The University of Pennsylvania Orthopaedic Journal

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The University of Pennsylvania Orthopaedic Journal

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Editorial Board

U·P·O·J

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Table of Contents

Clinical Research

Pediatrics

Shoulder & Elbow

Spine

Sports

Department Updates

Division Updates

About the Cover:
The cover art features an anatomical drawing done by Jan Van Rymsdyk, a prominent medical illustrator of the 18th century. William Shippen, Jr of Philadelphia traveled to England in 1758 to study medicine where he befriended John Fothergill, an influential English physician. Fothergill developed an interest in promoting medical teaching in Philadelphia and so he sent 18 anatomical drawings by Van Rymsdyk to Pennsylvania Hospital as a gift following its inception, of which the cover art was one.

At Children's Hospital of Philadelphia's Division of Orthopaedics, we strive to help kids move better so they can enjoy all the adventures of childhood. Ours is one of the largest and most active pediatric orthopaedic centers in the world. Our multidisciplinary team offers safe, state-of-the-art care for every type of orthopaedic condition children face and is dedicated to advancing therapeutic discoveries that benefit children worldwide.

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

Children's Hospital of Philadelphia℠
Division of Orthopaedics

Letter from the Editors in Chief

Blair Ashley, MD and Daniel Gittings, MD

Welcome to the 27th edition of the University of Pennsylvania Orthopaedic Journal (UPOJ). The UPOJ began in 1986 under the leadership of Dr. Carl T. Brighton as the nation's first fully resident-run journal of orthopaedic surgery. The UPOJ has been a source of pride for the department since its inception. The UPOJ would not be possible without the support from many contributors throughout the years. This edition is a testament to how we stand on the shoulders of giants both of the present and of the past.

We proudly dedicate this edition to Malcom Ecker, M.D. Dr. Ecker continues to be a gifted clinician and educator at both Children's Hospital of Philadelphia and also the Corporal Michael J. Cresence Vetarans Affairs Medical Center of Philadelphia to students, residents, and fellows. Additionally, Dr. Ecker is a stalwart for life-long learning. He is unfailingly in the front and center at every Penn Orthopaedic Surgery Department Grand Rounds each Thursday morning in the Agnew Grice Auditorium. Furthermore, while Dr. Ecker was just over sixty years of age, he elected to take the GRE exam and pursue a master's degree in computer science at Drexel University to keep his skills current. He is a role model for the consummate physician and life-long learner.

The theme for this year's UPOJ was inspired by Dr. Ecker's passion for education. This edition includes many articles to facilitate education and also provide an update of the events that have occurred in the department over the past academic year. The content includes extended abstracts highlighting original research, tips and tricks articles about various surgical techniques, editorials about the happenings in the department, and also a spotlight about Penn Orthopaedic Residency Program alumni that are now celebrating their ten-year anniversary.

As a resident organized journal, the UPOJ would not be possible without the vision of our leadership. "We thank our chairman, Dr. L. Scott Levin, and our faculty advisors, Dr. Jaimo Ahn and Dr. Samir Mehta for their unwavering support. We also would like to recognize our section editors for their contributions: Dr. Matthew Sloan (Arthroplasty), Dr. Adnan Cheema (Foot and Ankle), Dr. Kristin Buterbaugh (Hand), Dr. Mark Hasenauer (Pediatrics), Dr. Zachary Zimmer (Shoulder and Elbow), Dr. Michael Eby (Spine), Dr. Joshua Rozell (Sports), Dr. Tyler Morris (Trauma), Dr. Andrew Tyler (Tumor), Dr. Luke Lopas (Bone), Dr. Nicole Zelenski (Cartilage), and Dr. Chia Wu (Tendon and Ligament).

Similar to the first journal clubs pioneered by Sir William Osler in the 19th century, we hope that this issue continues to embody the spirit of education and academic discussion that the Father of Modern Medicine promoted during his tenure at Penn. We are excited to announce that the UPOJ is available online and easily viewable on your computer, Android tablet, or iPad at www.upoj.org. On behalf of all the contributors to the UPOJ this year, we hope that you find this edition informative and inspiring.

Sincerely,

Blair S. Ashley, MD and Daniel J. Gittings, MD
Editors-in-Chief
The University of Pennsylvania Orthopaedic Journal
Volume 27

Dedication to Malcolm Ecker

Blair Ashley, MD and Daniel Gittings, MD

We are honored to dedicate the 27th volume of The University of Pennsylvania Orthopaedic Journal to Dr. Malcolm L. Ecker who has touched the lives of many generations of Penn Orthopaedic graduates, in addition to the many pediatric and adult patients he has served.

Dr. Ecker states, "My best advice is to be curious in life," and both his career and family life exemplify this sentiment. Originally from Philadelphia, Dr. Ecker proceeded to Temple University for his undergraduate studies in physics, and then onto Temple University School of Medicine graduating in 1961. He then completed his rotating internship at Albert Einstein Medical Center in Philadelphia, where he did everything from reducing fractures, to caring for medical patients, to delivering babies. He subsequently moved to Boston to become a junior assistant resident in surgery at Boston City Hospital. During this time, Dr. Ecker spent time practicing as a general surgeon at the only hospital with an ambulance, and thus was forced to rapidly hone his surgical skills. During this era, surgical residents had very little help. Dr. Ecker and his co-residents were responsible for obtaining their own blood samples and looking at said samples under the microscope in addition to mixing the intravenous fluids for their patients, all while caring for upwards of 60 patients on the floor. During his early years of training, Dr. Ecker was expected to be a consummate physician.

The demanding environment of Boston City Hospital prepared Dr. Ecker for his next adventure: Platsburg Air Froce Base. The beginning of Dr. Ecker's military service marked a challenging time for the military, at which time they were so desperate for military physicians that many doctors bypassed basic training. At only 25 years of age and following only 1 year of general surgery residency, Dr. Ecker was the only physician on a base of 18,000 people with surgical training for approximately 6 months. He recalls managing many orthopaedic injuries closed, learning how to do spinals from CRNAs, and performing surgeries without anesthesia or EKG monitoring. In two years, the young surgeon did approximately 400 cases with minimal help or supervision.

Dr. Ecker then went to The Hospital for Special Surgery (HSS) to complete his orthopaedic residency. HSS provided a nurturing learning environment, where the Chairman and Chief of Surgery at the time, Dr. Robert Lee Patterson, considered the job of teaching residents to be paramount. It was at this stage that Dr. Ecker began to develop into the great surgical teacher we know today. Dr. Ecker acknowledges that teaching surgery is exceptionally challenging, and requires the teacher to, "be willing to sit and watch someone fumble." Training at HSS inculcated the importance of a thorough knowledge of anatomy, evidence based discussion of cases and self-critique when examining patients at follow up.

Throughout Dr. Ecker's practice, he has worked in both private practice and academic settings. His practice evolved to include pediatrics and adults, to pediatrics only, to focusing on spine and pioneering spinal cord monitoring, and so on. He states, "you always want to be open to things," and in a field driven by innovation, this is an important tenet to keep in mind as residents while we learn seemingly impossible volumes of information, only to realize that in ten years our techniques and tools may look much different.

Given Dr. Ecker's diverse training background and early experiences, it is no surprise that his career focused on taking care of the patient rather than just an isolated surgical problem. Dr. Ecker jokingly admits to not being "the best marketer," but no one can argue that he is one of the best patient advocates. This is perhaps the most impressive and impactful way that Dr. Ecker influences the Penn residents. Practicing in a nonoperative capacity now, Dr. Ecker still influences the lives of his patients by listening to their problems and concerns and treating their maladies in the clinical setting. Additionally, he teaches all the residents who have the pleasure of working with him at the VA hospital and CHOP the importance of listening to the patient, focusing on a good exam, and providing the appropriate treatment—surgical or otherwise. He encourages trainees to derive satisfaction from what you can do for a patient—the unique ability to go to work and to fix something—rather than other material gains.

In addition to being an excellent surgeon and educator, Dr. Ecker is a proud husband and father of three children who are his greatest source of pride. Since retirement, he returned to Drexel to learn about computer programming—inspired by his granddaughter—and proved that he remains curious. He notes that his "life review has been positive," and he exudes a humility and graciousness when discussing his journey and his accomplishments that demands respect and admiration. We are proud to dedicate this edition of the UPOJ to Dr. Ecker, who proves to be a significant role model as an innovative surgeon, a dedicated patient advocate, a comprehensive educator, and a well-rounded individual.

Letter from the Dedicated

Malcolm Ecker, MD

I was frankly astonished when the editors informed me of my selection for the dedication of this issue as I have been a rather quiet presence in the Orthopaedic Department of the University of Pennsylvania since 1970. It is most gratifying that I have had some influence on the many medical students, residents, fellows, and colleagues that I have been privileged to know.

My education was in the Philadelphia public schools. After majoring in physics at Temple University, I entered its medical school in 1957. It was at Temple that I was given a solid foundation in how to practice medicine, i.e take a thorough history, do a good physical and only then order or review laboratory studies and imaging. At Temple I was also instilled with the need to always consider the patient's emotional content. The founders of psychosomatic medicine, Edward Weiss and O. Spurgeon English, were my professors and their concepts have been "rediscovered" as holistic medicine. Every illness, even a fractured radius, has some emotional content or implications. My introduction to orthopaedics was from John Royal Moore and indeed we only reduced fractures on Tuesdays.

As was typical in those days, I took a rotating internship at Einstein Medical center. I did a year of general surgery at the Boston City Hospital where I worked every other night except for the three months in which I worked very night. These were the days of wooden ships and iron men and we of necessity provided our care with a minimum of staff support, learning our skills from the residents above us. As this was the time of the physician draft and I was only deferred for one year, I was then sent to the USAF base at Plattsburgh New York, never going through basic training, and being the only person with surgical skills on a base with 18,000 souls, a 75-bed hospital, and nurse anesthetists. With great anxiety, I learned to be independent with no back up and doing the trauma, surgery and orthopaedics. Eventually, a board eligible and orthopaedist arrived.

I began my residency at Hospital for Special Surgery, arriving with my faithful wife and three children under three. Under the direction of Robert Lee Patterson, it was a fantastic experience as he believed that the hospital's main purpose was to train residents. Actual patients were presented at conferences three times a week and all the residents could be expected to stand up and orate on the physical findings, indications, the treatment options, and the literature to support them, the cases having been posted the prior evening. My surgical teachers emphasized a detailed knowledge of the anatomy, attention to tissue handling and sharp dissection. Efficiency was emphasized rather than speed for its own sake. It was a hands-on residency with much opportunity for closely supervised surgery. The residents had priority over the few fellows in choice of cases. We did also rotate to the fracture service at The New York Hospital as well as the Bronx VA and Newington Hospital for Crippled Children. My final five months was as the hand fellow. I have endeavored to pass my teachers' approach and philosophy to those with whom I have had contact.

We returned to Philadelphia in a private practice. I soon began my association with Penn Orthopaedics as an attending at The Philadelphia General Hospital. In 1975, when there was a need for another orthopaedist at The Children's Hospital, I joined and started the scoliosis service while doing general pediatric orthopaedist but still doing general orthopaedics at a community hospital. In 1969, I was one of the first in the Philadelphia area to use cemented total hips. Through a series of chiefs at Children's, I continued this arrangement. As medicine continued to evolve, I merged my practice and became part of the full-time Penn faculty in 1997 which incorporated my community practice. The decision was made in 2003 to close this practice and as I was 65, I decided to stop surgery. It is better to quit when you are at the peak of your game rather than when folks say it is about time. Since then I have been privileged to see outpatients at Children's while continuing to impart my surgical thoughts to the residents at the VA. My colleagues at Children's have been most supportive of my role in sorting our seemingly never ending stream of non-operative patients, some the worried well, and being able to find the signal in the noise who needs a referral to a real doctor.

I am greatly indebted to my wife, best friend, and supporter of approaching 62 years who has never complained about the usual erratic orthopaedic surgery life. We have been blessed with three children who have become successful adults and whom I think that their best attribute is that they are kind to people and appreciate their station in life. I did try to be present at their various games, theater and dance performances. When asked how we were so lucky, we answer that some of it is luck and a good deal is by the example of their hardworking and honest parents. We are also blessed with what we consider five utterly amazing grandchildren who seem to enjoy spending some time with their grandparents.

I also have enjoyed the benefit of excellent support staff. Always remember to thank everyone as you leave the operating room. When making rounds, always find the patients' nurses and ask them their thoughts and what else we should be doing for the patients. They spend at least eight hours a day with the patient compared with your five minutes. I have watched various chiefs of Penn Orthopaedics expand and make it a national first choice. The latest, Dr. L. Scott Levin,

with his incredible work ethic, has exponentially expanded our prominence in an exceedingly challenging environment. I am indebted to the many residents and fellows who have taught me and keep me up to date.They also seem to tolerate my continued skepticism of why the latest technique is not something in search of an indication. Ten years out of training, you do not want to have never changed. Investigate new approaches with skepticism. Do they have supporting data and do they really improve on the older results? In our byzantine health care system, we must have outcomes to justify costs as resources are not infinite.

For the future, I believe that medicine and orthopaedics in particular, will always be a satisfying profession. You can avoid burn out by remembering the importance of your family and making the patient's outcome the primary goal. You will always have an income sufficient for your family and your children's education but perhaps not the exotic sports car. The gratitude of the patient lasts longer than the bigger boat.

Good luck in the challenging future and I hope to be sharing it with you for a few more years. Every day is a blessing.

Arthroplasty Tips & Tricks: The Use of Big Clinical Databases for Orthopedic Research

Matthew Sloan, MD, MS
Neil Sheth, MD

Introduction

Research has changed. This is nowhere more evident than the ubiquitous appearance of articles published using data derived from big clinical databases across the most popular research journals in every field of medicine. For example, the National Surgical Quality Improvement Project (NSQIP) database, which is produced by the American College of Surgeons, reports that its database has been used to publish over 1,100 articles in peer-reviewed journals as of June 30, 2016.[1]

There are numerous big clinical databases available, both administrative and clinically derived, which use data collected from clinical settings across the United States. The administrative databases derive data from payments and claim information which include: Medicare claims database, Hospital Cost and Utilization Project (HCUP), and University Healthsystem Consortium. The clinical databases derive data from review of direct patient information which include: Automated Central Tumor Registry, NSQIP, National Trauma Data Bank, National Cancer Database, and the Surveillance, Epidemiology, and End Results (SEER) Program. There are also innumerable state-based and institution-based administrative and clinical databases and registries in use.[2]

What is driving the use of these big clinical databases? The obvious answer is time and money. While randomized controlled trials represent the gold standard of clinical research, they require enormous financial investment and time to be performed properly. Consider the requirements to perform a randomized trial that hopes to evaluate the superiority of low molecular weight heparin versus aspirin in prevention of venous thromboembolic events following total joint replacement. How many patients must be enrolled in such a trial? In order to evaluate this complication with sufficient power to detect a difference between these interventions, if one should exist, thousands of patients must be enrolled. If this study were conducted at a single institution, enrollment on that scale would take several years.A multi-center collaborative effort would require additional funds for oversight among participant sites and quality of data collection.Who is going to collect and analyze all this data? Research assistants and analysts need to be compensated to organize and interpret the collected data.

The performance of this rigorous investigation is essential to the scientific and medical community. However, before such investments can be made, preliminary research must establish a basis for embarking on a project of this scale. Herein lies the fundamental role for the big clinical database: readily available data on millions of patients that can be queried in minutes with minimal cost.

How to Perform Research Using Big Clinical Databases

The first step to beginning any research project is asking a question. The question should be informed by a rigorous literature review to determine what is known on the topic and what questions remain. Once the question is identified, one can determine if using a big clinical database is an option.All databases have their own benefits and limitations. It is imperative to understand the limitations of a database prior to acquiring it for research purposes. To illustrate the importance of understanding database limitations, we will walk through the process of using a big clinical database to answer the following question:

> How has the volume of primary and revision Total Joint Arthroplasty (TJA) changed in the United States since the year 2000?

This question is ideally suited for a big clinical database. It is not a question that can be answered by prospective study. Furthermore, the answer to this question may generate future questions that may be evaluated initially with data already present in the database. This work may then be used to inform a prospective study to evaluate these subsequent questions.

Identify the Database

To identify the appropriate database to answer this question, we will require one that has nationally collected data. This rules out institutional and state databases.We are interested in TJA performed among all patients, bearing in mind that a subsequent question may assess demographic (age, sex, race, socioeconomic)

or clinical (obesity, diabetes, comorbidity index) variations among patients over time. So, Medicare claims database would be a poor choice, as it does not provide comprehensive data for patients under 65-years-old, a rapidly growing segment of TJA recipients.

One tip is to evaluate what database has been used to ask similar questions in the past. We reviewed a highly-cited article by Kurtz and colleagues that predicts expected growth in primary and revision TJA between 2005 to 2030.[3] To build their prediction model, the HCUP National Inpatient Sample (NIS) was used. This database collects patient data from a nationally representative sample of 1,000 hospitals and includes data on over 8 million patient discharges with demographic and clinical variables.[4,5] Patient data is not limited by age or region, which makes this database an ideal candidate for following national trends in clinical procedures.

Methods

Access to national databases varies in cost and restrictions of use. For our preferred database, the HCUP NIS, one must complete an online course and a data use agreement. After completion, each year of the database is available for purchase. The files are large, 5-10 GB per year, in a compressed file format.

After downloading the database files, the majority of the work involved in accessing the data is unzipping and merging the files. Data files of this scale, with roughly 8 million patient observations per year, cannot be opened using standard spreadsheet software. Common statistical packages with this capability include SAS, SPSS, Stata, and R. Depending upon familiarity, these program are more or less user friendly to those with a statistical programming background. However, R is the least user friendly and will require significant familiarity with the coding procedures even to upload the files into the program for analysis. Stata, on the other hand, uses numerous dropdown menus to enabling a novice to upload files and perform analyses with minimal prior experience.

We used Stata for our analysis. The steps for accessing data are outlined in Figure 1. Briefly, after download, each file set must be unzipped into a file type readable by the statistics program (an ASCII file in this case). Once all the files have been converted to ASCII format the files can be read into Stata and converted to a data (.DTA) file. The distributor of HCUP NIS provides coding to add labels to the variables. The various raw data files can then be merged so that the dataset with the patient procedures can be combined with the patient comorbidities and hospital characteristics files, for example. Once the data has been organized, it is ready for analysis.

To start, it is recommended to run simple means on patient ages and other demographic variables for comparison to reference values. This ensures that all the data was uploaded and merged correctly. If these values match, you can proceed to perform the analysis of interest. In our case, we wanted to know about trends in TJA and revision TJA since 2000. Each patient admission lists up to 15 procedure codes obtained from the patient discharge record. Using the 2000-2014 database years, we coded for all patients who underwent total

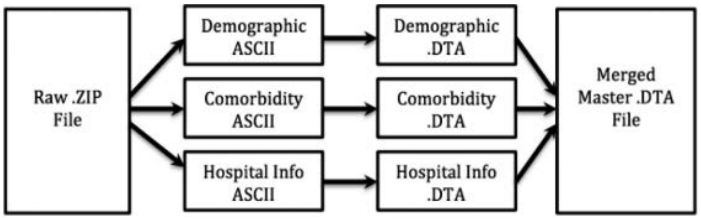

Figure 1. Process for unzipping and merging big clinical data file for use in statistical analysis programs.

hip arthroplasty (THA), total knee arthroplasty (TKA), revision THA, or revision TKA procedures in each year. The HCUP NIS database provides a representative weighted sample of 20% of hospital discharges from hospitals in the United States. Using each hospital's weighted average data, a national estimate for each procedure can be determined and cross-referenced against distributor data for sample procedures.

Once the trend data is obtained, outside data is combined with the raw volume data. We obtained data from the American Association of Orthopaedic Surgeons (AAOS) Orthopaedic Surgeon Census[6] to determine the change in annual cases per surgeon on a regional and national scale.

Results

Analysis of overall TJA demonstrates an increase in THA from 278,596 in 1997 to 523,280 in 2014. TKA procedures increased from 316,257 in 1997 to 752,941 in 2014. (Figure 2) Over the time period from 2000-2014 revision THA rose from 34,493 to 50,425. During the same period, revision TKA increased from 24,763 to 63,205, surpassing the number of revision THA performed annually. (Figure 3) From 2004 to 2016 the total number of orthopedic surgeon in the United States rose from 17,486 to 29,585. (Figure 4)

The volume of TJA per surgeon and revision TJA per surgeon annually remained constant over the time period 2004-2014. In 2004 overall TJA per surgeon was 47.2, with an insignificant change to 47.4 in 2014. Revision TJA per surgeon was 4.15 in 2004 and 4.22 in 2014. (Figure 5) Similar trends were seen regionally, with rises in TJA procedures, revision TJA

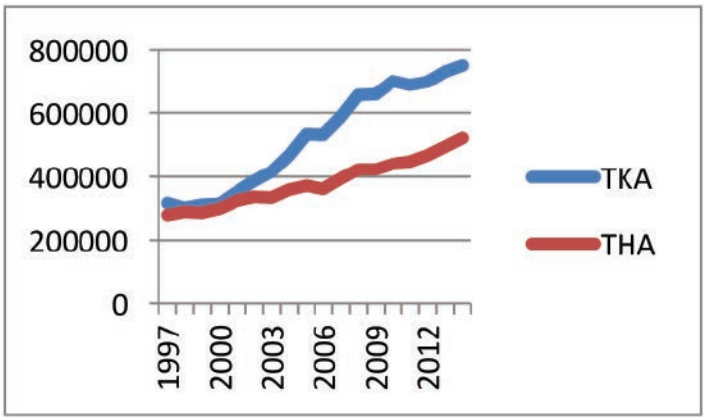

Figure 2. Total hip arthroplasty and total knee arthroplasty overall volume in the United States, 1997-2014.

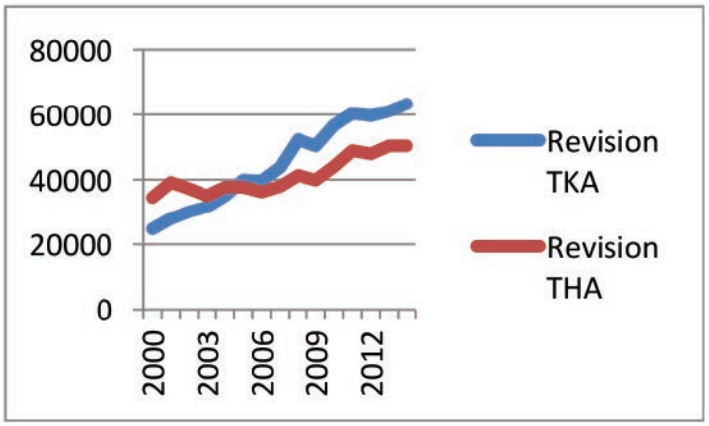

Figure 3. Revision total hip arthroplasty and revision total knee arthroplasty volume in the United States, 2000-2014.

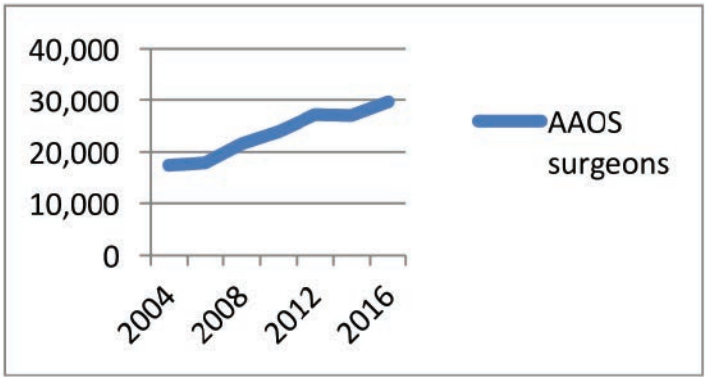

Figure 4. AAOS orthopedic surgeons in the United States according to AAOS Orthopaedic Surgeon Census, 2004-2016.

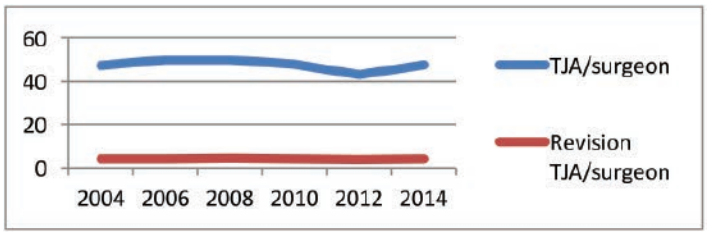

Figure 5. Overall total joint arthroplasty procedure and revision total joint arthroplasty procedure per orthopedic surgeon in the United States, 2004-2014.

procedures, and orthopedic surgeon volume in the Northeast, Midwest, South, and West. TJA and revision TJA procedures per surgeon, however, remained stable over the time period.

Table 1 demonstrates projected primary and revision TJA procedures for 2010 and 2020 according to the Kurtz paper. Comparison is made with the actual 2010 and 2014 data.

Discussion

The use of big clinical databases is allowing analysis of trends in orthopedics on a national level. In 2007, Kurtz and colleagues used this type of database to project growth of primary and revision total joint arthroplasty.[3] Using data from the HCUP NIS survey from 1990-2003, their team projected exponential growth of primary and revision TKA and continued linear growth of primary and revision THA. In the development of the Kurtz predictions, the model incorporated United States population estimates to develop estimates by age subgroup. The assumption inherent to this model was that projected increases in the aging population are driving increased demand for TJA procedures.

This is a logical assumption: older Americans are the primary recipients of TJA, thus an aging population drives demand for TJA procedures. However, the outcome modeled, that is total TJA performed in the United States is not a marker of demand, it is a demonstration of surgical performance, and thus, directly related to supply of surgeons available to perform these procedures. Our study incorporates the number of surgeries performed per orthopedic surgeon over the time period from 2004-2014. This analysis demonstrates a flat growth rate of surgeries performed per surgeon.

We assert that the dramatic rise that has been observed in TJA over the past two decades may be related to the rise in orthopedic surgeons in the United States. Furthermore, demand may be well above the saturation point at which surgeries can be performed. The ramifications of such unmet demand could be continued growth in TJA in parallel with increasing orthopedic surgeon density. It may be that the number of TJA procedures is far below patient demand, limited by the number of available surgeons. This would negate the Kurtz projection that primary and revision TKA will proceed to undergo exponential growth.

The year 2010 and 2020 Kurtz projections are demonstrated in Table 1. Their study uses a more narrow definition of TJA,

Table 1. Comparison of Predicted 2010 and 2020 primary and revision TJA procedures from Kurtz et. al with Actual primary and revision data from 2010 and 2014 using same coding scheme. * *Denotes significant difference from estimate*

Procedure	Predicted 2010	Actual 2010	Predicted 2020	Actual 2014
Primary THA	253,000 (232,000-276,000)	291,994*	384,000 (339,000-435,000)	371,605
Primary TKA	663,000 (618,000-711,000)	632,862	1,520,000 (1,362,000-1,700,000)	680,886*
Revision THA	47,800 (40,300-56,100)	44,032	67,600 (54,000-83,900)	50,425*
Revision TKA	55,300 (46,500-65,100)	56,586	55,300 (46,500-65,100)	63,205

incorporating only a single ICD-9 code for each of these procedures. Using the same coding scheme, actual data for primary and revision TJA procedures is provided for 2010 and 2014, the most recent available data year in the HCUP NIS database. It is clear that even at this earliest projected time point, 2010, the Kurtz projection has underestimated the number of primary THA procedures. For 2020, it appears the Kurtz projection has grossly underestimated the number of primary THA procedures that will be performed, as this estimate has already been met in 2014. The primary TKA projection, however, has not yet reached half of its 2020 estimate in 2014. Similarly for revision TJA, the 2020 estimate for revision TKA procedures has already been met and revision THA procedures have nearly been met by 2014. It may be the case that primary TKA procedures have not yet begun their exponential growth. However, it is evident that the Kurtz projections have been much too conservative for primary and revision THA, and revision TKA. We believe that the outlook is overly optimistic with regard to primary TKA procedures.

Following analysis of the Kurtz et al. methodology, we propose modeling future projections by taking into account expected surgeon growth as the strongest predictive variable. In addition, we plan to categorize the analysis into trends by demographic and comorbidity variables such as age, gender, and obesity to better understand what other factors are playing a significant role in driving the rise in TJA procedures.

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Validation of Utilizing a Modern Pedometer as a Measure of Patient Activity

Russell Stitzlein, MD
Alexander Neuwirth, MD
Keith Baldwin, MD MPH
Neil Sheth, MD

Introduction

Pedometers have been used for several years to measure the number of steps taken by users. Their recent popularization and advanced technologies such as Fitbit™ as well as digitized recording and applications linked to smartphones provides an opportunity for widespread clinical use by orthopaedic surgeons to evaluate patients pre-operatively and post-operatively.

Pedometers have been used with mixed results as a measure of patient activity in patients with total joint arthroplasty, with most studies reporting accuracy rates within 3%-5% of the true value.[1–7] Previous studies have found that following total joint arthroplasty, patients average approximately 5,000-7000 steps per day.[3,4] Age <60 years and male gender were found to be associated with increased steps per day. Multiple authors have commented on the wide variation in steps per day by patients undergoing total joint arthroplasty, with one group reporting a standard deviation of 3,040 steps per day[3] and another reporting a 15-fold difference in average daily steps among patients with the same UCLA activity scale score.[4]

Recent studies have been conducted to assess the use of smartphone pedometers in measuring patient activity. Results have been mixed, with most authors finding that smartphone application-based pedometers are too inaccurate for clinical evaluation/application.[8–10] Nolan, *et al*; however, showed that newer iPhone® models are 99% accurate in determining walking versus running and are able to accurately predict speed.[11] The iPhone® Health App calculates step-count and distance by integrating data obtained from the accelerometers, gyroscopes and compasses included in the phone. To date, no studies have reported on the accuracy or outcomes utilizing the iPhone® Health App available on iOS8 or later for the iPhone 5S or later smartphone models.

Hypothesis: Step counts as recorded by a modern pedometer (Health App on iPhone® 5S or later version) will correlate with the UCLA activity scale, Short Form (SF)-36 physical domain scores, Timed Up and Go (TUG) test scores, as well as Hip disability and Osteoarthritis Outcome Score (HOOS) and Knee injury and Osteoarthritis Outcome Score (KOOS) scores.

Specific Aims

1. Evaluate the accuracy of a modern pedometer (Health App).
2. Establish baseline values (T-score) for each of the outcomes measures and baseline pedometer step and distance values in a young healthy population.
3. Establish baseline values (Z-score) for each of the outcomes measures and baseline pedometer step and distance values in an elderly healthy population.
4. Correlate outcomes measures and pedometer step and distance values in patients with hip or knee osteoarthritis.

Methods

Institutional IRB approval was obtained prior to enrollment of subjects. A total of 110 subjects were enrolled in the preliminary study groups (validation and young healthy cohorts) with a plan to enroll 300 additional subjects for the final validation.

Patient Populations

1. Accuracy Cohort: Ten young healthy residents were recruited to assess the accuracy of a modern pedometer (Health App on iPhone® 5S or later version). Subjects all performed ten trials of 100 manually counted steps on both flat ground and on stairs. Pedometer data for each trial was then recorded for accuracy analysis.
2. Young Healthy Cohort: One hundred subjects aged 18-40 (medical students and residents) without chronic orthopaedic spine or lower extremity conditions were recruited to serve as young healthy control group. Each subject completed the UCLA activity scale, the SF-36, the HOOS and KOOS surveys and underwent a Timed Up and Go (TUG) test at the time of initial enrollment. The data from the Health App on the subject's smartphone was then extracted and the values for steps and distance for the 30-days immediately preceding the enrollment date were recorded and used for analysis.
3. Elderly Healthy Cohort *(Future Enrollment Group)*: This group will consist of 100 patients age ≥60-years old presenting to

orthopaedic surgery clinic with no history of chronic spine or lower extremity condition.

4. Hip Osteoarthritis Cohort *(Future Enrollment Group)*: This group will consist of 100 patients presenting to orthopaedic clinic with clinical and radiographic evidence of unilateral or bilateral **hip** degenerative joint disease with no ***clinical*** evidence of additional lower extremity joint or spine disease.
5. Knee Osteoarthritis Cohort *(Future Enrollment Group)*: This group will consist of 100 patients presenting to orthopaedic clinic with clinical and radiographic evidence of unilateral or bilateral **knee** degenerative joint disease with no ***clinical*** evidence of additional lower extremity joint or spine disease.

Results

Pedometer Accuracy

Five male and five female residents participated in the pedometer accuracy cohort. The male subjects had an average age of 29.4 years compared to 28.0 years for the female subjects ($p = 0.5$). Male subjects were an average of 72.2 inches tall compared to 63.8 inches for the female subjects ($p < 0.001$). Male subjects weighed an average of 203.0 pounds compared to an average of 121.4 pounds for female subjects ($p = 0.01$).

The accuracy analysis is summarized in Table 1. For all subjects, the pedometer recorded 2.1% more steps on flat ground than were manually counted by subjects. The discrepancy on flat ground for male subjects was +0.6% versus +3.5% for female subjects ($p = 0.26$). For all subjects, the pedometer recorded 5.9% more steps on stairs than were manually counted by subjects. The discrepancy on stairs for male subjects versus female subjects was statistically significant (1.6% vs. +10.2%, $p = 0.02$). Overall, there was no statistical difference between the pedometer data for all subjects on flat ground versus stairs ($p = 0.10$); this was also true for flat ground versus stairs for both the male ($p = 0.67$) and female ($p = 0.11$) subgroups.

Table 1. Pedometer accuracy meas ured as steps recorded on flat ground and on stairs when subjects manu ally counted 100 steps.

Flat Ground	**N**	**Mean**	**STDEV**	**Range**
Male	5	100.6	2.0	89–114
Female	5	103.5	5.0	90–128
Total	10	120.1	3.9	89–128
Stairs	**N**	**Mean**	**STDEV**	**Range**
Male	5	101.6	3 .0	86–105
Female	5	110.2	5.5	93–133
Total	10	105.9	6.1	86–133
Group	**vs**	**Group**	**p-value**	
Total Flat		Total Stain	0.10	
Male Flat		Male Stairs	0.67	
Female Flat		Female Stairs	0.11	
Male Flat		Female Flat	0.26	
Male Stairs		Female Stairs	0.02	

Young Healthy Cohort

Demographic analysis for the young healthy cohort is summarized in Table 2. Seventy-four males and twenty-six females participated. The cohort was predominantly Caucasian (87%). Twenty-four subjects reported a history of a prior lower extremity injury; no subjects reported an active acute or chronic lower extremity condition. Examples of prior injuries reported include meniscus tears, septic hip arthritis, metatarsal stress fracture, femoral shaft stress fracture, hip avulsion injury, pediatric femur fracture, pediatric tibial fracture, Osgood-Schlatter and aneurysmal bone cyst. Seventeen subjects reported prior lower extremity surgery. Examples of prior surgical procedures include knee arthroscopy, irrigation & debridement of open fracture, curettage and bone grafting and total hip arthroplasty.

Results of outcome instruments and pedometer data for the young healthy cohort is summarized in Table 3. The mean UCLA activity scale score was 8.9 (range, 5-10). Mean scores on the SF-36 were >95 for physical domains. Mean and median scores were lower for the energy/fatigue domain (62.0 and 65.0, respectively), the emotional well-being domain (82.2 and 84.0, respectively), and the general health domain (80.8 and 85.0, respectively). Mean scores for the HOOS were ≥ 89.9 for all domains. Median scores for all HOOS domains were 100. Mean scores for the KOOS were ≥ 96.6 for all domains.

Table 2. Demographic variables for the young healthy cohort.

Demographics	**N**	**Mean**	**STDEV**	**Range**
Gender				
Male	74			
Female	26			
Age		28.6	2.9	24.9–36.6
Height (inches)		70.2	4.5	56–77
Weight (lbs.)		171.8	37.3	105–265
BMI		24.3	3.3	19.2–33.4
Ethnicity				
Cacuasian (non-Hispanic)	87			
Caucasian (Hispanic)	3			
African-Amercan/Black	0			
Asian/Pacificl Islander	10			
Native American	0			
Prior Lower Extremity Injury	24			
Prior Lower Extremity Surgery	17			

Table 3. Outcomes measures by instrument and pedometer data for the young healthy cohort.

Outcome Measures	Mean	Median	STDEV	Range
UCLA Activity Scale	8.9	10	1.6	5–10
SF-36				
Physical Functioning	99.5	100	1.6	95.0–100
Role Limitations Due to Physical Health	100	100	0	
Energy/Fatigue	62.0	65.0	18.9	10.0–100
Emotional Well-Being	82.2	84.0	10.2	48.0–100
Social Functioning	96.8	100	8.1	62.5–100
Pain	95.	100	6.3	67.2–100
General Health	80.8	88	14.3	45.0–100
HOOS				
Pain	99.4	100	2.1	90.0–100
Symtpoms	89.9	100	2.5	90.0–100
Activities of Daily Living (ALDs)	100	100	0.3	98.5–100
Sports/Recreation	89.9	100	3.1	87.5–100
Quality of Life (QOL)	98.4	100	5.7	75.0–100
KOOS				
Pain	97.9	100	3.8	86.1–100
Symtpoms	96.8	100	5.0	85.7–1100
Activities of Daily Living (ALDs)	99.4	100	1.6	94.1–100
Sports/Recreation	96.6	100	7.6	70.0–100
Quality of Life (QOL)	97.8	100	5.5	75.0–100
Timed Up and Go (seconds)	5.50	5.35	1.40	2.55–9.52
Pedometer Data				
Steps	8118.2	7667.4	2257.5	4522–14478
Distance (meters)	6105.9	5697.4	1859.6	3067–11313
Distance (miles)	3.8	3.5	1.2	1.9–7.0

Median scores for all KOOS domains were 100. The mean TUG test time was 5.50 seconds. Subjects walked an average of 8118.2 steps [er day and 3.8 miles per day as recorded by the iPhone® Health App.

Discussion

The iPhone® Health App pedometer appears to accurately record steps and could represent a reliable way to measure patient activity. In our cohort, the iPhone® pedometer overestimated by 2.1% on flat ground and by 5.9% on stairs. If a larger study were to confirm the accuracy of the iPhone® Health App pedometer, it would be contrary to the findings of recent studies that have shown poor accuracy for smartphone pedometers.[8,9] Improved accuracy of iPhone® Health App pedometer could be due to decreased reliance on GPS data and/or improved data collection capabilities and programming in newer smartphones.

The SF-36 physical domain scores were high, on average, for the young healthy cohort as expected, with all physical domains displaying a mean >95. In comparison, the emotional domains demonstrated lower scores, with means from 62.0 for energy/fatigue to 82.2 for emotional well-being. At first glance, it might be surprising to find that there were deficits in the emotional domains on the SF-36, but a closer look at the domains and the study population provide a clear reasoning for these findings. The emotional domains of the SF-36 inquire about sleep habits, energy and stress levels. Given that our cohort exclusively included medical students and residents whose demanding academic and professional responsibilities result in chronic fatigue and stress, the lower scores are not unexpected.

The pedometer data for the young healthy controls demonstrated an average of 8,118.2 steps per day with a range of 4,522—14,478 steps per day. When compared to published step data on patients following total joint arthroplasty, it is somewhat surprising that our young healthy controls do not display a higher level of physical activity as recorded by the iPhone® Health App. It is quite possible that our mean value

under-represents the level of physical activity of our subjects and of the general population of young healthy individuals. Potential reasons for this measured discrepancy could be that our subjects are actually more active but fail to keep their smartphones on their person during periods of exercise. If this is the case, it could under-represent the true mean by a significant factor. An alternative explanation is that our study population of medical students and residents, while young and healthy, are less active than they otherwise would be due the nature of their school and professional responsibilities.

As a whole, the data obtained from the young healthy cohort should serve as an effective baseline for future analysis after the enrollment of the final cohorts. The young healthy cohort will serve to establish a T-score, much the same way is done for bone density evaluation and the diagnosis of osteopenia and osteoporosis. The elderly healthy cohort will serve to establish a Z-score for physical activity. We anticipate that the utilization of advanced pedometers will gain popularity in orthopaedics as a means to objectively and non-invasively follow the activity levels of patients and serve as a quick and reproducible proxy for patient-report outcomes.

Conclusions

The iPhone® Health App Pedometer records steps walked with acceptable accuracy. Young healthy controls have high levels of activity as measured by the UCLA activity scale, have excellent physical health as evidence by high scores on SF-36 physical domains and near perfect scores on the HOOS and KOOS tools. This group can be used to establish a baseline for comparison in a manner similar to the assignment of the T-score in bone density screening and diagnosis of osteopenia and osteoporosis.

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U·P·O·J

Evaluation and Treatment of Femoral Osteolysis Following Total Hip Arthroplasty

William Hardaker, MS
Daniel Gittings, MD
Jonathan Dattilo, MD
Neil Sheth, MD

Introduction

Total hip arthroplasty (THA) is widely successful for the treatment of end-stage hip disease. It significantly improves the quality of a patient's life by reducing both pain and functional limitation[1]. Many studies have demonstrated excellent survivorship following THA[2,3]. However, bone resorption, or osteolysis, has emerged as a major concern regarding long-term THA survival. The incidence of periprosthetic osteolysis is reported to be greater than the aggregate of all other complications[4].

Pathophysiology

Biomechanics of Femoral Component Design

Adaptive bone remodeling, or stress shielding, can occur in response to an altered mechanical environment following THA. Stress shielding leads to bone resorption, which can lead to an increased risk of periprosthetic fracture. Following implantation of a femoral prosthesis, there is redistribution of loads to the remaining femoral bone stock based on stem design. Most modern stem designs are manufactured with a coating that maximizes bone in-growth and minimize s stress shielding[3]. Reducing the amount of porous coating may decrease biologic fixation, whereas high amounts of porous coating may promote stress shielding[5,6].

Wear and Debris

Wear is defined as the loss of material from a surface due to motion. Linear wear rate refers to the degree of penetration of the metallic head into the plastic liner[6]. The incidence of osteolysis has been shown to rise significantly as linear wear rate rises above 0.1 mm/year, while osteolysis is rare below this threshold[7].

Implant material and design have important implications in wear and osteolysis. Highly cross-linked polyethylene (HXLPE), ceramic-on-ceramic, and metal-on-metal designs have all been employed as strategies in THA to reduce wear and subsequent osteolysis. Ultrahigh molecular weight polyethylene (UHMWPE) has been a reliable material used in THA acetabulum liners. However, the use of ceramic-on-polyethylene and metal-on-polyethylene implants has been associated with accelerated wear. HXLPE is a UHMWPE material that has been modified to resist wear.

Osteolysis

The concept of "effective joint space", which includes the prosthetic-bone interface, has been proposed as an explanation of the mechanism for wear particle migration and resulting osteolysis[8,9]. The flow of synovial fluid into the effective joint space delivers particulate matter that initiates localized macrophage-induced phagocytosis. The macrophages release cytokines, inducing a complex cellular response which initiates focal bone resorption primarily mediated by osteoclasts[5]. Circumferential implant coating has been shown to reduce wear particle migration along the effective joint space by creating a seal at the bone-implant interface[10,11,12].

Patient Evaluation

Evaluation begins with a comprehensive history and physical examination. The history should include the onset, provoking factors, quality, severity and delay between implantation and beginning of symptoms. In all cases of painful THA, infectious etiology must be ruled out.

Plain radiographs including an anterior-posterior (AP) view of the pelvis, AP and frog-leg lateral views of the femur that visualize the entire femoral component are necessary for initial evaluation. Radiographic signs of a stable uncemented implant include spot welds at the ends of the porous coating, absence of radiolucent lines, and calcar atrophy secondary to stress shielding. Osteolysis with a stable implant may be candidate for conservative treatment. Unstable implants may show component migration, divergent or progressing radiolucent lines, and pedestal formation (bony deposit at the distal tip of the implant)[13]. Loose femoral components also often remodel into varus and retroversion. Unstable implants require surgery to prevent further insult.

