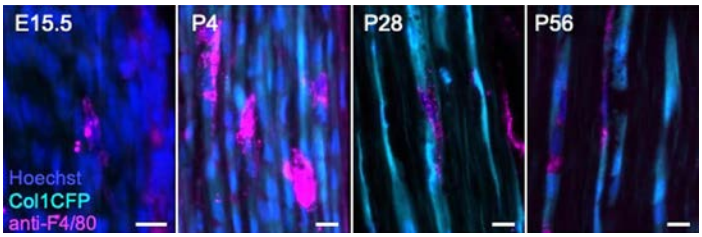

Figure 1. F4/80 immunofluorescence on Col1CFP patellar tendons (scale = 10μm).

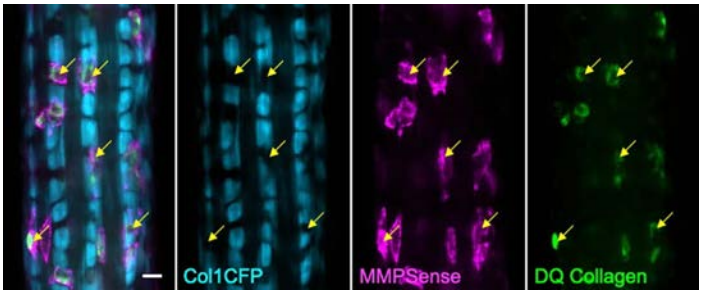

Figure 2. Col1CFP tendons cultured in medium containing MMPSense and DQ Collagen (scale = 10μm).

Potential cell signaling circuit between F4/80-enriched and F4/80-depleted cell populations

Due to the observed proximity of fibroblasts and macrophages and previous studies demonstrating cell-cell communication between macrophages and stromal cells, we investigated potential signaling pathways in F4/80-sorted tendon cell populations. The F4/80-enriched (macrophage-enriched) population expressed 53.5-fold higher levels of *Csf1r* compared to the F4/80-depleted (fibroblast-enriched) population, which expressed 5.85-fold higher levels of *Csf1* (Figure 3). Because TGFβ signaling plays a major role in tendon development [3] and macrophages have been shown to signal to fibroblasts via TGFβ [6], we analyzed expression levels of key TGFβ ligands and their receptor. All surveyed genes were detected in both populations. We found the macrophage-enriched population to have a 2.75-fold higher expression of *Tgfb1*, while the fibroblast-enriched population exhibited 2.38, 2.36, and 2.65-fold higher levels of *Tgfb2*, *Tgfb3,* and *Tgfbr2,* respectively.

scRNA-seq datasets confirm potential cell-cell communication between fibroblasts and macrophage

Analysis of two previously published scRNA-seq data sets showed that, among clusters enriched for *Adgre1* (F4/80), 78.0% (P7 forelimb and hindlimb tendons[3]) and 64.6% (3-month-old PTs[4]) of cells express *Csf1r*; of these *Csf1r*(+) cells, 44.4%[3] and 36.5%[4] express *Tgfb1*. Furthermore, among clusters enriched for *Tnmd* (tenocyte marker), 11.0%[3] and 18.3%[4] of cells express detectable levels of *Csf1* and 12.5%[3] and 14.4%[4] express *Tgfbr2*.

Discussion

In this study, we demonstrated that resident macrophages are present alongside fibroblasts during embryonic tendon development and throughout postnatal growth (Figure 1).

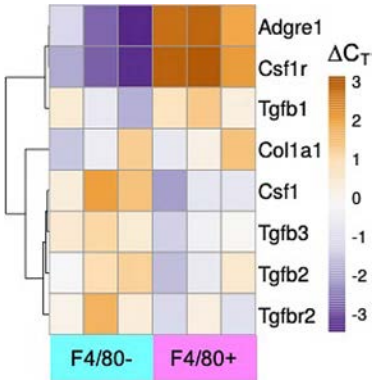

Figure 3. Gene expression of F4/80-sorted cells.

This macrophage population is capable of internalizing proteolytically cleaved DQ Collagen and MMPSense within their native environment (Figure 2), which suggests that these cells may be important in the degradation and/or clearance of ECM during development. We also established that fibroblasts express *Csf1* (Figure 3), a cytokine necessary for macrophage survival and function. scRNA-seq data showed that only a subset of fibroblasts expresses detectable levels of *Csf1*, suggesting that the spatial distribution of *Csf1r*(+) macrophages is dependent on *Csf1* expression by stromal cells, as is the case in other tissues. Our data and others' showed that tendon resident macrophages express TGFβ ligands and are especially enriched for *Tgfb1*, which supports our working hypothesis that macrophages provide trophic signaling to *Tgfbr2*(+) fibroblasts. Resident macrophages in other tissues are necessary for their development and contribute to ECM regulation and cell signaling circuits with surrounding resident cells. Our future studies aim to determine if analogous phenomena occur in tendons.

Significance

An improved understanding of the cells and signaling pathways that define and regulate the tendon lineage will be crucial to developing new therapies to attenuate the progression of pathologies and improve repair outcomes following injury. This study gives new insight into potential roles of resident macrophages during tendon development and growth and their interaction with *Col1a1*-expressing tendon fibroblasts.

Acknowledgements

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Collagen XII Regulates Tendon Dynamic Mechanical Properties and Collagen Fiber Realignment

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Disclosures

None

Introduction

Myopathic Ehlers-Danlos syndrome (mEDS) is a connective tissue disorder caused by mutations in the *Col12a1* gene, which encodes for collagen XII, a fibril-associated collagen with interrupted triple helices (FACIT). Patients with mEDS experience myopathy, joint hypermobility and contractures[1], indicating dysregulation of connective tissue function due to the absence of collagen XII. Our recent data showed that tendons from global collagen XII knockout (*Col12a1*$^{-/-}$) mice exhibited disrupted tendon fiber organization and assembly as well as increased cross-sectional area and stiffness. This suggests that the disruption of tendon structure function in the absence of collagen XII may be caused by a lack of distinct fiber domains resulting in reduced fiber sliding and increased stiffness. However, our previous findings may be confounded by the effects of collagen XII knockdown on other tissues, such as muscle and bone, and the isolated role of collagen XII on tendon mechanical function is still unknown. Therefore, the objectives of this study are to (1) evaluate the specific role of collagen XII in regulating tendon mechanical properties and the dynamic loading response in mature mice using tendon-targeted (scleraxis Cre) collagen XII knockout mice and (2) determine if the role of collagen XII is sex-specific. We hypothesized that a collagen XII knockout would lead to increased tendon stiffness and reduced collagen fiber realignment under loading due to disruptions in tendon matrix assembly in both sexes.

Methods

Patellar tendons from female and male, day 60 tendon-targeted collagen XII knockout (KO) mice (ScxCre;*Col12a1*$^{f/f}$, n = 6-8/group) and control (Cre- littermates, n = 4-6/group) mice (IACUC approved) were mechanically evaluated using viscoelastic and dynamic collagen fiber realignment methods, as described[2]. Tendons underwent a loading protocol of three stress relaxations at 3, 4, and 5% strain each with a dynamic frequency sweep (0.1, 1, 5, 10Hz), followed by a quasi-static ramp to failure. During the ramp, images were continuously acquired through rotating cross polarizers to evaluate dynamic collagen fiber realignment. For each sex, comparisons between genotypes were made using two-tailed, t-tests with significance set at $p \leq 0.05$ and trends at $p \leq 0.1$.

Results

Cross-sectional area was not different between female KO and control mice, while male KO tendons were smaller than control (Figure 1a). Contrary to our hypothesis, linear stiffness was significantly reduced in KO mice for both sexes (Figure 1b), and only female KO tendons exhibited a trending decrease in elastic modulus with no difference between male groups (Figure 1c). Additionally, percent relaxation was significantly reduced in female KO tendons at all strain levels (5% strain shown in Figure 1d). Despite only minor differences in elastic modulus, both sexes demonstrated striking differences in dynamic properties. Compared to their respective controls, dynamic modulus was significantly reduced in KO groups while phase shift was significantly elevated across all strain levels and frequencies (5% strain, 1Hz shown in Figures 1e and f, respectively). This suggests alterations in matrix structure leading to more viscous mechanical behavior during dynamic loading in the KO groups. This finding is further supported by a reduced degree of collagen fiber realignment (Figure 2a) in the female KO group,as shown by increased circular variance at all strain values (Figure 2b), and a reduced rate of fiber realignment in the male KO group (Figure 2c), as shown by increased circular variance at lower strain values (Figure 2d).

Discussion

This study investigated the isolated role of collagen XII on tendon mechanical function using female and male ScxCre;*Col12a1*$^{f/f}$ mice. Interestingly, KO patellar tendons had reduced stiffness, which contrasts the increased stiffness observed in flexor digitorum longus (FDL) tendons of global collagen XII knockout mice. This suggests that the effects of global knockout

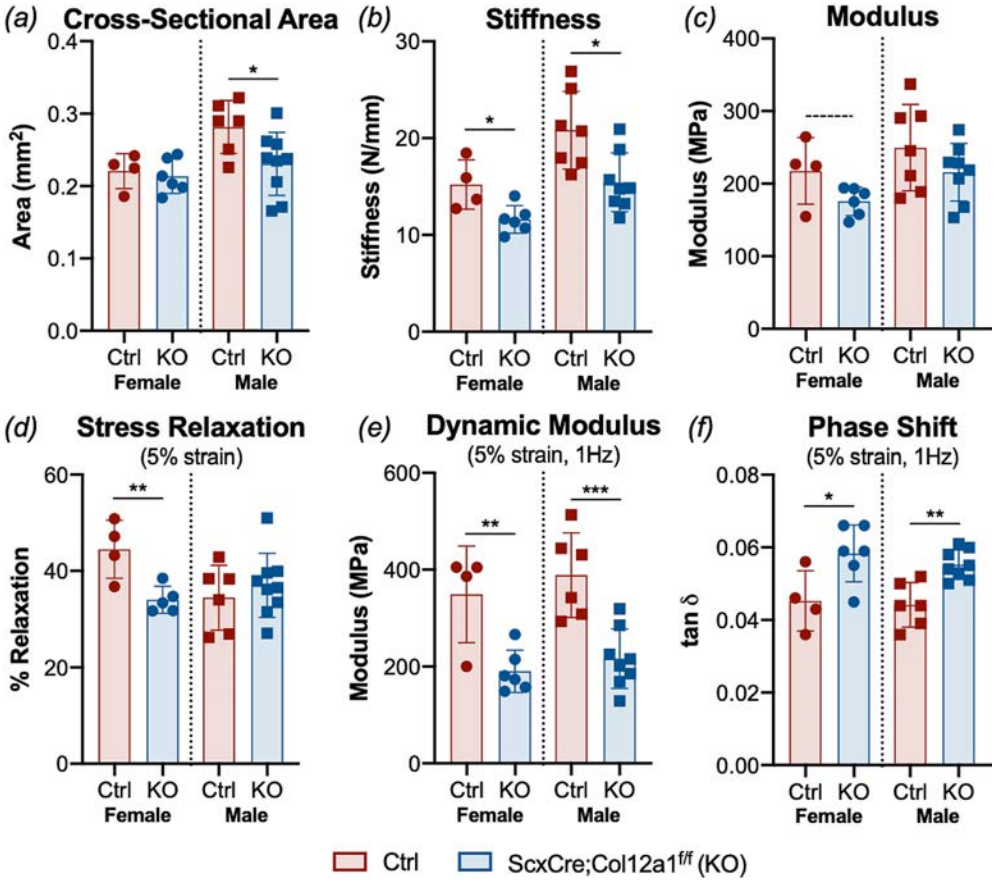

Figure 1. Male KO patellar tendons had **(A)** reduced cross-sectional area, while both sexes exhibited **(B)** reduced tendon stiffness. **(C)** Modulus and **(D)** percent relaxation were reduced in female KO tendons. **(E)** Dynamic modulus was reduced and **(F)** phase shift was elevated in KO groups for both sexes. Data presented as mean ± standard deviation. (---p ≤ .1, *p ≤ .05, **p ≤ .01,***p ≤ .0.001).

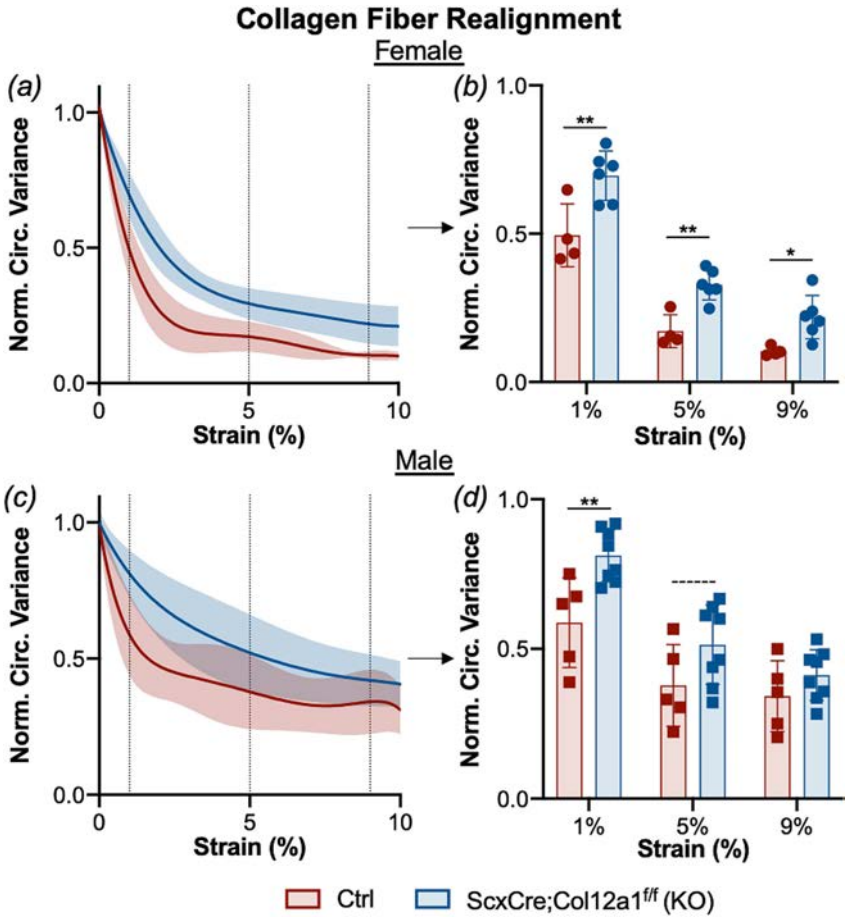

Figure 2. (A) Female KO tendons exhibited reduced collagen fiber realignment with increasing strain, as evidenced by **(B)** increased normalized circular variance at all strain levels compared to control. **(C)** Male KO tendons exhibited a reduced rate of collagen fiber realignment with **(D)** increased normalized circular variance at lower strain values compared to control. Data presented as mean ± standard deviation. (---p ≤ 0.1, *p ≤ 0.05, **p ≤ 0.01).

of collagen XII on muscle[3] and bone[4] may indirectly affect tendon, necessitating the use of this tendon-targeted mouse model. The effects of collagen XII knockout could also be tendon-specific, as mEDS patients present with both distal joint hypermobility and proximal joint contractures. Furthermore, female KO tendons exhibited less stress relaxation at all strain levels, suggesting alterations in the ability to effectively dissipate load. This could be attributed to a disruption in the establishment of proper hierarchical assembly leading to a reduction in fiber and fibril sliding. Matrix disorganization could also explain the striking differences in dynamic properties, as evidenced by reduced dynamic modulus, increased phase shift, and reduced collagen fiber realignment. Interestingly, our preliminary data shows that, in addition to its structural role, collagen XII may also be critical for regulating cellular organization necessary for establishing hierarchical structure and tendon function, and studies are ongoing to investigate these temporal roles of collagen XII throughout development. Finally, though similar trends were observed for both female and male groups in response to collagen XII knockout, there was a more pronounced effect in female mice. *Coll12a1* polymorphisms have been linked to an increased incidence of ACL ruptures in women[5], suggesting a possible sex-specific effect. Our study demonstrates that collagen XII knockout in tendons affects tendon matrix structure and organization, resulting in altered structural, viscoelastic, and dynamic collagen fiber realignment properties.

Significance

This study demonstrates the critical role of collagen XII in regulating tendon dynamic mechanical behavior, highlighting its importance in establishing tendon structure-function and its re-establishment following injury.

Acknowledgements

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Tendon Pathology Alters Chromatin Organization and Mechano-sensitivity in Human Tenocytes

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Disclosures

None

Introduction

Fibrous connective tissue injury or degeneration (e.g. tendinosis) is prevalent, with few treatments that restore function. Pathological changes in tendon alter the tissue chemo-physical environment, impacting endogenous cell behavior[1,2]. For instance, degeneration alters collagen orientation and changes tissue stiffness,[1,2] and lower local oxygen levels present in damaged tissues may promote early tendinopathy[2]. Furthermore, in the early phase of the injury/disease process, pro-inflammatory cytokines in the local milieu promote tendon cell catabolic response. These pathological changes in tissues impact cells across length scales, including at the level of chromatin organization. In a previous study, using super-resolution imaging, we found that tendinosis results in nano-scale chromatin reorganization in human tenocytes, with chromatin increasingly localized to the nuclear periphery, compared to healthy age matched controls[3]. Moreover, when healthy human tenocytes were cultured on a soft microenvironment (~3 kPa), we observed similar chromatin reorganization as seen in degenerative tenocytes[3]. Based on these findings, here we extended these studies to further investigate how cues from pathological chemo-physical environment (e.g. dynamic changes in stiffness, induction of hypoxia, and presence of inflammatory factors) impact chromatin remodeling in tenocytes.

Methods

Human tenocytes were isolated from young [Young (y), 42 years] or degenerative [Tendinosis (t), 35 years] tendons according to established protocols[2]. To investigate how changes in oxygen tension affect nanoscale chromatin organization, young healthy tenocytes were seeded on chambered-coverglass (500 cells/mm^2) for one day, followed by four days of culture under normoxic (21% O_2) or hypoxic (1% O_2) conditions. Next, to investigate how pro-inflammatory cytokines impact chromatin, young tenocytes were cultured on chambered-cover glasses for 1 day followed by additional culture for 24-hours with/without exposure to IL-1β (0.1-1ng/ml) or TNFα (1-10 ng/ml). Finally, to investigate how degeneration impacts mechano-sensitivity of tenocytes, young or tendinosis tenocytes were seeded onto a "stiffening" hydrogel system that provides rapid dynamic changes in substrate stiffness (for example, ~3→30 kPa) in the presence of cells[5]. For this, cells were pre-cultured for 24 hours followed by additional 24 hours of culture after stiffening. For all studies, fixed cells were immunostained for histone-H2B (H2B, Proteintech), and then incubated with secondary antibodies custom labeled with activator-reporter dye pairs (Alexa Fluor 405-Alexa Fluor 647, Invitrogen) for super-resolution stochastic optical reconstruction microscopy (STORM) imaging (Nanoimager, ONI)[3,4]. Obtained STORM images were analyzed by dividing the inner border of the nucleus (border: 15-20% determined from the image intensity profile across the diameter of the nucleus) from the rest of the nucleus and rendered these segments using custom MATLAB code and the Nanoimager software (ONI) respectively. For quantitative analysis, in MATLAB, Voronoi tessellation of the H2B localizations was adapted to segment super-resolution images[3,4].