Classification

The Paprosky classification, provides an algorithm for defining femoral bone loss and directing treatment for femoral revision[14]. The quality and quantity of proximal bone stock, defined by the Paprosky classification system, guides treatment for femoral component revision as summarized in Table 1.

Table I. Paprosky classification of femoral bone loss overview of defect type and treatment strategy.

Paprosky Classification of Femoral Bone Loss		
Type	**Description**	**Treatment**
Type I	Minimal metaphyseal bone loss	Extensively porous coated implant or tapered stem
Type II	Extensive metaphyseal bone loss with intact diaphysis	Extensively porous coated implant or tapered stem
Type III	Extensive metadiaphyseal bone loss, minimum of 4 cm of intact cortical bone in the diaphysis	Extensively porous coated implant or tapered stem
Type IIIb	Extensive metadiaph seal bone loss, less than 4 cm of intact cortical bone in the diaphysis	Tapered stem or cemented stem with impaction bone graft
Type IV	Extensive metadiaphyseal bone loss and a nonsupportive diaphysis	Allograft prosthetic composite, long cemented stem, or proximal femoral replacement

Treatment

Non-operative Management

Non-operative treatment, reserved for asymptomatic patients with stable implants, aims to stop or slow the progression of osteolysis. There is some evidence at short and mid-term follow up after THA that bisphosphonates lead to decreased bone loss from osteolysis. Long term effect, however, is unclear[15].

Operative Management—Surgical Planning

Meticulous pre-operative planning is paramount for revision THA. Planning includes determining the surgical approach, tools necessary for component removal, and implants for reconstruction. The surgical approach for revision THA is based on surgeon experience, prior incisions, region of bone loss, need for additional exposure such as osteotomy, distorted anatomy or presence of heterotopic ossification (associated with the posterior approach to the hip), and planned reconstruction technique[16].

It is helpful to determine prior implants used from a patient's operative report that includes implant serial number and registration information. Flexible osteotomes, trephines, high-speed burr (pencil tip, carbide tip, metal cutting wheel), ultrasonic cement removal instruments, and universal extraction tools are also useful to facilitate stem removal[16]. Use of an extended trochanteric osteotomy (ETO) for removal of a well-fixed implant or extraction of a long column of cement distal to the stem can also be helpful[17]. Ultimately, the extent of femoral bone loss determines the reconstructive technique used for treatment[16].

Paprosky Type I defect reconstruction

Paprosky Type I defects have minimal metaphyseal bone loss, an intact diaphysis, and little to no proximal remodeling of femoral component into varus or retroversion. Mainstays for treatment include proximally porous coated femoral stems, extensively porous coated cylindrical stems, and tapered fluted stems. Implant selection depends on surgeon preference, amount of remodeling encountered, and remaining bone stock[18,19].

Proximally-coated stems may be considered when there is minimal proximal metaphyseal bone loss. Extensively porous coated cylindrical stems are versatile and may be used to reconstruct Type I defects and defects with more severe bone loss. Tapered fluted stems achieve axial stability with their geometry and have longitudinal ribs that enhance femoral cortex rotational stability and bony apposition. They are designed to decrease proximal stress shielding and more closely match the implant's modulus to the femur in order to minimize thigh pain.

Paprosky Type II defect reconstruction

Paprosky Type II defects, the most common type of defect, have extensive metaphyseal bone loss with an intact diaphysis. They often present with proximal varus femoral remodeling, making reconstruction more challenging. Type II defects may be reconstructed using extensively porous coated cylindrical stems or tapered fluted stems. When considering reconstruction of these defects, it is most important to bypass metaphyseal bone loss and obtain stable fixation in intact bone.

Paprosky Type III defect reconstruction

PaproskyType IIIa defects include extensive metadiaphyseal bone loss with a minimum 4cm of intact isthmic cortical bone. These defects may be treated with extensively porous coated stems, tapered fluted stems with splines or cylindrical stems[20]. Modular stems, which offer a greater degree of versatility, can also be used for reconstruction. These stems provide the flexibility of restoring version when the lesser trochanter anatomy is altered by remodeling while also allowing for more adaptable correction of leg length by adjusting the proximal body[21]. They are, however, more expensive than non-modular stems and the modular junction is at risk of fretting corrosion, which may ultimately lead to fracture of the stem.

In contrast with Type IIIa defects, Type IIIb defects include extensive metadiaphyseal bone loss with less than 4cm isthmic cortical bone remaining. Although fully porous coated stems may be used successfully in select patients, the stem is technically challenging to insert and the stiffness of implant may lead to thigh pain. The poor isthmic bone stock in type

IIIb defects necessitates alternative treatment strategies to achieve stable fixation of the prosthesis. Strategies to treat these defects include tapered stems, modular fully porous coated stems, and polished tapered cemented stems.

Another strategy to treat Type IIIb defects is with impaction bone grafting. Impaction grafting may be used to treat scenarios where there is inadequate diaphysis (femoral canal >18mm in diameter or <4cm isthmic bone stock) to achieve a "scratch fit" for a cementless implant. Contraindications include significant segmental defects with proximal femoral deficiency greater than 10cm. Supporters of impaction grafting advocate its ability to restore bone stock. Although long-term results for impaction grafting are encouraging, this reconstruction technique is labor intensive and requires experience.

Paprosky Type IV defect reconstruction

Paprosky Type IV defects are the most extensive, with complete loss of the isthmus. Successful reconstruction of these defects is unlikely to be achieved using biologic fixation alone. To augment fixation, multiple strategies can be employed including impaction grafting with a long cemented femoral component, allograft prosthetic composite (APC) and proximal femoral replacement (PFR) [22].

APC can be performed by removing deficient proximal bone and cementing a long-stem prosthesis into a proximal femoral allograft, and press fitting or cementing the distal stem into the femoral canal. APC may be particularly advantageous to restore bone stock in young patients. Disadvantages of APC include potential for infectious transmission, difficulty in obtaining an allograft, risk of nonunion or resorption of the allograft, and high technical demand of the procedure[23].

PFR is traditionally used to treat elderly and low demand patients with massive bone loss. A sufficient amount of bone must be present distally to ensure secure fixation of the implant or cementation of the megaprosthesis. The main advantages of PFR are early return to weight bearing and no risk of disease transmission. Disadvantages of PFR include poor soft tissue attachment to the prosthesis that may lead to instability and dislocation, severe stress shielding and bone remodeling, and difficulty with fixation.

Summary

Femoral osteolysis following THA is a complex problem that requires meticulous evaluation and pre-operative planning. Location of bone loss, available proximal femoral bone stock, and the residual isthmus available for diaphyseal fixation determine which treatment option should be employed. The Paprosky classification system may be used to define bone loss and determine treatment strategies. Our preference is to treat defects with less bone loss and an intact isthmus (Type I, II, IIIa) with an extensively porous coated implant. Tapered fluted stems may also be used. We treat large diameter IIIa defects and IIIb defects with modular or non-modular tapered stems to decrease modular mismatch and prevent thigh pain. Defects with more extensive bone loss and limited or non-existent isthmic support (Type IIIb and IV) are treated with more complex reconstruction including impaction bone grafting with cement, long cemented stem fixation, allograft prosthetic composite, or proximal femoral replacement with reconstruction technique determined on a case by case basis.

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Preoperative Risk Factor Score Predicts Malnutrition in Total Joint Arthroplasty Patients

Sarah Rudasill[1]
Daniel Gittings, MD[2]
Nabil Elkassabany, MD[3]
Jiabin Liu, M.D, PhD[3]
Charles Nelson, MD[4]
Atul Kamath, MD[4]

[1]Research Specialist
3737 Market Street, 6th Floor
Philadelphia, PA 19104

[2]Resident, Orthopaedic Surgery
University of Pennsylvania
3737 Market Street, 6th Floor
Philadelphia, PA 19104

[3]Attending Anesthesiologist
University of Pennsylvania
3400 Spruce Street, 6 Dulles Building
Philadelphia, PA 19104

[4]Attending Orthopaedic Surgeon
University of Pennsylvania
Department of Orthopaedic Surgery
800 Spruce Street
Philadelphia, PA 19107

Introduction

Malnutrition is a modifiable risk factor associated with greater risk of perioperative complications and hospital lengths of stay in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA)[1,4,3,11]. Previous literature has identified hypoalbuminemia (serum albumin < 3.5 g/dL) as a reliable measure for malnutrition[2,6,7,10]. Preoperative diagnosis of hypoalbuminemia allows intervention with evidenced-based nutrition regimens that may correct malnutrition prior to joint arthroplasty and improve outcomes[2,5]. While advanced age, male gender, emergency cases, and high American Society of Anesthesiologists (ASA) physical status classifications have been previously associated with malnutrition, identification of patients at-risk for hypoalbuminemia has proven difficult[4,8,9]. The purpose of this study is to examine risk factors for hypoalbuminemia and develop a predictive model that identifies at-risk patients prior to elective total joint arthroplasty.

Methods

We retrospectively reviewed the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database from 2006 to 2014 to analyze preoperative independent risk factors for a diagnosis of hypoalbuminemia in adult patients with Current Procedural Terminology (CPT) codes for primary THA (CPT 2130) and primary TKA (CPT 27447). Missing serum albumin levels, emergent cases, or ASA $\geq$ 4 were excluded. Multivariate regression analysis was used to evaluate the impact of independent risk factors, including age, sex, race, date of operation, surgery within the past thirty days, tobacco use, alcohol consumption, functional status, dyspnea at rest or with moderate exercise, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM) type I and II, liver disease, congestive heart failure (CHF), coronary artery disease (CAD), hypertension necessitating medications, peripheral vascular disease, renal failure, central nervous system disease, spinal cord injury, and chronic steroid use.

THA and TKA were analyzed separately. Significant risk factors were used to develop a seven-point preoperative risk model to predict hypoalbuminemia in joint arthroplasty patients. Continuous variables were analyzed via t-test, categorical variables were analyzed with Fisher's exact test and chi-square test, and predictive validity was assessed by comparing hypoalbuminemia diagnosis to a calculated hypoalbuminemia risk score.

Results

There were 35,837 complete THA records and 56,008 complete TKA records. Among THA patients, 1,684 (4.7%) had hypoalbuminemia and 34,153 (95.3%) did not. Among TKA patients, 2,327 (4.15%) had hypoalbuminemia and 53,681 (95.85%) did not. According to Table 1, seven factors emerged as significant, independent predictors of hypoalbuminemia prior to both hip and knee arthroplasty: age, sex, surgery within the prior 30 days, diabetes mellitus (DM) type I, liver disease, central nervous system disease, and chronic steroid use. Poor functional status and tobacco use were unique independent risk factors for malnutrition in THA patients, while ethnic race and dyspnea at rest were unique factors in TKA patients.

The proposed model is a seven-point scale, with one point assigned to each shared risk factor for hypoalbuminemia (Table 2). A score of three or greater indicates a high pre-test probability of hypoalbuminemia. According to Table 3, 1.7% of the THA cohort (608 patients) and 2.0% of the TKA cohort (1,138 patients) were identified as at-risk for hypoalbuminemia. The positive predictive value for THA patients scoring three or greater was 20.4%, while the negative predictive value for scoring below three was 95.6%. For TKA, the positive predictive value for patients scoring three or greater was 10.54%, while the negative predictive value for below three was 96.0%.

Discussion

The purpose of this study was to identify risk factors for hypoalbuminemia in THA and TKA patients and develop a model that preoperatively predicts malnutrition. Since hypoalbuminemia is associated with a higher risk of complications following joint arthroplasty, a targeted, cost-effective screening method for hypoalbuminemic patients may improve outcomes through more extensive preoperative nutrition management[2,5,6,7,10].

Table 1. Identification of risk factors that predict hypoalbuminemia in patients undergoing THA and TKA.

	THA (27130)			TKA (27447)		
Risk Factor	**Odds Ratio**	**95% Confidence Interval**	**P-value**	**Odds Ratio**	**95% Confidence Interval**	**P-value**
Age						
60-69 years	1.10	0.77 - 1.58	0.591	0.94	0.73 - 1.20	0.601
70-79 years	1.42	0.98 - 2.07	0.067	1.05	0.81 - 1.37	0.685
≥ 80 years	1.87	1.22 - 2.87	0.004	1.76	1.30 - 2.37	<0.001
Female	1.41	1.07 - 1.85	0.014	1.29	1.06 - 1.58	0.010
Race						
Black	1.27	0.81 - 1.97	0.296	1.40	1.04 - 1.88	0.027
Hispanic	0.51	0.24 - 1.11	0.090	1.05	0.77 - 1.41	0.767
Asian, Pacific Islander, and Other	1.75	0.65 - 4.72	0.271	1.06	0.59 - 1.93	0.837
Year of Operation	1.09	0.99 - 1.21	0.091	1.01	0.95 - 1.08	0.708
Diabetes						
Type II	0.80	0.51 - 1.26	0.337	1.11	0.87 - 1.43	0.394
Type I	3.12	1.95 - 5.00	<0.001	2.31	1.69 - 3.16	<0.001
Dyspnea						
At rest	1.36	0.89 - 2.06	0.151	1.56	1.21 - 2.00	0.001
Moderate exertion	2.02	0.58 - 6.98	0.267	0.44	0.06 - 3.25	0.420
Functional status	3.51	2.61 - 4.74	<0.001	1.22	0.86 - 1.75	0.262
Smoking status	1.77	1.26 - 2.49	0.001	1.20	0.88 - 1.63	0.253
Alcohol consumption	0.51	0.22 - 1.19	0.119	1.57	0.90 - 2.76	0.114
COPD Diagnosis	1.52	0.94 - 2.44	0.085	1.44	0.99 - 2.08	0.056
Liver disease	23.38	2.93 - 186.49	0.003	7.77	1.11 - 54.60	0.039
Congestive heart failure	2.13	0.47 - 9.61	0.325	2.58	0.55 - 12.08	0.230
Coronary artery disease	0.94	0.62 - 1.43	0.772	0.81	0.60 - 1.10	0.179
Hypertension	1.18	0.88 - 1.57	0.273	1.17	0.95 - 1.45	0.144
Peripheral vascular disease	0.90	0.26 - 3.13	0.874	0.60	0.18 - 1.98	0.401
Renal failure	1.50	0.36 - 6.21	0.579	2.86	0.92 - 8.88	0.070
Central nervous system disease	2.55	1.74 - 3.76	<0.001	1.47	1.07 - 2.03	0.019
Spinal cord injury		omitted		0.31	0.04 - 2.37	0.261
Chronic steroid use	2.00	1.27 - 3.16		2.50	1.76 - 3.57	<0.001
Surgery within past 30 days	15.59	5.23 - 46.44		3.36	1.32 - 8.52	0.011
_constant	1.61e-80	7.40e-171 to 3.48e10		2.41e-13	8.19e-71 - 7.12e44	0.667

There were seven significant, independent predictors of hypoalbuminemia prior to hip and knee arthroplasty: age, sex, surgery within the prior 30 days, diabetes mellitus (DM) type I, liver disease, central nervous system disease, and chronic steroid use. Advanced age as a risk factor for malnutrition is consistent with previously published literature[4,8]. However, our analysis found that females are more likely to be malnourished for both THA (OR 1.41, p = 0.014, CI 1.07-1.85) and TKA (OR 1.29, p = 0.010, CI 1.06 − 1.58), differing from a previous report that found male sex as a risk factor for hypoalbuminemia[8]. The previous report included emergent cases in their analysis, so the discrepancy may result from our focus on elective primary arthroplasty patients.

The seven-point model in Table 2 is useful for clinical decision making in patients undergoing both THA and TKA. One in five of the model's designated high-risk THA patients, and one in ten of the model's designated high-risk TKA patients, had hypoalbuminemia. Previous studies have found that the incidence of malnutrition in patients undergoing THA or TKA was 8.5%[4]. In this study, only 4.70% of THA patients and 4.15% of TKA had hypoalbuminemia. This quick scoring mechanism thus identifies THA patients with nearly five times the risk, and TKA patients with double the risk, of hypoalbuminemia relative to all patients undergoing procedures.

We were limited by a retrospective study design and the small proportion of patients scoring three or greater in the model. A majority of patients using this model remain false positives, but optimization of the model could reduce large standard errors and permit weighting of risk factors to improve accuracy. Future research should attempt to weight factors, incorporate a larger patient population, and focus on improving predictions prior to TKA, for which predictions are half as accurate as THA.

Conclusion

Efforts to identify joint arthroplasty patients at risk for hypoalbuminemia resulted in a model that predicts prevalence above rates of malnutrition observed in the general population. Accurate identification of hypoalbuminemic patients may allow preoperative nutrition interventions to improve postoperative outcomes and to serve as a framework for prospective studies on malnutrition optimization pre-operatively.

Table 2. Predictive model for hypoalbuminemia

Seven-Point Model		THA		TKA	
Factor	**Points**	**Odds Ratio**	**Standard Error**	**Odds Ratio**	**Standard Error**
Age ≥ 80 years	1	1.87	0.41	1.76	0.27
Female	1	1.41	0.20	1.29	0.13
Diabetes Mellitus Type I	1	3.12	0.75	2.31	0.37
Liver disease	1	23.38	24.77	7.77	7.73
Central nervous system disease	1	2.55	0.50	1.47	0.24
Chronic steroid use	1	2.00	0.47	2.50	0.45
Surgery within past 30 days	1	15.59	8.68	3.36	1.60

Table 3. Model's predictive value for hypoalbuminemia prior to THA and TKA

	THA			TKA		
Albumin Risk Score	**Normal Albumin**	**Hypo-albuminemia**	**Total**	**Normal Albumin**	**Hypo-albuminemia**	**Total**
0	97.41%	2.59%	13,295 (37.1%)	97.56%	2.44%	16,717 (29.8%)
1	95.57%	4.43%	17626 (49.2%)	96.01%	3.99%	30,627 (54.7%)
2	89.90%	10.10%	4,308 (12.0%)	92.69%	7.31%	8,072 (14.4%)
3	80.94%	19.06%	551 (1.5%)	89.86%	10.14%	1,065 (1.9%)
4	66.07%	33.93%	56 (0.15%)	84.72%	15.28%	72 (0.13%)
5	100%	0%	1 (0%)	0%	100%	1 (0%)
Total	34,153 (95.30%)	1,684 (4.70%)	35,837 (100%)	53,681 (95.8%)	2,327 (4.2%)	56,008 (100%)
+ Predictive Value (≥3)		20.4%			10.5%	
- Predictive Value (≥3)		95.6%			96.0%	

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U·P·O·J

Foot & Ankle Tips & Tricks: The Essentials of Physical Examination

Adnan Cheema, MD
Kathryn O'Connor, MD

Introduction

A thorough physical examination is an essential part of any clinical encounter for patients presenting with foot and ankle (F&A) complaints. In this article, we review the essentials of physical examination, which combined with the history, can assist the clinician in making accurate diagnoses. Physical examination of the F&A can be broadly divided into the following: inspection, palpation, gait, range of motion (ROM), neurological exam, vascular exam, and special testing.

Inspection

Inspection of the foot and ankle can provide valuable clues as to the underlying disease process. Firstly, it is important to note whether the patient has any swelling. Diffuse swelling/edema, especially that which extends proximal to the malleoli or is bilateral, can be a sign of systemic disease such as kidney disease, hepatic compromise, congestive heart failure, vascular insufficiency or lymphedema. Localized swelling over a joint can be a sign of rheumatoid or osteoarthritis. Swelling along the course of a tendon may indicate a tendinopathy. Areas with both swelling and ecchymosis may indicate a fracture or sprain.

Inspection of the skin is also a vital component of the F&A exam. Bluish pigmentation of the skin represents hemosiderin deposits from extravasation and subsequent lysis of red blood cells. It can be a sign of venous stasis, varicose veins, or even a chronic deep venous thrombosis. Hypertrophic nails, decreased hair growth on the lower leg, and thin, shiny, pearlescent skin can also be signs of poor vascular supply. With the high prevalence of diabetes, skin ulcerations should be noted, their size documented and the wounds probed to assess their depth. In patients with diffuse erythema, the limb can be elevated to determine if the erythema improves. Lack of improvement may point to an infectious etiology while improvement can indicate Charcot arthropathy.

Inspection of the patient's standing alignment is a key part of the examination. Weight bearing is essential to understand the orientation of the joints, the position or splaying of the toes, and the extent of deformities. The alignment of the hindfoot should be assessed with the clinician standing behind the patient to determine whether the hindfoot is in neutral, valgus, or varus. Subtle differences in where the calcaneus contacts the ground in relation to the tibia should be noted, as it may indicate risk factors for other pathologies. The alignment of the knees and tibia should be noted as it may help identify other deformities. For example, a patient with a severe valgus knee may also have a valgus hindfoot to compensate. The shape of the arch should be examined to determine whether the patient is flat-footed or high-arched.

The forefoot should be examined with the patient standing to determine if it is abducted or adducted. The forefoot should also be examined with the patient seated, to assess for compensatory rotational pronation/supination, which may manifest only when the foot is unweighted.

The alignment of the toes should also be assessed with the patient standing. Standing examination makes varus, valgus, and cross-over deformities of the toes more apparent, allowing the clinician to understand how the pull of the long flexors and extensors are affecting the deformity. Claw toes, hammer toes, and mallet toes present similarly and should be differentiated.

The soles of the feet should be examined for plantar calluses, or mechanical hyperkeratoses. The location of these calluses can provide valuable clues into the underlying disease process. For example, a child with lateral plantar calluses may have a rigid varus hindfoot alignment that causes him to walk on the lateral aspect of his foot.

Palpation

Due to the foot's thin skin and superficial contours, surface anatomy can be an excellent guide to identify the location of pathologic processes. Ligamentous, boney, and tendinous injuries are usually painful immediately over the site of injury. For example, ankle and syndesmotic ligaments are located in areas with very little overlying tissue, making them easily identifiable with palpation. In the neuropathic population, however, palpation may not be as helpful, given the diminished sensation.

In the midfoot, boney osteophytes can be easily palpated, despite the small size of these

joints, again due to the thin soft tissue coverage. Masses can be identified easily on the dorsum of the foot and most commonly represent ganglion cysts.

In the traumatic setting, all four compartments of the affected leg should be palpated to assess for compartment syndrome. Pain with passive stretching of the toes can also be used to aid in the detection of this emergent diagnosis.

Some of the common areas of tenderness and their correlating differential diagnoses are listed in the Figure 1 and Figure 2.

Gait Examination

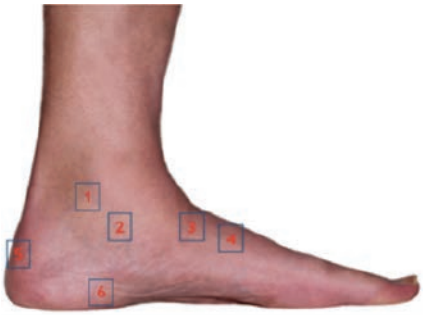
The patient should be asked to ambulate in the hallway for best assessment. Asymmetry of the direction in which the toes point, known as the foot progression angle, can be a clue to underlying pathology. For example, a patient who walks with his toes pointed in may have metatarsus adductus, internal tibial torsion, or increased femoral anteversion.

The stride length and rhythm should also be noted. A high steppage gait with slapping of the foot on the ground may be a result of a peroneal nerve palsy. Truncal balance should be assessed as well. A truncal thrust may represent a Trendelenberg gait and can be a sign of proximal muscle weakness.

A decrease in the stance phase on one leg results in an antalgic gait and should warrant further testing. In the normal gait cycle, the heel strikes the ground first. This is followed by the foot landing flat and then to toe off. If this sequence is disrupted, an underlying pathology should be investigated.

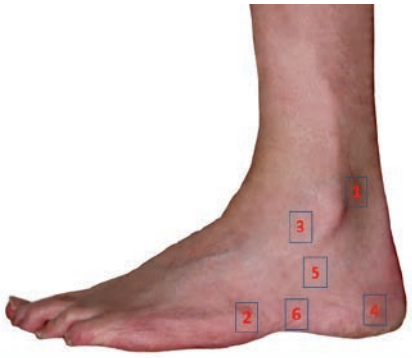
Range Of Motion Testing

ROM of the ankle and foot joints should be assessed in a systematic fashion. Like all joints, it is important to assess both passive and active ROM and compare to the contralateral side.



Labeled Point	Differential Diagnosis
1	Posterior Tibialis Tendon
2	Deltoid Ligament
3	Navicular, Accessory Navicular
4	First Tarsometatarsal Joint
5	Achilles Tendon Insertion
6	Plantar Fascia Insertion

Figure 1. Lateral view of the foot and ankle.



Labeled Point	Differential Diagnosis
1	Peroneal tendons
2	Base of the 5th Metatarsal
3	Anterior Talofibular ligament
4	Calcaneus body
5	Peroneal Tubercle
6	Groove for Peronus Longus at the Cuboid

Figure 2. Medial view of the foot and ankle.

The ankle joint is primarily responsible for dorsiflexion and plantar flexion. Restriction of ankle ROM can have multiple causes, including ankle arthritis and heel cord tightness. The subtalar joint is primarily responsible for eversion and inversion.

In patients with equinus contractures, the Silfverskiold test can be used to determine the role of the Achilles tendon on the limited range of motion. The degree of ankle dorsiflexion is measured with the knee extended, which engages both the gastrocnemius and the soleus. Thereafter, the degree of dorsiflexion is measured with the knee flexed, which engages only the soleus—the gastrocnemius has been taken off tension because it crosses the knee joint in addition to the ankle. If dorsiflexion improves with flexion of the knee, the equinus contracture is the result of the gastrocnemius tightness. If dorsiflexion does not improve with knee flexion, the contracture is a result of both the gastrocnemius and the soleus in the Achilles tendon.

The motion of the first MTP joint should also be assessed, especially in the setting of hallux valgus. It is important to note if the first MTP joint is correctable to a neutral alignment, as this affects treatment options.

Throughout the foot, understanding the relative flexibility of each joint is important, as options for surgery frequently differ based on the range of motion. In some instances, if a foot deformity is passively correctible, then conservative therapy or soft tissue procedures alone may be sufficient to correct it. For rigid deformities, however, osteotomies or fusions may be necessary.

While deficits in the range of motion of the foot may be caused by pathology within the foot and ankle, it is important to remember that the culprit may be in a different anatomic location. For example, a patient who is unable to extend the

first toe may have a laceration of the extensor hallucis longus tendon or severe MTP arthritis, but may also have a higher deep peroneal nerve injury or even an L5 radiculopathy.

Neurological Examination

A comprehensive neurological examination is critical, particularly in diabetics who commonly present with foot and ankle ailments. Sensation of the five nerves to the foot—sural, saphenous, superficial peroneal, deep peroneal, and tibial—should be evaluated. Specific testing with 5.07 monofilament is imperative to identify underlying neuropathy. Loss of "protective" sensations can lead to an increased incidence of foot wounds, amputations, Charcot arthropathy and generalized foot pain. Operative and post-operative management can also change dramatically in patients with underlying neuropathy, making proper identification of neuropathy all the more important.

Manual muscle testing of all the major extrinsic muscles to the foot is also a standard part of the examination. A careful strength examination can help differentiate between neurologic and musculoskeletal causes of weakness.

Reflexes should also be tested, namely the S1 reflex. Loss of the S1 reflex can be part of the normal aging process. However, when the S1 reflex is lost in combination with the inability to plantar flex the foot, the clinician should investigate for a true neurological injury.

Vascular Examination

Understanding the health of the patient's blood supply is important for surgical planning and identifying when other interventions may be needed. Skin changes associated with compromised blood supply are detailed in the inspection section above.

The dorsalis pedis and posterior tibialis pulses must be identified at every examination. In patients without palpable pulses, Doppler ultrasound should be used to identify flow. Ankle-brachial indices can be obtained to quantify the degree of vascular compromise. While a small percentage of the population does not have a clear dorsalis pedis pulse, patients with skin changes or risk factors for vascular disease should be considered for referral to a vascular surgeon.

Special Testing

In addition to the physical exam findings listed above, a few special tests can be performed to identify specific injuries. A description of the Silfverskiold test can be found in the ROM section.

In patients with cavovarus deformity of the foot, the Coleman block test can be used to assess the flexibility of the hindfoot. The patient stands with the affected foot on a block approximately 1-2cm thick, with the lateral heel and lateral foot firmly planted as the first ray hangs free. If the hindfoot varus corrects to neutral upon standing on the block, the hindfoot is deemed flexible. As such, one can infer that the pathology is likely in the forefoot, resulting in a compensatory varus hindfoot.

Single leg heel rise is a specific test to assess the function of the posterior tibial tendon. The patient is asked to stand on one limb and onto their toes as the clinician examines him from behind. Normally, the posterior tibial tendon initiates heel rise by locking the mid-tarsal joints and turns the hindfoot into varus. Patients with posterior tibial tendon dysfunction are unable to initiate the heel rise and lack the associated heel inversion.

The anterior drawer test can be used to examine the integrity of the anterior talofibular ligament, which is commonly injured during inversion ankle sprains. The clinician stabilizes the lower leg with one hand while applying an anteriorly directed force on the heel, assessing for translation. It is often helpful to perform the test bilaterally and compare both sides to better judge the degree of translation. A torn anterior talofibuar ligament results in increased translation.

The Thompson test can be used to assess for Achilles tendon tears. The patient lays prone on the table with the feet hanging freely of the edge. The clinician squeezes the calf and determines whether the foot plantar-flexes. Lack of plantar flexion or decreased plantar flexion compared to the contralateral side is a sign of an Achilles tendon tear.

Conclusion

The physical examination of the foot and ankle is a valuable tool to help clinicians make accurate diagnoses. Combined with the history and a thorough knowledge of anatomy, the physical exam can help not only in making diagnoses but also with surgical planning.

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Integrating Functional Ultrasonography and Motion Analysis into the Clinical Treatment of Patients with Achilles Tendon Ruptures

Josh Baxter, PhD
Todd Hullfish, BS
Kathryn O'Connor, MD
Daniel Farber, MD
Keith Wapner, MD
Wen Chao, MD

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

Introduction

Achilles tendon ruptures can lead to elongated and abnormal tendons that limit patient function[1–4]. While the links between musculo-tendon structure and locomotor function have been well described[5–9], the effects of altered tendon properties[10,11] on muscle remodeling[12,13] and locomotor function resulting from Achilles tendon injuries remain poorly understood. Animal studies have shown that muscles rapidly remodel in order to maintain sarcomere shortening dynamics and function[14,15]. However, the muscular response to extreme changes in shortening demands imposed by Achilles tendon injuries have not yet been described and may provide critical information for clinical decision making.

Therefore, the purpose of this study was to establish a framework that can be integrated into the clinical setting to link muscle remodeling and functional deficits in patients recovering from Achilles tendon ruptures. In particular, we aim to identify clinically relevant benchmarks that will guide treatment and better manage expectations. This case presents a framework that is currently being implemented in a prospective patient registry to rigorously characterize the muscle remodeling response to Achilles tendon injuries and establish clinical benchmarks for patient success.

Methods

A 27-year old male (1.83 m and 84 kg) presented 2.5 years following an acute Achilles tendon rupture that was surgically repaired by another provider using an open repair technique within 1 week of the initial injury. He had a poor outcome that was confirmed by a clinical outcome score (ATRS score of 49)[16] evaluation by a fellowship-trained foot and ankle surgeon, and an inability to perform a single-leg heel raise. This functional assessment is part of an IRB approved research registry.

Plantarflexor architecture was measured under ultrasonography[6,8] and muscle remodeling was quantified by contrasting the medial gastrocnemius muscles of the affected and unaffected sides. Muscle thickness as well as fascicle length and pennation were quantified by identifying the superficial and deep aponeuroses and clearly identifiable fascicles[6,7].

Plantarflexor function was assessed through a battery of tests that included isometric strength testing, walking, and single-leg heel raise. During these activities, the ultrasonography probe acquired images synchronously with motion capture, dynamometer, and force plate data[17]recording of the electrical activity of the muscle, measurement of knee- and ankle-joint rotations, and measurement of ground reaction forces in six men during walking at 3 km h(-1. Plantarflexion motion, torque, and power along with fascicle shortening dynamics were calculated to establish the link between muscular and patient function. Fascicle shortening dynamics were quantified using an automated tracking routine utilizing MATLAB's Computer Vision System Toolbox.

Results

Plantarflexor muscle architecture of the affected limb was comprised of shorter and more pennated muscle fascicles as well as a muscle belly that was less thick compared to the unaffected side (Table 1). The resting fascicle length shortened by nearly 60% and demonstrated a 3-fold increase in pennation. Muscle belly thickness also decreased by one-quarter of the unaffected side.

Patient function measurements demonstrated varying degrees of sensitivity to the underlying skeletal muscle adaptations (Table 2). The affected limb demonstrated a 47% decrease in active plantarflexion torque while the fascicles on each limb went through similar amounts of relative shortening. Walking at a self-selected speed did not elicit any functional differences between the affected and unaffected sides. Single-leg heel raises were highly sensitive to deficiencies in muscle architecture, both at the

Table 1. Architectural parameters of the medial gastrocnemius muscle of the affected side (surgically repaired tendon) and unaffected (healthy) sides.

	Affected	Unaffected	%change
Pennation	34°	13°	162%
Length	4.6cm	11.2cm	-59%
Thickness	2.2cm	2.9cm	-24%

Table 2: Plantarflexion biomechanics and fascicle shortening during isometric contractions, walking, and single-leg heel raise. (,) denotes nominal differences between groups.

	Affected	Unaffected	% Change
Torque	70 Nm	133 Nm	−47%
Shortening	41% (1.9cm)	46% (5.1cm)	~ (−63%)
Plantarflexion	16°	15°	~
Torque	160 Nm	156 Nm	~
Shortening	<1 cm	<1 cm	~
Plantarflexion	12°	40°	−70%
Torque	140 Nm	140 Nm	~
Power	100 W	260 W	−62%
Shortening	1.0 cm	5.4 cm	−81%

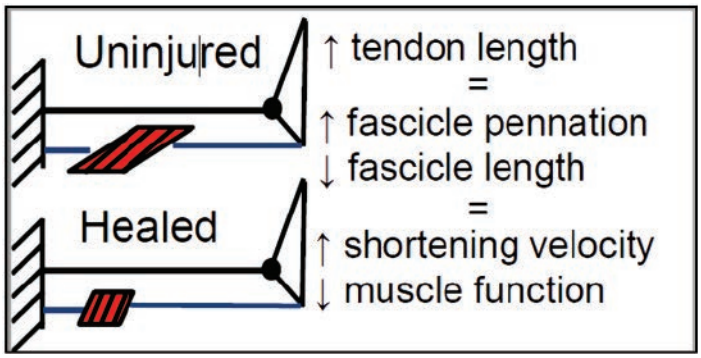

Figure 1. Achilles tendon elongation following repair, which appears to elicit muscle remodeling in order to maintain resting tendon tension. This muscle remodeling reduced muscle shortening and function in this study.

patient-function level (70% decrease in plantarflexion motion and 62% decrease in plantarflexion power) and at the muscle-level (80% decrease in muscle shortening).

Discussion

This study introduces a framework that rigorously quantifies muscle remodeling in response to Achilles tendon injuries—establishing a means to prospectively study the implications of injury and treatments on lower extremity function. Despite the clinical understanding that patients recovering from Achilles tendon ruptures may have elongated tendons with intrinsic differences from a normal, never ruptured tendon resulting in reduced function[1–4], there has not yet been prospective research that characterizes the effects of tendon injury on plantarflexor muscle remodeling and patient function. Establishing this relationship will provide clinicians with a greater ability to plan treatment based on patient factors—leading to improved function and outcomes.

Our central hypothesis that tendon elongation and intrinsic abnormalities resulting from tendon injuries and treatment will elicit rapid muscle remodeling—which we propose as a mechanism of maintaining tendon tension (Figure 1)—will be tested in a large-prospective cohort using this framework. Initial testing is underway to identify measures of tendon, muscle, and patient function that are most sensitive to changes in patient outcomes and status in order to streamline this framework in order to implement it into clinical settings. Simple musculoskeletal models[5,8,18] may also be informed by patient data as part of this prospective framework in order to predict patient function using cost-effective measures of musculoskeletal structure as model inputs.

This research framework is not without limitations. Prospective-functional registries are logistically challenging due to patient attrition and time constraints. In order to minimize these concerns, our methodology will collect a minimal amount of standardized information from all patients being treated for Achilles tendon pathology. Clinical experience suggests that other foot and ankle pathologies may result from compromised plantarflexor function following Achilles tendon rupture. For example, posterior tibialis tendon insufficiency—commonly referred to as flatfoot deformity—may result from increased mechanical demands placed on smaller muscles neighboring the triceps surae group, which was observed in this current case. Smaller muscles of the posterior compartment remodel in response to tendon injury and treatment[12,13] as a compensatory mechanism to preserve some amount of foot function[19]. To account for these compensatory changes in nearby muscles, we will acquire cross-sectional ultrasonography images of posterior compartment muscles[20].

Conclusions

We propose a framework for prospectively quantifying plantarflexor function and structure in patients treated for Achilles tendon ruptures. Current work is focused on streamlining this framework using low-cost measurement equipment in order to integrate these tests into the clinical setting. Characterizing the interaction between tendon structure and elongation, muscle remodeling, and functional limitations will aid clinicians in managing patient expectations, prescribing rehabilitation, and intervening in patients at risk of becoming functionally limited.

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U·P·O·J

Mechanical and Histological, but not Functional, Properties Remain Inferior in Conservatively Treated Achilles Tendons in Rodents: Long Term Evaluation

Benjamin Freedman, PhD
George Fryhofer, MD
Nabil Salka, BD
Harina Raja, MS
Cody Hillin, MD, MS
Courtney Nuss, MD
Daniel Farber, MD
Louis Soslowsky, PhD

McKay Orthopedic Research Laboratory
Philadelphia, PA

Introduction

Conservative treatment (non-operative) for Achilles tendon ruptures is suggested to produce equivalent capacity for return to function as operative repair[1]. In a rodent study, coupling conservative treatment with early return to activity (RTA) further improved healing and limb function 3- and 6-weeks post-injury[2,3]. However, the long-term biomechanical effects of conservative treatment and RTA timing on limb function, Achilles tendon properties, and gastrocnemius/soleus muscle properties are unknown and are essential to fully understand the effects of this treatment paradigm. Therefore, the purpose of this study was to evaluate the long-term response of conservatively treated Achilles tendons in rodents with varied RTA. We hypothesized that tendon and muscle properties would be superior with earlier RTA compared to delayed RTA, but both injured groups would remain inferior to uninjured controls 16-weeks post-injury. We also hypothesized that no differences in limb function would exist between groups by 16-weeks post-injury, but early RTA would have accelerated return to normal limb function.

Methods

Study Design

Sprague Dawley rats (n = 42) at 16-weeks of age were used (IACUC approved). Animals had treadmill training[2,3] prior to blunt midsubstance transection of the right Achilles tendon and resection of the plantaris longus tendon[4]. Animals were randomized into groups that returned to activity after 1-week (RTA1) or 3-weeks (RTA3), and all hind limbs were immobilized in plantarflexion. Uninjured age-matched animals (n = 10) allowed only cage activity were used as controls. Functional evaluation (n = 10-16/group) of passive ankle joint range of motion (ROM) and stiffness was performed on anesthetized animals prior to injury, as well as 4, 6, 10 and 16 weeks post-injury.

Ex vivo Assays

After sacrifice 16-weeks post-injury, tendons (n = 10/group) were harvested and prepared for viscoelastic, quasi-static, and fatigue testing, as described[2,3]. An additional set of tendons (n = 6/group) was used for histological and immunohistochemical analyses. Sagittal sections (7 μm) were stained with Hematoxylin-Eosin (H&E) and Safranin-O and Fast Green (SAF-O). Additionally, the gastrocnemius/soleus muscle complex was harvested, sectioned axially, and stained for antibodies against laminin (L9393, Sigma Aldrich) and myosin heavy chain (MyHC) types 1, 2a, and 2b (type 1: BA-D5; type 2a: SC-71; type 2b: BF-F3), as described[4].

Analysis

Functional ankle joint properties (i.e., ankle ROM and stiffness) for both dorsiflexion and plantarflexion were evaluated. Achilles tendon viscoelastic, quasi-static, and fatigue properties were computed. The tendon midsubstance was evaluated for cell density, nuclear shape, and GAG staining through grading by 3 independent, blinded investigators. Deep and superficial muscle regions were analyzed for fiber size (min Feret diameter) and fiber type distribution using the SMASH application[5]. One-way ANOVAs with post hoc t-tests with Bonferroni corrections were used to compare the effect of RTA on mechanical, functional, structural, and muscle properties. Kruskal-Wallis tests with post hoc Mann-Whitney U-tests were used for histological scoring.

Results

Functional deficits due to injury and due to RTA timing were present 4-weeks post-injury for ambulatory measures including the vertical ground reaction force (Fig. 1A) and for passive dorsiflexion ROM (not shown), both of which gradually returned to baseline levels by 16-weeks. Although functional properties achieved pre-injury levels by 16-weeks post-injury, mechanical properties remained inferior. RTA1 and RTA3 groups had increased cross sectional area (Fig. 2A) and decreased dynamic modulus (|E*|) (Fig. 2B) compared to uninjured control tendons. With regard to fatigue properties, the secant modulus (material property) was decreased in RTA1 and RTA3 groups compared to control (not shown), while the secant stiffness (structural

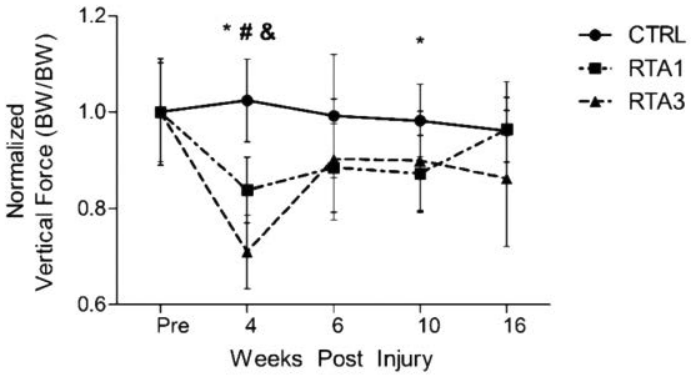

Figure 1. Ambulatory Assessment. RTA1 and RTA3 groups had decreased vertical force 4-weeks post-injury and returned to control levels by 6-weeks post-injury. Data shown as mean ± SD. Symbols indicate significant differences ($p < 0.017$) between groups (*-CTRL v. RTA1; #-CTRL v. RTA3, &-RTA1 v. RTA3).

property) was not different between groups (Fig.2C). In addition, tendon laxity (Fig.2D) was elevated in RTA1 and RTA3 groups compared to control levels. Histologically, RTA1 and RTA3 groups had increased cellularity compared to control tendons (Fig.3A), but had no differences in cell shape or SAF-O staining. Muscle staining revealed that RTA1 groups had decreased fraction of type-2x positive fibers compared to control and RTA3 groups, but no changes in the fraction of type-1, type-2a, or type-2b fibers (Fig.3B). No changes in fiber size were detected.