Results

Consistent with our previous findings[3], super-resolution imaging H2B heat maps showed that, while dense chromatin was distributed through the nucleus in young healthy tenocytes (Young), H2B was more condensed and primary localized to the nuclear periphery in young degenerative nuclei (Tendinosis) (Figure 1a-c). Strikingly, when healthy tenocytes were cultured under the hypoxic conditions, chromatin relocalized to the nuclear periphery and became more condensed (Figure 1a-c). This suggests that altered oxygen tension in tendon after injury or during degeneration may promote aberrant chromatin remodeling. Given that injury and degeneration increase inflammation, we next investigated how pro-inflammatory cytokines impact nanoscale chromatin organization in young healthy tenocytes. These studies showed that exposure to pro-inflammatory

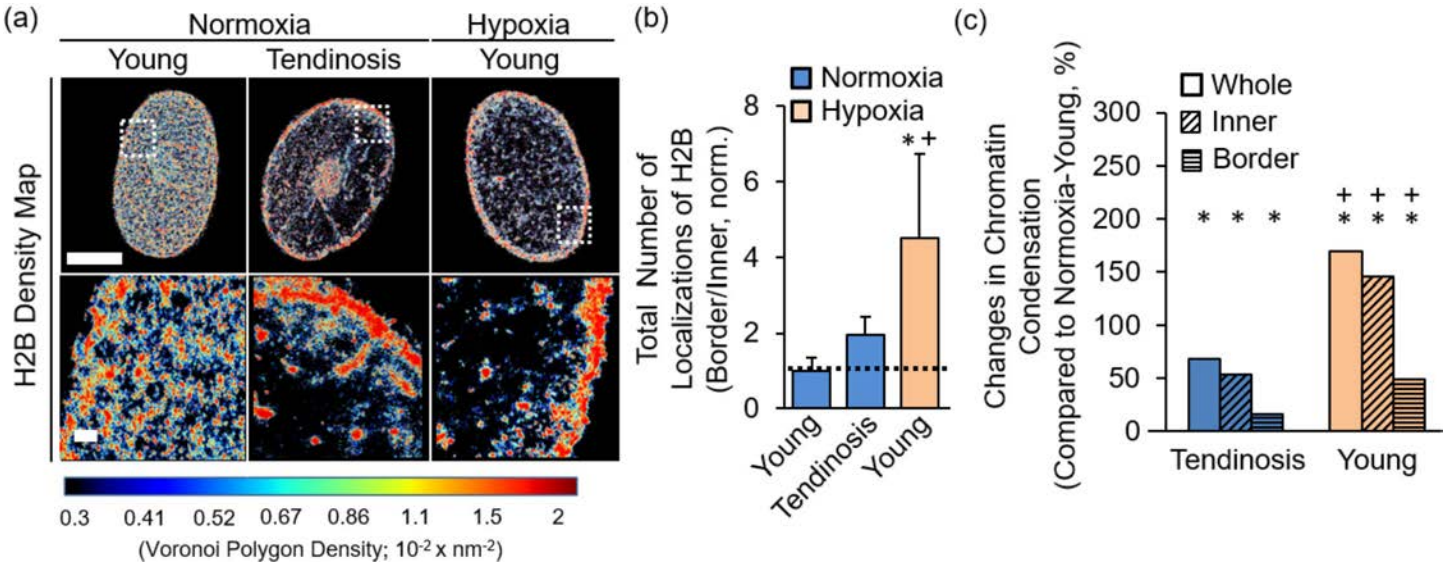

Figure 1: (A) Heat maps showing H2B localization density in young or tendinosis under normoxia or hypoxia culture condition (scale bars: top = 5μm, bottom = 500 nm). Quantification of the ratio of the total number of H2B localizations in the border to the inner **(B)** and changes in chromatin condensation (compared to young tenocyte in the normoxia culture condition). n = 5 cells, *:p < 0.05 vs. Young-normoxia, +:p < 0.05 vs. Tendinosis-normoxia.

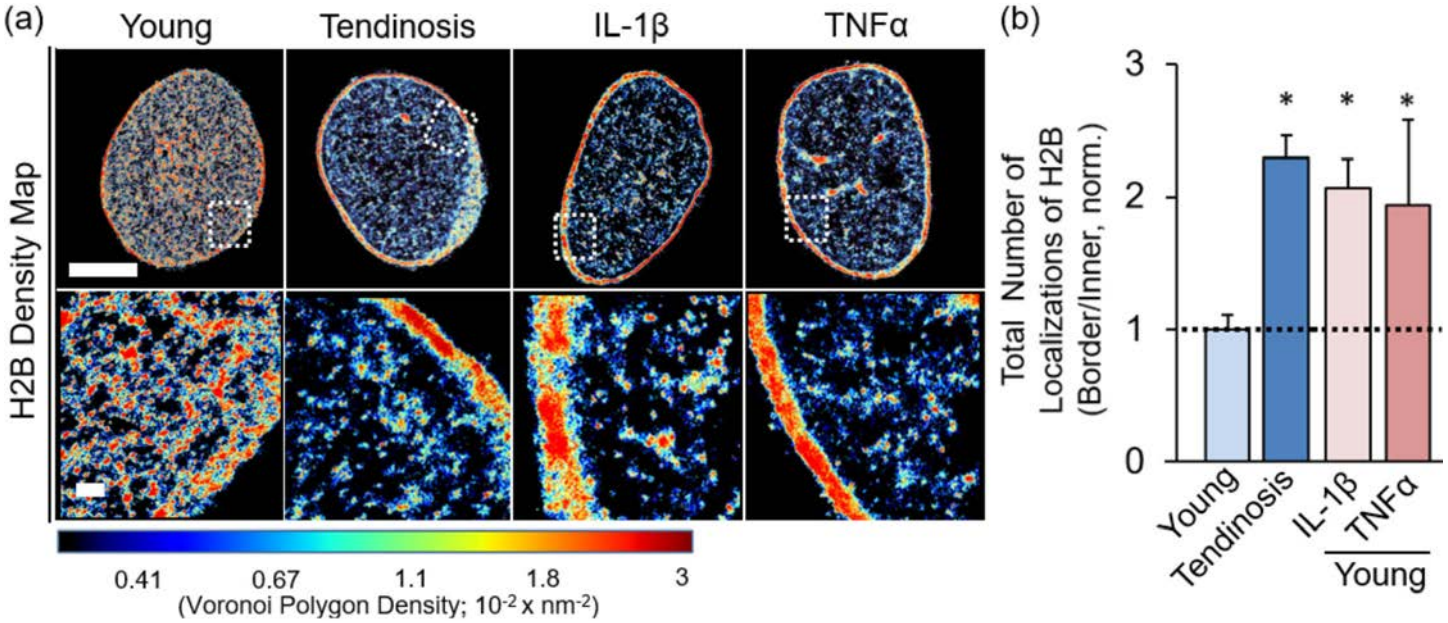

Figure 2: (A) Heat maps showing H2B localization density in young, tendinosis, or young human tenocytes with IL-1β (1 ng/ml) or TNFα (10 ng/ml) treatment. (B) Quantification of the ratio of the total number of H2B localizations in the border to the inner. n = 5 cells, *:p < 0.05 vs. Young human tenocyte (normalized). (scale bars: top = 5μm, bottom = 500 nm).

cytokines (IL-1β or TNFα) for one day resulted in rapid led chromatin reorganization to the nuclear periphery (Figure 2a-b) and increased chromatin condensation (not shown). This suggests that pro-inflammatory factors present in the wound environment impact chromatin organization in tenocytes during repair. Finally, we examined how a change in tissue stiffness impacts chromatin mechano-response in tendons. As was seen in soft substrates[3], H2B in young or tenocytes with tendinosis was primarily localized to the nuclear periphery within 4 hours after stiffening (Figure 3a-b). With 24 hours of stiffening, H2B became more uniformly dispersed and de-compacted in young healthy tenocyte nuclei. Conversely, in tendinopathic cells, no change in the spatial organization of chromatin and less de-compaction was observed (Figure 3a-c). This may suggest that prolonged changes in chromatin organization in diseased tenocytes may be associated with a loss of mechanical sensitivity and chromatin reorganization capacity with tissue degeneration.

Discussion

In this study, we show that tendon degeneration alters nanoscale chromatin organization in tenocytes and impacts their mechanical sensitivity. These data indicate that alterations in the chemo-physical environment that arise with tendon injury or degeneration induces phenotypic and chromatin alterations that are apparent at the nanoscale. Chromatin

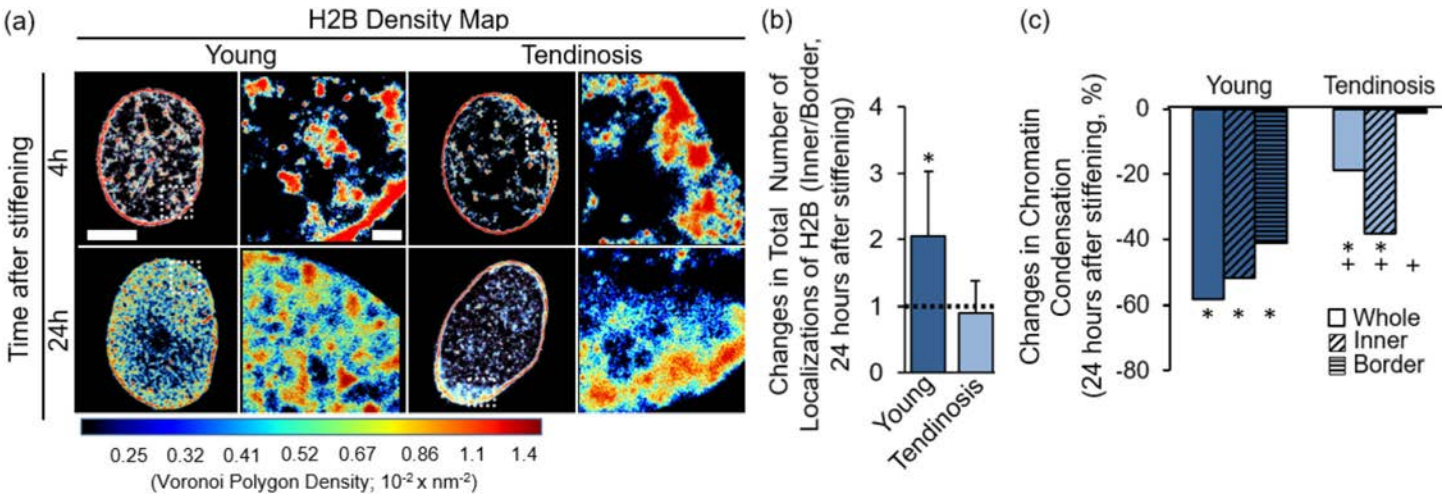

Figure 3: (A) Heat maps showing H2B localization density in young or tendinosis cultured on stiffening hydrogel system (4 hours or 24 hours after stiffening, scale bars: left = 5μm, right = 500 nm). Quantification of the ratio of the total number of H2B localizations in the inner to the border **(B)** or changes in chromatin condensation at 24 hours after stiffening **(C)**. n = 5 cells, *:$p < 0.05$ vs. before the stiffening, +:$p < 0.05$ vs. Young tenocyte.

reorganization to the nuclear periphery has been described as silent chromatin (heterochromatin) suppressing transitional activation[6]. Current work is identifying specific genetic loci that move to the periphery and the transcriptional activity of these loci in diseased tenocytes.