Discussion

This study investigated the long-term effects of conservative treatment on Achilles tendon healing in rodents. Long-term functional outcomes were improved compared to those

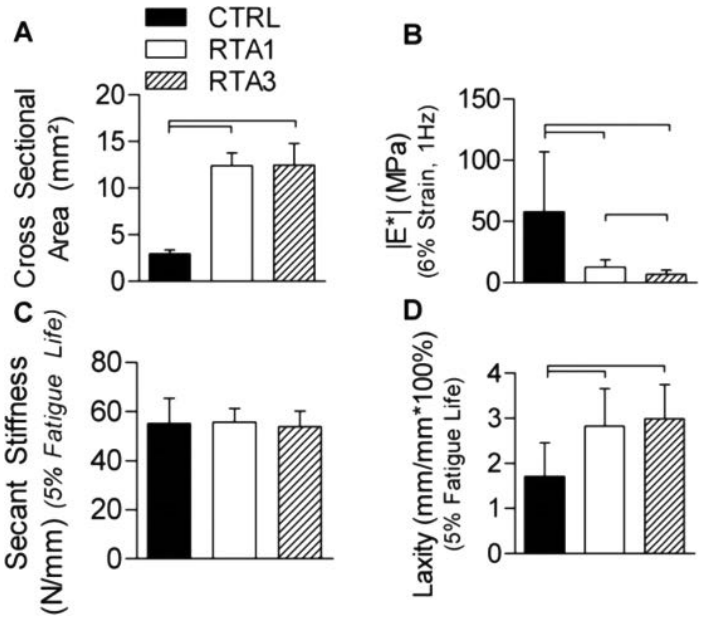

Figure 2. Mechanical Properties. RTA1 and RTA3 groups had increased **(A)** cross sectional area, decreased **(B)** IE*I, and increased **(D)** laxity compared to uninjured control tendons 16-weeks post injury. No differences in secant stiffness were found between groups. Data shown as mean ± SD. Lines indicate significant differences ($p < 0.017$).

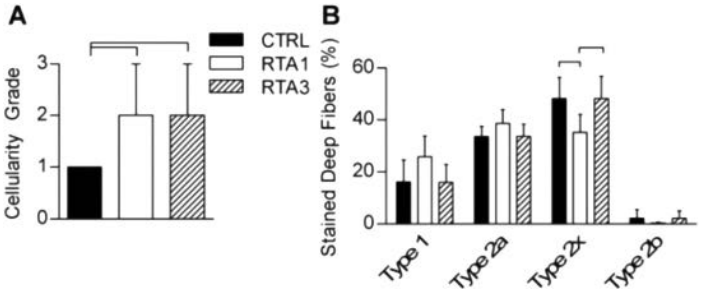

Figure 3: Tendon and Muscle Histological Properties. **(A)** Cellularity was increased in RTA1 and RTA3 tendons compared to uninjured control tendons when assessed at the midsubstance 16-weeks post-injury. **(B)** There was a lower percentage of type 2x fibers in RTA1 tendons compared to control and RTA3 groups. A- Data shown as median ± IQR. B- Data shown as mea n ± SD. Lines indicate significant differences ($p < 0.017$).

described in previous clinical literature[7, 8], potentially since an initial period of full plantarflexion casting was used to reduce tendon gapping, and that the function assessed was voluntary and not during high dynamic loading. Although mechanical properties improved compared to earlier time points in our rat model[2, 3] (similar to humans[6]), biomechanical properties at the tissue level remained significantly lower than controls. RTA1 and RTA3 groups displayed a much larger scar cross sectional area that was not fully remodeled, along with persistent high cell counts. Interestingly, although material properties were inferior in RTA1 and RTA3 tendons, structural properties were similar to controls, suggesting that healing tendons can achieve similar mechanical stiffness, which may explain the lack of changes in muscle properties between groups. Indeed, the majority of muscle properties assessed were not different from control levels 16-weeks post-injury, suggesting that conservative treatment does not have adverse effects on long-term muscle properties at the fiber level. The relatively low SAF-O staining contrasts to early RTA groups at 6-weeks post-injury[3], which suggests that a more tendon-like phenotype is achieved 16-weeks post-injury. Future studies will examine structural properties and sex differences in long term Achilles healing.

Significance

As conservative management of Achilles tendon ruptures becomes more popular, it is necessary to evaluate the long-term biomechanical effects of this treatment paradigm. Although functional properties return to baseline levels by 16-weeks in this rodent model, tendon properties remain altered mechanically and histologically, and gastrocnemius muscle properties may also be affected. Despite these changes, tendons 16-weeks post injury achieved many structural property characteristics (e.g., stiffness) of uninjured tendons, and differences created by prolonged casting were minimal.

Acknowledgements

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Aging Decreases Rat Achilles Tendon Vessel Density and Blood Flow after Injury

Corinne Riggin, BS[1]
Susan Schultz, RDMS[2]
Chandra Sehgal, PhD[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Research Laboratory, University of Pennsylvania, PA

[2]Department of Radiology University of Pennsylvania, PA

Introduction

Aging has significant effects on both maintenance of tendon health and tendon healing potential after injury[1,2]. Clinical ultrasound studies have demonstrated reduced blood flow in uninjured tendons due to aging[3,4] and cellular studies have demonstrated reduced vascular endothelial cell expansion and differentiation potential in tendon cell populations harvested from older age groups[5]. This suggests that tendons are subject to changes in vasculature that could alter their cellular responses, contributing to reduced healing capacity in the aged population. However, how aging affects the vascular response to injury in tendon is unknown. Therefore, the objective of this study is to evaluate the vascular response following Achilles tendon injury in adult and aged rats using both in vivo ultrasound measures of blood flow and ex vivo histological measures of vascular structure. We hypothesize that when compared to adult rats, aged rats will demonstrate a decrease in blood flow parameters, as well as a decrease in vascular density following injury.

Methods

Study Design

Under IACUC approval, 4 adult rats (4-5 months) and 5 aged rats (14-16 months) were used for this study. All animals underwent a bilateral Achilles incisional injury, followed by ultrasound imaging (n = 8-9 tendons/group) on day 7 post-injury, and sacrifice on the same day for histological evaluation (n = 8-9 tendons/group).

Surgical Protocol

Using aseptic technique, a skin incision was made on the medial side of the ankle, and the Achilles tendon was isolated. Using a 1.5mm flat scalpel blade, an incisional injury was made in the center of the tendon width in the mid-substance region. The tendon was left unrepaired and the skin was sutured closed.

Color Doppler Imaging

All animals underwent color Doppler imaging (Fig1A,B) on day 7 post-injury using the Vevo 2100 ultrasound system (VisualSonics Inc, Toronto) with a 40 MHz linear array transducer (MS550). Briefly, animals were anesthetized and positioned with the ultrasound probe parallel to the long axis of the tendon, imaging the sagittal plane. The mean color level (average blood flow velocity), the fractional area (% area of Doppler signal), and the color weighted fractional area (weighted average of blood flow velocity/unit area) were quantified over the entire tendon area. Results were compared using Student's t-tests with significance set at $p < 0.05$.

Histological Analysis

After sacrifice, the Achilles tendons were dissected and processed using standard techniques. Sections were stained with hematoxylin-eosin (H&E) and graded by 3 blinded, independent graders for cell shape (1 = spindle to 3 = round) and cellularity (1 = less cells to 3 = more cells). Additionally, sections underwent immunohistological staining for CD34, a vascular endothelial cell marker, and graded by 3 blinded, independent graders for vessel density (1 = less dense to 4 = more dense) and vessel size (1 = small lumen diameter to 4 = large lumen diameter). Results were compared using Mann-Whitney t-tests with significance set at $p < 0.05$.

Results

Ultrasound analysis demonstrated a significant decrease in fractional area (Fig1C), mean color level (Fig1D), and color weighted fractional area (Fig1E) following injury in the aged group. Additionally, immunohistochemical evaluation (Fig2A,B) demonstrated a significant decrease in vessel density (Fig2C), but no change in vessel size (Fig2D) following injury in the aged group. H&E analysis of cell number and cell shape did not demonstrate differences between groups (data not shown).

Discussion

Results demonstrate significant changes in both blood flow, as shown by the decreased mean color level and color weighted fractional area measures, as well as vascular structure, as shown by the ultrasound fractional area and histological vessel density measures. Interestingly, the vessel size did not change, suggesting that the maturation of vessels that form is similar between groups. This data supports previous human

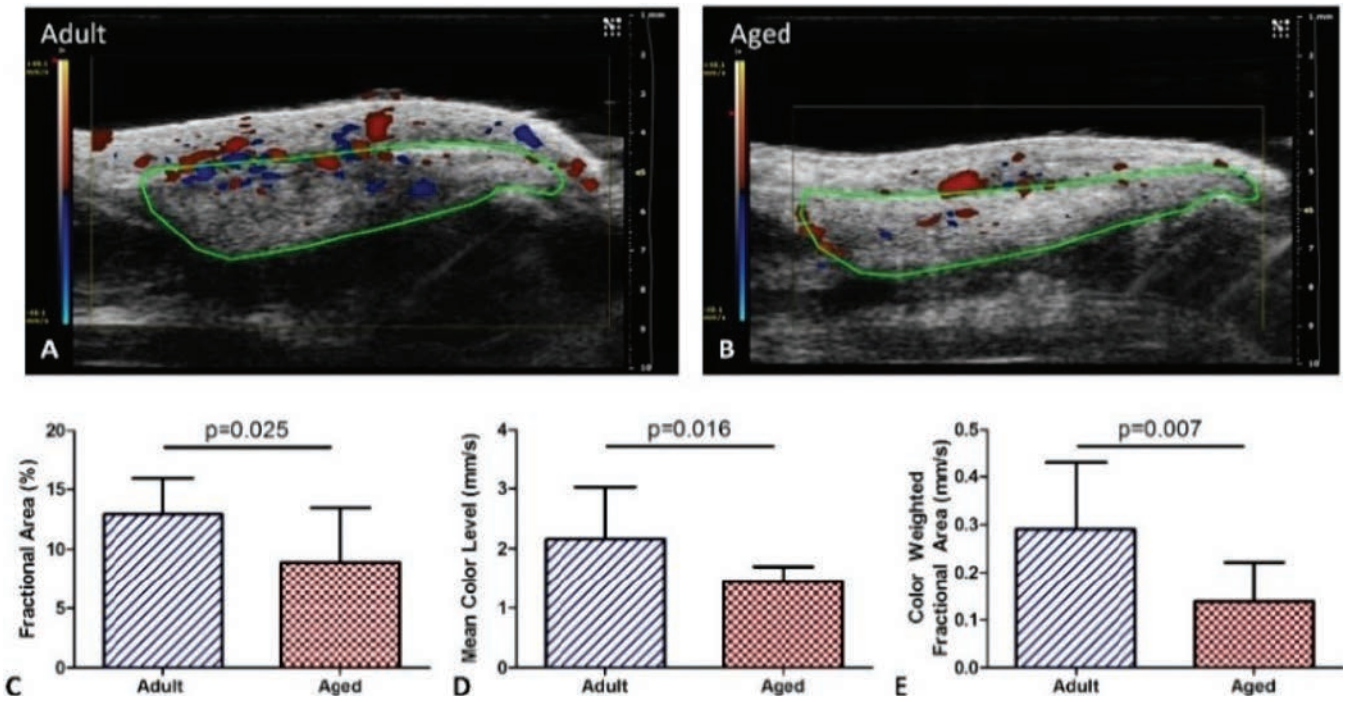

Figure 1. Representative color Doppler ultrasound images of **(A)** adult and **(B)** aged animals 1 week after injury (tendon ROI outlined in green). Ultrasound analysis of **(C)** fractional area, **(D)** mean color level, **(E)** color weighted fractional area demonstrating decreases in the aged group.

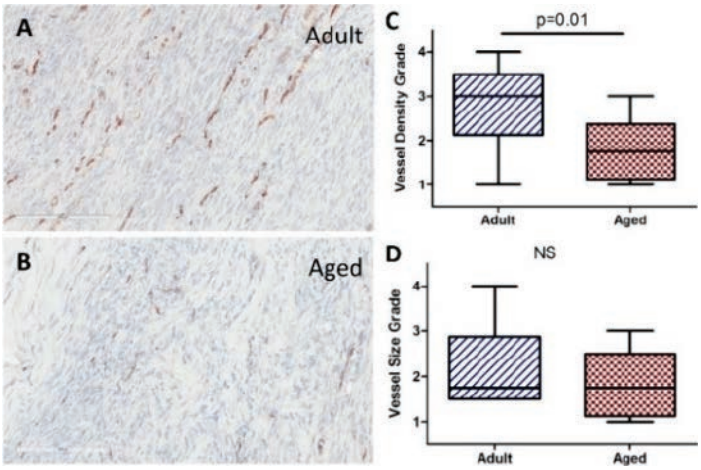

Figure 2. Representative images of **(A)** adult and **(B)** aged CD34 immunohistochemical staining (brown indicates presence of vascular endothelial cells). **(A)** Vessel density and **(B)** vessel size of adult and aged animals 1 week after injury.

ultrasound studies[3,4], showing decreased blood flow in elderly patients in both the uninjured Achilles and supraspinatus tendons. Additionally, the reduced vessel density could be explained by the decreased cell expansion or differentiation potential for vascular endothelial cells previously reported[5]. Future studies will evaluate the effect of vascular modulation on healing potential in both aged and adult animals using the delivery of pro- and anti-angiogenic factors after injury.

Significance

This study is the first to evaluate changes in vascular response due to aging after tendon injury in an animal model using both in vivo measures of blood flow as well as ex vivo structural measures of vascularity. Data suggests that aging tendons undergo changes in both vasculature structure and function, which can alter cellular responses and healing capacity after injury, and could help explain the reduced healing potential of the aged population.

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Immobilization Angle Effects on Tendon Healing in Achilles Tendon Rupture

Cody Hillin, MD, MS
George Fryhofer, MD
Benjamin Freedman, PhD
Daniel Choi, BS
Stephanie Weiss, BS
Louis Soslowsky, PhD

Introduction

Management of Achilles tendon ruptures in the elderly and overweight population is most commonly nonoperative[1] given their higher surgical complication rate. Nonoperative treatment includes immobilizing the ankle in plantarflexion, which is thought to improve ruptured tendon end apposition, and has been shown to produce the best outcomes when combined with early physical therapy.[2] However, the effect of ankle position during immobilization on Achilles tendon healing and limb function is unknown. Therefore, the objective of this study was to investigate the effects of the ankle immobilization angle, with or without angle manipulation, as well as immobilization time on hindlimb function and Achilles tendon mechanical, structural and histological properties 6 weeks after injury in a rat model. We hypothesized that a more dorsiflexed immobilization would result in inferior tendon properties and function compared to full ankle plantarflexion immobilization, and that this effect would be exacerbated with increased time spent immobilized. Additionally, we hypothesized that manipulating the ankle into a more dorsiflexed position during immobilization would improve tendon properties and function.

Methods

Study Design

Male Sprague-Dawley rats (n = 128) received 2 weeks of increasing treadmill acclimation (at 10m/min, up to 60min/day, 5 days/week)[3](IACUC approved) prior to surgical blunt midsubstance transection of the right Achilles tendon and plantaris tendon resection. Animals were then assigned to one of eight hindlimb immobilization groups (n = 16/group) before being sacrificed at 6 weeks post-injury. Immobilization was performed for 1 or 3 weeks at 160°, 90°, or 20° (Figure 1). Two additional groups were manipulated halfway through a 3-week immobilization period, from either 160° to 90° or from 90° to 20°.

In vivo Assays (Pre-injury, 4 & 6 weeks post-injury)

Hindlimb ground reaction forces and gait metrics were quantified using an instrumented walkway.[4]

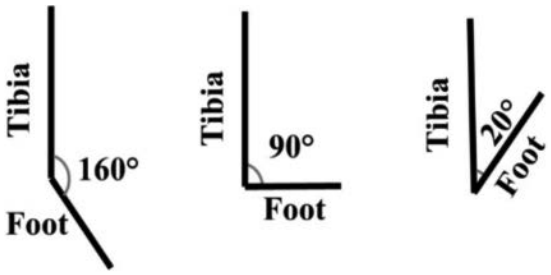

Figure 1. Immobilization position. Tibiopedal angle used to define ankle position. Rat ankle range of motion (10-160deg), was divided into three positions for immobilization.

Ex vivo Assays (6 weeks post-injury)

After sacrifice, the Achilles tendon-foot complex was carefully dissected (n = 10/group), measured for cross-sectional area, and secured in testing fixtures. Tendons were assessed for collagen fiber organization (circular standard deviation) and fiber density (echogenicity) using high frequency ultrasound while loaded at 1N in a PBS bath.[5] These same tendons were mechanically tested (n = 10/group) to evaluate their relaxation, low-strain frequency response (0.1 to 10Hz), and fatigue properties using mechanical and optical testing data.[6] Additional tendon samples were harvested at time of sacrifice, processed by paraffin procedures (n = 5-6/group) and stained with Hematoxylin-Eosin and Safranin-O/Fast Green to measure cell density, nuclear shape, glycosaminoglycan content, and tendon length. *Analysis:* Data was analyzed in a blinded fashion, with comparisons to the clinical standard of full plantarflexion at 160°. Manipulated immobilization was compared to non-manipulated immobilization of the same starting angle and duration. Normally distributed data was evaluated with Student's t-test or one-way ANOVAs, and functional data that was collected over time was assessed using two-way ANOVAs. Significant relationships ($p < 0.05$) were analyzed with post-hoc Student's t-tests with Bonferroni correction for multiple comparisons.

Results

90º Immobilization

There was no difference between 90° and 160° immobilization with regard to Achilles tendon length, histology, or echogenicity following 1 or 3 weeks of immobilization. With 1 week of 90°

immobilization, there was increased collagen fiber alignment (decreased CSD) (Figure 2) and stiffness (5% fatigue life), with decreased hysteresis (5 & 50% fatigue life), laxity (95% fatigue life) and stride length as compared to 160° (full plantarflexed) immobilization. With 3 weeks of 90° immobilization there was also increased alignment (Figure 2) and decreased hysteresis (5% fatigue life) compared to 160° immobilization. Additionally, 3 weeks of 90° immobilization had increased stiffness (95% fatigue life) (Figure 3) and stride length with decreased laxity (5, 50 & 95% fatigue life) and cycles to failure compared to 160° immobilization. Increasing the time immobilized at 90° from 1 to 3 weeks resulted in increased cycles to failure, stride length and echogenicity and decreased propulsion force, but no changes in other mechanical properties, cross-sectional area, tendon length, alignment, or histology metrics.

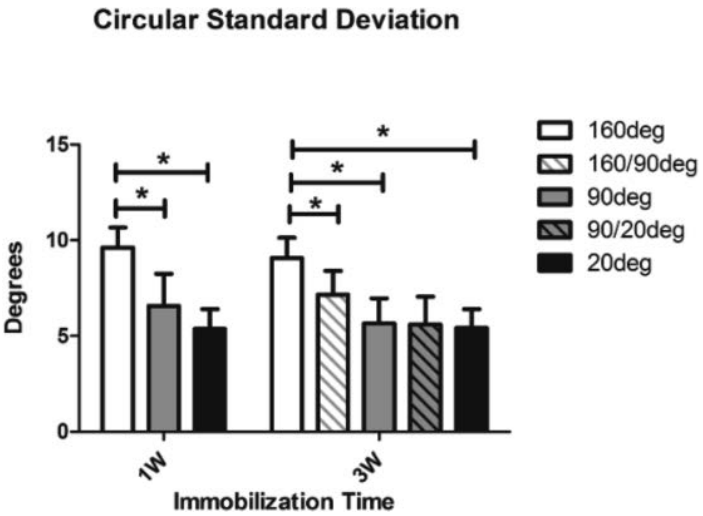

Figure 2. Tendon alignment. Using sequential HFUS images, tissue orientation is assessed. Decreased circular standard deviation indicates increased alignment. Asterisks indicate significant differences ($p < 0.05$).

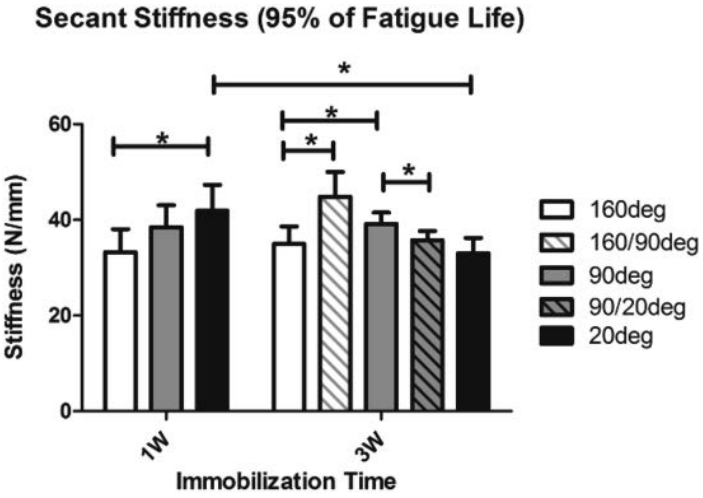

Figure 3. Late fatigue life stiffness. Calculated from force and displacement data at 95% fatigue life, where increased values indicate greater resistance to deformation. Asterisks indicate significant differences ($p < 0.05$).

20° Immobilization

Animals immobilized at 20° had increased tendon length, alignment (decreased CSD) (Figure 2) with decreased hysteresis (5% fatigue life) and laxity (50 & 95% fatigue life) compared to those immobilized at 160° regardless of immobilization duration. Additionally, with 1 week at 20° of immobilization there was increased stiffness (95% fatigue life) (Figure 3) and a sustained reduction in propulsion force measured at 4 (28% decrease) and 6 (22% decrease) weeks post-injury, compared to those in 160° immobilization. Increasing time immobilized at 20° from 1 to 3 weeks was associated with an increase in tendon cross sectional area and hysteresis (5% fatigue life) while also having a decrease in stiffness (5, 50 & 95% fatigue life) (Figure 3) and modulus (5, 50 & 95% fatigue life) but no differences in gait, histology, tendon length or HFUS parameters.

Angle Manipulation (160°-90°, 90°-20°)

Changing the ankle immobilization angle from 160° to 90° (increased dorsiflexion) midway through a 3-week immobilization showed increased stiffness (5, 50 & 95% fatigue life) (Figure 3), alignment (Figure 2) and Safranin-O staining, with decreased echogenicity, hysteresis (5% fatigue life) and cycles to failure but no change in tendon length or gait as compared to those that remained immobilized at 160°. Moving the ankle from 90° to 20° midway through the 3 week immobilization period resulted in increased tendon length, with decreased stiffness (50 & 95% fatigue life) (Figure 3) and stride length, but no changes in histology, cross sectional area, cycles to failure, laxity, modulus or HFUS parameters when compared to those that remained immobilized at 90° for 3 weeks.

Discussion

Achilles tendon properties and hindlimb function are influenced by the position and duration of immobilization. After just 1 week of immobilization at 20°, there was Achilles tendon lengthening and a consistent loss of propulsion force, perhaps due to early consolidation of scar tissue. This relation between Achilles tendon lengthening and reduction in plantarflexion strength and muscle activation has also been seen in humans, impacting function.[7,8] Dorsiflexing the ankle during the immobilization period from 160° to 90° produced a stiffer and more aligned tendon but no functional changes compared to remaining at 160°. However, immobilization angle manipulation from 90° to 20° caused a decrease in stiffness compared to remaining at 90°. These findings could be explained by the partially dorsiflexed foot providing the animal the ability to weight bear, without excess tendon end diastasis. Lastly, although increased tendon alignment at 90° or 20° immobilization resulted in decreased echogenicity, potentially reflecting changes in matrix density or collagen content, it also suggests improved collagen organization. Future work will investigate changes in muscle associated with immobilization angle following Achilles tendon rupture, given clinical changes seen in muscle activation[8] and volume [9] even with surgical repair.

Significance

Dorsiflexed immobilization can be used to enhance the tissue properties and function of healing Achilles tendon ruptures. However, excess dorsiflexion, even for short periods of time, can have lasting detrimental effects on the tendon and gait.

Acknowledgments

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Hand Tips & Tricks: Wrist and Hand Radiography

Kristin Buterbaugh MD
Glenn Buterbaugh MD

Radiographs of the hand and wrist are frequently first line assessments in the work up of both acute and chronic hand and wrist complaints. However, there are a multitude of views, measurements, and variations in anatomy that can make evaluation of hand and wrist radiography daunting. When approaching radiography of the hand and wrist, it is best to have a systematic way to evaluate imaging. This article provides a framework for systematic review of radiographs of the wrist and hand.

Evaluation of the Hand

Standard hand radiographic projections include the posterior-anterior (PA) view, lateral view, and oblique view. In the PA view, the hand is placed palm down on the cassette with the X-ray beam angled at 90 degrees. The articular surface of distal radius makes smooth concentric arc with proximal carpal row, and the arcs of the articular surfaces of midcarpal joint are congruent and concentric. These arcs are frequentlyl referred to as Gilula's Lines. Metacarpalphalangeal (MCP) and interphalangeal (IP) joints should appear open in digits two through five. The soft tissues of the phalanges should be symmetric. In the lateral view, the radius and ulna should be superimposed along with the metacarpals. Fanning the fingers and abducting the thumb allow for visualization of all digits with open joint spaces. In the oblique view the hand is externally rotated 45 degrees from the PA position. In an appropriately positioned oblique view, the midshafts of the third through fifth metacarpals will not overlap, though the distal heads will. There should be no overlap of the second and third metacarpals.

When assessing these standard radiographs, common variations in anatomy include the presence of sesamoids. Sesamoids are rounded well corticated ossicles at palmar aspect of the metacarpal heads. These can be confused for fracture, so it is important to remember locations where they are typically noted. There are two sesamoids at the MCP joint of thumb and occasionally one at the IP joint. There is frequently a sesamoid present in the MCP joint of small finger and one or two in MCP joint of index finger[5]. An accessory ulnar styloid ossicle may also be noted on radiographs, a less common anatomical variant which can be confused for fracture.

Since there is significant overlap between the carpal bones on standard views, many specific views have been developed to better visualize the carpus. We will focus on several of the carpal bone specific views including the scaphoid view, the carpal tunnel view, the semisupinated oblique view, the pisotriquetral view, and the Robert's view.

The scaphoid is best evaluated by an elongated PA view where the beam is angled 30 degrees cephalad with the wrist positioned in 10-15 degrees of ulnar deviation (Figure 1[2]). Ulnar deviation moves the scaphoid from the radius and presents its axis longitudinally. Angling the beam 30 degrees accounts for the volar tilt of the scaphoid allowing it to be evaluated en face with minimal superimposition.

The pisiform and the hook of hamate can be examined using the carpal tunnel view and the semisupinated oblique view. These views project the pisiform and the hook of the hamate volar to rest of carpus. The carpal tunnel view is an axial projection of the carpal tunnel. The hand placed in a hyperdorsiflexed position and

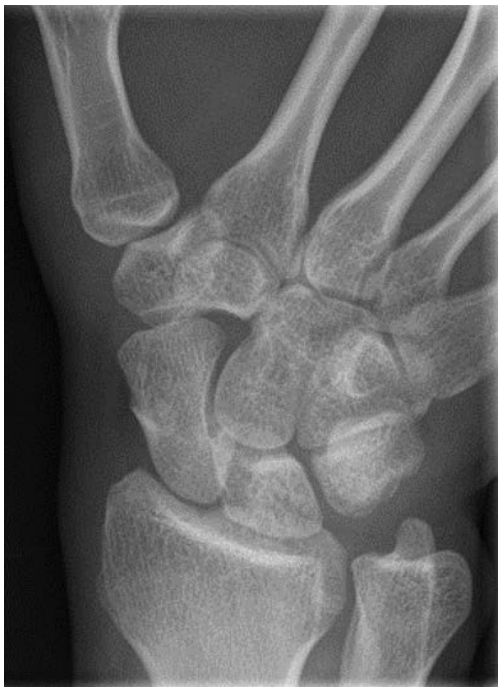

Figure 1. Photo credit: Daffner

the beam is aimed through the carpal tunnel. The view can be used to visualize hook of hamate, trapezium, and pisiform fractures (Hart Gaynor JBJS 1941). An alternative view for evaluating the hook of the hamate when concerned for fracture is the semi supine oblique radiograph. Positioning for a carpal tunnel view can be too painful in the setting of fracture. The semi supine oblique view positions the forearm in a neutral position with the beam centered on the thumb webspace. The thumb is maximally opposed and hand radially deviated. This brings the hook of the hamate into the thumb webspace (Figure 2[8]). Even with these specialized views, hook of the hamate fracture can be difficult to diagnose. If X-rays are negative but there remains clinical concern for fracture, a CT scan should be obtained.

The pisotriquetral view—also known as the All State View—is useful for the diagnosis or exclusion of pisotriquetral osteoarthritis. For this image, the hand is place in a 30 degree supinated from neutral so that Lister's tubercle is most dorsal structure (Figure 3[4]). Although pisotriquetral osteoarthritis is uncommon, it is a well-described cause of pain over the ulnar aspect of the wrist.

The Roberts view evaluates the first trapeziometacarpal and the scaphotrapezial joints the diagnosis of osteoarthritis. The trapezium is oblique to the remainder of the palm. Thus, in the Roberts view, the dorsum of thumb is placed on the plate in forced pronation as bulk of palm precludes joint from lying flat (Roberts 1936). We advocate the utilization of the Lewis modification which angles the beam 15 degrees proximally to correct the offset of the trapeziometacarpal joint from the horizontal (Figure 4[6]).

Evaluation of the Wrist

Standard wrist radiographs include the PA, lateral, and 45-degree semi-pronated oblique. These allow for improved evaluation of the distal radioulnar joint (DRUJ) and the distal radius.

In all views, it is important to note the position of wrist in space. Forearm orientation of wrist is based on the location of ulnar styloid, which always follows the olecranon. In neutral, the ulnar styloid is at the ulnar most aspect of the ulnar head on the PA view. However, in supination and pronation, the ulnar styloid will be in the center of the ulnar head. On the lateral view, the ulnar styloid will be dorsal in relation to the radius in supination and volar in pronation. Proximal convergence of the radial and ulnar shafts suggests pronation on the PA view. In contrast, parallel or proximally diverging shafts suggests supination. Additionally, the position of the wrist dynamically affects the measurement of ulnar variance. In supination and in radial deviation, the ulna appears relatively shorter. Negative ulnar variance also increases as the X-ray beam moves proximally[3]. Finally, wrist deviation should be noted in the assessment of the PA view. In radial deviation, lunate is half on and half off the ulnar border of the radius, whereas in ulnar deviation, the lunate is completely congruent with the radius.

When evaluating the DRUJ, the PA view assesses of degeneration and ulnar variance at the DRUJ, whereas the lateral view assesses alignment. Normal alignment should illustrate overlap of the radius and ulna on the lateral view with no dorsal or volar displacement. To ensure a good lateral in the unstable DRUJ, compare the relative positions of the distal pole of scaphoid and the pisiform (the most volar portions of the carpus) with the volar cortex of the capitate, which represents a relative midpoint. The pisiform should be transected in half by the volar cortex of the capitate, and pisiform should overlie the distal pole of the scaphoid. If the pisiform is volar to capitate anterior cortex, the image is supinated. If more dorsal, image is pronated (Figure 5[1]).

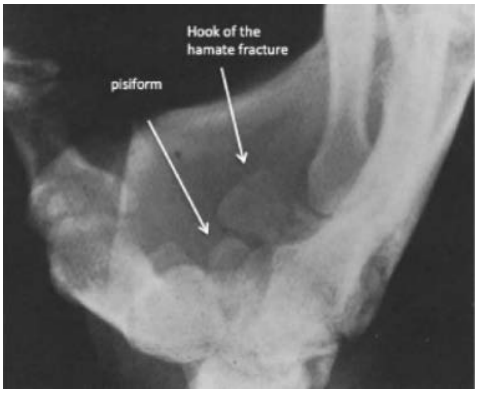

Figure 2. Photo credit: Papilion 1988

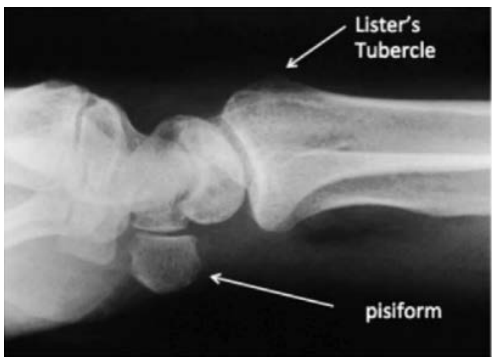

Figure 3. Photo credit: Gardner-Thorpe 1999

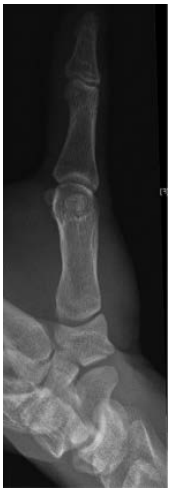

Figure 4. Photo credit: Ladd 2013

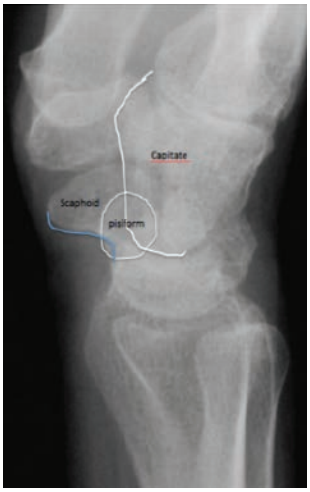

Figure 5. Photo credit: Amrami 2010

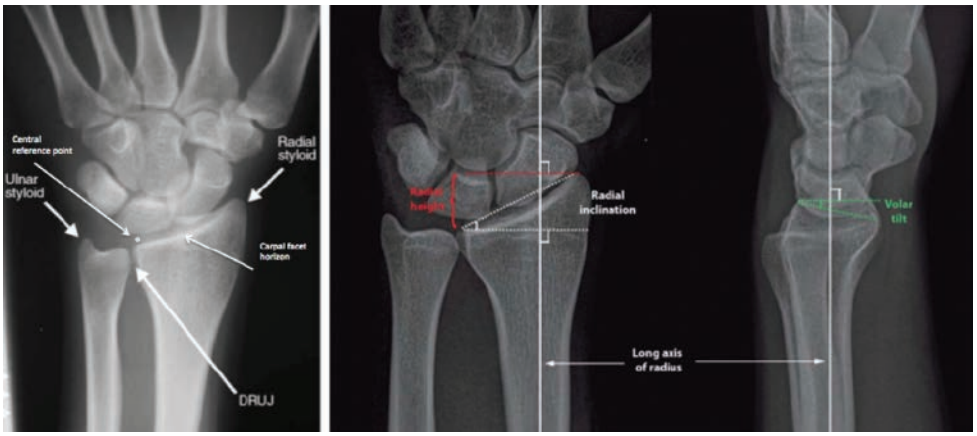

Figure 6. Photo credit: Medoff

When evaluating the distal radius, the PA view projects the profile of the radial styloid and the articular surface of the distal radius. The carpal facet horizon should be noted at 3-5 mm proximal to distal border of radius. The volar tilt of the distal radius places volar rim more proximally than the dorsal rim. The carpal facet horizon is the projection of the subcortical bone of the volar rim of the lunate facet. This is typically reversed in distal radius fractures due to dorsal tilt of the distal fragment. Therefore, it is important to correlate with a lateral radiograph (Figure 6[7]). Medoff measured average radiographic parameters on the PA view in 40 adults using the central reference point of the ulnar border to measure average radial inclination (23.6 degrees), radial height (11.6 mm), and ulnar variance (-0.6 mm)[7].

Medoff also advocates for a modified lateral view with the X-ray beam angled 10 degrees proximally in order to provide a more detailed evaluation of the radial articular surface in profile[7]. This is due to the fact that the radial inclination of the ulnar two thirds of the articular surface is 10 degrees to the long axis of the shaft. The lateral view will project the radial styloid as a v-shaped outline superimposed over the lunate. The central axis of lunate will be collinear with volar cortex of radial shaft. The teardrop—the volar rim of lunate facet—will form an angle of an average of 70 degrees with the radial shaft. Finally, the volar tilt is measured by a line perpendicular to the radial shaft axis and a line between the apex of volar rim and apex of the dorsal rim. Medoff measures an average 11.2 degrees volar tilt[7].

When assessing radiographs of the hand and wrist, the position of the forearm and hand in space is critical to achieving reliable and reproducible images. Due to the complexity hand and wrist anatomy, evaluation of radiographs can be a daunting task. Beginning with appropriately positioned PA and lateral views will complement rather than confuse diagnostic work up for hand and wrist pain.

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Ultrasonographic Evaluation of Zone II Flexor Tendon Lacerations and Repairs: A Cadaveric Study

Kristin Buterbaugh, MD[1]
Joshua Gordon, MD[1]
Nikolas Kazmers, MD[2]
Viviane Khoury, MD[3]
David Bozentka, MD[1]
David Steinberg, MD[1]

[1]University of Pennsylvania
Department of Orthopedic Surgery

[2]University of Utah
Department of Orthopaedics

[3]University of Pennsylvania
Department of Radiology

Introduction

Identifying zone II flexor tendon lacerations is a clinical challenge. Based upon thresholds described in the literature, the percentage of tendon laceration may influence whether surgical repair versus observation is recommended.[1] Flexor tendon lacerations involving greater than 50% of the tendon are thought to have improved outcomes with surgical repair.[2] Lacerations involving less than 50% typically undergo a trial of nonoperative management. Some controversy exists regarding the cutoff at which surgical repair is indicated.[3,4,5]

Accurately determining the percentage of tendon laceration involvement is difficult short of an exploratory operation, which may ultimately reveal a laceration that does not require repair. Validation of a noninvasive test that accurately characterizes partial lacerations may improve clinical decision making by avoiding unnecessary surgery or missed near-complete ruptures. Ultrasound is a potential candidate for this purpose, however validation studies are lacking. In a focused cadaveric pilot study, our team explored the use of ultrasound to evaluate the extent of partial zone II flexor tendon lacerations of non-thumb digits.

Materials and Methods

This study was performed in the Human Tissue Lab of the Department of Orthopaedic Surgery at the University of Pennsylvania. Non-thumb digits were prepared in eight fresh-frozen below-elbow cadaveric specimens. 32 flexor tendons were randomized into three groups: no laceration, low grade laceration (10-40% tendon laceration), and high grade laceration (60-90% tendon laceration).

The flexor digitorum profundus was exposed between A3 and A4 pulleys through midlateral incisions. A flap was raised as a single soft tissue sleeve to avoid air within the tissue planes. Tendons were randomly selected to remain intact, receive low-grade or high-grade lacerations. Partial lacerations were randomly assigned to the radial or ulnar aspects of the tendon, and the intended segment was measured with digital calipers. A keith needle was placed based on caliper measurement to mark the exact extent to which the tendon should be lacerated. Lacerations were carried out sharply with a knife in the transverse plane. Static and dynamic ultrasound were performed on each specimen with a linear-array 14 MHz transducer by a blinded fellowship-trained musculoskeletal radiologist. Actual values and ultrasound measurements of the percentage of tendon laceration were compared using the paired t-test. Sensitivities and specificities were calculated.

Results

Our study found that ultrasound was accurate in identifying and characterizing clinically relevant high-grade zone II flexor digitorum profundus partial lacerations as evaluated by a single fellowship-trained musculoskeletal radiologist. It was inaccurate in detecting and characterizing the extent of low-grade partial lacerations.

For high-grade lacerations, sensitivity and specificity were 0.83 and 0.85, with positive likelihood ratio and negative likelihood ratio values of 5.56 and 0.20, respectively. When considering lacerations accurately diagnosed as low- or high-grade, the percentage of tendon involvement was underestimated by ultrasound for low-grade lacerations (absolute difference -14.1%, $p = 0.03$), but no different than actual values for high-grade lacerations (-6.7%, $p = 0.22$). For lacerations that were detected, ultrasound correctly identified the side of laceration in 100% of specimens. Three (25%) of high-grade tears were misdiagnosed as low-grade. These results are summarized in Tables 1 and 2.

Discussion

Ultrasound provides a viable alternative for the evaluation of partial flexor tendon lacerations, with accuracy for clinically-pertinent high-grade lacerations that are likely to require repair. Validation of a noninvasive, fast, reliable test that accurately identifies partial lacerations may reduce the need for exploratory surgery in flexor tendon injuries. Ultrasound is dynamic, inexpensive, and readily available to hand surgeons and emergency departments, making it particularly attractive.

Other work has evaluated the use of ultrasound in the diagnosis of complete extensor tendon transection,[6] trigger finger diagnosis,[7]

Table 1. Summary of anatomic and ultrasonoi,ranbic data

Ultrasound Imaging Findings	Surgically-Created Laceration (Gold Standard)			
	Intact	Low-Grade Partial Laceration	High-Grade Partial Laceration	Total
Intact	6	9	2	17
Low-grade Partial Laceration	2	3	3	8
High-Grade Partial Laceration	0	0	7	7
Total:	8	12	12	32

Table 2. Ultrasound Test Characteristics by Laceration Type

Test Characteristic	Laceration Type	
	Low-Grade	High-Grade
Sensitivity	0.25	0.83
Specificity	0.85	0.85
LR+	1.67	5.56
LR-	0.88	0.20
PPV	0.50	0.77
NPV	0.65	0.89

Abbreviations: LR - likelihood ratio, NPV - negative predictive value, PPV - positive predictive value

tendon excursion,[8,9] and the presence of flexor tendon injury.[10,11] Despite these advances, complete characterization of the ability of ultrasound to differentiate partial flexor tendon lacerations is lacking. Only one study performed by Zhang *et al*. evaluated the efficacy of ultrasound in diagnosing flexor tendon lacerations in the hands of a single experienced ultrasonographer.[15] However, it does not systematically validate the ability of ultrasound to measure the extent of lacerations.

Conclusions

Our findings support the optimal use of ultrasound, ideally decreasing the number of unnecessary surgical explorations or missed high grade partial lacerations. It helps characterize the potential clinical use of this imaging modality and elucidates the limitations of ultrasound in evaluating low-grade partial flexor tendon lacerations. These results provide hand surgeons and radiologists with clinically-important data not currently in the literature. Future directions include introducing a second fellowship-trained musculoskeletal radiologist ultrasonographer to further validate inter and intra observer reliability.

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Acute Deep Infections of the Upper Extremity: The Utility of Obtaining Atypical Cultures and Factors Associated with Culture Positivity

George Fryhofer, BA[1]
Nikolas Kazmers, MD MSE[2]
Daniel Gittings, MD[3]
David Bozentka, MD[3]
David Steinberg, MD[3]
Benjamin Gray, MD[3]

[1]Perelman School of Medicine at the University of Pennsylvania

[2]University of Utah Department of Orthopaedics

[3]University of Pennsylvania Department of Orthopaedic Surgery

Introduction

Deep infections of the hand, wrist, and elbow are an important clinical entity[1-13] that may result in patient morbidity and loss of productivity. Treatment with surgical irrigation and debridement is the gold standard. These infections are typically caused by bacterial rather than atypical pathogens (fungus or acid-fast bacillus [AFB])[6], and the utility of ordering aerobic and anaerobic cultures has been established[1]. Although atypical pathogens may also be causative—especially in the immunocompromised population—there is no evidence to guide the decision whether or not to obtain atypical cultures during surgical debridement of deep infections of the hand or wrist[10].

The primary purpose of this study was to determine the incidence of positive fungal and AFB cultures in a patient cohort undergoing surgical debridement of acute deep infections of the hand, wrist, and elbow and to determine the rate at which the treatment plan was altered by atypical culture results. Secondarily, we aimed to identify patient and disease factors that affected the positivity of atypical cultures.

Methods

This retrospective cohort study (IRB-approved) reviewed 203 consecutive patients undergoing surgical debridement for acute deep space infections of the hand, wrist, and elbow by three hand fellowship-trained orthopaedic surgeons at an urban academic medical center between October 2013 and December 2015. Patients with diagnoses of superficial infections of skin or nail structures and necrotizing infections were excluded.

Adult patients ($\geq$ 18 years of age) with acute onset of symptoms were considered for inclusion. Sub-acute and chronic infections with symptoms >30 days were excluded. Documentation of intraoperative microbiological cultures, including bacterial (aerobic and/or aerobic) plus at least one atypical culture (fungal and/or AFB) was required. 100 patients meeting all criteria were identified for further analysis.

For each included patient, clinical, operative, and microbiological documentation were reviewed. Infections were classified as subjectively purulent if the operative note included one of five possible descriptors: "pus," "purulence," "purulent," "seropurulent," or "cloudy." When applicable, charts were further reviewed regarding the interpretation of positive atypical cultures, and a determination was made whether atypical culture results altered clinical management (infectious disease consultation, change in antibiotic regimen).