Significance

Our data show that degeneration alters the nanoscale chromatin organization of tenocytes and changes their mechano-sensitivity. This study may inform new directions to identify novel therapeutic targets for the treatment of connective tissue pathologies.

Acknowledgements

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Segment Mass Property Errors Have Less Impact on Estimated Joint Loading in Human Gait Than Ground Reaction Force Errors

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Introduction

Estimating joint loading during human movement is a cornerstone of biomechanics research. Traditionally, joint loads are estimated using musculoskeletal models to solve the inverse dynamics problem. Relying on Newton's second law of motion, we sum the external forces acting on a body segment and set that equal to the body segment dynamics[1]. This approach is powerful because it allows researchers to estimate the reaction loads at each joint that are impossible to physically measure without invasive surgeries[2]. However, this approach relies on assumptions and physical measurements that are difficult to quantify and prone to measurement error.

Therefore, the purpose of this study was to evaluate how the accuracy of joint load estimates are impacted by errors in both segment mass properties. To further explore the impact of experimental measurements, we tested the sensitivity to shear ground reaction force errors. We hypothesized that changing the mass properties and shear ground reaction forces would differentially impact estimated joint loading, with the smallest effects on the ankle and the greatest effects on the hip.

Methods

We recruited 8 healthy adults (6 males, 2 females; 30 ± 4 years; BMI, 24.1 ± 3.2 kg / m^2) who provided written informed consent. We collected traditional motion capture data during flat ground walking at self-selected speeds and performed inverse dynamics to establish a gold-standard range for sagittal joint load estimates. We then systematically introduced error by manipulating the mass properties of the musculoskeletal model and the magnitude of the externally applied loads. To this end, we scaled both by 0 to 200% in 5% increments, resulting in 1,600 simulations per subject. From this, we compared the peak joint load estimates from each error condition with the gold-standard across the joints in the lower extremities.

Results and Discussion

We found that shear ground reaction force errors had large impacts on joint load estimates while segment mass errors had less of an impact. These joint load estimate errors increased in the more proximal joints. The hip saw changes in mass resulting in around 35% error, changes in shear resulting in 82% error, and a worst-case scenario of 116% error. The knee saw changes in mass resulting in errors of 8%, changes in shear resulting in 140% error, and a worst-case scenario of 147% error. The ankle was least affected, with changes in mass resulting in errors of less than 2%, changes in shear resulting in 17%, and a worst-case scenario of 18%.

These results confirm our hypothesis that the ankle would be least sensitive to changes in mass and shear. This makes sense, as the segments distal to the ankle joint have relatively little inertial force potential compared to the loads experienced by the joint. It was surprising to see that the knee was very sensitive to changes in shear. This is likely due to the ratio of peak joint load to shear force, which in this case is roughly half that of the ankle. Errors in the hip were largely expected as it has the largest distal segment in the lower limbs. In addition to walking, we analyzed other activities of daily living and found that vertical movements like bouncing and heel raises had much smaller errors caused by ground reaction force differences.

Significance

Our results show that while some research areas such as forward simulation in rehabilitation and tendon transfer simulation might require very high-fidelity measurement techniques, there are many scenarios where faster, more convenient measurement solutions would result in very accurate data. Specifically, the ankle appears to be a largely unaffected by inertial factors and even some errors in shear measurements. These results are encouraging for researchers interested in making measurements outside of the biomechanics lab, both in the clinic and in the field.

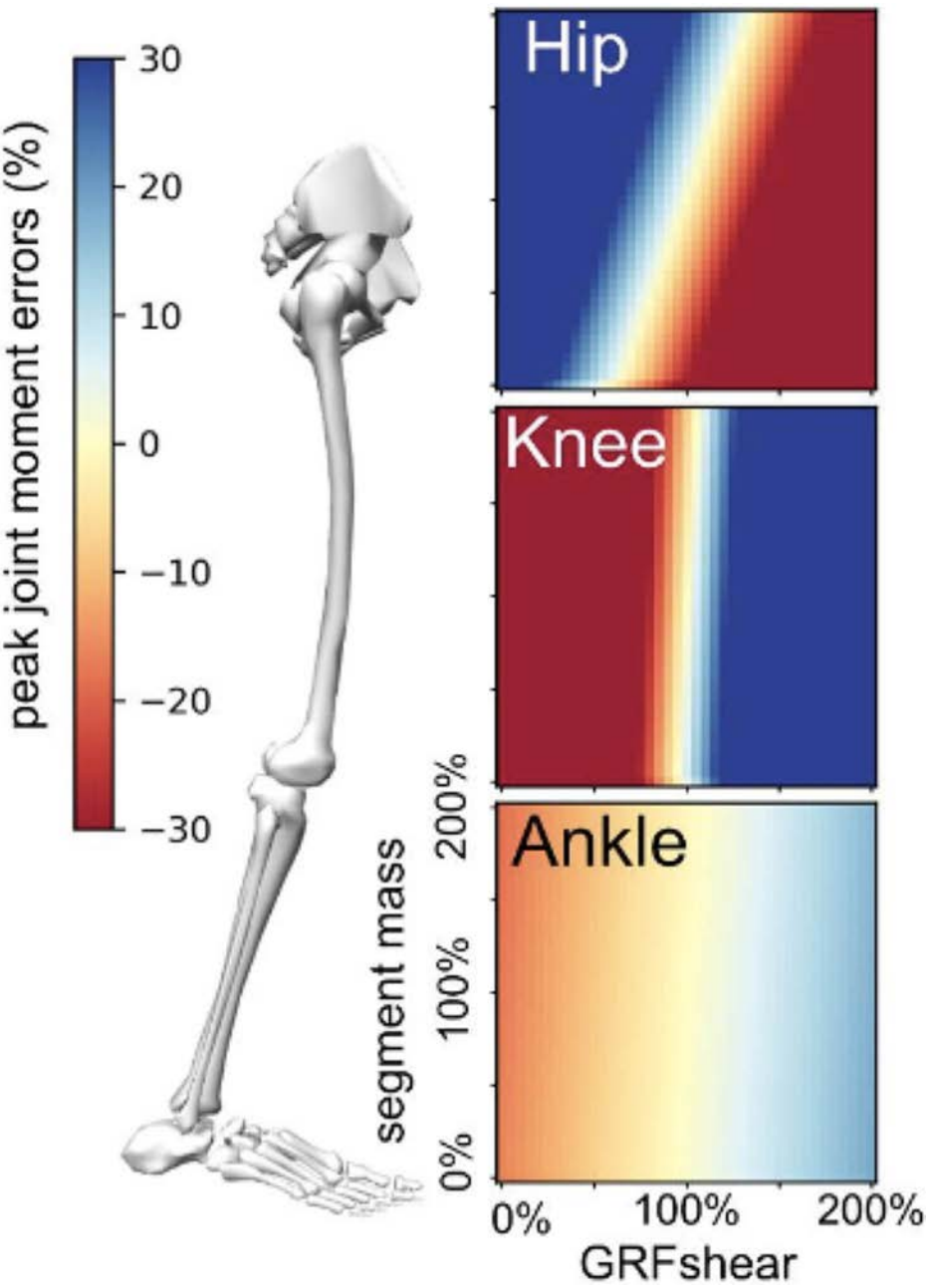

Figure 1. We visualized the precent errors in peak hip, knee, and ankle moments between each error condition and the gold standard measurement through diverging heat maps. Here, blue represents over approximations, red represents under approximations, and light yellow represents accurate approximations of joint moments.

Acknowledgments

This work was supported by the PennPORT IRACDA Fellowship Program (NIH grant# K12GM081259) and NIH/NIAMS K01AR075877.

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Collagen V Knockdown During Phases of Tendon Healing Differentially Impacts Gene Expression

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Disclosures

None

Introduction

Classic Ehlers-Danlos Syndrome (cEDS) is a connective tissue disorder often caused by mutations in *COL5A1*, which encodes the primary collagen V alpha chain[1]. Surprisingly, acute *Col5a1* knockdown at the time of murine tendon injury mitigated the quasi-static mechanical deficits of healing tendons[2]. This effect on mechanical parameters was reversed and diminished with *Col5a1* knockdown during the late inflammatory and early remodeling phases of tendon healing, respectively[3]. While this demonstrates that the timing of *Col5a1* knockdown during tendon healing differentially impacts tendon mechanics, the genetic mechanisms underlying this regulation remain unknown. Therefore, the objective of this study was to define the effect of acute *Col5a1* knockdown throughout the phases of tendon healing on injured tendon gene expression.

Based on prior mechanical findings, we hypothesized that *Col5a1* knockdown at the time of tendon injury would lead to diminished inflammatory expression and an earlier increase in matrix remodeling gene expression. We hypothesized that this effect would be reversed with *Col5a1* knockdown in the late inflammatory phase, leading to increased inflammatory expression at later healing timepoints. We also hypothesized that *Col5a1* knockdown in the early remodeling phase would cause negligible changes in gene expression.

Methods

Animals

Male wild-type (WT) (n = 20), bitransgenic *Col5a1*$^{flox/+}$ (n = 34) and *Col5a1*$^{flox/flox}$ (n = 34) mice with a tamoxifen (TM)-inducible *ROSA-CreER*^{T2} were used (IACUC approved). At 120 days old, mice received bilateral, full-thickness partial width patellar tendon injuries[4]. Mice received two consecutive daily doses of TM (2 mg/40 g body weight) for Cre-mediated excision of the *Col5a1* gene, resulting in I-*Col5a1*$^{+/-}$ and I-*Col5a1*$^{-/-}$ mice. The first TM injections were administered on the day of injury (WT, TM0), 5 days post-injury (TM5), or 21 days post-injury (TM21) for *Col5a1* knockdown during the different phases of tendon healing. Mice were sacrificed at 1 week (WT, TM0), 3 weeks (WT, TM0, TM5), or 6 weeks (WT, TM0, TM5, TM21) post-injury. Healthy WT control mice received TM doses (3 days of 4mg/40g body weight) at 120 days old and were sacrificed 30 days later. At sacrifice, right patellar tendons were dissected and immediately flash frozen at −80°C.

Gene Expression

For RNA extraction, patellar tendons were thawed in RNA*later* ICE. Tendons were homogenized with plastic pestles in TRIzol and vortexed. RNA was extracted (Direct-zol RNA Microprep, Zymo), and cDNA was reverse transcribed (High Capacity cDNA RT, Thermo). cDNA was pre-amplified for 15 cycles with Taqman assays for 96 target genes and was loaded into a Fluidigm 96.96 Dynamic Array. The 96 target genes included categories of collagens, non-collagenous matrix, matrix remodeling, cell-ECM proteins, cell markers, inflammatory markers, and housekeepers (*Abl1* and *Rps17*). ΔCt was calculated by subtracting the gene Ct from average housekeeping Ct.

Statistics

One-way ANOVAs with Tukey post-hoc tests were used to compare ΔCt values across genotypes within knockdown induction timepoint and healing timepoint. Significance was set at $p \pm 0.05$, and trends were set at $p \pm 0.1$.

Results

I-*Col5a1*$^{-/-}$ tendons had decreased *Col5a1* expression compared to WT tendons at each healing timepoint (TM0: 2.2-fold decrease, TM5: 2.4-fold decrease, TM21: 1.4-fold decrease). I-*Col5a1*$^{+/-}$ tendons had decreased *Col5a1* expression compared to WT tendons at 3 weeks post-injury (1.3-fold decrease, TM0 trend).

TM0: I-*Col5a1*$^{+/-}$ (trend) and I-*Col5a1*$^{-/-}$ tendons had increased *Postn* expression compared to WT tendons at 3 weeks post-injury, which persisted at 6 weeks post-injury

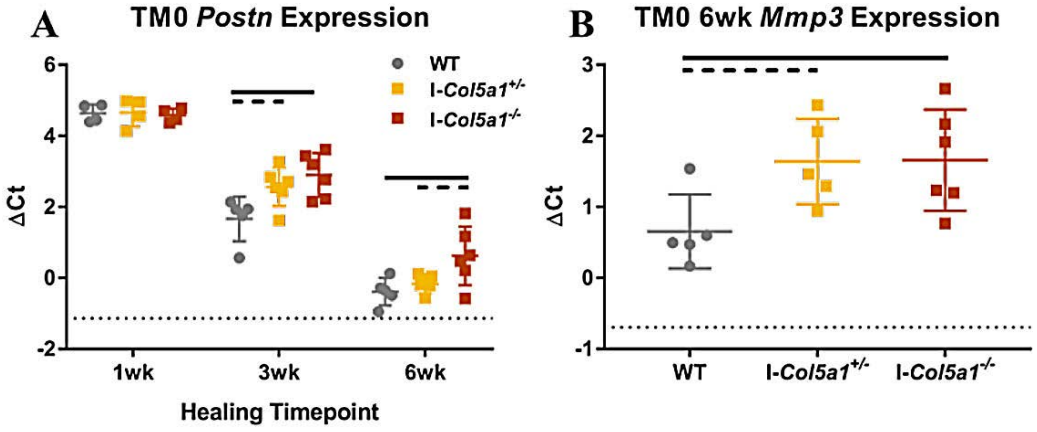

Figure 1. TM0 Gene Expression. (A) I-*Col5a1*$^{-/-}$ tendons had increased Postn expression at 3 weeks post-injury that persisted at 6 weeks post-injury. **(B)** TM0 *Mmp 3* expression was increased in collagen V-deficient tendons at 6 weeks post-injury. Dotted lines indicate WT uninjured expression. Solid lines denote $p \leq 0.05$, while dashed lines denote $p \leq 0.1$.

for I-*Col5a1*$^{-/-}$ tendons (Figure 1A). At 6 weeks post-injury, I-*Col5a1*$^{+/-}$ (trend) and I-*Col5a1*$^{-/-}$ tendons had increased *Mmp3* expression compared to WT tendons (Figure 1B).

TM5: At 6 weeks post-injury, I-*Col5a1*$^{+/-}$ and I-*Col5a1*$^{-/-}$ tendons had increased expression of *Aspn*, *Lum*, *Igf1*, *Mmp3*, and *Thbs4* compared to WT tendons (Figure 2). At this timepoint, I-*Col5a1*$^{+/-}$(trend) and I-*Col5a1*$^{-/-}$ tendons also had increased expression of *Bgn*, *Lox*, and *Mmp2* compared to WT tendons.

TM21: I-*Col5a1*$^{+/-}$ and I-*Col5a1*$^{-/-}$ tendons had increased expression of *Thbs4* compared to WT tendons at 6 weeks post-injury (data not shown). I-*Col5a1*$^{-/-}$ tendons had increased *Mmp3* expression compared to WT tendons at 6 weeks post-injury.

Discussion

Results indicate that collagen V temporally regulates healing tendon gene expression. Effective *Col5a1* knockdown was demonstrated in the *Col5a1*$^{flox/flox}$ model at all healing timepoints. When *Col5a1* was knocked down at the time of injury (TM0), *Postn* and *Mmp3* expression was increased. In addition to increased matrix remodeling expression (*Lox, Mmp2, Mmp3,* and *Thbs4*), *Col5a1* knockdown during the late inflammatory phase of tendon healing (TM5) led to increased small leucine rich proteoglycan expression (SLRPs, here *Aspn, Bgn,* and *Lum*). When *Col5a1* was knocked down during the early remodeling phase of tendon healing (TM21), less robust increases in matrix remodeling expression were observed. The observed expression changes support the mechanical changes seen with *Col5a1* knockdown during different tendon healing phases[2,3]. While *Col5a1* knockdown at the time of injury mitigated mechanical deficits of healing tendons, *Col5a1* knockdown during the late inflammatory phase worsened the mechanical deficits seen with wild-type healing. Compared to TM0 tendons, TM5 tendons exhibited more robust changes in gene expression, including increased SLRP expression. Limitations of this study are the global nature of the *Col5a1* knockdown, which could lead to off-

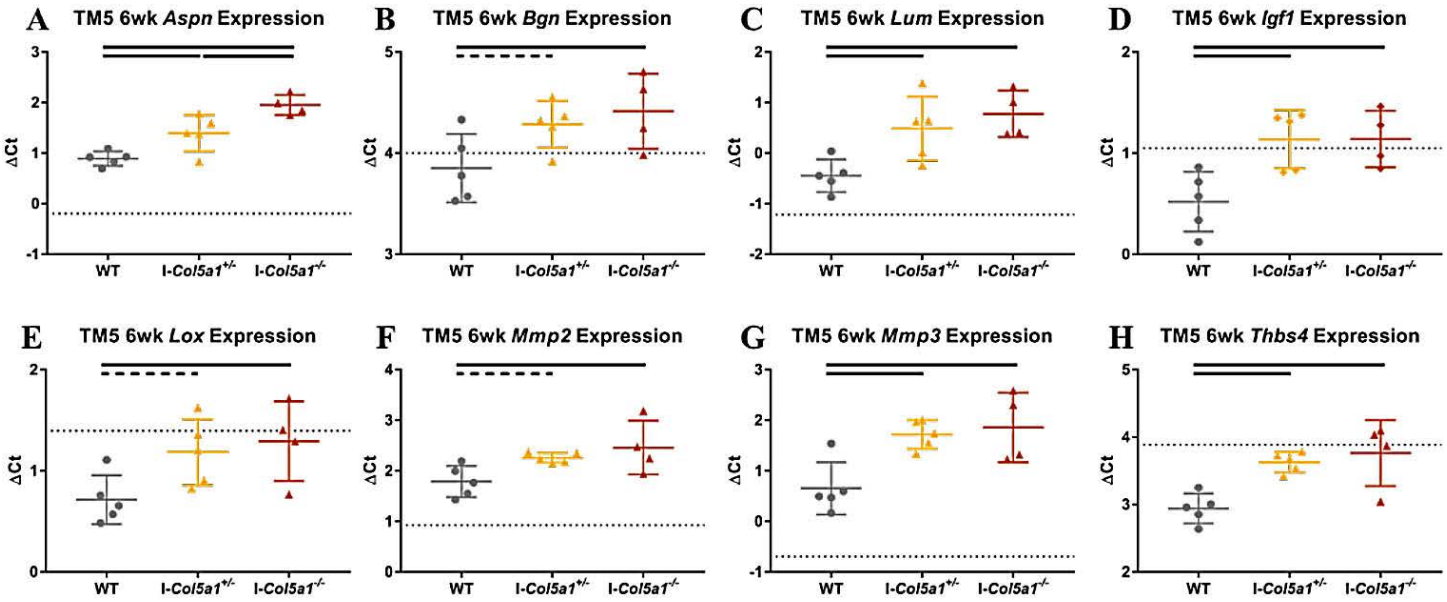

Figure 2. TM5 Gene Expression. At 6 weeks post-injury, *Col5a1* knockdown during the late inflammatory phase of tendon healing lead to increased expression of small leucine-rich proteoglycans **(A-C)**, *Igf1* **(D)**, and matrix remodeling genes **(E-H)**. Dotted lines indicate WT uninjured expression. Solid lines denote $p \leq 0.05$, while dashed lines denote $p \leq 0.1$.

target effects on neighboring tissues, particularly if longer knockdown periods were studied, and the study of gene expression without the addition of protein quantitation. Future work will analyze healing tendon matrix content to define how observed expression changes translate to functional matrix changes.

Significance

This work elucidates the temporally dynamic role of collagen V on regulating healing tendon gene expression. These results inform which phases of tendon healing are most sensitive to collagen V presence.

Acknowledgements

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Moving Outside the Lab: Markerless Motion Capture Accurately Quantifies Planar Kinematics During the Vertical Jump

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Introduction

The COVID-19 pandemic has created a need for easy-to- use, socially distanced methods of data collection for biomechanical research. The rise of mature, deep learning software packages provides a unique opportunity for a low cost, socially distant, high fidelity alternative to traditional motion capture. One such example of these software packages is DeepLabCut[1], an open source software developed for pose tracking of laboratory animals. This software has been applied to track human movement, however, there exist concerns about the accuracy of markerless motion capture relative to the marker-based gold standard. The purpose of this study was to evaluate the performance of markerless motion tracking as a method to measure lower limb angles during the vertical jump using a large cohort of subjects from a publicly available data set with time synchronized motion capture and video data.