Descriptive statistics were used to summarize patient demographic and disease-specific data. The reported culture data were obtained from operating room cultures only. To evaluate risk factors associated with atypical culture positivity, cohorts with positive and negative atypical cultures were compared with bivariate analysis for all collected variables (continuous variables—Student t-test or Mann-Whitney; categorical variables—Fisher exact test). A significance level of $\alpha = 0.05$ was used.

Results

One hundred patients were included in the final analysis. Mean age was 47.8 years (range: 20 to 85 years; median: 48 years), and preoperative infectious symptoms were present for a median of 5 days (range: 1 to 30 days) prior to surgical treatment (Table 1). Preoperative antibiotics had been given in 87% of cases, and 46% of all patients had one or more immunocompromising comorbidities. Infection diagnoses included soft tissue abscess (46%), suppurative flexor tenosynovitis (22%), septic arthritis (21%), osteomyelitis (9%), and septic bursitis (2%). Aerobic bacterial, anaerobic bacterial, fungal, and AFB cultures were sent in 100%, 99%, 94%, and 82% of patients for each culture type, respectively. Corresponding rates of culture positivity were 74% (74/100), 34.3% (34/99), 5.3% (5/94), and 2.4% (2/82), respectively (Table 2). Median postoperative follow up duration for all patients was 22 days (range 0-472 d). Patients with positive atypical cultures had a median follow up of 40 days (range 4-318 d).

Atypical cultures were positive for 7% of all patients (7 of 100) and 2.9% (7 of 238) of all atypical tests (cultures, stains) sent (Table 2). Of the patients with positive AFB cultures, one

Table 1. Baseline patient characteristics, including patient- and disease-specific factors.

Patient Factors		Disease Factors	
Mean age (years)	47.8	Mean pre-op symptom duration (days)	7.8
Sex		> 3 days (%)	69.0
Male (%)	37.0	> 7 days (%)	32.0
Female (%)	63.0	Recent hand procedure (%)	23.0
Mean BMI (kg/m^2)	28.8	Initial I&D in emergency room (%)	25.0
Obesity (%)	34.0	Subjective purulence in ER (%)	16.0
Morbid obesity(%)	7.0	Received pre-operative antibiotics (%)	87.0
Smoker (%)	32.0	IV (%)	61.0
Immunocompromising condition (%)	46.0	PO(%)	26.0
Diabetes (%)	22.0	Mean number of OR events	1.2
Cardiac disease (%)	14.0	Subjective purulence in OR(%)	69.0
IV Drug Use (%)	9.0	Mean post-op antibiotic duration (weeks)	3.4
Immunocompromising medication (%)	6.0	Mean post-op follow-up (weeks)	
Rheumatic disease or on DMARD (%)	5.0	Orthopaedic	6.5
End stage renal disease	3.0	Infectiousdisease	4.3
Active malignancy (%)	3.0	Infectious disease consulted (%)	43.0
HIV positive (%)	2.0	For bacterial infection (%)	40.0
Organ transplant (%)	1.0	For atypical infection(%)	3.0

patient with flexor tenosynovitis and underlying systemic lupus erythematosus on multiple immunosuppressants grew *Mycobacterium avium*. The positive fungal culture patients grew *Candida* species most frequently (3 of 5).

Patients with positive atypical cultures had an average duration of 12.0 days of symptoms compared to 7.5 days for negative atypical culture patients ($p = 0.11$; refer to Table 3). Of the 69 patients that exhibited subjective purulence during the index procedure, six patients had atypical positive cultures (representing 86% of all atypical culture positive patients). Of the six patients with positive atypical cultures and subjective purulence, four (67%) had bacterial cultures that were also positive.

Of all variables tested (Table 3), bivariate analysis demonstrated an association with atypical culture positivity and only one studied factor, symptom duration > 7 days (OR 6.0, CI 1.2-44.8, $p < 0.05$).

Discussion

At the time of irrigation and debridement, it is common to obtain intraoperative cultures to guide postoperative infection pharmacologic treatment. Nonetheless, several studies have reported the difficulty in diagnosing and treating patients with atypical infections in the upper extremity[2,11,12]. Although the utility of atypical cultures has been studied in other fields of orthopaedic surgery, this has not been previously established in the setting of deep space infections of the upper extremity[14,15].

Atypical cultures were positive in 7% of all patients in our retrospective series. Interestingly, 86% of patients with positive atypical cultures demonstrated intraoperative purulence, which in the majority of cases was explained by concomitant bacterial infection. Therefore, although atypical culture results are uncommonly positive in the setting of surgically-treated acute deep infections of the upper extremity, infections that are purulent may still harbor atypical organisms. Our results are consistent with other orthopaedic literature reporting similarly low incidences of positive fungal cultures (1.7%) and AFB cultures (0.5%) in arthroplasty patients[15].

When evaluating the effect of atypical cultures on patient management, we observed that infectious diseases referrals were made for 43% (3 of 7) of patients and the antibiotic regimen altered in only 14% (1 of 7) of patients with positive

Table 2. Summary of culture results and infection diagnoses.

	Patients (%)	Aerobic / Anaerobic			Fungal			AFB		
			Number per			Number per			Number per	
Diagnosis		Sent (%)	Patient	Positive (%)	Sent (%)	Patient	Positive (%)	Sent (%)	Patient	Positive (%)
Abscess	46 (46.0%)	46 (46.0%)	2.50	39 (50.6%)	43 (45.7%)	1.24	2 (40.0%)	36 (43.9%)	0.96	1 (50.0%)
Flexor Teno.	22(22.0%)	22 (22.0%)	3.41	14 (18 .2%)	20 (21.3%)	1.45	0 (0.0%)	20 (24.4%)	1.59	1 (50.0%)
Septic Joint	21(21.0%)	21 (21.0%)	2.71	15 (19 .5%)	21 (22.3%)	1.33	2(40 .0%)	16 (19.5%)	1.05	0 (0.0%)
Osteomyelitis	9 (9.0%)	9 (9.0%)	2.44	9 (11.7%)	8 (8.5%)	1.11	1 (20.0%)	8 (9.8%)	1.11	0 (0.0%)
Septic Bursitis	2 (2.0%)	2 (2.0%)	2.00	0 (0.0%)	2 (2.1%)	1.00	0 (0.0%)	2 (2.4%)	1.00	0 (0.0%)
TOTAL:	100 (100%)	100 (100%)	2.73	77 (77.0%)	94 (94.0%)	1.29	5 (5.0%)	82 (82.0%)	1.13	2 (2.0%)

Table 3. Bivariate analysis to determine risk factors for atypical culture positivity.

	Difference	95% Confidence Interval		*p* value
Risk Factor (continuous)				
Mean age (years)	−9.8[a]	−21.8	2.2	0.11
Mean BMI (kg/m^2)	−3.1[a]	−8.7	2.5	0.19[b]
Mean pre-operative symptom duration (days)	4.5[a]	−1.1	10.1	0.11
	Odds Ratio	**95% Confidence Interval[c]**		**pvalue**
Risk Factor (categorical)				
Pre-operative symptoms > 7 days	6.0	1.2	44.8	0.03
Rheumatologic disease or on DMARD	3.6	0.1	33.8	0.31
Immunocompromising medication	2.9	0.1	27.9	0.36
Subjective purulence	2.8	0.4	66.8	0.43
Pre-operative symptoms > 3 days	1.1	0.2	8.5	1.00
Smoker	0.8	0.1	4.3	1.00
Obese (BMI ≥ 30 kg/m^2)	0.8	0.1	53.9	1.00
Diabetes	0.6	0.0	4.3	1.00
Immunocompromsing condition	0.5	0.1	2.3	0.45
Cardiac disease	0.0	0.0	3.7	0.59
Intravenous drug use	0.0	0.0	6.9	1.00
Morbidly obese (BMI ≥ 40 kg/m^2)	0.0	0.0	10.1	1.00
Active malignancy	0.0	0.0	24.7	1.00
ESRD	0.0	0.0	24.7	1.00
HIV positive	0.0	0.0	48.6	1.00
Organ transplant	0.0	0.0	252.4	1.00

a. M eanatypical positive valueminus atypical negativevalue
b. Mann-Whitney performed due to non-normally distrib uted data
c. Calculated usingBlaker method

atypical cultures. Therefore, atypical cultures infrequently altered treatment (3% of patients)—even when positive—without evidence of adverse clinical consequence. Infectious disease referral may not be necessary for every patient with a positive atypical culture result, and a combination of clinical concern and surgeon discretion should guide this decision.

Interestingly, despite previous reports, (13, 16) we did not identify a statistically significant association between use of an immunosuppressant medication and atypical culture positivity. We did, however, observe that symptom duration > 7 days was positively associated with atypical culture positivity. This finding reinforces the notion that atypical infections may present in a more indolent fashion compared to typical bacterial infections.

This study has several limitations. We recognize the limitations of a retrospective chart review, including risk for selection bias. Moreover, the atypical culture yield of 7% observed in this study likely overestimates the true incidence of positive atypical cultures, given that only patients that had both bacterial as well as AFB and/or fungal cultures sent for analysis were included. Finally, the secondary objective of this study—to identify risk factors associated with atypical culture positivity—was limited by the relatively small number of patients with positive atypical cultures (n = 7) identified in this series, which may predispose to type-2 error.

Conclusions

We report a low incidence of positive atypical cultures in patients with acute deep space hand infections in our series. Symptom duration > 7 days was associated with positive atypical cultures, and management decisions were infrequently altered by positive atypical culture results. We recommend that physicians consider patient risk factors and the low incidence of atypical positivity before routinely sending atypical cultures in patients with acute deep space hand infections.

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Height-to-length Ratios to Assess Flexion Deformity in Scaphoid Fractures—a Comparison of Measurement Techniques

Adnan Cheema, MD[1]
Paul Niziolek, MD, PhD[2]
J. Bruce, Kneeland, MD[2]
David Bozentka, MD[1]
David Steinberg, MD[1]

[1]University of Pennsylvania
Department of Orthopedic Surgery

[2]University of Pennsylvania
Department of Radiology

Introduction

Scaphoid fractures, particularly those involving the waist, are prone to developing a flexion deformity in the sagittal plane. The distal pole flexes in relation to the proximal pole, which leads to a dorsal "humpback deformity" of the scaphoid. This deformity is important to recognize because it leads to destabilization of the wrist and carpal joints, which most commonly results in dorsal intercalated segment instability (DISI).

Height-to-length ratios can be used to assess the degree of flexion deformity and aid the surgeon in determining when surgery may be indicated. Historically, a height-to-length ratio of greater than 0.65 has been used as a cutoff to intervene surgically. However, there appears to be no consensus on how the height-to-length ratio should be measured. Some authors have tried to use software applications that assess the scaphoid three-dimensionally to obtain a "true" height-to-length ratio. Others have described identifying the sagittal CT cut with the worst deformity and measuring the height-to-length ratio in that plane.

Our null hypothesis for this study is that measuring height-to-length ratios on one sagittal CT cut will not be any more precise than measuring the height-to-length ratios three-dimensionally by taking all CT cuts into account.

Methods

After IRB approval was obtained, 33 patients were identified using an online database of radiology reports. We searched for patients 18 years and older with scaphoid fractures who had had a CT scan of the wrist. We excluded anyone who did not have a CT scan performed before undergoing surgical fixation and those who had any instrumentation in place. In patients with multiple wrist CT scans, we chose the earliest study available in the database. We identified patients in a reverse chronological order beginning from August, 2016 to April, 2011. All enrolled patients were identified from one institution. The CT scans were anonymized and removed of all patient identifiers. Two reformats of each scaphoid CT were created; one in a 'scaphoid' axis orientation and one in a 'wrist axis' orientation. They were then sent to two clinicians (Rater 1 and Rater 2) for measurement of height-to-length ratios. Rater 1 was asked to identify the sagittal cut with the largest flexion deformity and record the height-to-length ratio from that cut (Figure 1). Rater 2 was asked to measure the height-to-length ratio three-dimensionally. This was accomplished by first scrolling through all sagittal slices and drawing a line tangential to the two most-volar scaphoid surface curvatures to create the scaphoid long axis. Then, the most-proximal point of the scaphoid was determined similarly by scrolling through all cuts, and a tangential line to this point was drawn perpendicular to the scaphoid long axis. This process was repeated to determine the most distal point of the scaphoid to create a tangential line perpendicular to the long axis. The distance between these two proximal-distal lines determined the scaphoid length. Next, scaphoid height was measured by determining the most dorsal point projected from all slices and drawing a line perpendicular to the initially created long axis line (Figure 2). Each clinician measured the height-to-length ratio once for each axis orientation for a total of two measurements per scaphoid.

Results

The difference between the height-to-length ratio measurements was calculated for each of the 33 scaphoids for Rater 1. The height-to-length ratios varied by a mean of 0.09 and standard deviation of 0.07. The difference between the height-to-length ratio measurements was calculated for each of the 33 scaphoids for Rater 2. The height-to-length ratios varied by a mean of 0.14 and standard deviation of 0.12. Using a t-test, the two means were compared and found to be statistically different with a p value of 0.04. As such, identifying the sagittal cut with the greatest subjective flexion deformity to measure the height-to-length ratio was found to be the more precise method.

Conclusion

Identifying the more precise method to measure flexion deformities in scaphoid fractures has important clinic implications for hand surgeons in that it allows for easier identification of patients who may require surgical intervention. The technique used by Rater 2 is cumbersome and time-consuming,

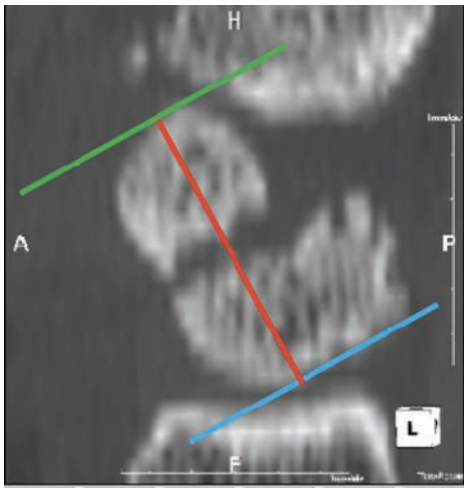

Figure 1. Measurement Technique for Rater 1. The blue line is drawn tangent to the most proximal extent of the scaphoid on this particular cut. The green line is drawn tangent to the most distal extent of the scaphoid on this particular cut. The red line is drawn in line with the long axis of the scaphoid connecting the blue and green lines. This represents the length.

making it less likely to be used in the office setting. Instead, subjectively choosing the sagittal cut with the worst-appearing deformity appears to lead to more precise measurements.

It is important to note that no gold standard exists for measuring flexion deformity in scaphoid fractures. Therefore, the above techniques cannot be compared to the "true" measurement of height-to-length ratios. As such, we cannot comment on the accuracy of the measurement techniques described above. We can only state that one is more precise than the other.

One limitation of this study is that only two measurements were made for each scaphoid. Having more points of reference would allow for more accurate measurement of the precision of each of the above techniques. Another limitation of this study was that each rater did not measure the height-to-length ratios using both techniques, which could potentially introduce observational bias into the analysis.

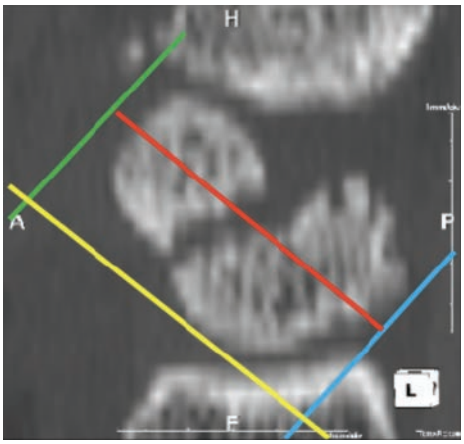

Figure 2. Measurement Technique for Rater 2. After scrolling through all sagittal slices, the yellow line is drawn tangential to the two most-volar scaphoid surfaces (not in the same plane as the cut shown). This designates the scaphoid long axis. The blue line is drawn perpendicular to the yellow line and tangential to the most proximal extent of the scaphoid after scrolling through all cuts. The green line is drawn perpendicular to the yellow line and tangential to the most distal extent of the scaphoid after scrolling through all cuts. The length of the scaphoid is measured by the red line. When compared to Figure 1, one can appreciate that the measurement length is increased and the orientation of the perceived long axis is changed, even though the same sagittal cut is being assessed.

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Variable-angle Locking Compression Plate Fixation of Distal Radius Volar Rim Fractures

Mengcun Chen, MD[1]
Daniel Gittings, MD[2]
Shuhua Yang, MD[1]
Guohui Liu, MD, PhD[1]
Tian Xia, MD, PhD[1]

[1]Department of Orthopaedics Surgery
Union Hospital, Tongji Medical College
Huazhong University of Science and
Technology, Wuhan, China

[2]Department of Orthopaedics
University of Pennsylvania
Philadelphia, Pennsylvania
United States of America

Introduction

The application of a volar buttress plate in open reduction and internal fixation (ORIF) for distal radius fractures provides both construct stability and recovery of wrist function.[1] A subset of distal radius fractures may propagate distal to the watershed line and involve the volar rim. These fractures have challenged current indications for fixed-angle volar plates.[2] Sufficient stabilization by buttressing this fragment requires placement of conventional volar locked plates distal to the watershed region. This far distal fixation strategy leads to plate prominence that may cause flexor tendon irritation. Furthermore, positioning these fixed angle devices far distally may also lead to inadvertent wrist joint penetration by distally directed screws.[3]

A variable-angle volar rim locking compression plate system (VA-LCP; Depuy-Synthes, West Chester, PA) was designed to be placed distal to the watershed line with a low-profile contour to prevent flexor tendon irritation. The VA-LCP system also has 15° off axis variable angle screws that may assist in avoiding penetrating the wrist joint. Furthermore, VA-LCP has distal radial and ulnar "teardrop" holes that may be used to augment fixation of the radial styloid, lunate facet, and distal radial-ulnar joint. The purpose of this study is to compare functional and radiographic outcomes of VA-LCP to traditional fixation strategies with fixed angle volar locking compression plates (FA-LCP).

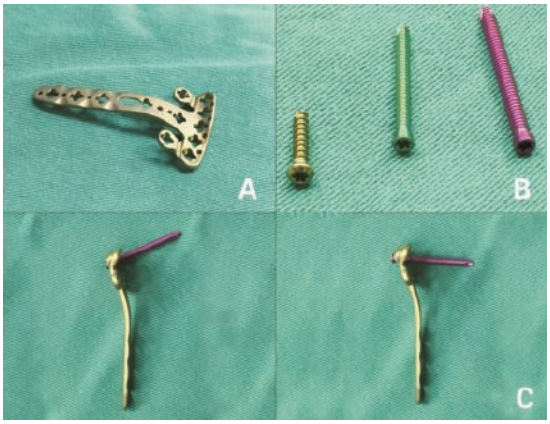

Figure 1. Variable angle locking compression plate for fragment-specific fracture fixation of fractures distal to the watershed line of the radius. **(A)**The pre-contoured variable angle volar rim plate (VA-LCP); **(B)** A 2.4 mm cortex screw and two 2.4 mm variable angle screws; **(C)** Low profile of the plate with holes allow up to 15° off-axis screw angulation in all directions.

Materials and Methods

A retrospective review of a consecutive series of patients who underwent open reduction and internal fixation (ORIF) using either VA-LCP (19 wrists) or traditional fixation with FA-LCP (28 wrists).

All patients underwent an extended volar approach of the distal radius to enable adequate visualization of the cortical rim of the distal radius.[4] In the FA-LCP group, a conventional volar locking plate was positioned as far distally as possible to stabilize the VMF. Auxiliary K-wires were added to augment fixation if stability was inadequate (Figure 1). In the VA-LCP group, a 2.4 mm VA-LCP low profile plating system was positioned straddling the watershed line, and held preliminarily in place with a K-wire in the distal end of the plate. The distal variable angle screws were placed as a "row of nails" to rafter and support the articular surface. Additional variable angle locking screws were placed in the radial and ulnar distal "teardrop" holes to augment fixation (Figure 2). Clinical outcomes were evaluated using the modified Mayo wrist score (MMWS), disabilities of the arm, shoulder, and hand (DASH) score, wrist range of motion (ROM) and grip strength relative to the uninjured contralateral side, and signs of flexor tendon irritation. Radiographic evaluation included radial height, radial inclination, volar tilt, and volar tear drop angle. All out comes were assessed at 3, 6, and 12 months postoperatively.

Results

The average follow-up period was 14.5 months (range 11-16 months) for the VA-LCP group and 15.8 months (range 12-18 months) for the FA-LCP group (Table 1). Both VA-LCP and FA-LCP groups improved MMWS and DASH scores with time postoperatively (Table 2). MMWS and DASH scores were improved in the VA-LCP group compared to the FA-LCP group at all time points after surgery ($p < 0.05$). Furthermore, relative ROM was improved in VA-LCP (flexion-extension 94.8%/ supination-pronation 93.8%) compared to the FA-LCP (flexion-extension 82.8%/ supination-pronation 84.5%) at 12 months ($p < 0.05$) (Figure 3). There was a 10.5%

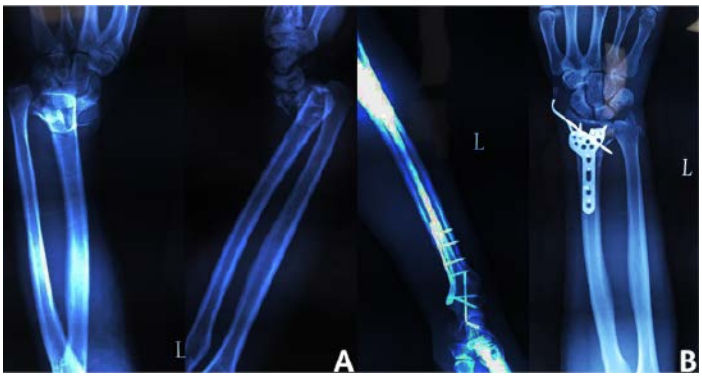

Figure 2. Radiograph obtained pre-operatively and two days postoperatively in a 43-year-old man who had undergone ORIF using a FA-LCP. **(A)** Pre-operative images demonstrate an intra-articular comminuted volar marginal rim fracture; **(B)** Postoperative images after ORIF with FA-LCP.

(2/19) and 21.4% (6/28) incidence of flexor tendon irritation with VA-LCP and FA-LCP fixation respectively ($p < 0.05$). There was a greater decrease in volar tilt from initial postoperative radiographs to latest follow up in the FA-LCP group (2.75 degrees) compared to the VA-LCP group (1.68 degrees) ($p < 0.05$).

Discussion

Intra-articular distal radius fractures that involve the volar rim are challenging to manage. A volar marginal fragment (VMF) may be either too small or too distal to the watershed line to be adequately supported with traditional fixation strategies[2]. Although conventional volar locked plates may provide a stable reduction,[5, 6] the geometry of the lunate facet poses exceptional challenges. Harness et al. reported loss of fixation of a volar lunate facet fragment with carpal dislocation in a series of seven patients with an average of 24-months of follow-up.[7] The VA-LCP low profile plating system was designed to be placed distal to the watershed line with an anatomically pre-contoured geometry that allows supplemental fixation into the lunate facet. Thus, the purpose of this study is to compare outcomes of VA-LCP to traditional fixation strategies with FA-LCP.

This study shows differences in functional outcomes between VA-LCP and FA-LCP. MMWS and DASH were improved at all time points in the VA-LCP compared to FA-LCP group. As discussed in the limitations section, although these results were statistically significant, the clinical significance of this difference is less apparent. When assessing the relative wrist ROM, the VA-LCP had better recovery compared to FA-LCP. This difference in relative wrist ROM may contribute to the difference in MMWS.[8] However, the difference in relative wrist ROM may be confounded by different postoperative immobilization protocols. The FA-LCP group was immobilized for a longer period of time (6 weeks FA-LCP vs 1 week VA-LCP) because there was concern the fixation construct was less stable than that used for VA-LCP. This increased period of immobilization and delayed rehabilitation may have introduced a lag time bias. Longer follow up is needed to whether FA-LCP patients will recover more ROM to catch up to the VA-LCP group.

Relative grip strength was also improved in VA-LCP compared to FA-LCP at early follow up at 3 months. Again, this difference may have been related to the longer immobilization protocol and delayed rehabilitation in FA-LCP. Interestingly, the FA-LCP group recovered grip strength more rapidly after 3 months and we were unable to detect a difference in grip strength between both groups at 12 month follow up. However, there was an apparent difference in flexor tendon irritation between both groups. The FA-LCP group had a high incidence of flexor tendon irritation (21.4% FA-LCP versus 10.5% VA-LCP) and a re-operation rate for removal of hard ware (7.1% FA-LCP versus 0% VA-LCP). In the FA-LCP group, the conventional plate had to be positioned distal to the watershed line to adequately stabilize the lunate facet, which may have contributed to flexor tendon irritation. Furthermore, the supplemental K-wires used for fixation may have also injured the tendons. A cadaveric study by Chia et al, found that volar radial styloid, transverse radial, and dorso-ulnar K-wires may penetrate both tendons and nerves about the wrist.[9] Although VA-LCP also straddled the watershed line, the low profile anatomically contoured design with highly polished cambered surface may have contributed to a lower incidence of flexor tendon irritation.

In addition to differences in clinical outcomes, we observed differences in radiographic outcomes. Radial height, radial inclination, and volar tear drop angle were not found to be different between groups at all time points. There was a larger loss of volar tilt in FA-LCP group compared to VA-LCP. Although K-wire augmentation has been reported to be effective to enhance stability of the reduction in these fractures, their trajectory from radial to ulnar in direction are biomechanically inferior to a volar buttress for these fragments that may experience shearing forces.[10]

Table 1. Comparison of patient demographics between both groups.

	VA-LCP	FA-LCP	P value
Number of Patients	19	28	–
Male / Female	4M / 15F	6M / 22F	0.77
Age (years)	52.9 (42-65)	53.5 (39-66)	0.74
Dominant hand injured	9	12	0.73
Time between injury and surgery(days)	2.8 (2-5)	2.9 (2-5)	0.89

Table 2. MMWS and DASH functional outcome scores over the 12 month follow up visit.

	3 Months		6 Months		12 Months	
	MMWS	**DASH**	**MMWS**	**DASH**	**MMWS**	**DASH**
VA-LCP	76.3(70-85)	24.4(20-28)	93.3(80-100)	10.5(2-14)	93.8(85-100)	9.2(2-12)
FA-LCP	67.4(60-75)	31.7(25-34)	80.6(70-90)	14.1(8-20)	83.5(75-90)	12.8(6-18)
p value	0.02	0.04	<0.01	0.03	<0.01	0.02

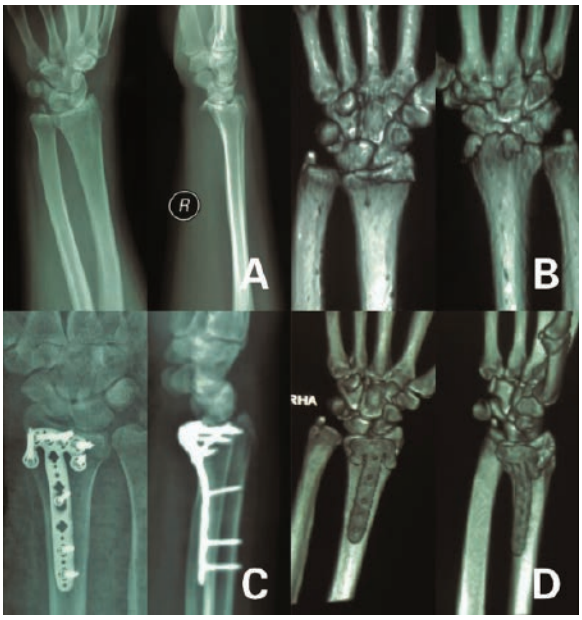

Figure 3. Radiograph obtained pre-operatively and two days postoperatively in a 49-year-old woman who had undergone ORIF using a VA-LCP. **(A)** Pre-operative images demonstrate an intra-articular distal volar marginal rim fracture with extension into the dorsal surface; **(B)** Postoperative images after ORIF with VA-LCP.

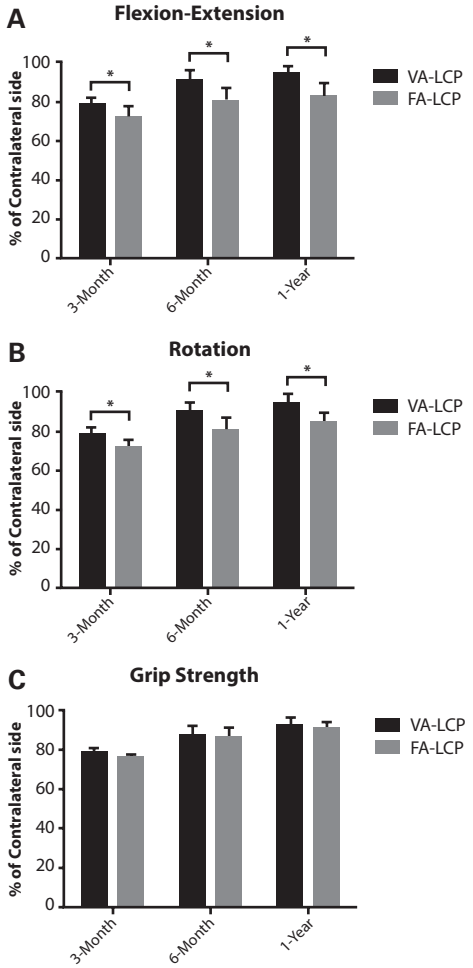

Figure 4. Relative ROM and grip strength throughout the 12 month follow up period. **(A)** Relative flexion-extension ROM **(B)** Relative supination-pronation ROM **(C)** Relative grip strength. *$p < 0.05$ when comparing between the two groups.

Conclusion

In conclusion, we report favorable clinical and radiographic results using the VA-LCP system compared to the FA-LCP. These results may be in part attributed to the VA-LCP system design with its low profile, anatomic contour, and multiple options for fixation that may decrease the incidence of joint penetration and improve lunate facet stability. Further research assessing the biomechanical properties of this system may further elucidate the mechanical properties of this plate and affect is has on the overlying flexor tendons. Furthermore, a long term prospective study is needed to assess long term clinical and radiographic implications when using this device compared to conventional plates. Surgeons should consider the VA-LCP system as an alternative to conventional plates when treating radius fractures distal to the watershed region.

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Pediatric Tips & Tricks: Management of Posterior Sternoclavicular Joint Injuries

Mark Hasenauer, MD
Apurva Shah, MD MBA
Keith Baldwin, MD MSPT MPH
David Spiegel, MD

Introduction

Posteriorly displaced physeal fractures or dislocations at the sternoclavicular joint (SCJ) are rare in the childhood and adolescent populations and require prompt diagnosis and treatment to optimize outcomes and prevent possible life threatening complications. We prefer open reduction and fixation for injuries with posterior displacement, with cardiothoracic "backup" in the rare event of vascular complication associated with the injury or it's treatment. Outcomes are generally successful with pain free range of motion and return to activity without disability.

Background

The medial epiphysis of the clavicle is the last to ossify and fuse, at approximately age 18-20 and age 22-25, respectively[1]. An injury to the medial clavicle can result in a true dislocation or a physeal fracture with displacement depending upon the patient's age, with the relative rates under debate[2]. The SCJ is a di-arthrodal saddle joint with minimal articular contact anteriorly and inferiorly, with stability depending upon ligamentous structures, particularly the posterior capsule. Many critical structures lie near the SCJ including the esophagus, trachea, brachiocephalic vein and subclavian artery, with the brachiocephalic an average of 6.6mm from the posterior clavicle[3]. Posterior displacement of the medial clavicle may be associated with compression of any of these structures including the brachial plexus.

While closed reduction and immobilization have been advocated, several studies in the pediatric population have suggested that re-displacement is common[2, 4, 5]. Many centers such as ours now routinely perform open reduction and internal fixation.

Preoperative Evaluation

SCJ injuries are rare and a high index of suspicion, with a careful history and physical examination, are required to make the diagnosis. In addition to pain, up to half of patients present with symptoms such as dyspnea or dysphagia[6], and up to 25% of injuries are missed initially[2]. Patients typically fall or sustain a blow to the lateral aspect of the shoulder and complain of "shoulder" pain. Asking the patient to place a finger where the site of maximal discomfort is can be helpful. Physical examination must include palpation of the entire shoulder girdle with assessment of airway, breathing, circulation and a neurovascular exam. Plain radiographs of the shoulder or clavicle often miss the diagnosis, although a serendipity (40-degree cephalic tilt) view may demonstrate the injury. A CT scan is suggested when there is clinical suspicion, and our cardiothoracic surgeons prefer the study is performed with contrast to assess for extravasation or compression[7] (Figure 1).

Procedure

Our cardiothoracic team is on standby during the procedure, and several units of packed red blood cells are available. A sternotomy tray should be in the room, with the cardiopulmonary bypass machine immediately available.

The patient is positioned supine on a radiolucent table with a bump between the scapulae. The prepping and draping include the upper extremity, chest, and both sides of the

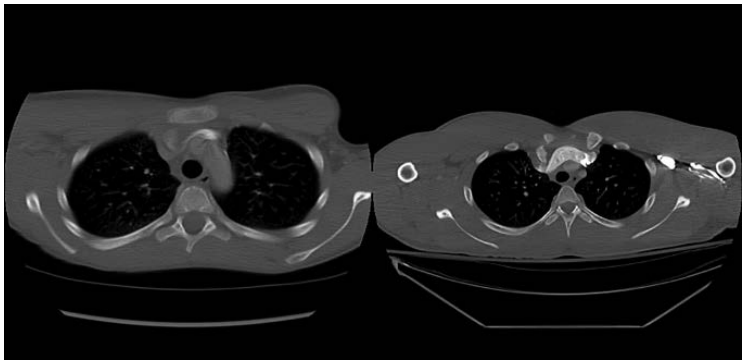

Figure 1. Posterior sternoclavicular dislocation demonstrating brachiocephalic compression.

neck and groin (Figure 2). An oblique incision is made starting along the medial clavicle at the first place it can be palpated, extending across the SCJ onto the manubrium below the sternal notch (Figure 2). The platysma is divided and periosteum incised. The pectoralis major is elevated off the manubrium, medial clavicle and SCJ. The anterior aspect of the clavicle is subperiosteally exposed between the pectoralis origin and the insertion of the trapezius/strap muscles, lateral to medial, and soft tissues/debris must often be removed anterior to the clavicle where it dives posteriorly under the manubrium (or epiphysis). Sub-periosteal dissection only needs to be enough to grasp the medial clavicle with a blunt bone holding clap, and a freer elevator may also be used to subperiosteally dissect medially until the clavicle has been sufficiently mobilized for reduction. Two drill holes in the clavicle can also be made to grasp the bone with a towel clamp. Lateral force is applied either directly through the clamp with traction on the arm. Occasionally, a periosteal elevator is used as a "shoehorn" or "skid" to lever the medial clavicle from under the epiphysis or manubrium. Direct inspection will reveal if the injury was a fracture or dislocation.

Different techniques have been described for fixation of acute injuries including suture repair, suture anchors, cerclage wire or sternal cables, plate and screw fixation[8]. Kirschner wire fixation has been abandoned due to risk of intra-thoracic migration with visceral damage which could result in death[9, 10]. Plate fixation techniques include anterior plating and Balser plate application. These techniques are not well studied in the adolescent population and have a high rate of removal[8, 11]. A reconstruction using allograft is utilized for chronic injuries. We prefer to utilize a heavy non-absorbable suture technique. In physeal fractures, the medial aspect of the metaphysis is sutured to the epiphysis with or without the addition of a figure-of-eight suture from the medial clavicle into the manubrium via unicortical drill holes, whereas the figure-of-eight technique is required in dislocations (Figure 3). An attempt is made to repair the periosteum and deep soft tissue envelope, followed by repair of platysma, subcutaneous tissues, and skin.

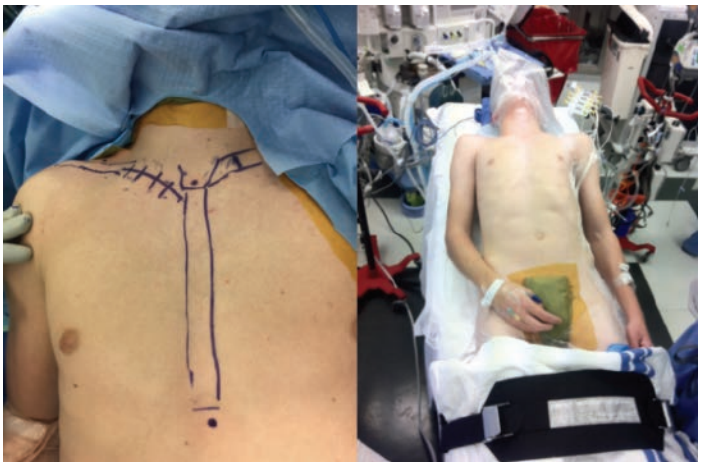

Figure 2. Relevant anatomy showing a direct anterior approach to the medial clavicle with prep and drape in case of need of bypass.

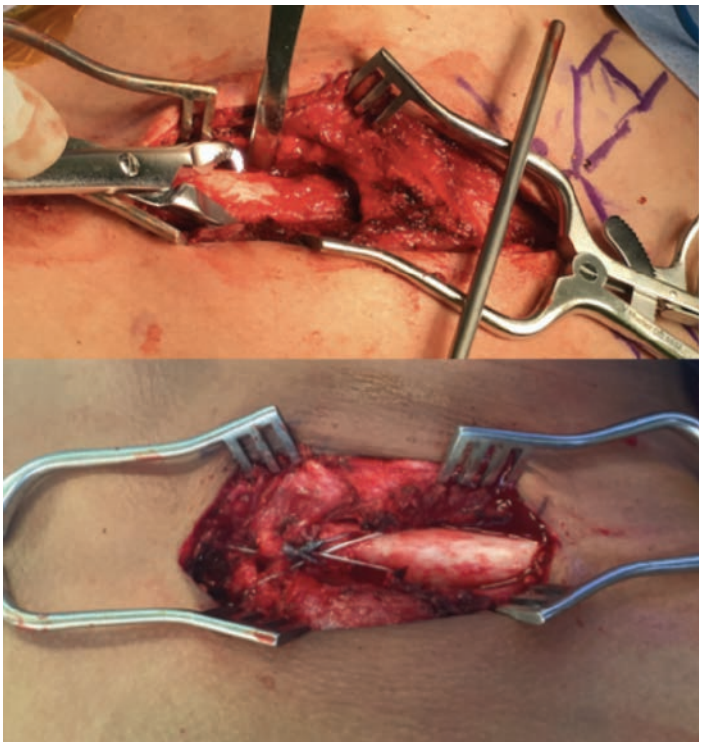

Figure 3. Posterior fracture dislocation and an example of figure of eight suture repair

Postoperative Protocol

Patients are admitted overnight for monitoring. A shoulder immobilizer is utilized for 4-6 weeks, and physical therapy is considered after 6 weeks. Return to sports is permitted 6 months after surgery if patient is asymptomatic.

Discussion

Posterior sternoclavicular joint injuries can be potentially life threatening and require proper identification and treatment. Although pediatric literature for these injuries is sparse, closed reduction has a high rate of redisplacement, and open reduction and fixation is currently recommended in many treatment centers. Outcomes appear favorable, with Waters et al demonstrating full return to activity in 13/13 patients at an average of 22 months[5], and other authors reporting full return to function and excellent outcomes in acute and chronic settings[4, 12, 13].

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U·P·O·J

Single Leg Spica Casting for Low Energy Pediatric Femur Fractures—Operative Technique

Daniel Miller, MD
Susan Nelson, MD MPH
Todd Blumberg, MD
Andrew Gambone, MD
Joseph Monteleone

[1]Divison of Orthopaedic Surgery
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Introduction

Femoral shaft fractures are common pediatric injuries, with treatment strategies depending on patient age, weight, skeletal maturity, fracture location, comminution, soft tissue integrity, and associated injuries. The American Academy of Orthopaedic Surgeons (AAOS) Clinical Practice Guidelines suggest early spica casting or traction with delayed spica casting for children aged 6 months to 5 years with a diaphyseal femur fracture with <2 cm of shortening.[1] Historically spica casting for pediatric femoral shaft fractures consisted of a two or one and a half leg spica with the injured leg in 90° of hip flexion and 90° of knee flexion.[2,3] While this is associated with good long term results, there is a significant burden of care on the patient, family, and community.[4] The single leg "walking spica" is safe and efficacious for treatment of low energy pediatric femoral shaft fractures[2,3,5] that decreases burden of care for the patient and family by facilitating safe mobilization with the well leg free.[3,5] Because of this, single leg spica casting has become the preferred technique at our institution. The purpose of this article is to describe this technique for the treatment of low energy pediatric femoral shaft fracture.

Preoperative Evaluation and Indications

Single leg spica casting is indicated in patients aged 6 months—4 years after low energy trauma (e.g. falling off a bed). Contraindication include high energy injury patterns suggested by significant fracture comminution, fracture shortening > 2 cm, or polytrauma.

All patients should undergo a history and physical and screened for concomitant injuries. Children less than 3 years of age should be evaluated for non-accidental trauma, particularly in those patients who are not yet walking. Families should be warned about the potential for complications including fracture displacement, skin related issues, and need for wedging or additional procedures.

Procedure

Closed reduction and spica casting can be performed in the operating room or emergency department provided that appropriate personnel, materials, and sedation are available[6] (Figure 1). Muscle relaxation may be requested to facilitate closed reduction. We suggest at least two skilled personnel in addition to the surgeon be present to facilitate cast application. A time out should be performed as per institutional protocol.

After induction of anesthesia, an appropriately sized Gore-tex Pantaloon (W. R. Gore and Associates, Inc., Flagstaff, AZ) is applied to act as a waterproof barrier in the event of soiling. Excess liner is removed from the patient's well leg. Layers of six inch stockinette or folded surgical towels are placed between the patient's abdomen and liner to provide room for abdominal expansion following cast application. While the anesthesiologist controls the airway, the child is carefully lifted onto a spica casting table.

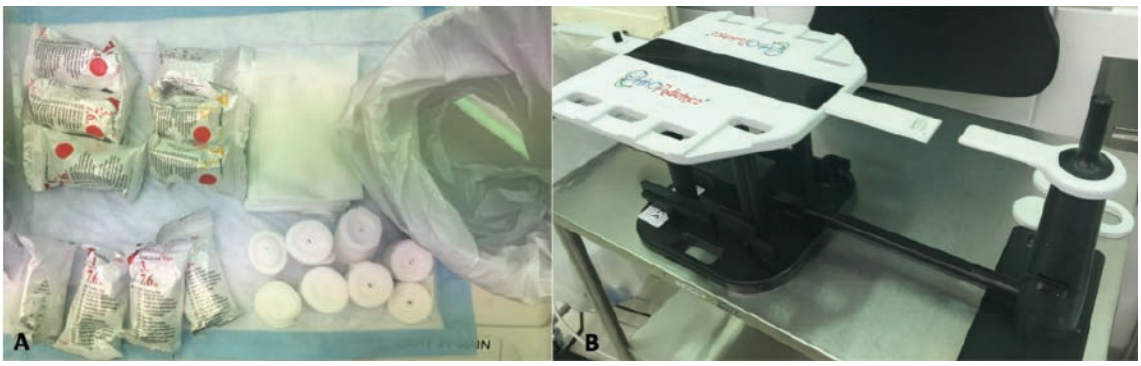

Figure 1. (A) Supplies include 2 and 3 inch fiberglass cast tape, soft roll, and stockinette folded to be placed on the stomach **(B)** One variation of hip spica table.

The proximal (box) portion of the spica table should end on the mid thoracic spine (approximately T7), fully supporting the shoulders. The well-padded distal post of the spica table should be adjusted so that it rests snugly against the patient's perineum, supporting the sacrum. The patient's arms may be secured to the side or overhead with cast padding or held in place by an assistant depending on the configuration of the available spica table.