Methods

Data were compiled from the open data set[2]. The marker-based motion capture data were captured at 120 Hz with a 67-point marker set. Video for markerless tracking was captured on two orthogonal cameras at 30 Hz. We split the data set into a 69 subject training set and a 16 subject test set. To train the model, four people labeled 19 points of interest across 12 frames per subject. Each of these frames were automatically selected via a DeepLabCut clustering algorithm. To test consistency across labelers, a set of five shared subjects were labelled by all four labelers (60 total images). Agreement between labelers was evaluated via the C-1 formulation of the Intraclass Correlation Coefficient (ICC). The data consisted of each of the subjects performing 20 actions. Researchers identified the start and end times of each instance of the subjects' vertical jump and added a one second buffer period to each end of this period. Vertical jump was chosen for further analysis because of its relevance as a common test in sports performance testing. Hip, ankle, and knee angles were extracted from the 1-3 vertical jumps that each subjects performed. The markerless results were compared with the traditional motion tracking results using root mean squared error in addition to coefficient of multiple correlation (CMC) metrics. For both ICC and CMC measurements, r values above 0.9 indicate "very strong agreement."

Results and Discussion

The level of agreement between labelers was very high across the five shared subjects, with an ICC = 0.998 and RMSE = 4.52 pixels. Results generated from CMC across the whole movement showed very strong agreement between the markerless approach and the traditional motion capture data with a CMC $<$ 0.991 and a RMSE $<$ 3.22°. Across the hip, knee, and ankle angles extracted, the CMC values were similarly high, being 0.970 $\pm$ 0.055, 0.963 $\pm$ 0.471, and 0.853 $\pm$ 0.23 respectively (Figure 1).

The results of the study show that free, easy-to-use, open source markerless tracking is a viable alternative to traditional motion capture technology, especially for data collection outside of traditional laboratory spaces. As the CMC values all indicate strong to very strong agreement between the two methods of motion tracking, this represents a significant development in increasing accessibility to accurate motion tracking technology for human subject research. These findings provide evidence that basic cameras can be used to collect human kinematic data remotely without the need for specialized equipment which provides researchers with the ability to reach historically underrepresented groups that are less likely to participate in studies that take place in a laboratory.

Significance

Markerless motion capture has potential – like other devices including mobile dynamometry, instrumented insoles, tensiometers, and inertial measurement units – to transform biomechanical research away from traditional laboratory settings into venues convenient to populations that are under sampled with present approaches without sacrificing measurement fidelity.

Acknowledgements

This work was funded in part by NIH K12GM081259 and NIH/NIAMS K01AR075877.

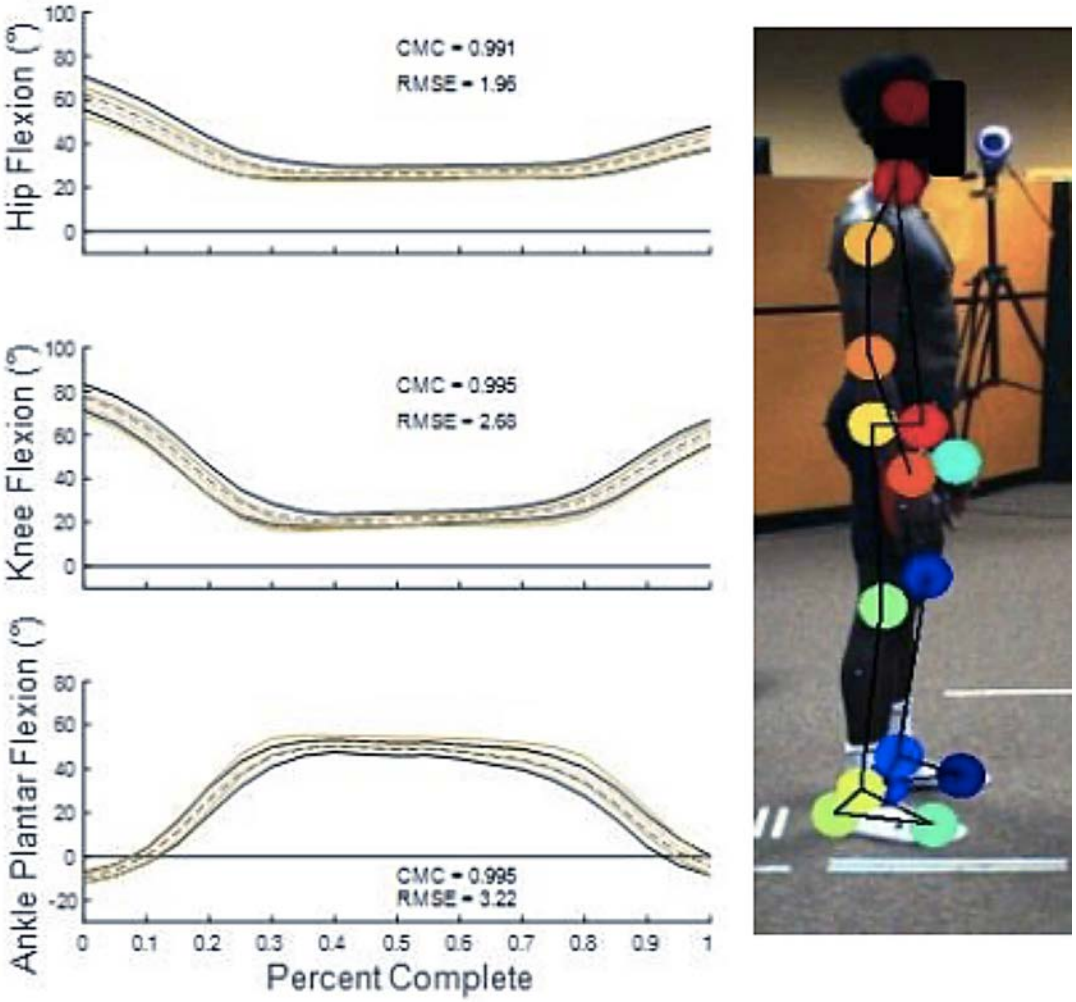

Figure 1. (Left) Gold-motion capture, Black-markerless motion tracking. Dashed-means across all subjects and solid-95% confidence intervals. **(Right)** example of tracked frame.

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U·P·O·J

Morphogenesis of Fibrous Structures in the Embryonic Knee is Severely Disrupted by a Lack of Muscle Contraction

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Introduction

Precise tissue morphology and positioning within the knee are critical for the patellar tendon, cruciate ligaments, and menisci to mechanically support joint function. Shape and organization of these knee fibrous elements is coordinately established during embryonic joint formation, whereby joint cells are specified and patterned within the hindlimb cartilage anlagen, and become distinct structures following joint cavitation[1,2]. Contraction of skeletal muscle is a key regulator of the joint morphogenesis process[3]. In particular, Splotch-delayed (*Spd*) and Muscular Dysgenesis (*mdg*) mouse models, in which skeletal muscle fails to develop (*Spd*), or is non-contractile (*mdg*), exhibit joint cavitation failure, resulting in fusion of most articulating joints[4]. Surprisingly, aside from patellar fusion, few overt changes have been reported in the knee joints of these mice, leading to the belief that muscle contraction does not significantly contribute to knee development[4,5]. This notion, however, is confounded by chick studies showing meniscus dissociation and molecular signaling alterations following embryonic hindlimb paralysis[6,7]. To date, however, no study using the available murine models has assessed how absence of muscle contraction impacts the fibrous tissues unique to the knee joint. Here, we demonstrate that deficiency in muscle loading in mice causes aberrant changes in the establishment of fibrous tissues of the developing knee that far exceed those previously reported[4,5].

Methods

mdg mutant mouse embryos were harvested alongside littermate wild-type (WT) controls at Thieler Stage (TS) 24 and 27, along with TS27 *Spd* mutant embryos and littermate WT controls. Knee joints from three animals per time point and genotype were dissected, fixed in formalin, cryo-embedded, and serially cryosectioned (8-16μm) in the sagittal and/or coronal planes across the width of the joint. Sections were permeabilized (0.1% Triton-X), stained with Alexa-Fluor Phalloidin 546 (actin), and counterstained with Hoechst-33342 (nuclei). Imaging was done by laser-scanning confocal. Second harmonic generation (SHG) for visualization of fibrillar collagen was performed by multiphoton microscopy (20X objective). For nuclear aspect ratio (NAR), z-stacks (60X, 0.2μm step-size) for individual nuclei were acquired (from PT sections of two TS24 animals/genotype), and aspect ratios were calculated from maximum intensity projections using Fiji. Measurements were pooled for WT/mdg samples and compared via a Mann-Whitney U Test ($p < 0.05$ cutoff).

Results

Knee joints of TS27 *mdg* (non-contractile muscle) mutants contained patellar tendon (PT), ACL, and PCL structures, though all were greatly reduced in thickness (Figure 1a; Figure 1b (PT)). Likewise, SHG imaging showed aligned collagen fibers in the *mdg* PT and cruciate tissues that were diminished compared to WT controls at this time point (Figure 1c). Strikingly, an extra tissue structure–aligned parallel to the PT and with femoral and tibial attachments anterior to the ACL/ PCL was observed in all TS27 *mdg* mutants (Figure 1a, red arrowhead). This element appeared to be a fibrous ectopic ligament, as it contained both linearly aligned cells and collagen fibrils, similar to the adjacent tendon/ligaments (Figure 1b, c, "Ect. Lig.").