One member of the surgical team should be dedicated to holding the leg in the planned casting position of 45° of hip flexion and 45° of knee flexion with slight abduction (30-45°) and longitudinal traction. The well leg should be flexed and abducted as well to prevent pelvic tilt. Web roll cast padding is circumferentially rolled around the injured leg from just proximal to the malleoli to the xiphoid process with careful attention to padding bony prominences. The foot and ankle are left completely free. Longitudinal strips of 2 inch cast padding are applied anterior to posterior to provide additional padding in the groin and perineal region.

Fiberglass casting material is applied first proximal to distal to create a long leg cast and a valgus mold is applied at the fracture site to prevent varus malalignment (Figure 2). Bi-planar fluoroscopy is used to confirm appropriate length, alignment, rotation and cast molding. Up to 2 cm of shortening, 10 degrees of Varus, and 20 degrees of sagittal displacement are acceptable criteria for reduction. Fiberglass is subsequently applied to reinforce the connection between leg and pelvis. A figure of 8 pattern is useful when circumnavigating the pelvis. Fiberglass struts consisting of 6-8 layers of casting tape are added to provide additional mechanical integrity between the trunk and leg along the anterior thigh, lateral thigh, and medial groin (Figure 3).

The liner is folded back and a final layer of fiberglass is applied. The child should be removed from the casting table and rotated into the lateral position so that all portions of the cast can be inspected for sharp edges that may need to be trimmed. Fluoroscopy is used to confirm acceptable reduction and a radiopaque object should be used to annotate the cast at the fracture location in the event that cast wedging is needed at follow up (Figure 4). The stockinette or towels are removed from the abdomen and two diapers (one small to be placed under the cast edges and one larger overtop) are applied to prevent cast soiling.

Postoperative Protocol

Perioperative management includes pain management, cast care instruction by trained staff, and physical therapy evaluation to ensure safe transport. Follow-up examinations with x-rays are performed at one, two, three, and six weeks post-

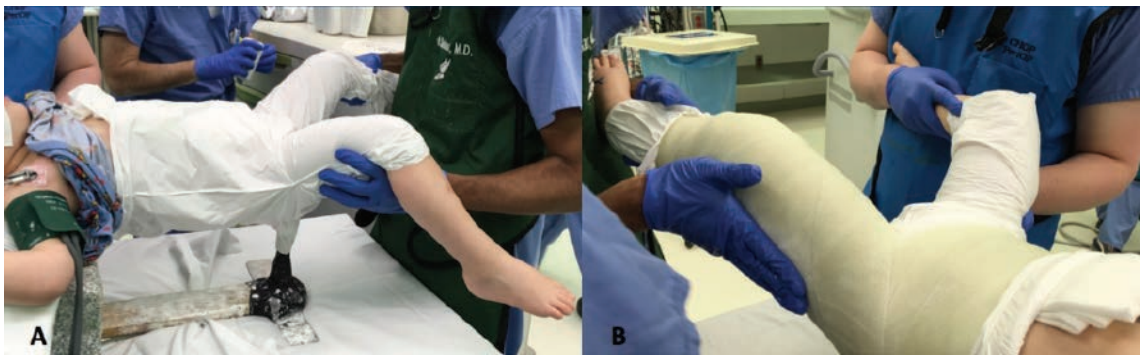

Figure 2. (A) Once the liner is in place the child is lifted onto the spica table and soft roll applied **(B)** Initial layer of cast tape is placed and a valgus mold applied.

Figure 3. (A) 6-8 layer fiberglass struts are added to enhance the mechanical stability between the leg and pelvis portion of the cast and **(B)** overwrapped with one layer of casting tape.

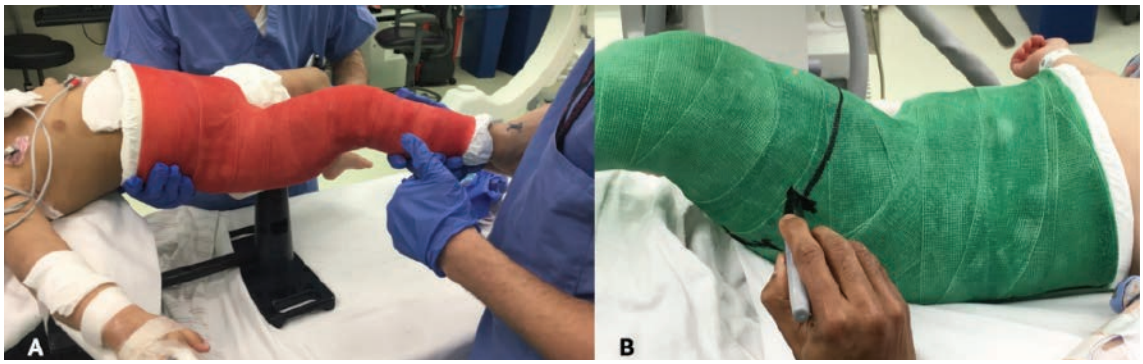

Figure 4. (A) Final casting position. The child can now be removed from the spica table and final fluoroscopy taken **(B)** The cast can be annotated using fluoroscopy to facilitate future wedging.

operatively. Young children will self-restrict weight bearing as comfort allows, with formal clearance for weight bearing when callus is visualized on radiographs. Cast wedging can be performed for coronal or sagittal displacement, typically within the first two weeks following reduction. Loss of reduction may require repeat closed reduction or surgical intervention. Casts are removed after clinical and radiographic evidence of union. Reluctance to walk is common following cast removal and limping may persist for up to a year.[7] Physical therapy is generally not indicated. Additional follow up visits are scheduled for 3 months and 1 year post operatively, with subsequent visits on an as needed basis.

Discussion

Single leg spica casting provides an attractive alternative to the traditional one and a half leg spica cast when used appropriately. This technique can be used safely in children aged 6 months to 4 years with low energy fractures to obtain satisfactory outcomes while minimizing the treatment burden on the patient and family.

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Concomitant Injury and Complications Following Pediatric Tibial Spine Fractures

Taylor Jackson, BA
Eileen Storey, BA
Theodore Ganley, MD

Introduction

Tibial spine fractures are avulsion fractures of the tibial intercondylar eminence at the insertion of the anterior cruciate ligament. These injuries were once considered the childhood equivalent of the ACL injury, and though rare, occur most commonly in 8 to 14-year-old patients.[1]

Tibial spine fractures were originally classified as Type I, II, or III by Meyers and McKeever in 1959, and later modified to include type IV factures.[2, 3] Type I fractures are non-displaced, type II are displaced with an intact posterior hinge, type III are completely displaced, and type IV fractures are displaced and comminuted fractures.[2,3]

Management of these injuries is controversial, especially for type II injuries since there is no consensus on optimal management in the literature.[4-6] Type I fractures may be managed with closed reduction, while types III and IV are best managed with surgical fixation.[1,5,6] For type II fractures, debate remains about whether they should first be managed with closed reduction rather than directly proceeding to internal fixation.[5-7]

These injuries are frequently associated with additional pathology. The most commonly seen concomitant pathology include meniscal tears, chondral injuries, and soft tissue entrapment in the fracture site.[8-10] Importantly, many of these injuries may prevent adequate reduction and can be treated at the time of surgical fixation. Early treatment may prevent further morbidity in the long term.

Methods and Materials

We retrospectively reviewed all patients treated surgically for tibial spine fractures between January 1, 2009 and December 31, 2015 at our institution. Pediatric patients 18 years or younger who presented and were initially treated surgically for a tibial spine fracture were included if followed for at least 3 months after surgery. Patients were excluded if they did not meet inclusion criteria, were initially treated at an outside institution, or lacked adequate follow-up or clinical data. Multi-trauma patients and those with additional lower extremity factures were also excluded.

82 patients with tibial spine fractures were identified between January 1, 2009 and December 31, 2015. After medical record review, 17 were excluded as they were managed non-operatively, 2 were excluded as they were initially treated at an outside hospital, 7 were excluded due to the presence of additional lower extremity fractures in the setting of severe trauma, and 7 were excluded for inadequate follow-up. An additional patient was excluded, as the fracture could not be classified since radiographs were not available and the operative note did not specify the degree of displacement. Thus, a total of 48 patients with tibial spine fractures were included in the analysis. All patients were treated surgically with arthroscopic assisted internal fixation. For the purpose of our analysis, arthrofibrosis was defined as a 10° extension deficit and/or 25° flexion loss 3 months after treatment that persisted despite physical therapy and was not caused by nonunion, malunion, a new injury, a ligamentous or meniscal injury, or a bony deformity.

Patient demographics, fracture classification, mechanism of injury, length of immobilization, concomitant injury patterns, and reoperation rates were collected. All fractures were classified as either Type I, II, or III according the Meyers & McKeever system and comminuted injuries were classified as Type IV as described by Zaricznyj.[2,3]

Standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentage for categorical variables such as gender) were used to summarize demographic variables. Comparisons of categorical variables between groups were made using the Chi-Square or Fisher's exact test, depending on sample size. Statistical analysis was performed using the data analysis software SPSS® Version 24 (SPSS Inc., Chicago, IL) and Microsoft Excel 2011.

Results

There were 48 patients analyzed in the study, including 31 males and 17 females with an average age of 12.5 years (range, 7.4-17.5 years). There were no Type I, 14 Type II, 21 Type III, and 13 type IV fractures. The fractures most commonly resulted from twisting (20) or contact (18), but the injury also resulted from hyperextension in six patients. The mechanism of injury could not be determined from the patient record in four patients. Fifteen patients

Table 1. Patient Demographics

Average Age (years)	12.5 (7.4-17.5)
Average Age (years)	12.5 (7.4-17.5)
Sex	
Male	31
Female	17
Height (cm)	157.8 (122-180)
Weight (kg)	53.3 (22.7-89.8)
BMI	21.0 (14.9–32.1)
Fracture Type Type II	14
Type III	21
Type IV	13
Mechanism Twisting	20
Contact	18
Hyperextension	6
Immobilized	31.4%
Days Immobilized	18.1 (6-43)
Follow-up (months)	11.1 (3.0-40.0)

Table 2. Concomitant Pathology

	Type II N=14	Type III N=21	Type IV N=13	Total N=48	P-Value
Meniscal injury	4 (28.6%)	7 (33.3%)	8 (61.5%)	19 (39.6%)	.160
Lateral Meniscus	3 (75%)	7 (100%)	7 (87.5%)	17 (89.5%)	
Medial Meniscus	1 (25%)	0 (0.0%)	1 (12.5%)	2 (10.5%)	
Soft Tissue Entrapment	6 (42.8%)	7 (33.3%)	6 (46.2%)	19 (39.6%)	.726
Meniscus	1 (16.7%)	3 (50%)	1 (16.7)	5 (27.8%)	
Intermeniscal Ligament	5 (83.3%)	3 (50%)	5 (83.5%)	13 (72.2%)	
Ligamentous Injury	1 (7.1%)	0 (0.0%)	2 (15.4%)	3 (6.3%)	.101
ACL	1 (100%)	0 (0.0%)	1 (50%)	2 (66.7%)	
MCL	0 (0.0%)	0 (0.0%)	1 (50%)	1 (33.3%)	
Loose body	1 (6.7%)	7 (33.3%)	5 (38.5%)	13 (27.1%)	.121
Chondral Injury	2 (14.3%)	3 (14.3%)	5 (38.5%)	9 (18.8%)	.259
None	3 (21.4%)	6 (28.6%)	0 (0.0%)	9 (18.8%)	.099
Number of Injuries (per Patient)	17 (1.1)	27 (1.3)	25 (1.9)	66 (1.7)	.116

(31.3%) were immobilized for an average of 18.1 days (range 6-43 days). The remaining patients were treated with continuous passive motion machines (CPM). (Table 1)

At the time of initial surgery, concomitant pathology was very common. Overall 81.2% of the patients suffered additional injuries, with an average of 1.7 injuries per patient. All of the type IV fractures suffered concomitant injuries, while only 78.6% of the type II fractures and 71.4% of the type III injuries were found to have suffered additional injuries, though a significant difference in the rate of concomitant pathology was not found ($p = 0.099$). The most common injuries were meniscal tears, soft tissue entrapment, chondral injuries, and loose bodies. Overall, there was a 39.6% incidence of meniscal pathology. Although meniscal injury was found in 61.5% of type IV fractures compared to only 28.6% of type II fractures and 33.3% of type III fractures, this difference was not significant ($p = .160$).

There was an overall 39.6% incidence of soft tissue entrapment. Soft tissue entrapment was found at similar rates across different fracture types with involvement in 42.8% of type II fractures, 33.3% of type III fractures, and 46.2% of type IV fractures ($p = .726$). The incidence of loose bodies was 6.7% in type II fractures, 33.3% in type III fractures, and 38.5% in type IV fractures for an overall incidence of 27.1%, and no statistical difference between fracture types ($p = .121$). 14.3% of type II fractures, 14.3% type III fractures, and 38.5% of type IV fractures were found to have chondral lesions for an overall incidence of 18.8%. There was no significant difference in the presence of associated chondral lesions between fracture types ($p = .259$). The most common finding was grade 1 chondromalacia of the patella, though three of the type IV fractures had more severe grade 2-3 chondromalacia or fissuring of the tibial plateau or femoral condyles. One patient required chondroplasty. 7.1% of type II fractures, no type III fractures, and 15.4% of type IV fractures were found to have ligamentous injuries for an overall incidence of 6.3% with no significant difference between fracture types ($p = .101$). Table 2 demonstrates the concomitant injury pattern for each fracture type.

Ten of forty-eight (20.8%) patients underwent reoperation during their treatment course, but half of the reoperation cases were for scheduled removal of hardware (10.4%). For the remaining patients, there were three cases of arthrofibrosis, two were in type IV fractures and one was in a type II fracture in the setting of a surgical infection. All were treated with lysis of adhesions and manipulation under anesthesia. There were two ACL reconstructions. One patient was treated for a newly ruptured ACL. A second patient had an ACLR for a rupture that occurred at the time of the initial injury, but reconstruction was delayed until after fixation of the tibial spine. This patient also underwent manipulation for knee stiffness at the time of the ACLR. (Table 3).

Discussion

Though tibial spine fractures are rare injuries, they can be significant due to the high risk for concomitant pathology and

the potential for complications. Mitchell et al. conducted a review of 58 patients with tibial spine injuries and found no concomitant injuries in type I fractures, meniscal injury in 29% of type II fractures and 12% of type III fractures, entrapment in 33% of type II fractures and 48% of type III fractures, and chondral injury in 7% of type II fractures and 8% of type III fractures.[9] Overall, the authors found 59% of patients had concomitant pathology with 48 injuries occurring in 34 patients for an average of 1.4 injuries per patient. We found higher rates of concomitant pathology in our cohort (81.2%) with 66 injuries occurring in 39 patients for an average of 1.7 injuries per patient.

A wide range of incidence for associated meniscal and chondral injuries, ranging from 3.8% to 40%, has been reported in the literature.[9-14] Kocher et al. found only three meniscal injuries in a series of 80 skeletally immature patients treated for tibial spine fractures, which differs by over a factor of ten from the 39.6% that we report.[10] This wide range may owe to the differing definitions and methods of detection. Some studies use direct visualization under arthroscopy while others may rely on MRI, which has been found to be less reliable than direct visualization.[8, 9] Additionally, it is unclear how fracture classification affects injury rates as few studies distinguish between type III and type IV fractures. Our results are near the upper end of the reported spectrum, which may in part be due to selection bias of limiting our investigation to surgical patients as well as the relatively high proportion of type III and IV fractures in our sample. Classification of injury or method of detection may also play a role as we relied on arthroscopy in this cohort, however Shea et al. found 8 of 20 (40%) skeletally immature patients had associated meniscal injury based solely on MRI.[11]

Soft tissue entrapment, most commonly of either the anterior horn of the meniscus or the intermeniscal ligament, is known to block adequate reduction of type II and III fractures, though the incidence is less well characterized in type IV fractures.[10, 15] Kocher et al. also found soft tissue entrapment in 54% of cases with 26% occurring with type II and 65% occurring with type III fractures.[10] In most cases, the anterior horn of the meniscus was interposed. A prior study had also found interposition of the anterior horn of the meniscus in 90% of cases of type III fractures.[16] However, in our cohort, the intermeniscal ligament was interposed in the majority of cases of soft tissue entrapment (72.2%) with similar rates for type II, III, and IV fractures (42.8%, 33.3%, 46.2%, p=.726)

The incidence of chondral injury in tibial spine fractures is not well characterized. Mitchell et al reported a 7% rate of chondral injury in type II injuries and 8% in type III injuries.[9] We found an overall 18.8% rate, with 14.3% in both type II and type III and 38.5% in type IV fractures. While there were more chondral lesions in type IV fractures, this did not reach statistical significance. However, the group did have the most severe chondral injuries, with one requiring chondroplasty for grade 2-3 chondromalacia of the lateral femoral condyle.

The most debated fracture pattern is the type II fracture, as there is no consensus in the literature regarding optimal treatment.[1, 5, 6] However, some have recommended that first line treatment should be closed reduction, and advancing to surgery only if conservative management fails or if the fracture is not adequately reduced in extension.[10, 17] While similar outcomes have been found across open reduction, arthroscopic reduction, and closed reduction, one study did find a 16.7% reoperation for type II fractures that were managed conservatively due to loose bodies, continued instability, and soft tissue impingement.[4, 6, 18] Furthermore, a review of large series of consecutive tibial spine fractures found 47% of type II fractures would not reduce in extension, and of those, 26% had meniscal entrapment in the fracture site.[10]

In our series, we found a 20.8% reoperation rate (10 of 48 patients). The most common reason for reoperation was for removal of hardware, though this may be avoided with suture, suture anchor, or bioabsorable screw fixation methods. Other than removal of hardware, the most common reasons for reoperation were arthrofibrosis and ACLR. One patient had a ruptured ACL at the time of the tibial spine injury, and so delayed reconstruction was indicated. At the time of reconstruction, the patient also underwent manipulation for knee stiffness. There were three patients who developed arthrofibrosis and were treated with lysis of adhesions and manipulation under anesthesia. Overall, the rate of arthrofibrosis in this study was low (6.25%) compared to reported rates, which range from 2.7% to 38% and most commonly are reported between 10% and 15%.[4, 6, 7, 18-20] The lower rate in our series may be attributed to the early range of motion (ROM) treatment initiated in the majority of patients (68.6%). Patel et al. reviewed 40 tibial

Table 3. Reoperation and Complications

Patient	Fracture Type	Procedure	Indication	Associated Pathology
1	II	Lysis of Adhesions and Manipulation Under Anesthesia	Arthrofibrosis and Infection	
2	III	ACL Reconstruction	New ACL Rupture	
3	IV	ACL Reconstruction and Manipulation Under Anesthesia	Delayed ACL Reconstruction	Knee Stiffness
4	IV	Lysis of Adhesions and Manipulation Under Anesthesia	Arthrofibrosis	Meniscal Tear
5	IV	Lysis of Adhesions and Manipulation Under Anesthesia	Arthrofibrosis	
6	III	Removal of hardware	Retained Hardware	
7	II	Removal of hardware	Retained Hardware	
8	III	Removal of hardware	Retained Hardware	Chondral Injury and Meniscal Tear
9	II	Removal of hardware	Retained Hardware	
10	IV	Removal of hardware	Retained Hardware	Chondral Injury

spine fracture patients and found that there was a 12-fold increase in arthrofibrosis for patients who initiated ROM later than 4 weeks.[20]

Limitations of this study include its retrospective nature and small sample size. A convenience sample was used owing to the rare nature of the condition. Larger sample sizes may aid in detecting difference in injury patterns and injury rates between fracture types. Furthermore, only surgical patients were evaluated, which have introduced selection bias as less severe fractures, such as type I fractures or minimally displaced type II fractures, may have been more likely to be treated with closed reduction.

We noted a high rate of additional knee pathologies in this series of tibial spine fractures. The most common injuries are soft tissue interposed in the fracture site and meniscal injury. Chondral injuries are less common, except in type IV fractures, and ligamentous injury is rare. Types II, III, and IV fractures had similar rates of overall concomitant pathology. Other than hardware removal, the most common reason for reoperation were arthrofibrosis and ACL injuries. Given the high rate of additional injuries, MRI evaluation and a low threshold for surgical fixation should be considered, even for type II fractures. A high index of suspicion for additional injuries is required when treating tibial spine fractures as concomitant pathology is very common.

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Current Concepts in Management of Unstable Slipped Capital Femoral Epiphysis

Brendan Striano, BA[1]
Taylor Jackson, BA[1]
Daniel Miller, MD[1]
Wudbhav Sankar, MD[1]

[1]Division of Orthopaedic Surgery, The Children's Hospital of Philadelphia, 3400 Civic Center Boulevard, 2nd Floor Wood Building, Philadelphia, Pennsylvania, USA 19104

Introduction

Slipped capital femoral epiphysis (SCFE) is the most common hip condition in the adolescent population and represents mechanical failure of the physis, which allows displacement of the proximal femoral epiphysis relative to the metaphysis[1]. As described by Loder, SCFE can be classified as stable or an unstable based on clinical presentation, with unstable SCFE being painful enough to prevent ambulation, even with crutches or other walking aids[2]. The most worrisome outcome with SCFE is osteonecrosis of the femoral head[3], for which Loder's classification is prognostic. Stable slips typically have good prognosis with essentially a 0% risk of osteonecrosis, while unstable slips have been reported to develop AVN in 0%-58% of cases, with an overall rate thought to be 24%[4-7]. Osteonecrosis is devastating because it results in immediate disability, loss of function, and places patients at high risk for premature osteoarthritis[5, 7-9].

There is currently little consensus on the management for unstable SCFE, with significant variation in surgeon preference for management[10, 11]. Treatment options vary in several realms, including timing of treatment, choosing in-situ fixation v. reduction, number of implants, and whether or not to perform a capsulotomy. Because vast treatment options exist and providers lack consensus, it is worthwhile to review recent research and current concepts of the treatment of unstable SCFE.

Operative Considerations

Timing of Surgery

When treating an unstable SCFE, timing has long been considered an important factor. Despite considerable research, there is still some controversy about the optimal timing of SCFE fixation[12-14]. Chen et al. demonstrated good outcomes when fixation was performed urgently, within 12-24 hours of presentation[13]. Similarly, Parsch et al. had excellent results in patients treated within 24 hours of the onset of pain[15]. Other studies have suggested that timing may not be as significant[8]. Interestingly, a European study suggested "windows" of opportunity. Kalogrianitis et al. recommended treating patients within 24 hours if possible or waiting for almost a week to allow an "inflammatory effusion" to resolve[16] A systematic review by Alshryda et al. showed that timing of surgery was an independent predictor of AVN, but also supported the concept of "windows" of opportunity[17]. In spite of this data, most centers in the United States favor urgent treatment of unstable slips whenever possible.

Role of capsular decompression

The periosteal tearing associated with an unstable SCFE often results in considerable intra-capsular hematoma. From the femoral neck fracture literature, it is known that intra-capsular hematoma can increase capsular pressure and tamponade the epiphyseal vasculature[18, 19]. Herrera-Soto et al. demonstrated that attempted closed reduction can contribute to increased capsular pressure to levels above those seen in myofascial compartment syndrome[20]. Therefore, with an unstable SCFE, surgeons should consider capsular decompression with either needle decompression, percutaneous capsulotomy, or formal open capsulotomy[33].

"In-situ" Fixation vs. Closed reduction and fixation

When treating an unstable SCFE, most surgeons perform "in-situ" fixation, which may be more accurately termed a positional reduction, or attempt a formal, purposeful closed reduction[4]. These options offer the benefit of familiarity for nearly all orthopaedists, regardless of training, and allow for prompt stabilization[21]. In-situ fixation has long been a standard procedure, with low rates of osteonecrosis (9-12%) and good initial clinical outcomes[12, 22]. However, recent data has demonstrated that for some unstable SCFEs, in-situ fixation may have poor long-term, patient reported functional outcomes, due to high rates of residual deformity[15, 23]. These findings, which may previously have been underappreciated, are an expected consequence of in-situ fixation because there is no attempt at reducing the deformity. Driven by these recent data, there has been renewed interest in achieving more anatomic reduction. Historically, purposeful closed reduction has been discouraged because a partial or complete purposeful reduction has been associated with an increased incidence of AVN[5, 14, 24]. However, recent advances in the ability to assess femoral head perfusion have led to renewed interest in purposeful reduction.

Epiphyseal Perfusion Monitoring

One of these most significant recent advances has been the development of intra-operative monitoring techniques, which may allow improvements in both closed and open treatment options[3,4,7]. Assessment of blood flow may help identify patients at high risk for osteonecrosis and allow for early intervention before hip deformity occurs[9]. Options include assessing epiphyseal bleeding with drilling, laser flometry probe, and using an intracranial pressure (ICP) catheter[3,4,7]. One significant advantage of ICP probe monitoring is that it can be done percutaneously[4]. A recent study by Schrader et al. described a technique of perfusion monitoring using an ICP probe inserted through a percutaneously placed cannulated screw (Figure 1). The series included 13 patients with unstable SCFE. Initially, flow was identified in seven patients, and no perfusion was detected in the remaining six. Perfusion was restored in all six following percutaneous capsular decompression. At two years follow-up, there was no radiographic evidence of AVN and no complications from use of ICP monitoring[3].

Open reduction and internal fixation

Parsch et al. described a technique which consists of an urgent open approach, capsulotomy, and direct visualization of the femoral neck, followed by gentle, finger-tip reduction[12,21]. The proximal femur is exposed through an anterolateral Watson-Jones approach with a longitudinal capsulotomy, which also allows for evacuation of the joint effusion. A Kirschner wire is then inserted through lateral cortex and advanced to the metaphyseal edge of the slip. The surgeon then palpates the gap between the metaphysis and epiphysis, keeping a finger on the femoral head to allow for a more controlled, gentle reduction of the acute portion of the slip. Once adequate reduction is achieved, the multiple Kirschner wires are advanced into the epiphysis to achieve fixation.

The strengths of this approach are the timeliness of treatment, evacuation of the intraarticular hematoma through capsulotomy, and the gentleness of partial finger-tip reduction[12,21]. In a series of 64 slips treated with this technique, there were excellent outcome scores and extremely low rates of AVN, below 5%[12,21].

Modified Dunn

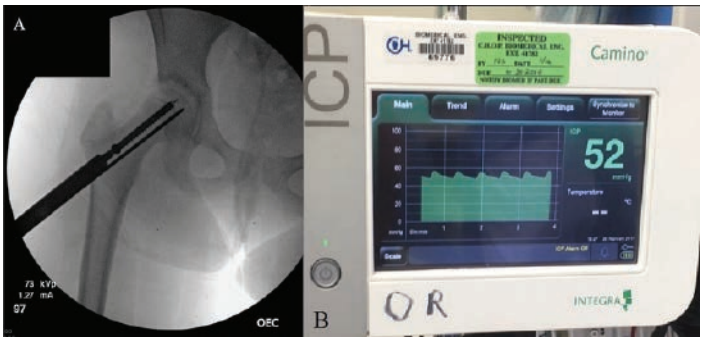

Figure 1. (A) Representative image of intracranial pressure probe in femoral epiphysis monitoring perfusion **(B)** Perfusion monitoring system demonstrating waveform and pulse pressure.

Recently, the so-called modified Dunn procedure has received much attention. This is an open capital realignment performed through a surgical dislocation approach, allowing for identification and preservation of the vascular supply, which allows for a controlled and anatomic reduction of the femoral epiphysis[7]. While the modified Dunn can restore near normal anatomy, the procedure is technically demanding and requires specialized training, which inhibits its widespread utilization. Despite these limitations, the procedure has rapidly gained popularity at several centers. Ziebarth et al. reported very low complication rates in 40 patients (12 with unstable SCFE), with no osteonecrosis and 2.5% residual impingement after an average follow-up of 54 months[7]. With a mean follow-up of 12 years, Ziebarth et al. reported improved radiographic alignment, but follow-up operative intervention for impingement was necessary in 14% of hips. Even with such long follow-up, there were still no cases of osteonecrosis, however, only 5 of these patients presented with unstable SCFE[25]. Sankar et al., in a multicenter series, reported on twenty-seven patients, and found a 27% rate of osteonecrosis after an average follow-up of 22.3 months[4]. The wide range in reported outcomes and complication rates may in part be related to the technical difficulty of the procedure. Subsequent studies have demonstrated that surgeon volume and experience play a significant role in complication rate. Reported rates range from 17% in the most experienced to 50-100% in the least experienced surgeons[26].

Author's Preferred Technique

With expanding options for treatment and perfusion monitoring, we find it important to have a treatment algorithm for unstable SCFE that incorporates information about epiphyseal perfusion, patient preference, and surgeon comfort level (Figure 1). At our institution, all unstable SCFEs are treated urgently. For mild, unstable slips, gentle positional reduction and fixation with two 6.5mm cannulated screws is an excellent treatment option. Femoral head perfusion is monitored using an ICP catheter through the cannulated screw as described by Schrader[3]. If after fixation, the epiphysis is ischemic, a percutaneous capsulotomy is performed. If monitored perfusion still remains absent, a formal open arthrotomy is performed. Finally, if perfusion continues to be impaired, consideration is given for removing the internal fixation and reattempting closed reduction versus performing an emergent modified Dunn procedure (Figure 2).

If the slip is moderate to severe at initial presentation, there is consideration of bypassing in-situ fixation and proceeding directly with a modified Dunn procedure. This route is considered only when a qualified hip specialist is available. It is important that the patient and family receive a full explanation of the risks and benefits of the more invasive modified Dunn procedure to allow for shared decision-making.

While at our institution the modified Dunn is the treatment of choice for severe SCFE or those with no measurable perfusion, it should be emphasized that other options, such as "in-situ" fixation and the Parsch method are certainly worthwhile depending on surgeon comfort level. The Parsch

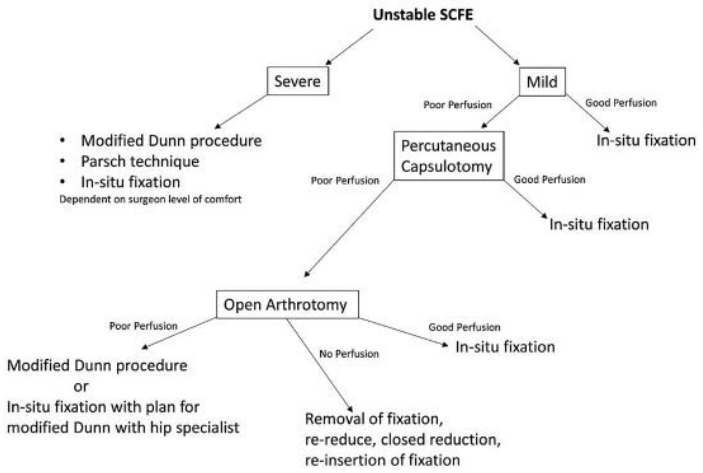

Figure 2. Decision making algorithm for treatment of unstable slipped capital femoral epiphysis. Perfusion is monitored with intra-cranial perfusion probe, as described by Schrader et al. This algorithm reflects the practice at our institution based on physician level of comfort, familiarity, and institutional experience.

method, in particular, can be performed safely in most centers and has very low rates of reported AVN[12].

Discussion

Osteonecrosis is the most serious consequences of an unstable SCFE[6,21]. It places the patient at risk for hip deformity, hip osteoarthritis, and need for total hip arthroplasty later in life[4,5,7,] . Furthermore, patients who develop osteonecrosis have worse functional and quality of life outcomes[4].Therefore, minimizing the risk of AVN is the top priority in treatment of unstable SCFE. Recent systematic review found the overall rate of osteonecrosis after unstable SCFE to be 24%[4-7].

The etiology of AVN in unstable slips is thought to be tamponade within the joint capsule from hematoma and/or kinking or tearing of the epiphyseal vessels[26]. Restoring blood flow may be achieved by gentle reduction and decompression of the joint capsule hematoma[3,2,20,21,26].The use of intraoperative epiphyseal perfusion monitoring can aid in detecting patients with reduced blood flow and potentially allow surgical interventions to improve femoral head perfusion. This advance, along with the development of the modified Dunn procedure, has increased our armamentarium for treating unstable SCFE. Although osteonecrosis may never be a "never event" following unstable slips, an appropriate algorithmic approach considering timing of surgery, decompression of the hip capsule, intraoperative perfusion monitoring, and a carefully chosen surgical technique, may mitigate the risk of osteonecrosis and optimize the long-term outcomes of this challenging condition.

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U·P·O·J

Hip Pain: A Case Report of Diagnosing Femoracetabular Impingement in an Adolescent Athlete

Jermonte Lowe, BS
Julien Aoyama, BA
Nancy Chauvin, MD
Lawrence Wells, MD

Introduction

Femoroacetabular impingement (FAI) is characterized by abnormal morphology of the proximal femur and/or acetabulum. FAI is a condition of abnormal contact that may arise as a result of either abnormal morphologic features involving the proximal femur and/or the acetabulum. It may also occur from excessive and supraphysiologic hip ROM leading to impingement.[1] Although there are several adult-specific reports of FAI in the literature, research involving skeletally immature subjects is sparse and there is no consensus on how to reach a definitive diagnosis for FAI. Consequently, it is not uncommon for pediatricians and pediatric radiologists to misdiagnose FAI as hip or groin strains, which can negatively affect prognosis. Here we characterize an FAI diagnosis in a 15-year-old female athlete and the management outcome.

Case Information

A 15-year-old female ice hockey and field hockey goalie presented to our hospital with a history of 4-week right hip pain after initial evaluation and conservative treatment by an outside orthopedic surgeon. Complaints of sharp pain in her right hip began when she was sprinting during field hockey practice. She was told she may have a hip labrum tear by an outside orthopedic surgeon and was prescribed 3 weeks of crutches and activity restrictions. After no significant improvement in right hip pain with activity modifications, she presented to our hospital for further evaluation and treatment. She reported her symptoms improved with rest but worsened anytime she moved her hips. She noted her right hip pain had not improved significantly with acetaminophen and crutch ambulation as prescribed. She also noted previous IT band injury to the right side but otherwise no significant past medical history.

Standing evaluation revealed no asymmetry in iliac crest height or scoliosis. Mild palpation tenderness was present around the right hip as well as comparatively reduced external rotation (45° on R, 60° on L), and abduction (40° on R, 70° on L) of the right hip. Strength was 5/5 bilaterally for all muscles of the hips and pelvis. Resistance tests elicited no pain and she was able to perform straight leg raises without issue. FABER, Thomas, and Ely special tests were negative bilaterally. However, flexion, adduction and internal rotation impingement and Ober tests were positive on the right hip.

Anterior-posterior and frog lateral radiographs of the hip and pelvis were obtained and initially interpreted as normal by the radiologist. (Figure 1) However, upon evaluation by our orthopedic surgeon, mild bilateral CAM deformities of the femoral necks were seen. (Figure 2) Alpha angles measured on the frog lateral radiographs were found to be 73 degrees on the right and 68 degrees on the left. A follow-up direct MR arthrogram of the right hip was performed which demonstrated a labral tear along the mid-portion of the superior labrum. (Figure 3) Axial oblique MR imaging and radial reformatted imaging showed a small osseous bump along the anterolateral aspect of the proximal femoral metaphysis. There was physiologic physeal closure within the central portion of the proximal femoral physis, which ruled out a possible slipped capital femoral epiphysis.

Management

We offered arthroscopic labral repair and osteoplasty of the bilateral FAI CAM deformities to the patient but she elected to receive treatment at an outside hospital. There she was treated with bilateral open osteoplasties of the femoral necks and an open labral repair of the right hip. Postoperatively she did well with no complaints of pain at either hip at the 2-month mark when she returned to see us. However, she reported she had given up ice hockey and would continue to play field hockey only.

Discussion

Young athletes repetitively flexing and/or internally rotating the hip joint with dance, lacrosse, field or ice hockey (especially goalies) are more susceptible to hip labral tears. Hockey players in particular tend to develop impingement at a much higher rate than other athletes. One study comparing hockey players and skiers found that CAM impingement affected 79% of ice hockey players versus only 40% of skiers.[2] When improperly treated, FAI may lead to persistent symptoms and early-onset osteoarthritis of the hip.[1] Surgery, including hip arthroscopy, surgical dislocation,

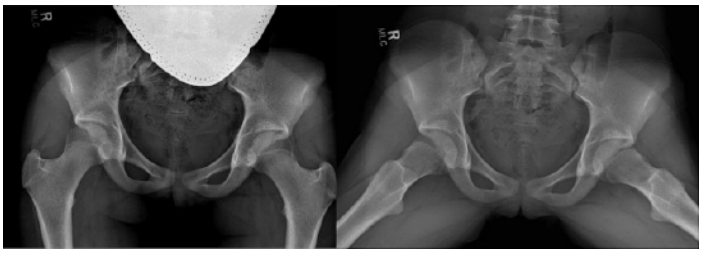

Figure 1. Anterior-posterior and frog lateral radiographs of the bilateral hips and pelvis. Mild CAM deformities can be seen on both femoral necks in the lateral view.

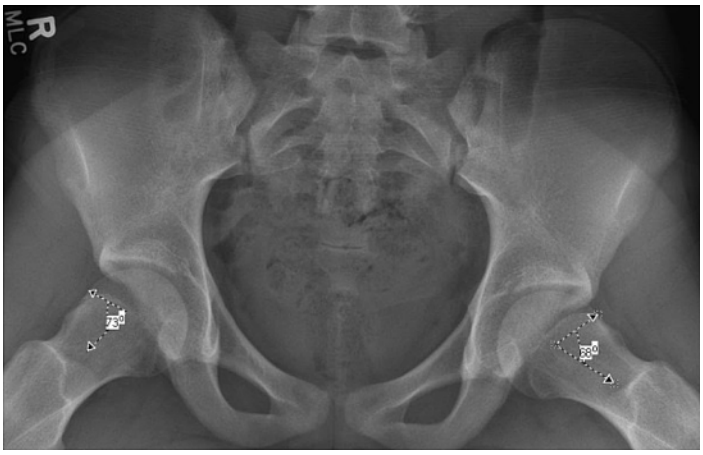

Figure 2. Frog lateral radiographs of the bilateral hips and pelvis with CAM deformities on both femoral necks (white asterisks). Alpha angles were measured and found to be 73 and 68 degrees for the right and left hips respectively.

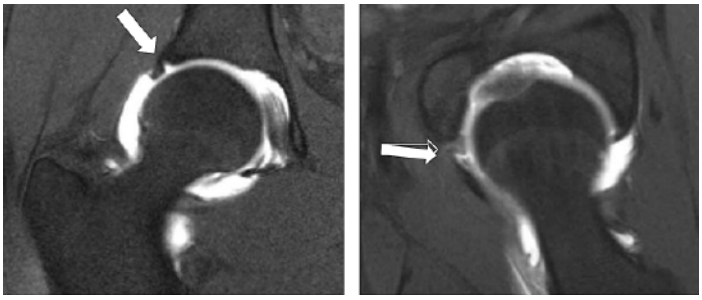

Figure 3. T1-weighted coronal (left) and axial (right) MR images of the right hip showing the superior labral tear (solid white arrow).

and osteochondroplasty are safe and successful treatment options for abnormal hip morphologies, and without surgical intervention CAM lesions may significantly reduce the length of an athlete's career and increase their risk for osteoarthritis.[3]

Many cases of FAI are underreported because they are misdiagnosed as hip or groin strains.[2] Fortunately, the physical findings of FAI are specific. Anterior FAI occurs when the hip is flexed and internally rotated, bringing the femoral neck against the anterior acetabulum and labrum. Posterior FAI occurs when the hip is extended and externally rotated. Given the patient with anterior or posterior hip pain, these maneuvers are crucial to progressing towards an appropriate diagnosis.[4]

Classical radiographic findings of CAM impingement include a pistol grip deformity with bony prominence at the anterolateral femoral head and neck junction on lateral radiograph of the hip.[5] Pincer impingement is seen in entities that result in a closer approximation of the femoral head-neck junction and the lateral acetabular rim (i.e., coxa vara, acetabular protrusion, retrotorsion of femoral head, coxa magna, ossification of acetabular rim, acetabular retroversion).[5]

Cross-sectional MR or CT imaging may also confirm FAI. Both exams are sufficient for measuring alpha angles of the hip joint. Alpha angles greater than 50 degrees are widely accepted for diagnosing CAM impingement. MR imaging is especially effective in discerning acetabular labral damage from impingement of the acetabulum and femoral head/neck junction, by illustrating increased labral signal on fluid sensitive images that extends to the articular surface.[5]

Differential diagnoses in adolescents include hip strain, overuse injury, and slipped capital femoral epiphysis (SCFE). Radiographic workup can exclude SCFE and confirm FAI.

Conclusion

In summary, the recognition of FAI in adolescent athletes is significant and often overlooked. We illustrate the history, physical and radiographic findings of FAI in a young athlete, including surgical results. Armed with the proper diagnosis and treatment, this patient was allowed to return to sport and pursue her aspiration to play field hockey in college.

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U·P·O·J

Medial Epicondyle Fractures in Adolescent Athletes: Two Cases where Conservative Treatment is Surgery

Dwayne Carney, BS
Alexander Akoto, BS
Jermonte Lowe, BS
Julien Aoyama, BS
Lawrence Wells, MD

Introduction

The medial epicondyle is the origin of the flexor pronator musculature and the proximal attachment of the medial ulnar collateral ligament (UCL). The flexor pronator mass functions as a dynamic stabilizer of valgus stress to the elbow while the UCL acts as a stabilizer of static stress to the same region. The medial epicondyle is the third of six main ossification centers which usually develops between the ages of 4-6.[1] However, an open apophysis is often present until the age of 14 to 15. The apophyseal cartilage is relatively weaker than the ligaments that attach to it, and therefore, is a major determinant of possible injury to the medial epicondyle in a subpopulation of individuals.

Fractures of the medial humeral epicondyle account for approximately 12% of all pediatric elbow fractures, occurring most frequently in males ages 9 to 14.[2,3] This injury can be due to excessive valgus stress placed on the elbow by the pronator mass that has a common point of origin at the medial epicondyle. It is especially common amongst youth baseball players and gymnasts. A recent trend in single-sport concentration and year-round participation renders these young athletes more susceptible to ulnar nerve dysfunction and avulsion fractures of the elbow.

The optimal method of treatment for medial humeral epicondyle fractures in pediatric patients is controversial. Non-operative as well as operative management have been reported to have positive outcomes so there is a lack of consensus when neither option is clearly indicated. Typically, avulsion fractures of the medial humeral epicondyle with more than 5mm of displacement, presence of significant instability, or containment of fragments incarcerated in the joint space, are treated with ORIF followed by range of motion and strength rehabilitation.[2,4] For those fractures with minimal displacement or no instability, treatment consists of immobilization in a long arm cast at 90 degrees for 3-4 weeks followed by similar rehabilitation.[2]

This report outlines the injury of a 15-year-old baseball player who injured his elbow while pitching. The physical examination and x-rays of the baseball player confirmed a right-sided medial humeral epicondyle fracture and treatment options were discussed. With the intention of a speedy return to sport and normal function, he opted for open reduction and internal fixation (ORIF).

Case Description

Case: The Baseball Player

A 15-year-old male, T.J., previously in good health, presented to an urgent care facility with a history of non-contact injury to his right elbow suffered earlier that day. A long-time baseball player, T.J. was throwing a pitch when he heard a loud pop immediately followed by intense pain. Plain anterior-posterior (AP) X-ray examination of the elbow showed a complete avulsion fracture with 2.7mm displacement of the medial epicondyle, and he was referred for consultation with a pediatric orthopedic surgeon (Figure 1).

Physical examination results revealed tenderness on the medial aspect of the right elbow and valgus laxity. Hoping to quickly return to baseball, T.J. elected to undergo open reduction and internal fixation (ORIF) of the fracture, which was performed 4 days after injury.

The patient's elbow was immobilized in a removable posterior splint 1-week post-operatively and converted to a sling after wound healing. Early protected active range-of-motion exercises were also started 1-week post-operatively. By 8 weeks T.J. had regained full strength and range of motion in the injured elbow and was cleared to participate in tryouts for his fall baseball team. His range of motion at 9 months is shown in Figure 2.

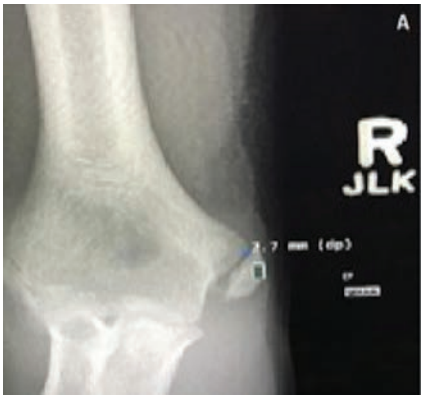

Figure 1. Pre-operative radiograph of distal humerus in baseball player with a medial epicondyle fracture.

Figure 2. Baseball player's range of motion 9-month postoperatively.

T.J.'s 9-month postoperative x-rays show appropriate bony union between the fracture fragment and the distal humerus (Figure 3). Despite having 2.7mm displacement based on AP plain films, he received surgical treatment allowing him to return to play faster. Non-operative management would have included 6 weeks of casting followed by further physical therapy.

Discussion

The management of medial epicondyle fractures in the pediatric population has remained controversial with some studies showing positive results for both operative and non-operative management.[1, 4-6] Traditionally, indications for operative versus non-operative management are dependent upon the degree of displacement of the fracture fragment from the fracture bed with displacement <5mm managed non-operatively and those 5mm-15mm managed operatively.[1,4-6]

With youth baseball pitchers playing for larger parts of the year, they are prone to developing avulsion fractures of the medial epicondyle depending on their degree of usage.[1, 5, 6] The atmosphere is more competitive in youth sports and with the prospect of collegiate and professional success, athletes are opting for opting for treatment that will allow quicker return to play. Despite the lack of high level evidence studies, there are a few lower level studies that show there is an earlier return to play in those athletes treated operatively.[2, 5, 6] One study shows a 9.33 odds of union for operative management as compared to non-operative treatment.[1] Prolonged casting might result in stiffening of the elbow as well as inappropriate lengthening of the ulnar collateral ligament as a result of malalignment of the fracture fragment which can result in increased valgus instability at the elbow.[7]

Displacement is mainly determined by the use of anterior-posterior (AP) and lateral elbow X-rays. Disagreement on measurements of fracture displacement on an X-ray was defined as a reading greater than 2mm difference between observers. A study demonstrated that surgical team members were shown to disagree in 54%, 87% and 64% of cases on

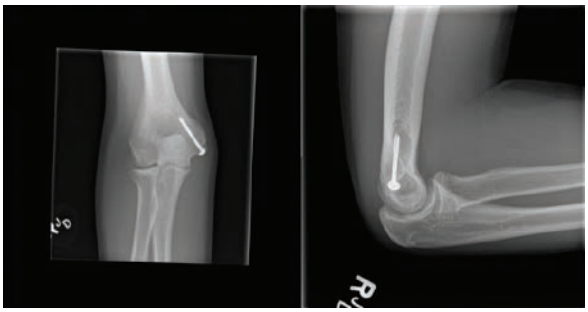

Figure 3. 9-month postoperative x-rays showing appropriate bony union between the fracture fragment and the distal humerus.

AP, lateral and oblique X-ray views, respectively.[3] Therefore, an oblique X-ray or computed tomography (CT) are better options for measurement.

Different types of ORIF can assure speedy return to full range of motion such as cannulated screw with washer fixation. Kirschner (K-wires) wires can also be used but should be removed 2 and 6 months after placement.[8] A cannulated screw and washer inter-fragmentary compression construct was used for T.J.

There have been some documented cases of late ulnar nerve palsy after ORIF; however, this was absent in our patient. The ulnar nerve may be damaged during the initial trauma or via iatrogenic means, such as during surgery or compressive effects of casting on the nerve.[9]

Conclusion

Adolescent athletes who play year-round are opting for surgery to repair medial epicondyle fractures to return to play quicker.Though there is a place for non-operative management with some minimally displaced fractures, athletes faced with the decision between operative and non-operative treatment can be assured that operative management can reliably expedite return to function and sport.

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U·P·O·J

Arthroscopic Assisted Reduction of a Salter-Harris Type III Fracture of the Distal Femur with Concomitant Anterior Cruciate Ligament Reconstruction: a Case Report

Andrew Gambone, MD
Alexander Akoto, BA
Todd Blumberg, MD
Susan Nelson, MD, MPH
Daniel Miller, MD
Lawrence Wells, MD

Abstract

Anterior Cruciate Ligament rupture in the presence of a Salter-Harris Type III fracture of the distal femur is an uncommon injury in the pediatric population. It can be caused by a combination of a valgus and rotational force applied to the knee. This injury most likely represents a sequence of events in which the distal femur fracture is preceded by rupture of the anterior cruciate ligament. Traditionally, these injuries have been addressed at separate operative settings, with fixation of the femur occurring on an acute basis and the ACL rupture being addressed later. However, this has the potential to prolong rehabilitation, result in chondral injury, and delay overall return to sports.[2] Here, we present a case of an arthroscopic assisted fixation of a Salter-Harris type III fracture of the distal femur along with concomitant ACL reconstruction.

Introduction

ACL rupture in the presence of a distal femoral physeal fracture is rare, however the presence of physeal fracture does not exclude concomitant ligament injury.[1] The incidence of ACL tears has increased over the years in the pediatric population likely due to increased sports participation and the use of advanced imaging.[2] A better understanding of the ACL anatomy, the physis, and the natural history of ACL insufficient knees has changed the management of these injuries. The current treatment for ACL tears is arthroscopic assisted reconstruction.

Isolated distal femur fractures may be managed operatively or non-operatively depending on the degree of displacement.[3] Salter Harris type III/IV fractures of the distal femur are particularly difficult injuries to manage both in the short and long term; the extent of physeal involvement and intra-articular nature increases the risk for growth arrest and future degenerative joint changes.[4] Anatomic reduction of the joint surface is required. Typically, this is achieved through open reduction and internal fixation. We present an alternative visualization of the joint surface arthroscopically.

We report the case of a 14-year-old soccer player with an ACL rupture in the presence of a Salter-Harris type III fracture of the distal femur who was treated with arthroscopy assisted fracture reduction and ACL reconstruction during the same operative setting.

Case Information

A 14-year-old female injured her right knee during a soccer game while attempting to make a shot on goal, colliding with the goaltender. The right knee was forced into valgus and internal rotation while her knee was extended and her foot planted. She presented immediately to the emergency department of an outside hospital with right knee pain and swelling. Anteroposterior, lateral, and oblique plain radiographs revealed widening of the medial distal femoral physis. An MRI was ordered to further evaluate the amount of displacement, and it confirmed a Salter-Harris type III fracture with minimal displacement and revealed a complete tear of the anterior cruciate ligament (Figure 1).

The patient was seen at our institution where operative and non-operative treatment options were discussed with the patient and her family. Given the patient's desire to return to athletics and start early range of motion, operative management of both the distal femur fracture and ACL tear during the same operative setting was chosen.

The patient was brought to the operating room placed in the supine position. Arthroscopic evaluation of the knee joint revealed a minimally displaced fracture of the medial femoral condyle extending into the intercondylar notch. A complete mid-substance of the ACL was visualized. The fracture was reduced closed, and reduction was confirmed under fluoroscopy as well as direct arthroscopic visualization of the joint surface. A 7.3 mm x 80 mm partially-threaded cannulated screw augmented with a washer was placed across the fracture site to obtain interfragmentary compression (Figure 2). Exam under anesthesia revealed that the fracture was stable. A guide pin was then placed in the epiphysis across the fracture site midline with the diaphysis to ensure screw placement did not violate the intercondylar notch and interfere with femoral tunnel placement for

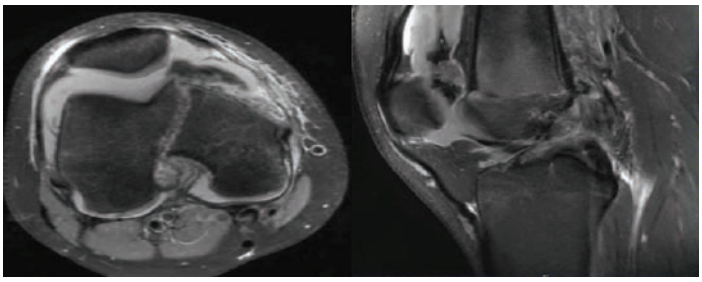

Figure 1. MRI of the right knee demonstrates a minimally displaced fracture of the medial femoral condyle extending into the intercondylar notch as well as a complete tear of the ACL.

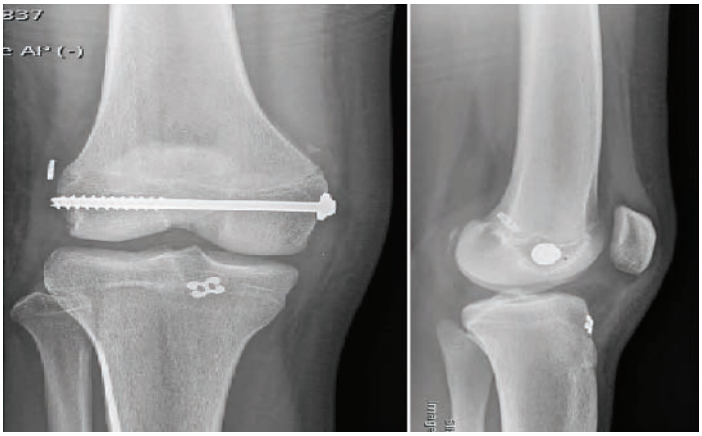

Figure 2. Intraoperative fluoroscopic images post percutaneous screw fixation and ACL reconstruction.

ACL reconstruction. The ACL was then reconstructed via an all inside technique utilizing a 6-strand semitendinosus and gracilis autograft (Figure 3).

The patient was placed in a hinged knee brace locked in 10 degrees of hyperextension. The brace was unlocked for range of motion exercises. The patient was brought back to the operating room at 7-weeks post-op for manipulation of her right knee under anesthesia for concerns of early arthrofibrosis. Afterwards, her post-operative course was uneventful and she regained full knee range of motion.

Discussion

Distal femoral physeal fractures with concomitant ligamentous knee injuries present a challenging problem for both the patient and clinician. The physeal injury itself carries with it a risk of growth arrest which can lead to a limb length discrepancy and angular deformity. [3,4] Depending on the amount of growth remaining, this can be significant and result in the need for additional surgical procedures. Salter-Harris type III/IV fractures are of particular concern given their intra-articular nature and inherent instability. Open reduction and internal fixation is typically recommended to achieve a congruent joint. However, the extensive soft tissue dissection required for knee arthrotomy is associated with increased surgical morbidity such as bleeding, infection, arthrofibrosis, and further injury to the physis.[3,5] Even in the absence of

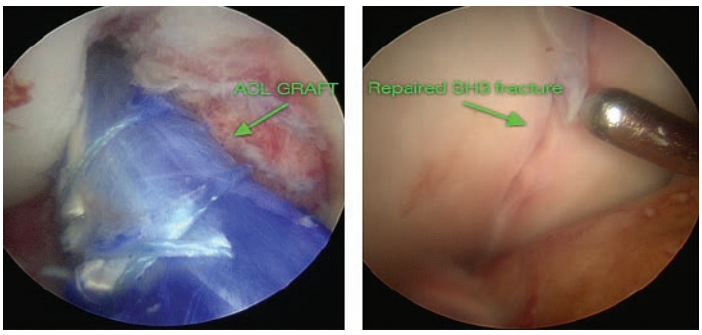

Figure 3. Arthroscopic images of ACL reconstruction with hamstring autograft and reduced Salter-Harris III fracture.

surgical complications, the expected scar formation can make future arthroscopic procedures much more challenging.

Besides the technical difficulties, staging the ACL reconstruction has the potential to negatively affect functional outcomes and quality of life. Closed reduction and casting is applicable only with a nondisplaced fracture or a stable fracture pattern and does not allow immediate range of motion. However, clinicians should have a low threshold for ordering advanced imaging such as CT or MRI to fully evaluate for any fracture displacement.[6] Open reduction and internal fixation with arthrotomy may result in higher morbidity and may also slow the return of full range of motion. Limited knee range of motion prior to ACL reconstruction has shown to adversely affect outcomes, compelling surgeons to postpone surgery until range of motion is improved.[7]

Prior Reports and Relevant Literature

Previous reports of Salter-Harris type III femur fractures with concomitant ACL injuries have detailed a staged strategy of surgical management.[1,8] In these cases, the distal femur fractures were addressed via open reduction and internal fixation. Removal of the fixation hardware and ACL reconstruction were then performed once the patient had regained adequate range of motion in the knee, 2-3 months later.[9] Importantly, the multiple operations involved in this staged strategy also provide multiple opportunities for perioperative complications contrasted with the single operation detailed here. Furthermore, the removal of fixation hardware during ACL reconstruction raises the question of increased risk for refracture of the distal femur. [9,10]

Conclusions

Arthroscopic assisted reduction and percutaneous fixation of intraarticular distal femur fractures minimizes soft tissue dissection, provides confirmation of anatomic reduction under direct visualization, allows for early range of motion, and obviates the need for an additional planned procedure when done in conjunction with ACL reconstruction.

The case presented in this study is, to our knowledge, the first documented arthroscopic assisted reduction of Salter-Harris type III fracture of the distal femur in conjunction with reconstruction of the anterior cruciate ligament during the same operative setting in the English literature.

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Mehta Casting for Early Onset Scoliosis—Operative Technique

Todd Blumberg, MD
Susan Nelson, MD, MPH
Daniel Miller, MD
Andrew Gambone, MD
Joseph Monteleone
Patrick Cahill, MD

Introduction

Management of early onset scoliosis (EOS) is a challenging endeavor for the pediatric orthopedic surgeon. While a number of "growth friendly" spinal implants exist, including growing rods, Vertical Expandable Prosthetic Titanium Rib (VEPTR), and MAGnetic Expansion Control (MAGEC), these techniques have high complication rates[1], require multiple expansion procedures, and have been shown to result in unintended autofusion in nearly 90% of patients.[2] Additionally, growing constructs exhibit signs of diminishing returns with subsequent lengthening procedures [3], reducing their effectiveness as the child ages.

Background

Many cases of infantile idiopathic scoliosis (IIS) resolve spontaneously as trunk and motor control rapidly develop in the neonate. However, for curves with documented progression treatment is recommended. Cotrel et al. managed EOS successfully with a casting method utilizing elongation, derotation, and flexion to correct the deformity[4]. Mehta adapted this technique to infantile scoliosis, finding 69% of patients completely resolved by an average age of 3.5 years when treated early.[5] Serial casting technique for EOS relies on the principle of guided growth, improving the deformity in the cast and allowing continued growth of the child to aid in the correction. Although serial casting has been associated with complete resolution of deformity in patients with IIS, the goal of casting is not necessarily complete cure. For more severe deformity or patients with other types of scoliosis, casting can be an effective tactic to delay surgical treatment with growing instrumentation [6,7].

Preoperative Evaluation and Indications

Mehta casting is indicated in patients with progressive curves beginning as young as 12 months of age. Patients with EOS should be evaluated with a thorough clinical history and physical exam. Appropriate imaging, including PA and lateral scoliosis radiographs, should be obtained as well as an MRI to evaluate for neural axis anomalies such as a tethered cord, syrinx, or Chiari malformation. Appropriate referrals for patients with syndromic scoliosis and evaluation of the cardiac and renal systems by the pediatrician are recommended. Contraindications to serial casting include resolving/non-progressive scoliosis and inability to receive general anesthesia. Families should be warned about the potential for skin complications. The expectations regarding curve improvement, need for a minimum commitment of 12 months of casting, and likelihood of additional procedures as the child grows, especially for older children and those with larger curves, should be discussed.

Procedure

The patient is administered a general anesthetic and intubated while supine on a stretcher. Laryngeal mask airway (LMA) is contraindicated due to the high peak inspiratory pressure that are created while the cast is being molded. A silver impregnated tank or other liner is applied. Tubular stockinette is fastened above the iliac crests and halter traction used at the chin to assist in elongation. The patient is moved to the Mehta table and arms are abducted to 90 degrees, padded, and secured with cast padding. Halter traction is connected and the legs are placed into a sling, allowing for both a mild flexion and traction force to be applied to the patient (Figure 1). Cast padding is applied and imaging is reviewed to plan hand positioning for derotation molding. Contrary to adolescent idiopathic scoliosis, the majority of infantile idiopathic curves are left major thoracic curves with the apex at the lower thoracic spine. Three to four layers of four-inch plaster are applied to the torso followed by the derotation molding. The surgeon derotates the thorax with one hand posteriorly at the apex of the deformity, just lateral to the costovertebral junction, and one hand anteriorly over the rib prominence. An assistant provides counter pressure on the upper chest/shoulder and another holds and molds the pelvis at the iliac crests to allow maximum derotation. A mirror at the base of the table is utilized to evaluate and adjust the hand position during derotation. After the plaster has set, fiberglass cast material is overwrapped (Figure 1).

Windows are cut from the front and back of the cast to allow for abdominal and chest wall expansion (Figure 2), with placement of the

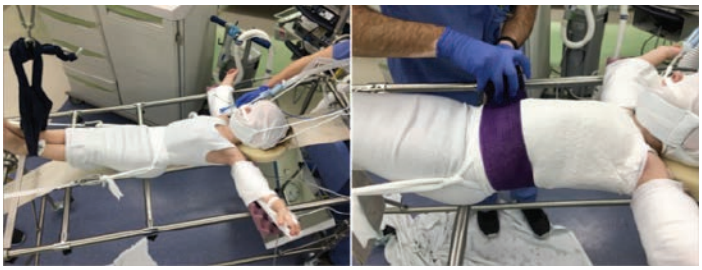

Figure 1. The patient is positioned on the Mehta table with arms abducted and padded. Halter traction is applied to the head, and stockinette overlying the iliac crest provides a traction force with the legs flexed, producing elongation and flexion. The plaster cast is applied and molded to derotate the rib cage.

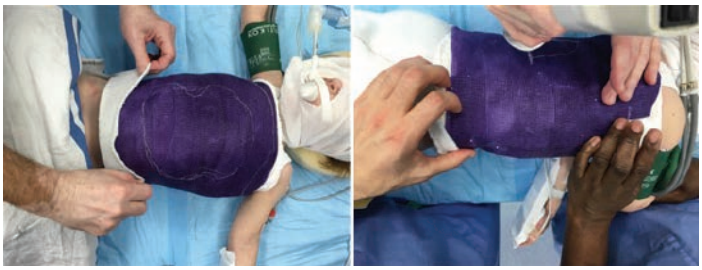

Figure 2. After the cast is applied, the patient is transferred back to the stretcher where windows in the cast are made to allow for improved respiratory mechanics. The posterior window is removed on the concavity of the deformity, in this case, the right side of the chest only.

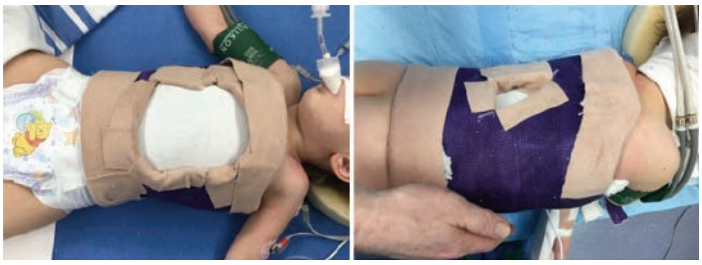

Figure 3. Moleskin is applied to the edges of the cast, covering all fiberglass surfaces.

posterior window on the opposite side of the curve. Cast edges are then padded with moleskin to prevent skin irritation (Figure 3).

Postoperative Protocol

Upright radiographs are obtained prior to discharge to assess the correction (Figure 4). Patients are typically admitted after the first cast to monitor respiratory status and provide cast care teaching. Subsequent cast changes are performed as outpatient procedures every 2-3 months. Casting is discontinued when curve resolution or stabilization occurs, or if serially casting fails to halt curve progression. After successful cast treatment, a brace is utilized to prevent progression with continued growth.

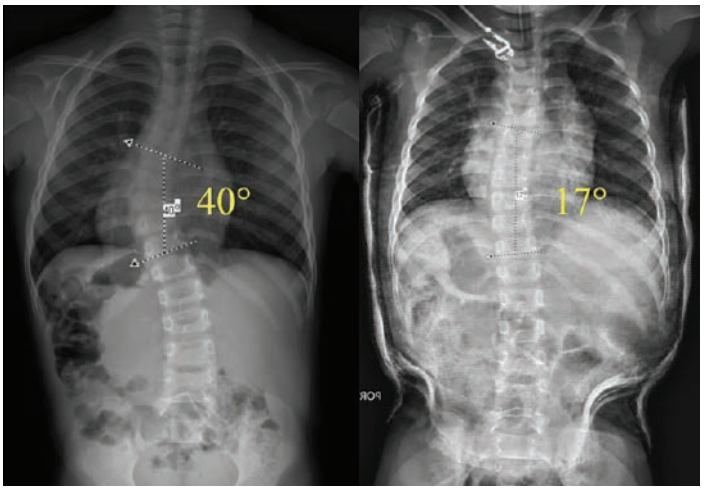

Figure 4. Pre- and post-casting imaging demonstrating a left thoracic curve (T9 apex) with 40 degrees of deformity in the coronal plane. Following cast application, the coronal deformity has decreased to 17 degrees and the thoracic spine has been largely de-rotated. Note the well-padded supra-pelvic mold.

Discussion

Mehta casting is an effective and reliable method to address early onset scoliosis. This technique can be curative for infantile idiopathic curves, and can help delay surgery in children with other forms of early onset scoliosis. It may offer an alternative to "growth friendly" spinal implants, which have a high rate of complication.

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Value in Pediatric Orthopaedics

Brendan Striano, BS
John Flynn, MD
Edited by Matthew Webb, MD

Introduction

Recent and ongoing changes in the healthcare landscape have redirected the focus of healthcare delivery toward the importance of value and cost effective care[1-4]. As a component of this reform, it is important that individual healthcare providers seek areas of improvement within their own area of expertise. These improvements in value can be sought in several distinct domains which include increased efficiency[6], prevention[5], and systems level changes[7]. To that end, we provide a review of recent work to improve value-based care in pediatric orthopaedics.

Efficiency

Healthcare is growing increasingly dependent on the collaborative work of multi-disciplinary teams, and this is especially true in the operating room (OR). In the OR, the surgical team must coordinate with team members from anesthesia, nursing, and radiology among others. In long, complex operations, these interdisciplinary teams often include many individuals with new individuals entering the team as the case proceeds. Lack of familiarity between team members or lack of case-specific knowledge for new individuals can result in delays that hinder efficiency. In the operating room, these inefficiencies add to patient risk (for instance, increased risk of surgical site infection (SSI) and increased blood loss if the procedure is prolonged), as well as increasing cost of care[15-20]. This financial impact is magnified by the expense of operating a surgical suite[16-18]. For these reasons, dedicated teams with static team members have drawn the interest of research groups, particularly for posterior spinal fusion (PSF) for scoliosis. PSF represents an ideal target for dedicated teams because of the inherent need for an interdisciplinary team, the complexity of the procedure, and the relatively high case volume. Recently, Miyanji et al. demonstrated that the implementation of a standardized, dedicated team reduced rates of surgical site infections, as well as time in the operating room[6].

In response to the growing need for improved value of care, at The Children's Hospital of Philadelphia (CHOP) we implemented our own dedicated spinal surgery team. This project initially began with a single surgeon and a small group of anesthesiologists and nurses who underwent training and practiced their role in a posterior spinal fusion. The key component of this training dealt with the standardization of positioning, prep, drape, imaging, wake-up, and transport. To track the effects of implementation of this dedicated team data on time in the operating room and financial impact were collected. Data from the initial stages of this project showed significant reductions in operating room time and cost of care with the dedicated team. Given its success, this project was then expanded to include a second surgeon and more anesthesiologists and nurses. The initiative has continued to demonstrate positive results, maintaining decreased operating room times by more than an hour on average and lower costs on the order of thousands of dollars per patient, even after expanding the number of providers involved.

Systems Level Change

In order to provide more efficient, value-based care, it is important for both healthcare providers and hospital administrations to seek avenues to improve efficiency. Change at the level of the hospital system allows broad implementation of value-based changes, and recent study has demonstrated that there are potential systems level changes in pediatric orthopaedics than could vastly improve efficiency and value.

Securing operating room time can be difficult in a busy in-patient pediatric hospital, and this can be particularly challenging for unplanned surgical operations such as trauma cases. Traumatic orthopaedic injuries do not often require emergent surgery. For this reason, these operations are often scheduled as "add-ons" to proceed after the end of regularly scheduled procedures, after regular business hours, or on a subsequent day. This delay is imparted by the organizational structure of the OR scheduling system and is not due to lack physician availability or willingness to proceed with an operation. Brusalis et al. demonstrated that this systematic inefficiency can be addressed by the institution of a dedicated orthopaedic trauma operating room scheduled exclusively for these "add-on" cases[7]. Within this new policy, a single operating room was set aside daily for orthopaedic "add-on" procedures, and it was not used for any regularly scheduled operations.

This new policy reduced not only the volume of costly "after-hours" procedures, but it also reduced the wait time to surgery, the length of hospitalization, and the overall cost of care. This finding is supported by similar findings in the adult orthopaedic trauma literature[22-24].

Recent data have also demonstrated the value of performing procedures at ambulatory surgical centers. Though many pediatric orthopaedic procedures need to be performed at in-patient hospitals, there are some operations that are amenable to being conducted at ambulatory surgery centers, and Fabricant et al. demonstrated that ambulatory surgery centers can provide 17-43% savings for several common pediatric orthopaedic procedures[3]. This cost reduction came from decreases in both surgery and anesthesia related time expenditures. Kadhim et al. demonstrated similar findings when comparing anterior cruciate ligament (ACL) reconstruction at an in-patient facility versus an ambulatory surgery center. Procedures at ambulatory centers had increased work efficiency and shorter procedure times[21].

It is likely that several factors contribute to the increased efficiency seen at ambulatory surgery centers. One possible mechanism of increased efficiency at out-patient surgical centers is a reduced staff volume. A lower number of staff members translate into teams with high levels of familiarity with one another and the tasks involved in the procedure. Kadhim et al. noted the importance of team members being well-versed in the intricacies of ACL reconstruction in their recent publication[21].

Prevention

Children suffer millions of musculoskeletal injuries annually, and research has demonstrated that a significant portion of injuries can be avoided with appropriate primary prevention[5,8,9]. Nearly 33 billion dollars are spent on the treatment of musculoskeletal injuries in children every year[10]. Preventing injuries reduces both morbidity and associated cost of care. Because surgical care is expensive, preventive interventions are particularly effective when they prevent injuries that typically require operative intervention.

One such injury is ACL tear. An ACL injury can cost $5,000 to $38,000 to repair[5,11]. ACL injuries have been shown to occur more often in individuals with poor biomechanics[12,13]. The resultant interest in neuromuscular training to reduce strain on the ACL has been shown to significantly reduce the risk of ACL injury[14]. Neuromuscualr training has also been shown to be cost effective in preventing ACL reconstruction. Swart et al. demonstrated, using a decision-analysis model, that implementation of a universal ACL tear prevention program reduced the incidence of ACL injury from 3.0% to 1.1% and reduced costs by $100 per player per season[5].

Data Collection

For effective value-based change, data must be brought together from both the clinical and financial realms. Currently, there are well-developed research infrastructures to track clinical data and patient outcomes, but avenues for collection and incorporation of financial data into pediatric orthopaedic research continues to need development. Often, the barrier to making financially minded care decisions is often the availability of information.

Recently, Zygourakis et al. published on the effect of distributing scorecards to surgeons with information about their monthly median expenditure in the operating room. Subsequently, orthopaedists demonstrated a 6% reduction in cost, representing more than $1000 dollars in savings per case, on average[27]. Similarly, Tabib et al. showed that after providing real-time cost information to physicians in the operating room, they were able to make an 8% decrease in modifiable costs per case[26].

Physicians have shown awareness and interest in reducing cost of care, but in order to do so they need readily available data[27]. To address this issue at CHOP, we partnered with a colleague from our hospital's billing department. This connection has allowed for ready access to financial data for several projects and has fostered a departmental interest in delivering more value-based care.

Discussion

Delivering high value care is a vital component of the changing healthcare landscape, and these improvements can be found at all levels from the healthcare provider to the hospital infrastructure. Recent work has demonstrated that improvements can made through streamlining the practice of interdisciplinary teams, increasing efficiency at the system level, and preventing injury in the community. The first step in instituting the principles of value-based care, however, is the collection of high-quality data, and more work of this kind will be necessary as the American healthcare landscape continues to evolve towards delivery of cost-effective, value-based care.

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U·P·O·J

Preliminary Biomechanical Analysis of Superior Capsular Reconstruction Grafts During Activities of Daily Living

Andrea Simi, BS
Matthew Chin, MD
John Kelly IV, PhD
Josh Baxter, PhD
Michael Hast, PhD

Introduction

Rotator cuff tears are painful and often debilitating injuries that are especially prevalent in older adults[1]. While many cuff tears can be surgically repaired, massive 'irreparable' tears present a special challenge for patients and shoulder surgeons alike. Recently, a superior capsular reconstruction (SCR) technique has been developed to address this problem, which utilizes a dermal allograft spanning the superior region of the glenohumeral joint that inserts into the glenoid rim and the greater tuberosity of the humerus. While SCR does not restore the cuff, the graft reinforces the superior capsule—thereby providing leverage and support to the proximal humerus that is normally provided by cuff tendons[2]. Preliminary studies indicate that SCR is effective in improving shoulder function[2,3]; however, the biomechanical limitations of this repair technique have yet to be sufficiently explored.

The goal of this study was to identify physical activities that may overburden the implanted graft and cause premature failure. To achieve this task, results from an in vitro experiment and an in vivo 3-D motion tracking session were used as inputs for the development of a musculoskeletal model (Fig 1).

Materials and Methods

A single cadaveric upper extremity (female, 96 years old) was used in this experiment. The specimen was skeletonized such that all muscle, tendon, and capsule tissues surrounding the shoulder joint were removed. The SCR repair was performed by an experienced surgeon using a single-row suturing technique. The scapula was secured to a test frame (TA ElectroForce 3550) and the potted humerus was secured to the actuator in the anatomic position. The humerus was driven superiorly at a rate of 0.5 mm/s until failure of the graft occurred.

Upper extremity kinematics during activities of daily living were captured using motion analysis on a young male (22 years old). Reflective markers were adhered the xyphoid process, sternum, C7 vertebra, right acromion, medial and lateral condyles of the elbow, radius and ulna of the wrist, and back of the hand. The subject performed six activities of daily living: combing his hair, a forward reach, an overhead reach, tucking the back of his shirt, washing his back, and washing his opposite shoulder. Marker traces were used to inform the computational model of upper extremity motions in 3-D space.

The musculoskeletal model of an SCR shoulder was developed in OpenSim and was based on a previously published upper extremity model[4]. The model consisted of six segments (thorax, clavicle, scapula, humerus, forearm, hand) and had 13 degrees of freedom. No active muscles were included, as this study was purely a kinematic assessment of glenohumeral motions to make estimations of strain and loads imparted onto the SCR graft.

The graft was modeled with four parallel ligament elements that were attached on the rim of the glenoid and the greater tuberosity to mimic the cadaveric insertion points. A wrapping sphere was used to represent the humeral head. Ligament resting lengths were based on fiber lengths when the shoulder was in the anatomic position. A simple simulation consisting of prescribed superior translation of the humerus at a rate of 0.5 mm/s was performed to mimic the in vitro experiment. Physiological cross sectional area forces and normalized force-length curves were adjusted to reproduce the force displacement data that was measured experimentally.

Joint kinematics were calculated using the OpenSim inverse kinematics tool to track in vivo data collected using motion analysis. Individual ligament forces and lengths, as well as average fiber lengths and total graft forces were quantified for each motion.

Results

Activities involving ligament-lengthening posterior shoulder rotation (back washing and shirt tucking) excessively loaded the graft, which may cause graft failure. Throughout these motions the average fiber length exceeded the experimentally determined ultimate strain (dashed line, Fig. 2A). Simulated graft failure is shown as sharp decreases of total force near 180N (Fig. 2B). These values are slightly lower than the experimentally measured ultimate force of 216N. This is explained by the fact that individual fiber lengths differed during motions, causing some fibers to reach ultimate strains and "break" while others remained intact. Fibers did

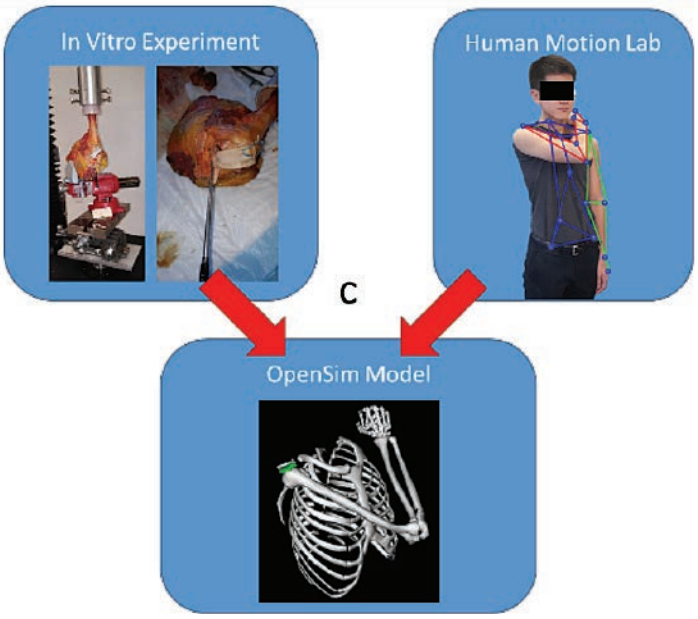

Figure 1. Mechanical properties of the grafts were characterized with an in vitro experiment, while activities of daily living were recorded in 3-D. Both experiments provided input to the OpenSim model.

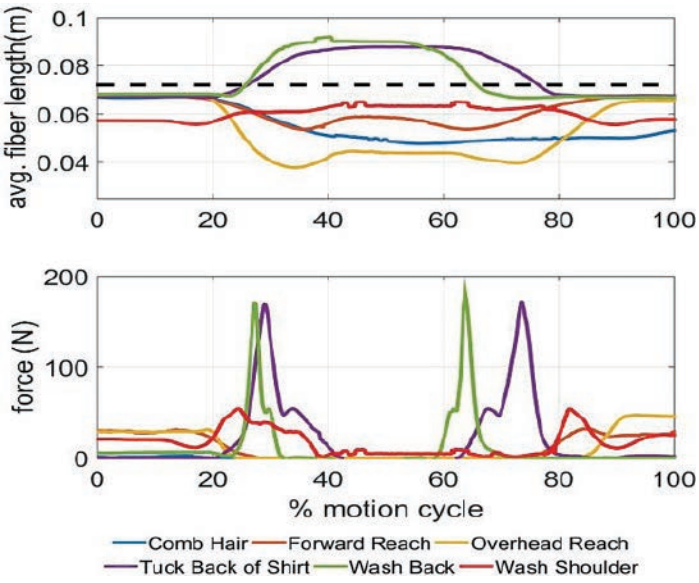

Figure 2. (A) Average fiber length and **(B)** total force exerted on SCR fibers throughout activities of daily living.

not exceed their failure points during hair combing, forward reaching, overhead reaching, or shoulder washing motions.

Discussion

While SCR has shown promise as a repair strategy for massive irreparable rotator cuff tears, the biomechanical limitations of the grafts are still not well-defined. This model identified post-surgical activity limitations that may better inform surgical outcome expectations. These preliminary results also demonstrate the capacity of coupling in vitro, in vivo, and in silico modeling techniques in one cohesive experiment. This approach has potential to provide valuable information to clinicians and rehabilitative specialists to manage patient expectations and guide rehabilitation.

This study was preliminary in nature and has several limitations. While the results suggest that this model is capable of identifying high-risk activities, the small sample size precludes our ability to make strong conclusions about its efficacy. Additionally, the modeling could be improved by including muscle forces and articular joint contact, so that the influence of internal and external loads on the shoulder joint could be assessed. Finally, failure of the in vitro graft occurred at the glenoid insertion, so graft failure biomechanics could be improved with stronger fixation (i.e. double-row suture techniques).

More work is needed to explore the full implications of this preliminary study. In future experiments, we intend to repeat cadaveric simulations, assign validated biomechanical properties to our model ligaments, and validate the model with motion capture data collected in patients treated with SCR.

Acknowledgement

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U·P·O·J

Current Trends in Treatment Options for Glenohumeral Arthritis in the Active Adult

Christopher DeFrancesco, BS[1]
Nicole Zelenski, MD[2]
John Kelly IV, MD[2]

1Perelman School of Medicine
University of Pennsylvania

2University of Pennsylvania
Department of Orthopaedics

Introduction

Glenohumeral (GH) degenerative joint disease (DJD) is a common cause of chronic shoulder pain in adults. In patients with this condition, clinical exam may reveal pain, and restricted range-of-motion (ROM), especially in external rotation[1]. Shoulder radiographs (Figure 1) and magnetic resonance imaging (MRI) can be helpful in assessing the joint surfaces, labrum, rotator cuff, and nearby structures. When DJD is diagnosed, the provider should note concomitant deficiencies such as musculotendinous tears. Treatment options are influenced by the patient's symptoms, age, underlying diagnosis (i.e. inflammatory arthritis, glenoid dysplasia, or humeral head AVN), concomitant injuries, activity demands, and overall health.

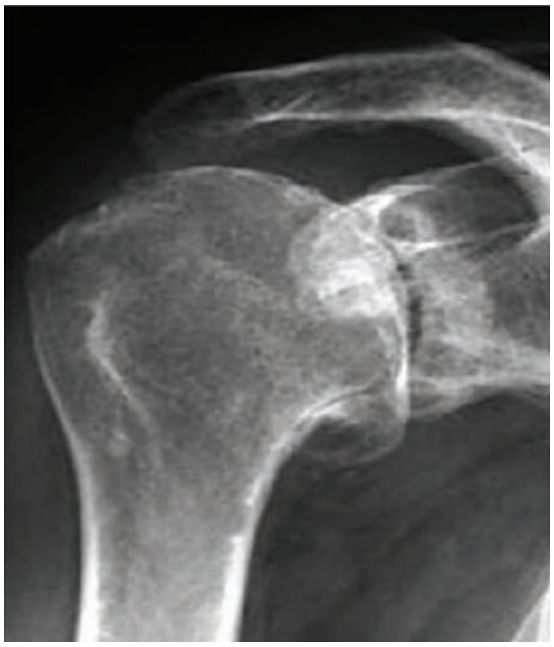

Figure 1. An anterior-posterior radiograph of a degenerative shoulder. Note the marked humeral head flattening, joint space narrowing, and osteophyte formation.

Non-operative Treatments

Activity Modification and Therapy

First attempts at treatment commonly include activity modification, over-the-counter (OTC) pain and anti-inflammatory medications, and formal or informal physical therapy focusing on flexibility and rotator cuff strengthening. Therapy should include ROM exercises and muscle strengthening, which may improve shoulder congruency and decrease pain. In the senior author's experience, the active adult with symptomatic GH DJD rarely achieves lasting improvement with physical therapy, activity modification, and OTC medications alone.

Joint Injections

A combined intra-articular injection of a corticosteroid with an anesthetic such as lidocaine or bupivicaine may provide the patient with temporary pain relief and functional improvement while medication effects last. Many providers are wary of these treatments since corticosteroid injections may hasten tendinopathy[2], pose a theoretical risk for increasing postoperative infection rates[3,4], and can cause systemic effects[5]. Recent research has further shown that methylprednisolone, lidocaine, bupivicaine, and a preservative commonly found in injection solutions can decrease in vitro chondrocyte viability[6-8]. Serial corticosteroid and/or anesthetic joint injections alone are therefore not recommended in the active patient seeking a return to activities.

Intra-articular injection of hyaluronan is now a promising treatment option. Noël et al. performed a prospective study of 39 patients with GH arthritis and an intact rotator cuff who were treated with hyaluronan injection. The authors found a mean pain decrease of 24 mm on the Visual Analog Scale (VAS) at 3 months post-injection, concluding that the treatment is safe and effective[9]. Another study reported similar clinical results[10], while a third reported in vitro findings suggesting that haluronan is chondro-protective[11]. Although these results are promising and American Academy of Orthopaedic Surgeons (AAOS) clinical practice guidelines endorse hyaluronan injection as a treatment option for GH DJD[12,13], these treatments still provide only temporary relief to the patient with advanced disease.

Operative Treatments

Although total shoulder arthroplasty (TSA) is the standard in surgical treatment of GH osteoarthritis, there remains debate regarding management of young, active adults with

advanced GH DJD.A large 2004 study by Sperling and Rowland assessed long-term outcomes after hemiarthroplasty (HA) or TSA in patients under age 50, finding that only 75% of HAs and 84% of TSAs survived without revision at 20-year follow-up. Although the patients in this study reported improved pain and ROM, assessment using the Neer rating system revealed unsatisfactory results in over half of HAs and almost half of TSAs. The authors' takeaway was that "great care must be exercised in offering HA or TSA to patients aged 50 years or younger, with active consideration of alternative treatment methods"[14]. These sobering findings stoked interest in GH joint preservation.

Arthroscopic Debridement

Arthroscopic debridement of the degenerative GH joint allows for a combination of procedures: removal of osteophytes and loose bodies, labral repair, rotator cuff repair, subacromial decompression, axillary neurolysis, and biceps tenodesis or tenotomy. Subacromial bursectomy should be performed at the time of debridement[15]. Capsular releases are commonly done to improve ROM. Chondral procedures including microfracture, autologous chondrocyte implantation, and osteochondral augmentation may also be performed, although their role in the shoulder remains unclear[16].

The Comprehensive Arthroscopic Management or "CAM" debridement procedure—consisting of glenohumeral chondroplasty, removal of loose bodies, humeral osteoplasty and osteophyte resection, 3-point capsular release, subacromial decompression, axillary neurolysis, and biceps tenodesis—has shown promising results leading to increased interest in debridement. Mitchell et al. reported mid-term results for a group of patients with mean age of 52 at the time of CAM. Out of 49 shoulders meeting the requirements for TSA at the outset of the study, only 23% advanced to TSA within 5-years after CAM[17]. Millett et al. separately found that patient satisfaction in a similar cohort at mean 2.6-year follow-up after CAM procedure was high with a median score of 9/10 (10 being "very satisfied")[18]. Another study similarly found high patient satisfaction scores persisting past 2-years postoperative[19]. Research suggests that debridement can delay the need for arthroplasty, with about 80% of patients avoiding TSA in the 5 years following debridement[1,17]. These procedures are attractive because they have a low risk of adverse outcomes[20], have minimal contraindications[15], and do not preclude future reconstructive operations. Arthroscopic debridement should be considered for concentric joints with visible radiographic joint space and no evidence of abnormal posterior glenoid shape[21,22]. Evidence shows that joint space under 2 mm, significant bipolar disease, and large osteophytes are associated with worse outcomes after debridement[23,24]. In the senior author's experience, arthroscopic debridement is best suited for patients with moderate, predominately glenoid-sided disease.

Some surgeons advocate for biologic glenoid resurfacing at the time of debridement in cases with extensive glenoid involvment. This involves first performing microfracture on exposed bony glenoid surfaces before arthroscopically affixing a patch of acellular dermal allograft or porcine intestinal submucosa to the glenoid surface (Figure 2). Early reports of these techniques have been promising, with one study showing a patient satisfaction rate of 75% at minimum 3-year follow-up[25] and another revealing a 6 point decrease in VAS pain scores at 2-4 year follow-up[25,26]. Future outcomes studies will help providers assess the utility of these procedures.