Additionally, all TS27 *mdg* knees had a complete absence of the medial meniscus anterior horn (Fig. 1b), a severe reduction in the medial meniscus body/posterior horn, and the majority of the lateral meniscus was missing (data not shown). These phenotypes were confirmed in the sagittal and coronal planes, and were also observed in TS27 *Spd* mice (data not shown). The vertical "ectopic ligament" and the missing anterior medial meniscus horn were already noted in *mdg* joints at TS24, around the time the knee joints cavitates (Figure 2a, b). However, at TS24, cells were properly positioned at the sites of the PT and cruciates in *mdg* samples (Figure 2a). While these resident cells exhibited linear alignment and fibrillar actin networks that

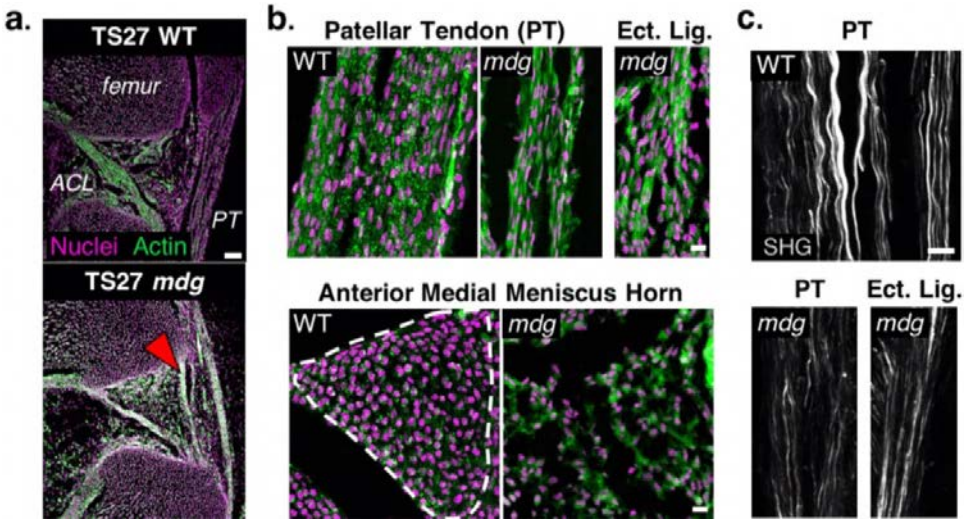

Figure 1. TS27 analysis. (A) Wild-type (WT) and *mdg* mutant sagittal knee sections stained for cell nuclei (magenta) and actin (green).Red arrowhead denotes an ectopic ligament structure ("ect. lig.") seen in the *mdg* joints. **(B)** Magnified views of WT and *mdg* indicated issues from sagittal serial sections.**(C)** Aligned collagen visualization by SHG (second harmonic generation) in the WT and *mdg* PTs and the *mdg*"ectopic ligament". SBs: 100μm **(A)**; 10μm **(B,C)**.

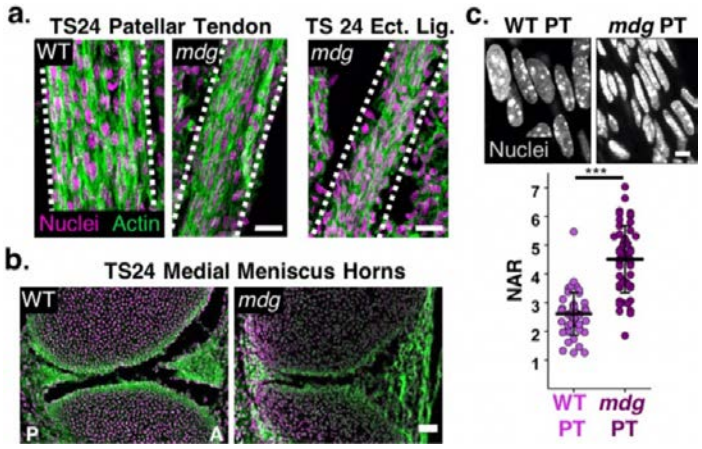

Figure 2. TS24 analysis. Sagittal views of cell organization in WT and *mdg* PTs and the *mdg* ectopic ligament ("ect lig.") **(A)** and medial meniscus horns **(B)** .A: anterior, P: posterior. **(C)** Nuclear aspect ratio (NAR) measures (n = 50/group, mean ± s.d) for nuclei of WT and *mdg* PT resident cells. ***: $p < 0.001$. SBs: 20μm **(A,B)**; 5 μm **(C)**.

resembled WT cells, their nuclei were significantly elongated (Figure 2c).

Discussion

This study demonstrates a varied, but overall profound, impact of muscle contraction on developing fibrous knee joint tissues. By the joint cavitation stage (TS24) in *mdg* mutants, cellular condensations were absent in the anterior regions of the medial meniscus (Figure 1b, Figure 2b) and throughout the lateral meniscus (data not presented), suggesting that defects in meniscus cell patterning may be responsible for the absence of these structures by TS27. Interestingly, meniscus morphogenesis phenotypes were asymmetric—with differential effects seen based on anterior-to-posterior and medial-to-lateral position. This highlights that location-specific biophysical and/or molecular cues may be guiding meniscus formation. Conversely, cells of the PT and cruciate ligament of *mdg* mice appropriately assembled by TS24 (Figure 2a) and were able to generate a fibrillar collagen network by TS27 (Figure 1c), suggesting that specification of the PT and cruciates initiates normally, despite abnormal muscle forces. However, the hyper-elongation of cell nuclei in the PT at TS24 (Figure 2c) points to an alteration in the mechanical microenvironment, perhaps due to increased resident cell contractility or a heightened level of tissue pre-stress. Either factor could contribute to the observed reduction in size of the PT and cruciates at TS27, through increased tissue micro-damage, cell shearing, or potentially cell death. Intriguingly, morphogenesis of an ectopic tissue consistently occurred when muscle was absent or non-contractile, with a defined position within the joint, and ligamentous tissue properties (Figure 1b, 2b). This finding demonstrates that cues downstream of a loss of muscle contraction may enable alternative cell condensations to persist; a mechanism that requires further investigation.

Significance

We demonstrate that, contrary to the established understanding, muscle contraction is critical for murine knee joint development, and acts to direct the proper morphogenesis of the PT, menisci, and cruciate fibrous tissues, rather than impacting knee joint cavitation.

Acknowledgements

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A Subset of FAP Cells Expressing Gli1 Promote Muscle Regeneration With Less Fat Accumulation

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Disclosures

None

Introduction

Skeletal muscle has a remarkable capacity for regeneration after injury. Recently, a new type of muscle-resident progenitor cell, referred to as fibro-adipogenic progenitors (FAPs), was identified to be critical in supporting the process of injured muscle regeneration. To date, FAPs remain a poorly defined, heterogeneous population without any specific genetic markers. Using a lineage tracing mouse model (*Gli1-CreER Tomato, Gli1ER/Td*), we recently discovered that Gli1 marks a small subset of muscle-resident FAPs (17%) that preferentially expand upon muscle injury (40% of FAPs at day 3 after injury). Here, we performed cell ablation, pharmacologic manipulation, and single cell transcriptomics to further investigate the role of Gli1$^+$ FAPs in muscle regeneration and fat deposition after injury.

Methods

Animals

All animal work was approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pennsylvania. *Gli1-CreER Rosa-tdTomato* (*Gli1ER/Td*) mice and *Gli1-CreER Rosa-tdTomato DTA* (*Gli1ER/Td/DTA*) mice were generated. To induce *CreER* activity, 2-month-old male mice received tamoxifen (Tam) injections (75 mg/kg/day) for 5 days. Acute muscle injury was induced by injection of 10 μl Notexin (NTX, 10 μg/mL) or 50 μl glycerol (50% vol/vol) into the Tibialis Anterior (TA) muscle.

Histology

TA muscles were processed for cryosections followed by H&E, WGA, or Perilipin antibodies staining.

Single cell RNA sequencing (scRNA-seq) analysis

Pre-aligned and filtered single-cell RNA-seq matrix files of mouse muscle cells were acquired from GEO: GSE110878. Unsupervised clustering was conducted by Seurat and GO/KEGG term enrichment were analyzed by Clusterprofiler.

Statistics

Data are expressed as means ± standard error of the mean and analyzed by t-tests or one-way ANOVA.

Results

In the TA muscle of *Gli1ER/Td* mice, Td$^+$ cells were exclusively FAPs located in the interstitial area of myofibers (Figure 1A). Though initially presented at a low level in freshly digested muscle cells, Td$^+$ cells constituted 40% of confluent cells after culturing. Sorted Td$^+$ FAPs formed 6.2-

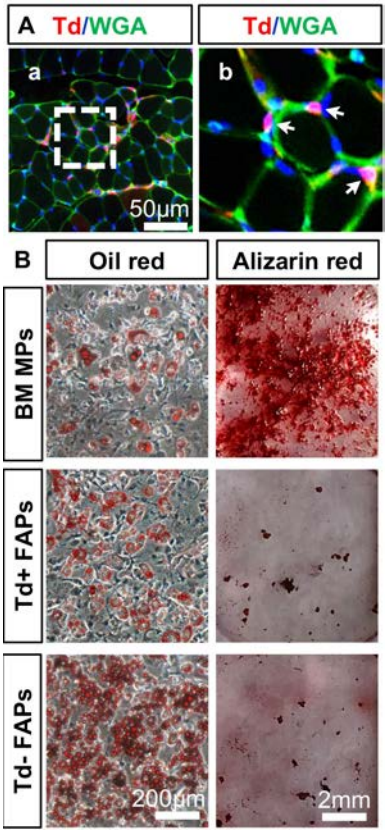

Figure 1. Td in the muscle of *Gli1ER/Td* mice labels a subpopulation of FAPs with less adipogenicity. (A) Td$^+$ cells located in the interstitial area of TA muscle in *Gli1ER/Td* mice. **(B)** Representative images of osteogenic and adipogenic differentiation of BM MPs (Bone marrow mesenchymal progenitors), Td$^+$ FAPs and Td$^-$ FAPs.

fold more CFU-Fs than Td$^-$ FAPs. They had fibroblastic and adipogenic differentiation abilities, but generated much fewer adipocytes than Td$^-$ FAPs (Figure 1B). Both Td$^+$ and Td$^-$ cells had no osteogenic differentiation ability (Figure 1B). To investigate their *in vivo* function, we generated *Gli1ER/Td/DTA* mice. At 2 months of age,Tam injections quickly reduced Td$^+$ cells by 80% and eliminated Td$^+$ CFU-F colonies from muscle (n = 3/group), indicating successful cell ablation. Interestingly, myofibers regenerated at day 7 and day 28 in *Gli1ER/Td/DTA* mice after Notexin injury were 34.1% and 22.7%, respectively. These were smaller than those in *Gli1ER/Td* mice (Figure 2A, n = 5/group), suggesting an impairment of myogenesis.