Hemiarthroplasty

Hemiarthroplasty, wherein a proximal humerus prosthetic implant is placed without glenoid replacement, can be an option in young adults with GH DJD, minimal glenoid pathology, and an intact coracoacromial ligament. While TSA is generally regarded as superior[12,13], prior work has suggested that this may not be the case in patients under the age of 50[27]. Various results have contributed to the lack of consensus concerning HA and TSA in this subpopulation. For example, research has shown that patients undergoing HA have a 28% chance of reoperation within 10 years, with most subsequent procedures involving conversion to TSA due to glenoid erosion[27]. Sperling and Rowland found a 76% rate of radiographic glenoid erosion at 15-year follow-up in their young HA cohort[14]. Despite these negative reports, one recent review of HA and TSA in young, active adults found that HA had a lower rate of complications such as loosening, erosion, and revision (13.2% versus 23.7%)[20]. In light of the clinical equipoise created by various findings, HA remains an option in those with humeral head-predominant disease.

Hetrrich et al. previously showed that HA outcomes are worse when the humeral head is not properly centered in the glenoid[28]. Centralization of the humeral head and concentricity of the glenoid is therefore of utmost important. In some patients, soft tissue balancing will be performed to yield a centered implant. Glenoid reaming may also be used to correct unsatisfactory glenoid shape or version[15]. This "ream-and-run" procedure induces the formation of a stable fibrocartilage glenoid surface that centralizes the humeral head, leading to improved patient-reported shoulder comfort and function[29]. The patient with a poorly centralized humeral head or a glenoid that is not concentric and not amenable to reaming is a poor candidate for HA.

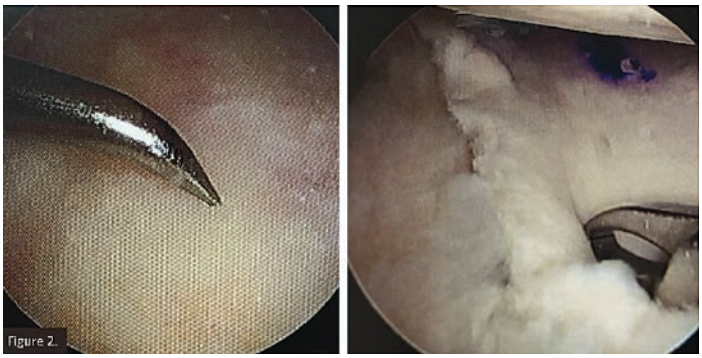

Figure 2. Preoperative (left) and intraoperative (right) arthroscopic photos in a patient undergoing arthroscopic biologic glenoid resurfacing.

Biologic glenoid resurfacing may be performed with HA (Figure 3). This can be done using adjacent anterior capsule, extracellular matrix product, or allograft obtained from the tensor fascia lata, meniscus, or achilles tendon[20,30]. Achilles allograft has been recommended as the superior material[31,32]. Although biologic resurfacing may help maintain radiographic joint space[30], evidence has not shown that it improves revision rates[30,33,34].

Humeral Head Resurfacing

An alternative to HA is humeral head resurfacing (HHR), which is similar to HA in that it replaces the humeral articulating surface and not the glenoid. However, HHR involves a smaller implant than HA with the goal of preserving the natural joint line[15]. In this technique, the humeral head is debrided and osteochondral tissue is removed to the level of the anatomic neck. A metal alloy prosthesis with polished or ceramicized surface is then implanted to replace the humeral articulating surface. Bailie et al. reported 2-year outcomes for patients age 55 or less who were managed with HHR. Out of 36 patients, 35 were satisfied with their outcomes at minimum 2-year follow-up. VAS pain scores showed statistically-significant improvement, and no cases of clinical or radiographic loosening were found[35]. The use of HHR in active patients is limited by high rates of glenoid erosion, with some surgeons advocating for simultaneous biologic glenoid resurfacing to lower this risk[36,37]. HHR yields its best results in cases of humeral predominant primary osteoarthritis and fares relatively poorly in patients with rotator cuff pathology or posttraumatic arthritis[15]. It should not be used in patients with >40% loss of the humeral articulating surface[15], those with severely injured or irreparable rotator cuff tears[15], or patients with marked humeral osteopenia. A more recent report of long-term outcomes with HHR in patients age 50 or younger found an 18.5% revision rate at 10-years, comparable to rates for HA or TSA. The authors concluded that HHR is a useful option in the treatment of GH DJD in the active adult[38]. In fact, some advocates of HHR believe that it is a better option than HA in young patients[39].

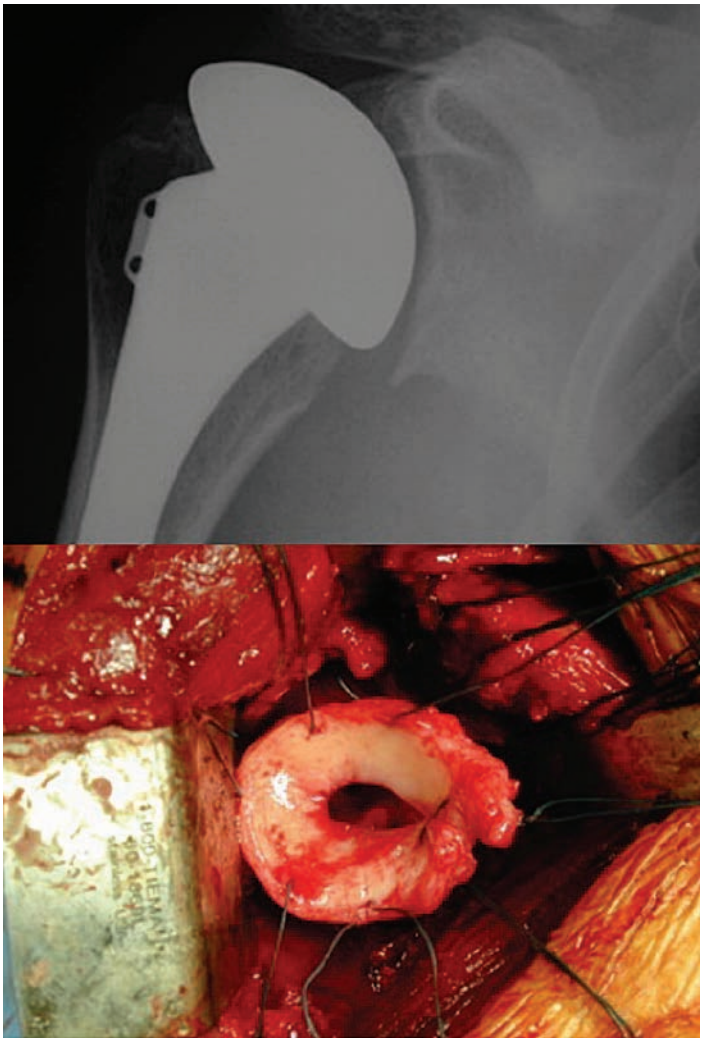

Figure 3. A postoperative radiograph showing a hemiarthroplasy implant in place (top) and an intraoperative photo illustrating simultaneous biologic glenoid resurfacing performed with the hemiarthroplasty (bottom).

Total Shoulder Arthroplasty

In a TSA, a long-stemmed metal humeral implant is placed along with a glenoid component, typically made of polyethylene. While HA is generally regarded as less technically-demanding with lower operative times, decreased blood loss, and lower cost, TSA is commonly considered the superior procedure for primary osteoarthritis because it provides reliable pain relief, improved ROM, and patient satisfaction[40]. Accordingly, AAOS clinical practice guidelines give a moderate-strength recommendation for TSA over HA in patients with GH DJD[12-13]. Despite this seeming endorsement, glenoid radiolucency and glenoid component loosening still pose a significant risk in TSA, particularly in younger, active adults. A recent systematic review of TSA in patients under age 65 found that, at mean 9.4-year follow-up, 54% had glenoid radiolucency and 17.4% had undergone revision[41]. Despite these issues, TSA can be a good option for treating young patients with severe GH DJD, especially those with extensive bipolar disease or concomitant shoulder deficiency such as chronic rotator cuff tear.

Conclusion

Due to uncertainty regarding the longevity of TSA implants, preservation of the native shoulder joint is a reasonable mid-term goal in relatively young adults with GH DJD. To move forward effectively, the provider and patient must understand the underlying disease and its severity, appreciate limitations in treatment, and manage expectations effectively. Nonoperative interventions rarely provide lasting improvement. Arthroscopic debridement can effectively decrease pain, improve ROM, and delay the need for arthroplasty. Hemiarthroplasty is reserved as an option for patients with minimal glenoid pathology. Some practitioners prefer HHR over HA. TSA remains an option for treating advanced GH DJD in adults of any age, although younger patients exhibit higher rates of component loosening. Future advances in the field may involve improved

biomaterials for glenoid resurfacing as well as reliable chondral tissue implants to repair articular surfaces.

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Supraspinatus Tendons Have Different Mechanical Properties Across Sex

Kelsey Robinson, MD
Adam Pardes, BS
Benjamin Freedman, PhD
Louis Soslowsky, PhD

McKay Orthopaedic Laboratory
University of Pennsylvania
Philadelphia, PA

Introduction

Degenerative rotator cuff tears are common[1] with known risk factors such as age, hypercholesterolemia, family history, and smoking[2-5]. Although there is a disproportionate incidence of Achilles ruptures in males[6] and ACL tears in females[7], sex is not a clear risk factor for degenerative rotator cuff tears. Previous work has demonstrated that male rat Achilles tendons have decreased modulus compared to females[8], which may provide a biomechanical explanation for some of the disproportionate clinical incidence of acute ruptures in males. However, whether the differences in mechanical properties in the Achilles tendon exist in the rotator cuff is unknown. Therefore, the objective of this study was to determine the mechanical properties of the uninjured male, female, and ovariectomized (OVX) supraspinatus tendon in a rat model and compare them to known sex differences in the Achilles tendon[8]. We hypothesized that, like the Achilles, female and OVX supraspinatus tendons would exhibit decreased cross-sectional area but, in contrast to the Achilles, there would be no differences in material properties compared to male supraspinatus tendons.

Methods

Shoulders were harvested from 36 aged-matched adult male (n = 12), female (n = 12), and OVX (6 weeks after OVX; n = 12) Sprague-Dawley rats (IACUC approved). The supraspinatus tendon was fine dissected and Verhoeff's stain lines were placed at the bony insertion site and 8 mm proximally. Tendon cross-sectional area was measured with a custom laser device[9]. Humeri were secured in PMMA, and cyanoacrylate was used to secure the tendon between two pieces of sandpaper leaving an 8mm gage length. A custom fixture was used to secure the potted samples in an Instron ElectroPuls E3000 affixed with a 250 N load cell. Tendons were submerged in a 1x PBS bath maintained at 37°C and underwent preconditioning, stress relaxation, low strain dynamic frequency sweep (0.1-10 Hz), and fatigue testing at 2 Hz (~7-40% maximum stress) until failure. Quasi-static, dynamic, and fatigue mechanical properties were computed and one way ANOVAs with post-hoc Bonferroni corrections (a = 0.05/3) were used to compare groups.

Results

The cross-sectional area of female supraspinatus tendons was significantly smaller than male (30%) tendons and OVX (15%) tendons (not shown). Percent relaxation was not different across groups (not shown). There were no differences in toe or linear moduli (Figure 1A) or transition strain across sex; however, toe and linear stiffness (Fig. 1B) and insertion stiffness were greater in male supraspinatus tendons (120%, 140%, and 190%, respectively) than in females. The dynamic modulus of male supraspinatus tendons was lower (80%) compared to female tendons at all frequencies (Figure 1A) and male tendons had higher (180%) hysteresis (Figure 1C) compared to females, but there were no differences in tan(δ) between groups (not shown). Fatigue testing showed that the secant modulus of male supraspinatus tendons was lower (80%) compared to females (Figure 1A) and secant stiffness was higher (115%) compared to females (Figure 1B). Previous sex differences research in the Achilles tendon demonstrated that male Achilles tendons have lower elastic, dynamic, and secant moduli compared to female tendons[8].

Discussion

We measured the uninjured mechanical properties of supraspinatus tendons of male, female, and ovariectomized rats. While male and female tendons were found to have similar quasi-static material properties, male tendons had lower dynamic and secant moduli compared to females at all frequencies tested. Their higher hysteresis throughout loading suggests that they may be less able to resist deformation under stress than female tendons. Male tendons also had higher stiffness under both quasi-static and fatigue loading conditions, which is expected, in part, given their larger cross-sectional area. Interestingly, some of these findings are different in the supraspinatus tendon based on previous work that quantified sex differences in the Achilles tendon[8]. Although similar differences in dynamic and fatigue mechanical properties were found in both supraspinatus and Achilles tendons, they differed under quasi-static loading conditions. Unlike male Achilles tendons, which had lower modulus compared to females[8], male supraspinatus tendons did not exhibit sex

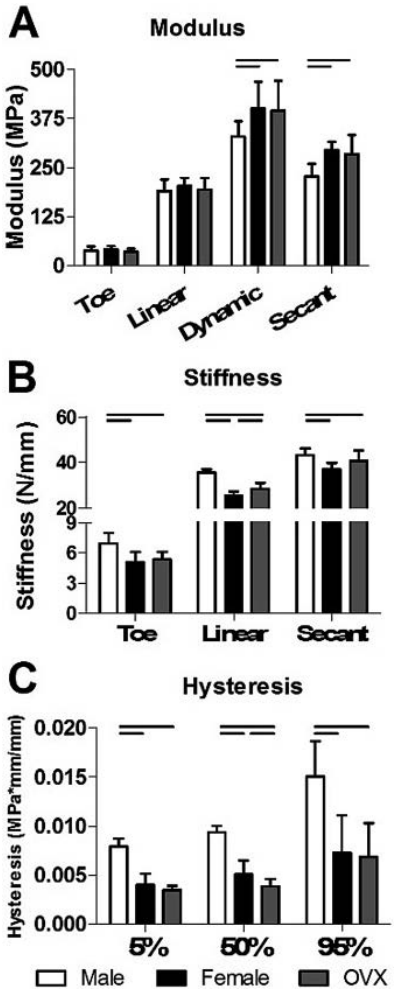

Figure 1. Mechanical testing results. Moduli **(A)** and stiffness **(B)** were calculated during quasi-static, dynamic, and fatigue loading of supraspinatus tendons. Hysteresis **(C)** was measured at 5%, 50%, and 95% fatigue life. Males have lower modulus during dynamic and fatigue loading, higher stiffness, and higher hysteresis than females.

differences in toe and linear modulus, but did have higher stiffness (Figure 2). Although male supraspinatus tendons demonstrated lower mechanical properties with fatigue loading and clinical tears of the supraspinatus tendon are usually degenerative, there is not a disproportionate rate of clinical supraspinatus tendon tears across sex as there is with the Achilles tendon. This may be because the supraspinatus is not subjected to the same loads as the Achilles in vivo. Nevertheless, it is interesting to note that males have increased rates of acute full thickness supraspinatus tears in humans[10] despite the fact that their quasi-static material properties do not differ across sex in the rat model. This clinical finding could be explained by differences in supraspinatus muscle composition across sex, which may lead to altered loading of the tendon and an increased rate of acute tears. Future work will investigate sex differences in histologic features of the supraspinatus tendon and muscle.

Conclusion

This work begins to define the differences in mechanical properties of the supraspinatus tendon across sex and

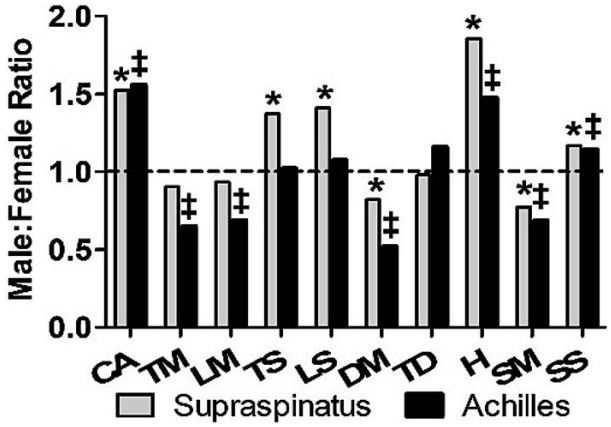

Figure 2. Tendon-specific sex differences in mechanical properties. Ratio of male to female means were taken for each parameter. Data that were significantly different between male and female supraspinatus or Achilles tendons are indicated by * and ‡, respectively. There were significant differences in dynamic and fatigue mechanical properties in both supraspinatus and Achilles tendons. Male supraspinatus tendons had higher stiffness while male Achilles tendons had lower elastic moduli compared to female tendons. No direct comparisons were made between supraspinatus and Achilles tendon property male:female ratio. Dotted line represents a ratio of 1.0. CA: cross-sectional area, TM: toe modulus, LM: linear modulus, TS: toe stiffness, LS: linear stiffness, DM: dynamic modulus (1 Hz), TD: tan(δ), H: hysteresis, SM: secant modulus, SS: secant stiffness.

indicates that sex differences can be tendon-specific which may have implications in the way clinical injuries are managed.

Acknowledgements

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U·P·O·J

Spine Tips & Tricks: Thoracolumbar Injury Anatomy, Biomechanics and Classification

Michael Eby, MD

Introduction

An understanding of the anatomy and biomechanics of the thoracolumbar junction is essential to appreciate the unique injury patterns that occur in this region of the spine. Due to the complexities of these injuries, there have been numerous attempts to effectively classify them. While there are many historical classification systems, review of their progression provides valuable insight into the nuances of this subject and allows context to better appreciate the current management of these injuries. This article aims to review the current and historical classification of these injuries and summarize how management can be best guided.

Anatomy and Biomechanics of the Thoracolumbar Junction

The thoracolumbar junction is comprised of the thoracic vertebrae from T10 to L2. There are several distinct anatomic features of the transition from thoracic to lumbar vertebrae that contribute to the patterns of injury seen. The thoracic spine is more rigid than the lumbar spine due to the attachments of the ribcage. This prevents motion in the stiff thoracic spine and concentrates any external forces acting on the spine at the junction of T10 to L2 (T11 and T12 articulate with floating ribs, which do not confer the same amount of stability as ribs connecting to the sternum) as opposed to diffusing the energy throughout a larger segment of the spine. The transition from thoracic kyphosis to lumbar lordosis in this region further reduces the ability of this segment of the spine to dissipate forces in the sagittal plane. In addition, the transition from coronally oriented facets in the thoracic spine to more sagitally oriented facets in the lumbar spine increases the amount of potential motion in this plane.[1]

The axial load of the body on the spine from the force of gravity is not centered on the spine, but approximately 3.5 cm anterior to the C7 plumb line.[2] Thus gravity creates a compressive force along the anterior column of the spine, resisted by the vertebral bodies, and a tensile force through the posterior column countered by the posterior ligamentous complex. The importance of the posterior ligamentous complex as a tension band construct is highlighted throughout numerous injury classifications. Finally, the compressive strength of the vertebrae in the thoracolumbar junction is less than the lower lumbar vertebrae[3], making this portion particularly susceptible to fracture.

Historical Classification Systems

There have been numerous classification systems introduced to objectively stratify thoracolumbar injury. These injuries have been classified by mechanism, fracture morphology, functional anatomic units, columns, presence of ligamentous injury and various assortments of those criteria. Reconciling all the different aspects of these potentially complex injuries into a reproducible and universally accepted system that can guide treatment makes this classification technically challenging.

The first classification system was described by Lorenz Bohler in 1930[4], separating injuries by mechanism such as compression, flexion, extension, distraction, shear and torsion. Watson Jones incorporated fracture morphology such as wedge fractures or comminution into classification in 1938. In addition, Watson Jones introduced the concept of the critical role of the posterior ligamentous complex in stability of the spine.[5] In 1949, Nicoll provided a basic but important component of classification: stable versus unstable fractures. Stability can be important in two functions. In the short term, acute stability of the spinal column requires ensuring the general relationship between vertebrae is maintained to prevent neurologic injury. Long term stability is important in preventing chronic pain or eventual deformity of the spine. Nicoll also proposed the concept of separating the spine into discrete structures to be examined separately: the vertebral body, disc, facet joints and inter-spinous ligament.[6] Holdsworth in 1970 drove the concept of classification by mechanism, thoroughly describing five distinct mechanisms of injury.[7] He also was a proponent, along with Kelly and Whitesides, of the two column model of the spine, with the anterior column being composed of vertebral body and disc, and the posterior column composed of pedicles, lamina, facets and posterior ligamentous complex.[7,8]

In 1983, Denis proposed a classification system that divided fractures by mechanisms of

compression, burst, seatbelt injuries and fracture dislocations with further subdivision of each category. With this classification system, Denis proposed the well-known three column model. The foundation of this model is that an intact middle column, which consists of posterior longitudinal ligament as well as the dorsal aspect of the disc and vertebral body, is crucial to stability.[9] Even more complicated classification systems have been introduced since, such as the AO classification introduced by Magerl in 1994. This consists of 53 types of fractures sorted based on three main mechanisms (flexion, distraction and rotation).[10] Ultimately, simplicity lends itself to strong inter-observer reliability, which is essential for a classification system to be useful. While many classification systems struggled to accommodate the multitude of aspects, lasting acceptance of these prior systems was limited due to their inability to ultimately guide treatment.

Thoracolumbar Injury Classification and Severity Scale

In 2005, the Spine Trauma Study Group led by Vaccaro proposed the Thoracolumbar Injury Classification and Severity Scale (TLICS)[11], which is currently a widely-adopted pathway to describe these injuries as it also guides management. The TLICS incorporates injury morphology, posterior ligamentous complex integrity, and neurologic status into a point based scale that identifies patients who would benefit from operative vs. non-operative treatment. The TLICS incorporates these facets by evaluating the injury morphologically on CT scan as well as the patient's clinical neurologic exam to assess for acute stability that may manifest with neurologic symptoms or cause deterioration of neurologic status. Long term stability of the spine is addressed by evaluation for posterior ligamentous complex injury by MRI. A point based scoring system makes the TLICS functionally useful in operative decision making, while morphologic stratification that is not overly burdensome or complex achieves high inter-observer reliability due to the simplicity of the system. This highlights the importance of a classification system where a consensus on operative intervention can be reached, as there is still significant controversy. While instrumentation provides assurance of spinal stability, excellent outcomes of non-operative treatment with bracing in thoracolumbar injury have been reported if the patients are appropriately selected.[12] Despite validation of the TLICS, including a study showing 96% of thoracolumbar injury treatments are accurately predicted by the TLICS[13], universal acceptance has not been achieved by this system.

AOSpine Thoracolumbar Classification System

The AOSpine classification system was introduced in 2013 by Vaccaro and an international group of surgeons to address the continued lack of universal acceptance of a classification system. The system expands upon the TLICS to incorporate a more detailed morphological classification modeled after the Magerl system. The posterior ligamentous complex and the neurologic status are still incorporated in the operative decision making.[13] The algorithm for determining treatment was designed with input from hundreds of surgeons across many international regions.[14] It remains to be seen if this will increase international acceptance of a single common system.

Conclusion

Unlike fracture classification systems in other parts of the skeleton, the thoracolumbar region has many unique biomechanical and anatomical considerations that must be understood to fully appreciate the injuries that occur. The many classification systems that have been introduced struggle to reconcile the vast complexity and variation of differences seen in morphology and mechanism with the more pertinent and simplistic determination of stability and need for operative intervention. While universal acceptance of a single classification system may eventually lend clarity to a complicated and controversial topic, studying the evolution of these classification systems allows for a more thorough understanding of injury to this region of the spine and the advantages and drawbacks of the various classification systems.

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U·P·O·J

Growth Modulation for Idiopathic Scoliosis with an Anterior Tether—Operative Technique

Susan Nelson, MD, MPH
Todd Blumberg, MD
Andrew Gambone, MD
Daniel Miller, MD
Patrick Cahill, MD

Introduction and Background

Adolescent idiopathic scoliosis (AIS) is a three-dimensional spinal deformity consisting of alterations in the coronal and sagittal plane as well as axial rotation.Treatment options include observation, bracing, or surgery depending on patient characteristics, curve magnitude, and skeletal maturity. Deformity correction and fusion is currently the gold standard for surgical treatment of AIS[1]. Recent advances in treatment of AIS include fusion-less strategies that harness spine growth to guide the deformity similar to asymmetric tethering of the physis to correct long bone deformities. The advantages of fusion-less technique are preserved spinal motion and future growth. Staples have been used to modulate spine growth in idiopathic scoliosis[2,3] and recently flexible tethering has been used[1,4,5]. A flexible anterolateral tether placed thoracoscopically allows for dynamic compression to modulate growth, while minimizing effects on disc health and motion[6].

Pre-operative Evaluation and Indications

Indications for anterior tethering are being established for this innovative approach to managing idiopathic scoliosis. Current relative indications include: age >9 years, >2 years of growth remaining, thoracic major scoliosis, Cobb angle 40-65 degrees, non-structural compensatory curves, cobb angle between vertebrae T5 and L1[5]. Contraindications include congenital malformations, patients who would not tolerate a thoracoscopic approach, skeletal maturity, and patients with vertebrae too small in the thoracic region to accommodate anterior instrumentation. All patients should have pre-operative physical examination and work up as appropriate for any patient with AIS. This includes neurologic examination, assessment of curve flexibility clinically and radiographically, and pre-operative MRI evaluation for neuraxial pathology. Levels selected for tethering are within the measured Cobb angle.Although there is not a precise method to determine correction, initial correction should be planned based on growth remaining.

Procedure

The presence or availability of general surgeon for the thoracoscopic approach may be required based on the primary surgeon's experience and comfort. Thoracoscopic exposure is facilitated by single lung ventilation anesthesia. After induction of anesthesia the patient is positioned on a radiolucent table in left lateral decubitus for a typical right thoracic curve. Using fluoroscopy, the upper and lower instrumented vertebrae are marked, as is a line over and parallel to the vertebral bodies in the sagittal plane (Fig. 1). Depending on surgeon preference, the coronal trajectory of each level may also be marked.Wide prep and draping of the chest is mandatory in case an extensile approach is required.

Anterior portals are established first in the anterior axillary line. A small amount of local anesthetic is infiltrated and incision is made with a 15 blade followed by blunt dissection with a hemostat for placement of a 5mm viewing cannula. The length of planned instrumentation is divided into quarters with the proximal anterior portal made at the bottom of the top 25% (Figure 1). A second anterior portal can be placed three interspaces distal to this. Posterior trajectory is maintained during entry into the thoracic cavity coming over the rib with the trocar. The chest cavity is insufflated with CO_2 and a 30 degree endoscope is placed. The lung is gently retracted using an endoscopic peanut until completely deflated. Levels are confirmed with fluoroscopy. The parietal pleura overlying the spine is divided and the segmental vessels cauterized using a harmonic scalpel/coagulation. Maintaining hemostasis is essential for adequate visualization. With the parietal pleura retracted a sponge may be placed between the spine and the esophagus and great vessels. This facilitates exposure and protects these structures.

Posterior portals are then established along the previously marked line to facilitate direct lateral trajectory to the spine for instrumentation. 15mm cannulas are used. Local anesthetic

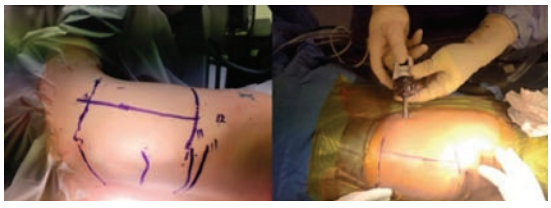

Figure I. Marking of levels is done prior to procedure start under fluorosc, guidance. Anterior portals are established in the anterior axillary line.

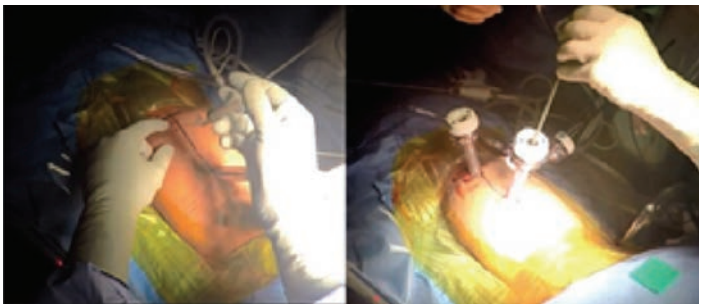

Figure 2. Posterior portals are established along previously marked area. Local anesthetic is infiltrated and can help localize.

infiltration into the intended interspace can be helpful and the needle used to directly visualize the trajectory (Figure 2). Usually two to three levels can be instrumented through one interspace portal. The number or posterior portals will be dictated by the number of instrumented levels planned. Levels are instrumented sequentially distally to proximally starting with pronged centering staples impacted into the mid portion of the lateral vertebral bodies. Bone wax is placed into the staple to maintain hemostasis and placement checked with fluoroscopy. A tap is used through the staple and trajectory confirmed fluoroscopically. The far cortex should be carefully penetrated for bicortical fixation. Screws are placed followed by the flexible tether which is manipulated into the tulips and secured with set screws. An external tensioning device is used to take any slack out of the tether and initiate correction before final tightening (Figure 3).

Once fluoroscopy confirms adequate initial correction the tether can be trimmed with the harmonic scalpel. Local anesthetic is injected posteriorly at the level of the transverse process at each level under direct thoracoscopic visualization to ensure the pleura is not penetrated. A chest tube is placed and portal sites are closed in layers.

Postoperative Protocol

Chest tube suction is set to -20cm H_2O. Output may initially be high due to any irrigation used intraoperatively. The chest tube is typically discontinued when output is <200cc/24hr.

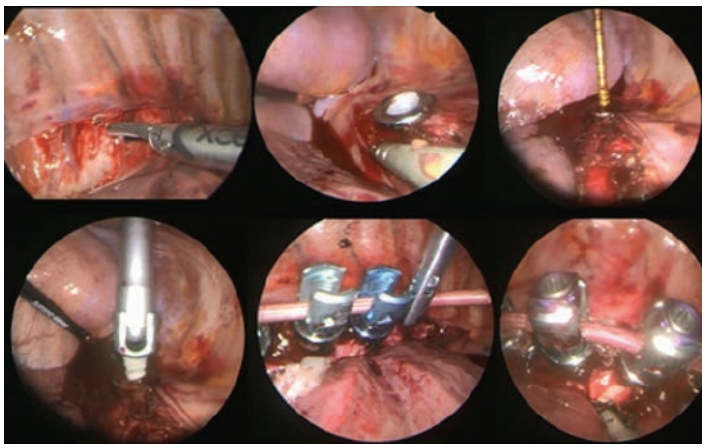

Figure 3. The segmental vessels are cauterized with the harmonic scalpel prior to instrumentation. A pronged staple has been placed and filled with bone wax followed by tapping and screw placement. Placement of the flexible tether and final position.

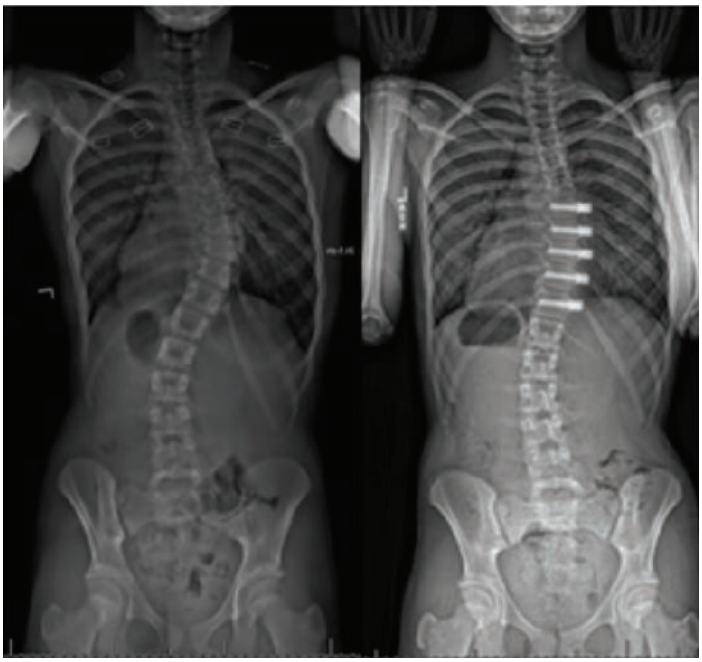

Figure 4. Pre- and post-standing radiographs showing instrumentation and initial correction.

Early mobilization and incentive spirometry are encouraged. The patient is seen 6 weeks post operatively with PA and lateral scoliosis radiographs (Figure 4).

Activity is advanced at this point. Patients are followed subsequently at 3 months and then every 6 months to monitor correction until skeletal maturity. If signs of overcorrection are noticed on follow-up imaging, the tether can be cut in a minor procedure to prevent progression.

Discussion

Anterior tethering for idiopathic scoliosis has the potential to harness growth for curve correction thus maintaining spine flexibility, allowing growth, and saving the patient from a larger spinal fusion operation. Indications for this technique are evolving and overcorrection may occur. However, in the appropriately selected patient growth modulation can successfully correct scoliosis while avoiding spinal fusion.

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Growth Factor and Extracellular Matrix Expression and Localization during Nucleus Pulposus Formation

Sun Peck, PhD[1]
Kendra McKee, MD[2]
Neil Malhotra, PhD[1]
Brian Harfe, PhD[2]
Lachlan Smith, PhD[1]

[1]University of Pennsylvania
Philadelphia, PA

[2]University of Florida
Gainesville, FL

Introduction

Intervertebral disc degeneration is implicated as a major cause of low back pain[1]. Current available treatment options primarily focus on relieving pain rather than regenerating disc tissue, and thus, there is a need for new therapeutic strategies that alleviate symptoms as well as restore disc structure and mechanical function. The earliest degenerative changes occur in the central nucleus pulposus (NP), where altered composition initiates a cascade that compromises mechanical function and culminates in structural failure. An impediment to the development of cell-based strategies for NP repair is the unique developmental origin of the NP, as NP cells are derived from the notochord and not the mesenchyme[2-4]. Improved understanding of embryonic NP formation may enable recapitulation of developmental signals that might drive therapeutic cell types, such as mesenchymal stem cells, towards an NP cell-like phenotype to optimize adult disc regeneration. Previously, we established changes in global mRNA expression profiles of resident cells as the notochord transforms into the NP using whole-transcriptome sequencing (RNA-Seq), and found that key signaling pathway elements that regulate patterning, growth, differentiation, as well as structural extracellular matrix (ECM) molecules, showed significant differential gene expression across this embryonic developmental window[5]. In this study, our objectives were to build on these findings by examining protein expression of growth factors and ECM molecules implicated in our RNA-Seq results at key developmental stages as the notochord transforms into the NP.

Methods

For these IACUC approved studies, we used the Shh-cre;ROSA:YFP mouse model[3], where all Sonic Hedgehog (Shh) expressing notochord-derived cells express YFP throughout the life of the mouse (i.e. creates a fate map). We examined two key developmental stages representing the immediate, opposite ends of the notochord to NP transformation: E12.5 (fully formed, intact notochord) and P0 (fully formed spine with distinct disc space). Whole embryos (E12.5) or isolated spines (P0) were fixed in formalin, and processed into paraffin. Midsagittal, 8 μm thick sections were stained with Alcian blue/picrosirius red (ABPR) for GAG and collagen respectively, hematoxylin and eosin (H&E) for cellularity, or immunostained with antibodies specific to proteins-of-interest (ECM: Collagens I, II and VI, and aggrecan; growth factors: Shh, transforming growth factor β1 (TGF-β1), and insulin-like growth factor 1 (IGF-1)) and counterstained with hematoxylin. Staining intensity in the notochord/NP and associated tissues was semi-quantitatively assessed.

Results

At E12.5, there was a discrete notochordal structure with a GAG-rich inner core and outer sheath, both of which were relatively acellular compared to the rest of the notochord (Figure 1). GAG-rich mesenchymal condensations in regions that will form future vertebral bodies were clearly present (Figure 1). At P0, the spine was fully formed with distinct vertebral bodies and disc spaces, including clear boundaries between the annulus fibrosus and the NP (Figure 1).

Extracellular matrix components collagens I, II, and VI, and aggrecan showed diffuse staining in non-cellular regions (core and sheath) of the E12.5 notochord. At P0, these molecules exhibited intense staining at the outer boundary of the NP. SHH, TGFβ1, and IGF1 all showed

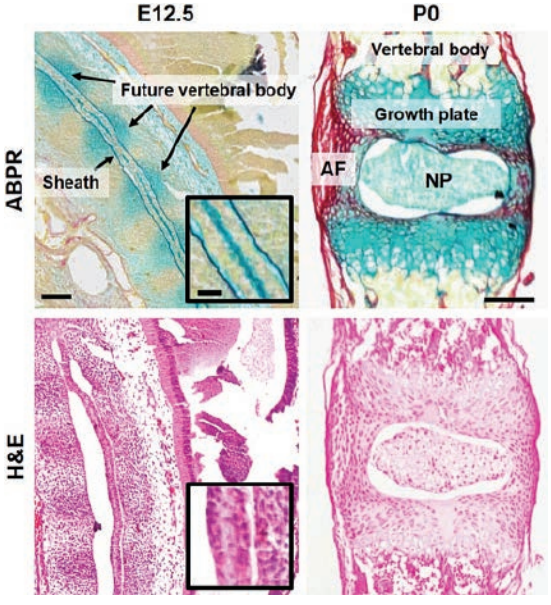

Figure 1. Overall morphology at E12.5 (notochord) and P0 (disc). AF: annulus fibrosus; NP: nucleus pulposus. Scale bar = 100 μm; inset scale bar = 20 μm.

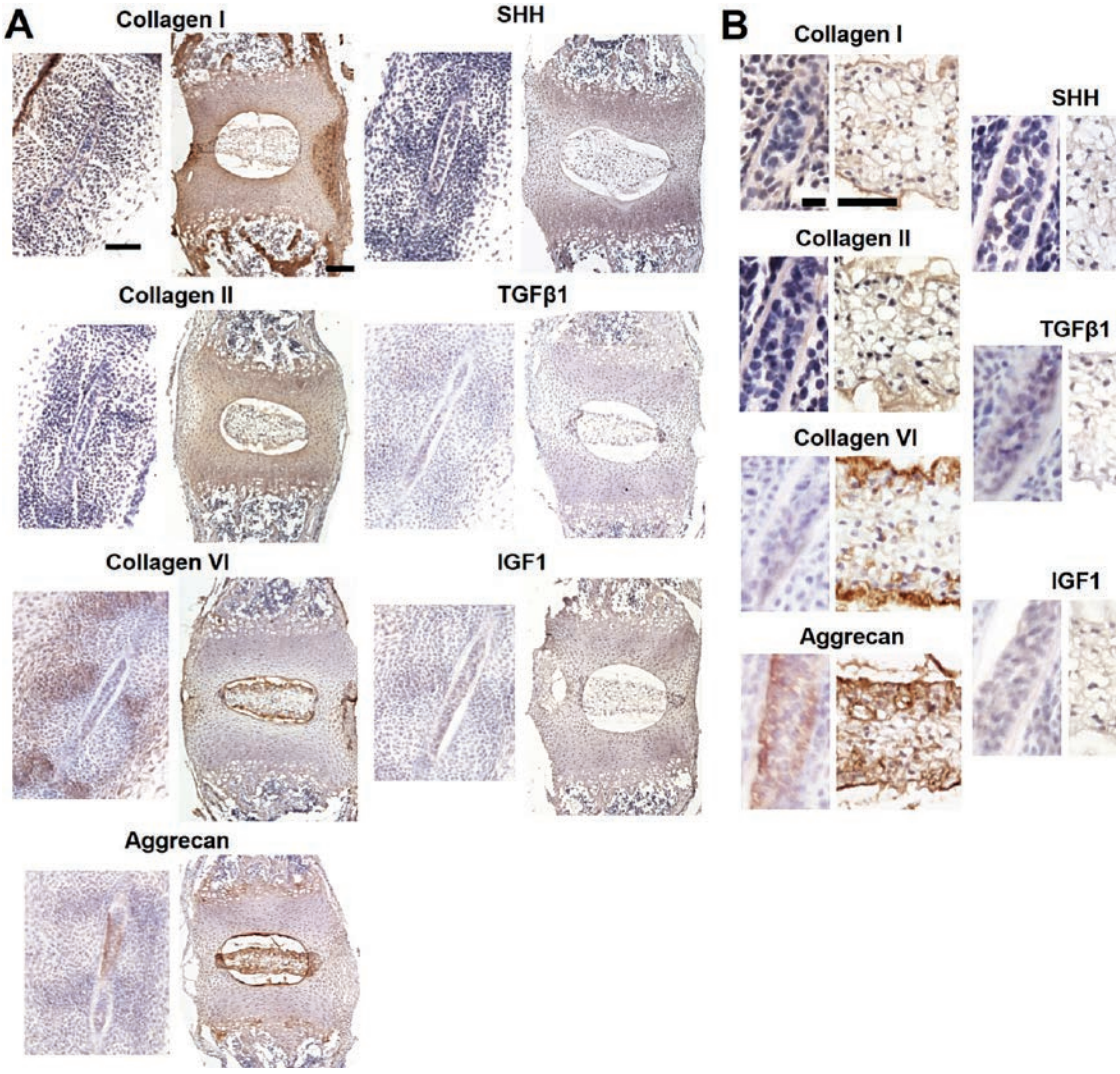

Figure 2. Representative immunostaining of ECM and growth factors at E12.5 and P0. For each pairing, the left image is E12.5, and the right image is P0. Panels in B represent higher magnification images of notochord/NP from A. Scales in A: E12.5 = 50 μm, P0 = 100 μm, and B: E12.5 = 10 μm, P0 = 50 μm.

Table 1 Developmental Staae and Region

	E12.5			P0			
Molecule	**N**	**DC**	**VC**	**NP**	**IAF**	**OAF**	**E**
SHH	**	-	-	*	-	-	-
TGFβ1	**	**	*	**	*	*	**
IGF1	**	**	*	*	-	-	**

Table 2 Developmental Stage and Region

	E12.5			P0			
Molecule	**N**	**DC**	**VC**	**NP**	**IAF**	**OAF**	**E**
Aggrecan	**	*	*	***	*	*	**
Collagen I	*	***		**		***	
Collagen II	*	*	*	*	**	*	***
Collagen VI	*	***	-	***	-	**	*

cellular expression in the E12.5 notochord. At P0, expression of TGFβ1 and IGF1 by NP cells was heterogeneous (strongly by some cells, weakly by others). SHH expression in the NP was weaker at P0 than at E12.5. In both the E12.5 and P0 samples, positive immunostaining of non-notochord/NP tissues for many of these molecules was also observed. Semi-quantitative scoring of protein localization is presented in Tables 1 and 2.

Discussion

In our previous whole-transcriptomic profiling study, we found a large number of differentially expressed growth factor and ECM genes at P0 compared to E12.5[5], which are largely reflected on the protein level in our current results. We demonstrated marked changes in protein localization and expression levels between E12.5 and P0. As mRNA and protein levels do not always directly correlate in expression, ongoing work is focused on elucidating regulatory and functional roles of these genes on both the transcriptional and translational levels. The changes observed most likely reflect a switch from patterning (decreased Shh signaling) to growth (increased TGFβ1, IGF1, and ECM structural genes) as the NP develops into a functional, load-bearing tissue. Heterogeneous expression within the NP at P0 suggests that resident cells may be undergoing progressive phenotypic changes to accommodate evolving functional requirements. Interestingly,

we also observed staining of non-notochord derived tissue in our studies, which will help to inform future studies exploring the roles of these molecules in embryonic spine development as a whole. Overall, these data support our long-term goal to establish and recapitulate the specific developmental signals required for embryonic NP formation in order to improve cell-based therapeutic strategies for disc regeneration.

Significance

Low back pain associated with intervertebral disc degeneration is a significant global health and economic burden. The results from this study further our knowledge and understanding of NP development and serves to inform development of improved cell-based therapeutics for disc regeneration.