Gli1 is an effector of Hedgehog (Hh) signaling. Intramuscular injection of purmorphamine (PUR), an Hh agonist, expanded Td$^+$ cells at day 4 and increased myofiber size by 1.6-fold at day 30 after Notexin injury (Figure 2B, C, n = 4/group). Local glycerol injection causes muscle degeneration with fat infiltration. Strikingly, Td$^+$ FAPs were less likely to become adipocytes compared to Td$^-$ FAPs and ablation of Td$^+$ cells led to 39.9% more adipocytes in muscle (Figure 3A-D, n = 4/group). Hh signaling inhibitor, GANT61, induced 78.3% more adipocytes, while PUR almost completely depleted adipocyte infiltration (n = 5/group). ScRNA-seq analysis of mouse muscle mononucleated cells showed that FAPs can be subclustered into Gli1$^+$ and Gli1$^-$ FAPs (Figure 3E, F). Pathway analysis suggested that Gli1$^+$ FAPs are more metabolic active and more related to tissue regeneration than Gli1$^-$ FAPs. For example, they have higher Interleukin-6 (Il6) production and TGF-beta signaling, two known positive regulators of myoblast proliferation and tissue regeneration. Furthermore, Gli1$^+$ FAPs express higher levels of known muscle regulators, such as *Tgfb1, Wisp1, Malat1, Igf1*, *Il15* and *Il33* (Figure 3G), compared with Gli1$^-$ FAPs, which was further validated by qRT-PCR (Figure 3H). *Il15* and *Wisp1*, are also involved in inhibiting FAPs differentiation into adipocytes. Further analysis revealed increased expression of anti-adipogenic regulators, such as *Tsc22d3*, *Dlk1*, *Ddit3* and *Nr4a1* (Figure 3I), and reduced expression of pro-adipogenic regulator, such as *Zfp423* and *Ebf1* (Figure 3J).

Discussion

Our study found that *Gli1-CreER* labels a subpopulation of FAP cells. Compared to Gli1$^-$ FAPs, Gli1$^+$ FAPs are more metabolically active for muscle repair and less likely to contribute to muscle adiposity. Our studies demonstrated that Hh/Gli1 signaling pathway is critical for regulating muscle regeneration and fat accumulation, indicating that

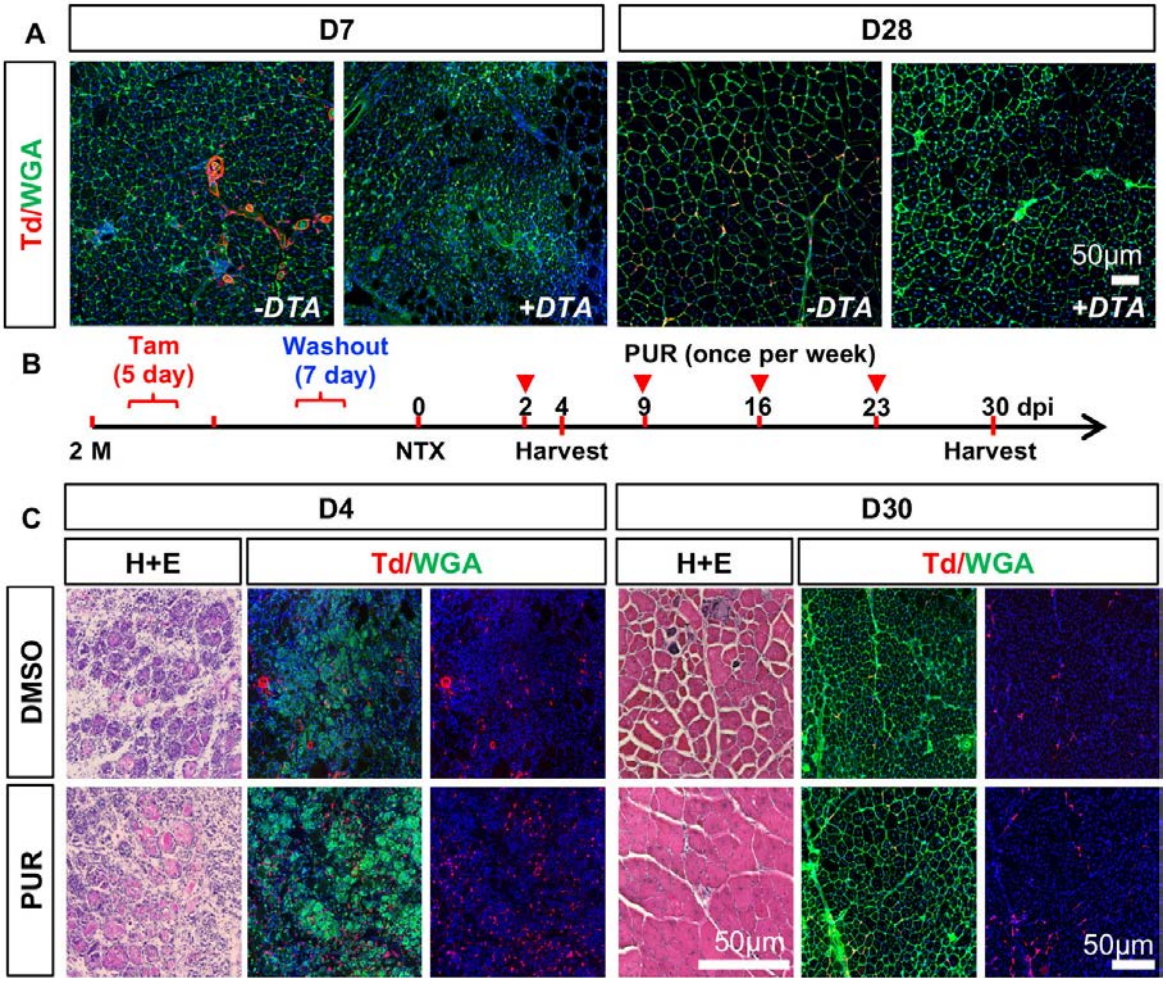

Figure 2. Ablation of Gli1$^+$ cells causes delayed muscle regeneration and activation of Hh signaling accelerates muscle healing. (A) Representative immunofluorescence imaging of *Gli1ER/Td* and *Gli1ER/Td/DTA* muscle at day 7 and 28 post NTX injury. **(B)** Schematic plot of mouse muscle NTX injury model with PUR treatment. **(C)** Representative H&E staining and immunofluorescence images of TA muscles with DMSO or PUR treatment group at day 4 and day 30 post NTX injury.

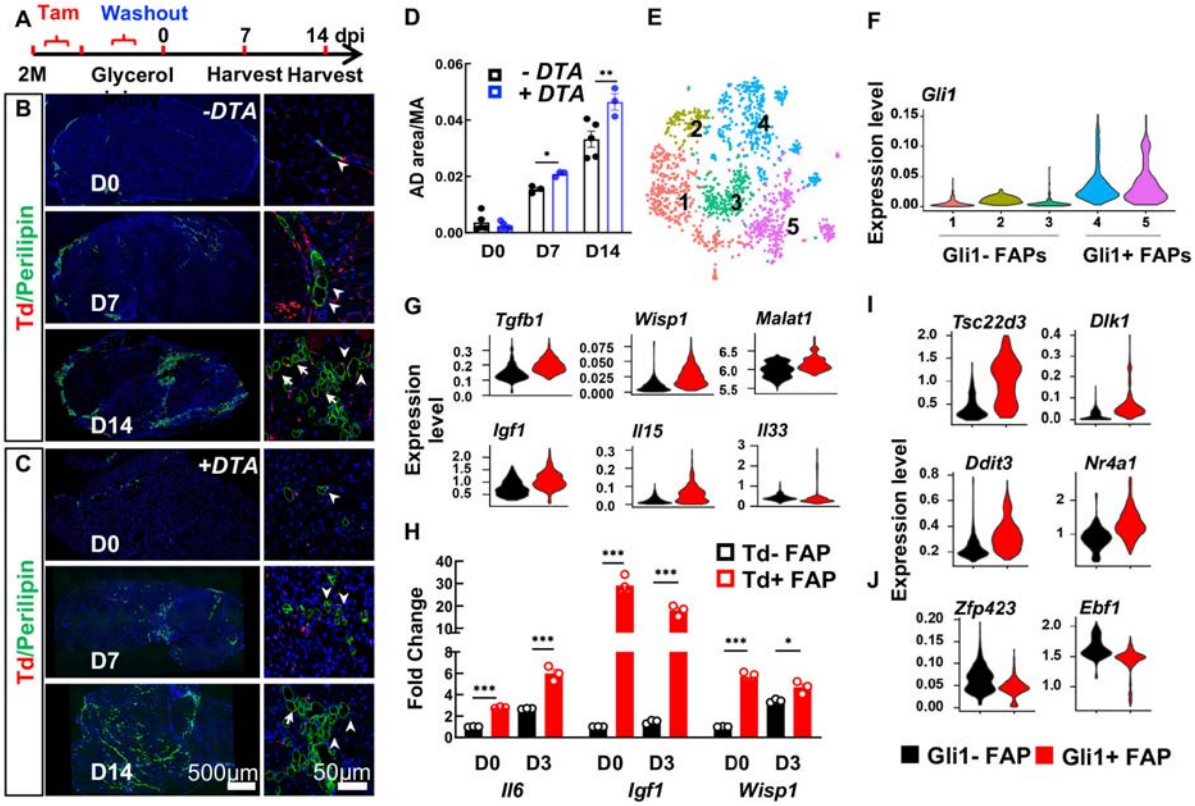

Figure 3. Gli1⁺ FAPs suppress intramuscular adipogenesis and Single cell RNA-seq analysis of FAPs. (A) Schematic plot of mouse muscle glycerol injury model. **(B, C)** Representative immunofluorescence images of TA muscle from *Gli1ER/Td* or *Gli1ER/Td/DTA* mice at day 0, 7, and 14 post glycerol injury with perilipin staining. Arrows point to Perilipin⁺Td⁺ cells and arrowheads point to Perilipin⁺Td⁻ cells. **(D)** Quantification of muscle adipocyte area revealed that muscle adiposity is increased in *Gli1ER/Td/DTA* mice. **(E)** Further subclustering of FAPs generates 5 subclusters. **(F)** Violin plots show clusters 4 and 5 express Gli1 at a higher level compared to clusters 1, 2 and 3. **(G)** Violin plot of myogenic factors expression. **(H)** qPCR of *Il6, Igf1* and *Wisp1* expression at D0 and D3 after injury of sorted Td⁻ and Td⁺ FAPs. **(I)** Violin plot of anti-adipogenic factors expression. **(J)** Violin plot of pro-adipogenic factors expression.

pharmacological activation of this pathway could be a therapeutic approach to boost muscle regeneration.

Significance

Our study revealed a subpopulation of FAPs that preferentially promotes muscle regeneration with less fat accumulation and implied a potential therapeutic effect of Hedgehog signaling in muscle diseases.

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