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Novel Techniques for the Evaluation of Physical Activity in a Large Animal Intervertebral Disc Degeneration Model

Justin Bendigo, BS[1,2]
Sarah Gullbrand, PhD[1,2]
Brendan Stoeck, MSE[1]
Zosia Zawacki, VMD[1]
Thomas Schaer, VMD[1]
Harvey Smith, MD[1,2]
Robert Mauck, PhD[1,2]
Neil Malhotra, MD[1]
Feini Qu, BS[1,2]
Lachlan Smith, PhD[1,2]

[1]University of Pennsylvania
Philadelphia, PA

[2]Philadelphia VA Medical Center,
Philadelphia, PA

Introduction

Intervertebral disc degeneration (IDD) is a progressive, age-related condition that leads to structural and mechanical failure of the disc. This deterioration is commonly associated with low back pain (LBP). Therefore, pain is the most clinically significant characteristic of IDD, and the ideal animal model should recapitulate pain and functional impairment in addition to structural and mechanical alterations to the disc. Our group previously developed a large animal goat model of IDD that effectively recapitulates the structural and mechanical changes that occur with degeneration[1]; however, intervertebral disc degeneration in sheep or goats does not result in clinically perceptible pain, even at very advanced stages. Various methods currently exist to evaluate activity and pain in small animal models, including: the LABORAS platform, which measures vibration/force for position and behavior tracking[2]; hindpaw withdrawal in response to mechanical (von Frey Test) and thermal (Hargreaves Test) hyperalgesia signifying increased pain sensitivity[3]; and the Rotarod Test, which uses a rotating rod to measure balance and activity endurance[3]. These techniques are not readily translatable to large animal models. An objective tool to assess functional change that is consequent to painful degeneration would be invaluable to evaluation of therapeutics in preclinical animal models. The objective of this study was to develop and validate two novel techniques for quantifying physical activity in an established caprine model of disc degeneration.

Methods

Two male large frame goats, ~2 years of age, were housed together in a 3-sided barn. IDD was induced at 4 lumbar levels per animal via intradiscal injection of 1U chondroitinase ABC. Our previous work showed that this insult results in moderate to severe degeneration of the disc after 12 weeks, as assessed via MRI, disc height, and histology[1]. Over this 12-week period, two methods of activity monitoring were investigated. *Overhead Video-Based Motion Tracking*: A GoPro HERO4 camera recording in SuperView mode was mounted to the barn ceiling to capture live images of the entire pen. Video was recorded for 1 hour per day when humans were not present to capture unprovoked activity. Motion was tracked for one goat in MATLAB using the DLTdv5 texture tracking program[4], which tracks a manually selected monochromatic texture region of interest—in this case the goat's body (Figure 1A). The center of this region for each video frame was then output to Excel as x-y coordinates mapped to the resolution of the video. Frames were grouped into 1-second increments, and the average x-y position was rounded to the nearest whole number. The distance formula was used to calculate change in position between each 1-second increment, and these values were summed over the hour-long video to yield total activity. Activity was monitored during 2 pre-operative weeks to establish baseline activity and from 1-12 weeks following induction of disc degeneration.

Daily activity measurements were binned into two-week periods for analysis. Differences between time points were assessed via unpaired Student's *t*-tests compared to pre-op activity. To test for inter-observer reliability of the video tracking software, pre-op videos were tracked by two observers, and the activity levels were compared via unpaired Student's *t*-test. *Step-Count Quantification using a Custom Wearable Device*: Step count was also measured on a daily basis in a separate goat to characterize activity. A custom built wearable device[5] consisting of a sensor board with gyroscope, accelerometer, and magnetometer; microcontroller; radio; data logger; and lithium polymer battery was attached to the right forelimb proximal to the carpus (Figure 1B). A neodymium magnet was attached distal to the carpus. Discrete steps were identified by local maxima in the magnetic field strength, which occurred with carpal flexion during ambulation. Data from the device was uploaded to a computer each day over a period of 4 weeks prior to surgery, and for 12 weeks following surgical induction of disc degeneration. MATLAB was used to count the number of steps in a 30-minute window each day. Prolonged periods of elevated magnetic field strength—indicating that the goat was lying down—were excluded from the analysis. As with the video tracking data, activity was binned into two-week periods for analysis. Differences between time points were assessed via unpaired Student's *t*-tests compared to pre-op activity.

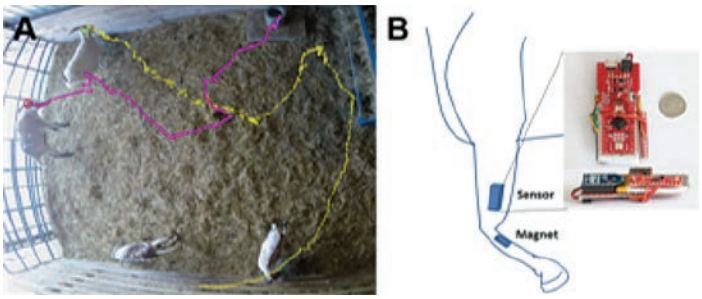

Figure 1. (A) Overhead tracking of goat locomotion from video footage via the DLTdv5MATLAB code. **(B)** Schematic illustrating placement of the custom wearable device on the goat forelimb.

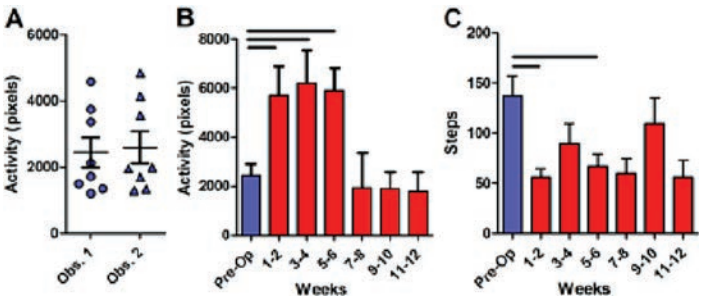

Figure 2. (A) Inter-observer video tracking. **(B)** Video tracking and **(C)** Custom wearable device tracking of daily activity pre-op and 1-12 weeks post-op in two separate goats.

Results

Overhead Video-Based Motion Tracking

No significant difference in pre-op activity level was found between observers (Figure 1A). There was a significant increase ($p < 0.05$) in activity from 1-6 weeks post-operative compared to pre-op baseline, followed by a return to baseline activity from 7-12 weeks post-op (Figure 2B).

Step-Count Quantification using a Custom Wearable Device

A significant reduction ($p < 0.05$) in activity 1-2 and 5-6 weeks post-op was observed compared to the pre-op baseline, with 7-12 weeks post-op also trending towards decreased activity ($p = 0.0614$ at 11-12 weeks) (Figure 2C).

Discussion

We developed two novel, independent methods for quantifying large animal activity in a model of lumbar disc degeneration and demonstrated that both methods are able to detect changes in activity over time. While activity levels differed between the two goats immediately post-surgery, both tracking methods show a long-term trend towards returning to or below baseline. Ongoing work will further validate these methodologies to explore and optimize relationships between disc degeneration and functional parameters in large animals. Concurrently we are assessing biomarker signatures such as serum inflammatory markers and immunohistochemistry for nociceptive nerve fibers. Recently, NIH leaders called for improved transparency and reproducibility in animal models[6,7]. Our activity monitor methodologies described here combined with competent physical examination will offer a platform for improved *in vivo* assessment when using large animal models. Other applications for the wearable device include tracking limb movement during augmentation of orthopedic hardware in fragility fractures or tracking three-dimensional head and neck kinematics in future work involving goats undergoing cervical total disc replacement.

Conclusions

Use of these novel activity monitoring techniques in large animal models of musculoskeletal disease will enhance the clinical relevance of these models by improving scientific rigor and model fidelity resulting in a more predictable translation to human clinical use.

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Sports Tips & Tricks: Technical Evaluation of ACL Graft Dimensions: Staying out of Trouble

Joshua Rozell, MD
Brian Sennett, MD

Background

The anterior cruciate ligament (ACL) is approximately 30mm long and 10mm wide.[1] It consists of two bundles, anteromedial (AM) and posterolateral (PL), which contribute in varying degrees to knee stability.With the knee extended, the PL bundle is tightened and the AM bundle is lax; as the knee is flexed, the AM bundle tightens and the PL bundle relaxes. Consequently, the PL bundle plays an important role in rotational stability in extension. Proximally, the ACL originates from the posteromedial surface of the lateral femoral condyle and inserts distally on the anterior aspect of the tibial plateau.

Today, ACL rupture is usually treated surgically, most commonly in young patients with bone-patellar tendon-bone (BPTB) or hamstring tendon (HT) autograft. While bone to bone healing remains the gold standard in ACL reconstruction, there are several postoperative disadvantages of the BPTB graft, including anterior knee pain, quadriceps weakness, possible patella fracture, patellar tendon rupture, and infrapatellar contracture.[1,2] During the last decade, there has been an increased use of HT grafts due to the lower rate of postoperative morbidity with fewer donor-site complications. While the quadrupled graft has been shown to have a higher load to failure compared with the BPTB,[3] there are also several concerns with the use of HT grafts: failure to achieve immediate rigid fixation to bone (slower than BPTB),[4] lower stiffness compared with the BPTB graft or the native ACL, risk of increased laxity at medium- to long-term follow-up, tunnel widening, weakness of the hamstring musculature with difficulties controlling internal tibial rotation, and reduced strength in deep flexion.

Regardless of graft used, preparing and sizing the graft intraoperatively is a very calculated process. This review provides a basis for the determination of certain graft parameters and illustrates tips for successful outcomes.

Technique

*BPTB **(Figure 1)***

While harvesting the graft, the osteotomy site on the tibia is started 8-10mm above the insertion of the patellar tendon to allow for a functionally shorter graft without compromising

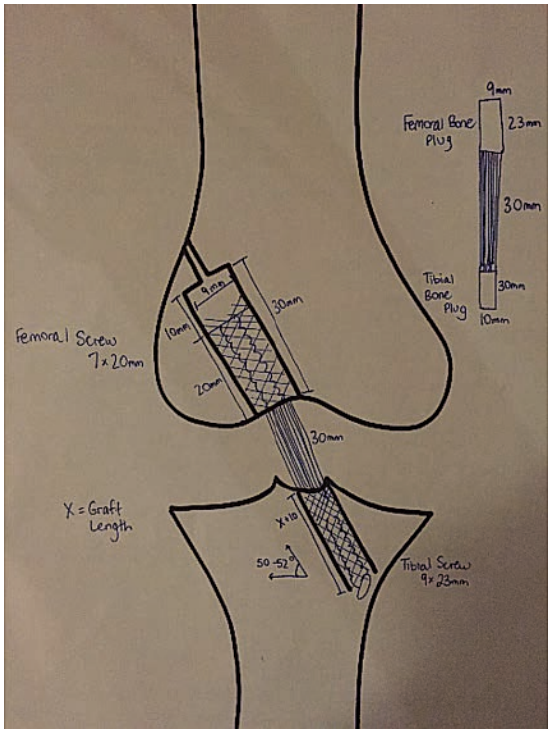

Figure 1. Bone patellar tendon bone graft schematic.

the insertion site on the tubercle. This allows the bone plug to be seated higher in the tunnel (i.e. closer to the joint). In contrast, creating the tibial limb of the osteotomy closer to the tibial tubercle may result in a shearing of the patellar tendon. The tibial tunnel is then drilled. The angle of the tunnel is generally approximately 50-52 degrees and the length of the tunnel is 10mm more than the length of the harvested graft. This ensures that the graft will remain entirely within the tunnel after fixation. The tibial bone plug is sized to 10x30mm. The goal of tibial tunnel fixation is to provide the most stable and robust fixation without protrusion of the plug from the tunnel distally. Once in place, 30mm of graft will be intraarticular and the remaining length of graft will be seated in the tibial tunnel.

The femoral tunnel is reamed to 9mm wide and 30mm long. The length of the tunnel avoids lateral femoral blowout. The femoral bone plug is sized to 9x23mm. When the knee is positioned in flexion on the operative table, the distance from the top of the tibial tunnel to the top of the intercondylar notch is approximately 25mm. As a result of the femoral and tibial tunnels being drilled independently (i.e. non-linear), if the

bone plug is greater than 25mm in length, the plug will be difficult to clear the tunnel and change direction to fit up into the femoral tunnel. The width of the plug corresponds to the amount of bone reamed for the femoral tunnel. Comparing a 9mm to 10mm tunnel, the radius of the tunnel is increased from 4.5mm to 5mm, therefore thinning the size of posterior wall by 0.5mm. This increases the risk of posterolateral condylar blowout and catastrophic graft failure. Once recessed to the appropriate level flush with the medial face of the lateral femoral condyle, the femoral tunnel is notched and tapped prior to insertion of the femoral interference screw (7x20mm).

Hamstring ***(Figure 2)***

After harvesting the hamstring tendons, any remaining muscle attached to the tendons is removed as this does not contribute to the overall tensile strength of the graft. The tendons are folded in half through a suture button (usually 180mm graft harvest results in 90mm quadrupled graft). To calculate the size of the button needed, the length of the femoral tunnel (30mm) is subtracted from the length of the entire femoral condyle (Z). Eight millimeters is then added to this. The 8mm represents the radius of the suture button that is required to be outside the tunnel for the button to flip on itself. Further, [(Z-X)+8] must be left than or equal to the button loop size. Since the buttons are sized in increments of 5mm, if the calculation, for example, yields 16mm, a 20mm button must be used. The graft is trimmed for a 9mm diameter tunnel. Again, 30 of graft remains intraarticular. The graft length remaining in the tibial tunnel plus 10mm is equal to the tibial tunnel length. This helps to account for the obliquity of the tunnel.[5] The graft in the tibial tunnel is whip stitched prior to insertion.

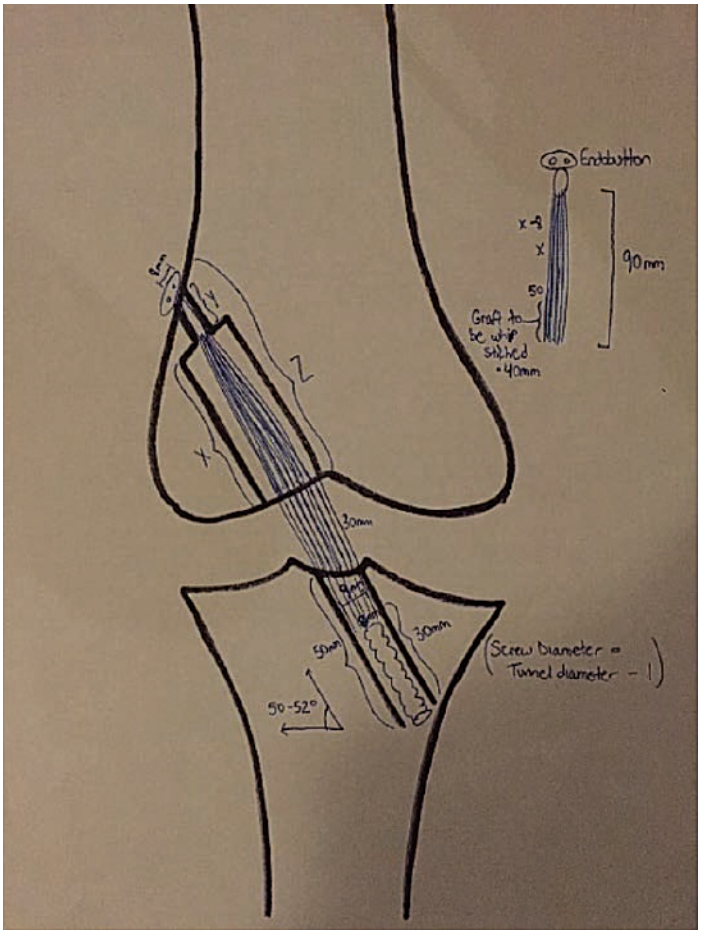

Figure 2. Hamstring graft schematic

Key Principles

Regardless of graft and tunnel preparation techniques, certain overarching principles should be taken into consideration when performing an ACL reconstruction:

Graft Size

Unlike bone-patellar tendon-bone grafts, the diameter of a hamstring autograft is quite variable.[6] In a retrospective analysis of 296 patients undergoing hamstring autograft ACL reconstruction, Park et al. did not observe any failures in patients with graft diameters of 8 mm or greater.[7] Among patients with a graft size of less than 8mm, they noted a revision risk of 5.2%. Similarly, in a retrospective review of 256 patients, Magnussen et al. report that 16 of 18 revision ACL reconstructions occurred in patients with hamstring autografts less than or equal to 8mm in diameter, with a revision risk of 16.4% noted in patients under age 20 among this cohort.[6] Thus, a graft >8mm in a young person portends the best outcome regarding re-rupture rate. Regarding, functional recovery, Mariscalco et al. retrospectively evaluated 263 consecutive patients undergoing hamstring autograft ACL reconstruction. After controlling for age, sex, BMI, graft parameters, and femoral tunnel drilling technique, a 1mm increase in graft size was noted to correlate with higher KOOS scores. Revision was not required in any patient with a graft >8mm in width, but in 18.3% of patients under 18 years old with grafts <8mm.[8]

Certain factors put patients at risk for smaller autografts. These include patient weight less than 50kg, height less than 140cm, body mass index less than 18, and leg circumference less than 37cm.[9] If graft width is not sufficient, there are several alternative options. First, augmentation with allograft is a possibility. This discussion must be undertaken with the patient prior to surgery. Second, the use of a 5-strand graft (3 strands from the longer and more robust semitendinosus and a doubled gracilis) can be employed.[10] Finally, conversion to a BPTB graft is also an option.[11]

Interference Screw Length and Width

Interference screw use is recognized as one of the standard techniques for ACL graft fixation. Initial work by Kurosaka in 1987 followed in 1994 by Kohn and Rose showed in a cadaveric model that using a 9mm interference screw afforded greater stability than using a 7mm screw with a gap size of 1mm. This is especially true on the tibial side.[12,13] With regard to screw length, earlier studies showed that at least a 20mm screw was required to maximize pullout strength. Brown et al. reported

no difference between 20mm and 25mm screws.[14] However, more recent studies, albeit in a porcine model, are beginning to show that there is no significance in displacement, load to failure, and stiffness between interference screws 12.5, 15, or 20mm in length.[15] Further study is required in humans to evaluate these differences and their effects on pullout strength.

Backup Fixation/Bailout

Tibial fixation is the weakest link in ACL reconstruction.[16] Possible reasons for relatively low fixation strength include decreased bone mineral density compared with the tibia or excess graft tension during flexion. In addition, the line of force relative to the tibial tunnel is in line, as opposed to the obliquely oriented femoral tunnel. Repetitive loading may then lead to graft slippage. Therefore, the surgeon should be prepared with multiple backup options should the fixation not prove adequate or if the surgeon believes the ultimate load to failure will be substantially augmented by supplemental fixation. These include tying the graft over a bicortical screw post, using staples, using a suture anchor, or recessing the graft further into the femoral tunnel. In one study evaluating three methods of tibial fixation, namely an interference screw alone, an interference screw backed by a suture anchor, and an interference screw backed by a 4.5mm bicortical screw, ultimate load to failure was substantially increased by adding backup fixation. There was no significant difference in load to failure between the backup fixation groups.[17]

Conclusion

Multiple techniques have been described for ACL reconstruction and there are several factors to consider when deciding upon graft choice, fixation options, and post-operative rehabilitation. Determination of graft size, tunnel size and position, and femoral and tibial fixation options are critical to a successful outcome. An understanding of the technical aspects is critical, but a conceptual grasp of the "why" is perhaps more important.

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U·P·O·J

A Surgeon's Case-Based Guide to the Management of Osteochondritis Dissecans of the Knee in the Pediatric Athlete

Scott LaValva, BS[1,2]
Eileen Storey, BA[1]
James Carey, MD, MPH
Kevin Shea, MD
Eric Wall, MD
Theodore Ganley, MD[1,2]

[1]The Children's Hospital of Philadelphia, Division of Orthopedic Surgery, Philadelphia, PA

[2]Perelman School of Medicine at The University of Pennsylvania Philadelphia, PA

Introduction

Given the lack of clinical studies investigating the comparative effectiveness of osteochondritis dissecans (OCD) treatments, orthopedic surgeons currently utilize different approaches for various types of lesions[1,2]. We present the standard-of-care treatment protocol used at the Children's Hospital of Philadelphia (CHOP), a high-volume center for juvenile OCD cases, as a comprehensive guide for treating common presentations of pediatric knee OCD.

Treatment Approach

Pre-Surgical Characterization of the Lesion

Characterizing the stability of an OCD lesion is critical for guiding non-operative or operative treatment recommendations. The stability of OCD lesions depends upon the mechanical integrity of the affected subchondral bone and the status of the adjacent articular cartilage. In general, a *stable* lesion will be immobile with healthy, intact articular cartilage whereas an *unstable* lesion may be mobile and demonstrate disrupted articular cartilage[3,4]. While arthroscopy is the gold standard for precisely characterizing a lesion, magnetic resonance imaging (MRI) provides useful diagnostic information to guide decision-making in potentially unstable lesions before making an incision[5]. Though multiple radiologic classification systems exist, evidence of distinct fragments, high T2 signal intensity between parent and progeny bone, disruption of the articular cartilage, and the presence of loose bodies on MRI are all accepted criteria for reliably determining stability[6]. Other strong predictors for failed non-operative healing include large lesion size on MRI[7,8] and mechanical symptoms at presentation[8].

Case 1. Stable, Intact Lesion

14 yo male with a 1-year history of diffuse medial-sided pain of the left knee who fell directly onto the anterior aspect of both knees during a basketball game 1 month ago. Since that fall he has experienced increased anteromedial knee pain. He was seen by his primary care physician who ordered radiographs and an MRI.

Stable lesions limited to the subchondral bone with intact articular cartilage are most common in pediatric patients[9]. Since stable lesions in patients with open physes tend to have a relatively high potential for healing[7], an initial trial of non-operative treatment is recommended. For an isolated intact lesion, the non-operative protocol includes a hinged knee brace locked in extension for 6 weeks followed by 6 weeks of no bracing but continued activity modification, including no high-impact running or jumping. After a 3-month trial of non-operative treatment, the patient receives a follow-up MRI to evaluate for signs of healing, which include re-ossification, disappearance of the radiolucent

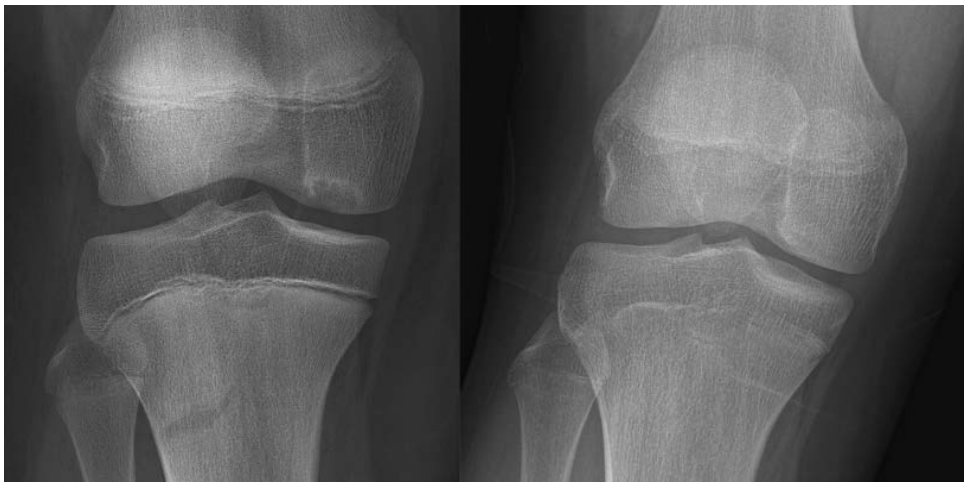

Figure 1. A comparison of pre-operative and 2-year post-operative radiographs show healing of a stable OCD lesion with intact cartilage on the lateral aspect of the medial femoral condyle (MFC).

zone, resolution of the sclerotic rim, radiographic union of the lesion, resolution of the lesion, and resolution of radiolucent demarcation[10]. If radiographic signs of some but not complete healing are present, a second 3-month trial of non-operative treatment, including 6 weeks of bracing and 6 weeks of continued activity modification, is recommended. Indications for operative management at 3-months follow-up include no evidence of healing or a worsening lesion on radiographs in a patient with closed/closing epiphyseal plates.

The standard operative procedure for stable, intact lesions is knee arthroscopy with multiple drilling through the progeny bone and into the parent bone in an effort to recruit marrow elements and evoke a healing response[11]. Transarticular and retroarticular drilling with a Kirschner wire have demonstrated similar efficacy in the treatment of these lesions[12,13]. While transarticular drilling has historically been performed more frequently at CHOP, retroarticular drilling may be valuable, especially for posterior lesions. Key technical recommendations for transarticular drilling include the use of a variety of knee flexion angles or accessory portals to maintain a perpendicular angle between the portals and articular cartilage. For retroarticular drilling, the use of a C-arm and a small parallel guide to ensure accurate pin placement is recommended. The surgeon should place a single pin at the center of the lesion and use the parallel guide to place adjacent pins.

Case 2. Unstable, Salvageable Lesion

12-year-old female presents with right knee pain that began 1-2 months ago. She has tenderness over the medial femoral condyle and decreased range of motion with no locking or giving way. Symptoms are made worse by activity.

While an initial non-operative trial is indicated for a stable, intact knee OCD lesion, radiographic evidence of an unstable lesion implies low healing potential regardless of patient age and thus typically warrants operative management without a non-operative trial. Though the specific operative technique may vary depending on the state of the lesion, unstable but salvageable lesions typically undergo surgical arthroscopy with internal screw fixation of any hinged portion[4]. During arthroscopy, the surgeon can evaluate for the amount of subchondral bone. We typically opt for fixation with a headless metal reverse threaded compression screw if sufficient subchondral bone is visualized on imaging or flathead screws when there is trace subchondral bone present. Members of the Research in Osteochondritis Dissecans of the Knee (ROCK) multicenter study group have provided a detailed overview of each of the common surgical techniques for internal fixation of hinged lesions[4]. In the case that fibrous tissue is discovered at the base of the lesion, the tissue should be curetted and a stable rim should be prepared such that the void can be filled with a local bone graft from the proximal tibia[14].

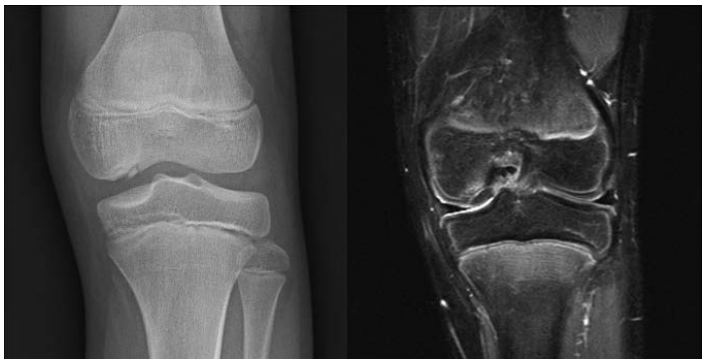

Figure 2. Pre-operative radiograph and MRI show unstable OCD lesion on the lateral aspect of the MFC requiring fixation.

Case 3. Unstable, Unsalvageable Lesion

16-year-old male basketball player who presents for follow-up for bilateral knee pain. He was last seen two years prior for left greater than right knee pain. His pain does not prevent him from participating in his activities, but he does have decreased ROM and intermittent buckling and swelling of the left knee when playing basketball.

While primary fixation is the most viable option for unstable, salvageable OCD lesions in the knee, other surgical options should be explored if the lesion has produced multiple fragments, the articular cartilage is excessively damaged, or there is a mismatch defect between the progeny and site of origin[15].

Surgical techniques often vary based on the size of the unsalvageable lesion. For small defects ($\sim$1cm^2), we typically opt for marrow stimulation via surgical arthroscopy to produce replacement fibrocartilage, including abrasion arthroplasty, drilling, or microfracture[15]. For intermediate defects ($\sim$1-2cm^2), we typically use osteochondral autograft. For larger unsalvageable defects ($>$2cm^2), we typically opt for either autologous chondrocyte implantation (ACI) or osteochondral allograft. To ensure the best possible outcome for osteochondral allograft, the surgeon should precisely log the size of the lesion and send advanced imaging studies to precisely match the graft to the patient's knee.

Conclusion

Although there is limited consensus in the literature for the optimal management of knee OCD, this multi-case report provides an overview of the current treatment practices at a high-volume center treating knee OCD for the various type of lesions both young and experienced surgeons may encounter in their practice.

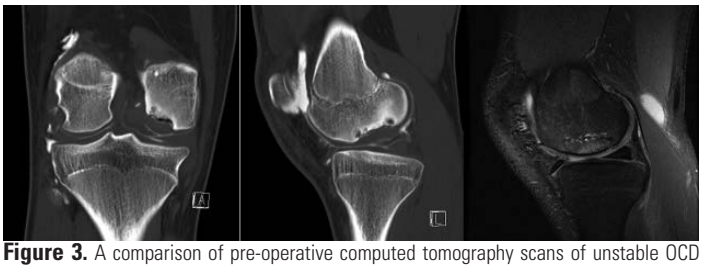

Figure 3. A comparison of pre-operative computed tomography scans of unstable OCD lesion showing a breach in the articular cartilage on the lateral aspect of the MFC and post-operative MRI after osteochondral allograft.

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Anterior Cruciate Ligament Reconstruction in the Adolescent: A Hybrid Approach to Physeal-respecting Autograft Reconstruction

R. Justin Mistovich, MD[1]
Rushyuan Jay Lee, MD[2]
Eileen Storey, BA[3]
Theodore Ganley, MD[3,4]

[1]Case Western Reserve University
Division of Orthopedic Surgery
Cleveland, OH

[2]Johns Hopkins University
Division of Orthopedic Surgery
Baltimore, MD

[3]The Children's Hospital of Philadelphia
Division of Orthopedic Surgery
Philadelphia, PA

[4]Perelman School of Medicine at The
University of Pennsylvania
Philadelphia, PA

Introduction

The incidence of anterior cruciate ligament (ACL) injuries in the pediatric and adolescent population continues to increase.[1] The literature supports earlier surgical intervention since nonoperative management is associated with chondral and meniscal damage.[2,3] While patients with wide-open physes who have more than two years of growth remaining benefit from physeal-avoiding techniques, patients approaching skeletal maturity may be addressed with a technically simpler hybrid reconstruction. We describe a technique that utilizes a femoral physeal-avoiding tunnel and a physeal-respecting tibial tunnel while still allowing use of a five-strand, larger diameter hamstring graft to stabilize the knee.

Background

Patients approaching skeletal maturity can be addressed with a hybrid technique that is technically simpler than complete physeal-sparing techniques. The hybrid ACL reconstruction consists of placing a physeal-sparing femoral tunnel and physeal-respecting tibial tunnel. Unlike the femoral tunnel, the tibial tunnel is drilled across the tibial physis and a soft tissue graft is placed across the physis with fixation distal to the physis. Surgeons must adhere to fundamental principles to minimize the risk of physeal damage, improve technical reproducibility, and fully utilize the autograft tissue available to maximize graft diameter. The overall goal of the hybrid reconstruction is to reconstruct the pediatric knee using autograft tissue with minimally invasive methods. These methods allow for both unrestricted growth and knee stability, a return to healthy fitness, and optimal outcomes.

Preoperative Evaluations and Indications

Before ACL reconstruction, a determination of skeletal maturity will guide the surgeon to choose the appropriate technique. On average, male adolescents cease lower extremity growth between ages 15 and 16, while females cease lower-extremity growth between ages 13 and 14.[4] The tibial physis begins to close in a central location and closes earlier than the femoral physis. In cases where skeletal age is ambiguous, a single anteroposterior radiograph of the left hand can determine maturity based on the Greulich and Pyle atlas.[5]

For a hybrid physeal-sparing or respecting approach to be indicated, one should note a tibial physis that demonstrates early evidence of approaching skeletal maturity, including physeal narrowing, central closure of the tibia, and increasing sclerosis about the physis.[6] These findings correlate to approximately two or fewer years of remaining lower extremity growth. If a greater amount of growth remains, a physeal-sparing surgery is indicated. Conversely, adolescents who are skeletally mature can be approached with the standard adult technique, though the five-strand autograft described may still be of benefit to minimize graft failure in these patients.

Procedure

For the adolescent approaching skeletal maturity, this technique uses a five-strand hamstring autograft hybrid reconstruction utilizing both an all-epiphyseal, physeal-avoiding femoral tunnel, and a physeal-respecting tibial tunnel with interference screw fixation supplemented with low-profile backup fixation.

Graft Preparation

The 5-strand hamstring autograft consists of a tripled semitendinosus and a doubled gracilis.[7] After the hamstring autograft is harvested and care is taken to maximize tendon length, the tendons are placed on the graft preparation table to assess the feasibility of obtaining a final graft length of 8 to 9 centimeters (cm) after folding. For the tripled semitendinosus, the folds are marked out on the tendon approximately 8, 16, and 24 cm from the end in order to ensure a folded length of 8 cm. An additional 1.5 cm is also marked for securing the tripled end. The gracilis is prepared similarly to ensure that it has a folded length matching that of the semitendinosus. Both the semitendinosus and gracilis are whipstitched using high strength non-resorbable sutures (Fiberloop, Arthrex,

Naples, FL). Femoral fixation is prepared using the TightRope RT (Arthrex, Naples, FL).

A 5-strand hamstring autograft utilizing both a tripled semitendinosus and a doubled gracilis allows for a larger diameter graft to overcome the biomechanical limitations of a smaller graft common in younger patients (Figure 1).[7] While a larger graft size will impart stronger biomechanical properties, a larger tunnel crossing the physis also presents a slightly increased risk of physeal arrest. Therefore, to minimize tunnel size without compromising graft diameter, graft ends are kept under compression using two, graft sizer blocks or graft tubes. This prevents the graft from swelling at the ends, thus minimizing tunnel size and potential physeal damage.[8] The femoral and tibial graft ends are sized independently for appropriate tunnel diameter. The graft is moistened with a gentamycin and saline solution to lower the risk of bacterial seeding.[9]

Preparing the Femoral Tunnel

When the patient is being prepared for surgery, both the lateral femoral condyle and the center of the condyle are outlined with a marking pen. To avoid the lateral collateral ligament, the starting point for drilling the femoral tunnel is anterior to the midline. Keeping the trajectory below and parallel to the physis in the coronal plane helps to maximize tunnel size while maintaining an all-epiphyseal position (Figure 2).

When debriding the residual ACL stump, a small portion of the native ACL fibers are left intact. This allows for ingrowth of the graft as well as a landmark for tunnel drilling.[10,11] The ACL guide is centered at the native femoral stump and the tunnel is directed to the proper area of the femoral condylar ring. Once the insertion point for the guide pin is determined, a small incision is made sharply through the iliotibial (IT) band. This will function as the trans-IT band endoscopic portal to later confirm that the button is resting securely on the lateral

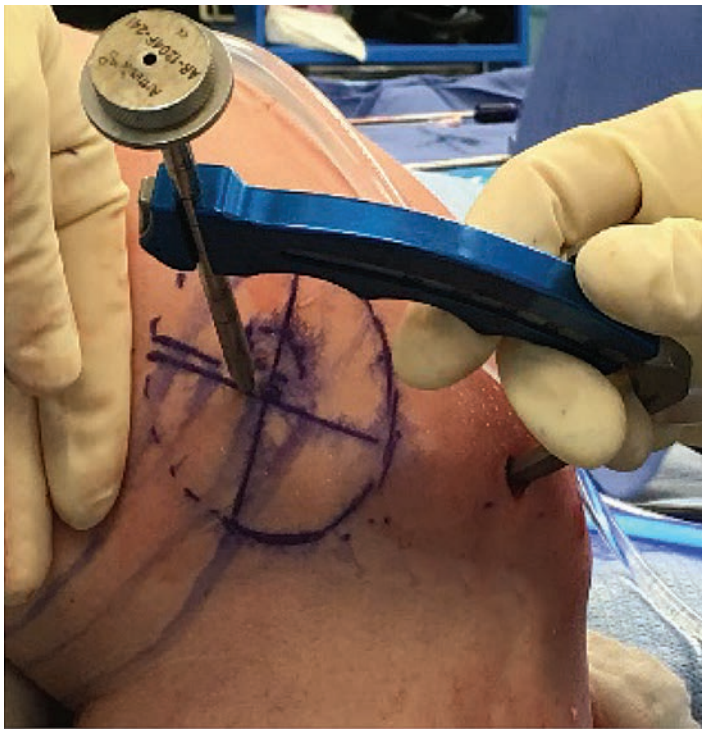

Figure 2. Intraoperative photograph of the outlined lateral femoral condyle to mark tunnel trajectory and the appropriate alignment of the femoral guide for tunnel drilling.

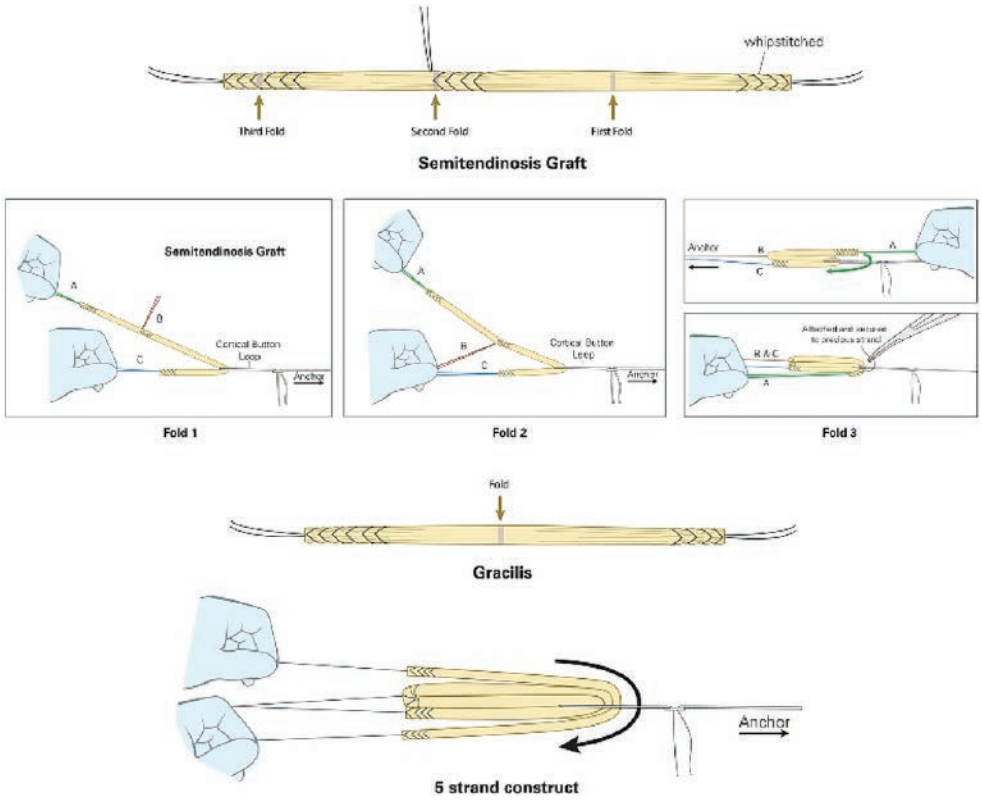

Figure 1. Illustration demonstrating measurements and technique for preparation of the five-strand hamstring autograft. *(Acknowledgement: Michael Mustar, medical illustrator, Case Western Reserve University).*

femoral cortex.[12] To maintain an all-epiphyseal position, the tunnel is typically drilled at an angle between 90-100°. A FlipCutter (Arthrex, Naples, FL) can be used to drill this angle.

Preparing the Tibial Tunnel

Since the proximal tibial physis ceases growth earlier than the femoral epiphysis and contributes significantly less to overall growth, the tibial tunnel can be prepared with a physeal-respecting rather than physeal-sparing approach.

As initial arthroscopy is performed, a small portion of the residual ACL is left at the tibial insertion to promote ingrowth of the graft as well as to provide an anatomic landmark for graft placement. An ACL guide is inserted into the anteromedial portal and centered over the native ACL stump. To minimize physeal damage, set the tunnel to be drilled at an angle of 60-70°. A guide pin is first inserted using the tibial guide, and the tunnel is drilled with a standard reamer based on the measured size of the tibial side of the prepared graft.

Measuring Interference Screw Length

The arthroscope is inserted through the tibial tunnel in a retrograde fashion to visualize the physis. If the physis is open and present, a small ruler is inserted to measure the distance from the distal aspect of the tunnel to the physis. The length of the interference screw should be just short of the physis as recent studies have demonstrated that screw fixation across the physis will cause a temporary growth arrest.[13]

Passing the Graft

Under arthroscopic visualization, the graft is advanced slowly to the point where the button is about to exit the guide pin hole. The button is flipped under arthroscopic visualization and gentle tension is maintained on the graft. Confirmation of the position of the button is performed by inserting the arthroscope through the incision at the distal lateral femur. This has previously been described as the trans-IT band endoscopic portal.[12] The suture limbs are followed with the arthroscope to find the button and ensure that it is resting flush of the femoral cortex and fully flipped (Figure 3). A small probe may be inserted through the endoscopic portal to gently maneuver the button if necessary. Short, quick bursts of fluid will allow for clear visualization.

The graft is fully advanced into the femoral tunnel. The knee is cycled while the graft is under tension. The appropriately sized tibial interference screw is inserted so its length remains short of physis. The authors use a bioabsorbable screw with bone ingrowth properties (Delta screw, Arthrex, Naples Fl).

Backup fixation

Two arthroscopic anchors are used to augment the distal tibial fixation (PushLock, Arthrex, Naples, FL). Two drill holes are created lateral to the medial collateral ligament (MCL) and distal to the tibial tunnel with a standard arthroscopic technique. Suture limbs from the ACL graft are then fed through the anchor and secured, allowing for low profile supplemental fixation while respecting the physis.[14]

Figure 3. Intraoperative photograph showing the arthroscope in the trans-IT band portal and visualization of the button fully flipped and resting on the lateral femoral cortex.

Postoperative Protocol

The post-operative rehabilitation protocol consists of a controlled progression of activity focused on returning athletes to full competitive return to play at 9 months. The rehabilitation protocol provides patients with early return to motion, endurance, and a graduated strengthening program. The protocol also incorporates a proprioceptive,

neuromuscular training program involving multiple hop tests that teaches injury prevention strategies for both lower extremities to prevent future knee injuries upon return to sports.

Discussion

Pediatric and adolescent ACL injuries continue to occur at an increasing rate. Based on the risk of further injury, operative reconstruction has typically been indicated for individuals planning to return to sports. While individuals who have greater than two years of growth remaining require specialized procedures, we describe a physeal-respecting hybrid approach that allows for autograft reconstruction with a five-strand hamstring graft in adolescents with fewer than two years of growth remaining. Using an all-epiphyseal femoral tunnel and a physeal-respecting approach to the tibia with graft fixation distal to the physis, this technique respects the remaining growth of pediatric patients while also stabilizing the affected knee.

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ACL Reconstruction in Children Using Growth Plate Sparing Techniques

Christopher DeFrancesco, BS[1]
Andrew Gambone, MD[1]
Theodore Ganley, MD[1]

[1]Children's Hospital of Philadelphia
Division of Orthopaedics

Background

Although previously considered rare in the pediatric population, recent work has found that 1-3.4% of children presenting for management of a knee injury are diagnosed with an ACL rupture.[1] In fact, the incidence of ACL rupture in pediatric patients has increased substantially.[2-4] With over 100,000 reconstructions annually in the United States[4] and a significant proportion attributable to children and adolescents, effective management of ACL ruptures in the skeletally immature is an important topic. Surgical techniques to address ACL insufficiency in these patients include primary repair, extra-articular tenodesis, transphyseal reconstruction, partial transphyseal reconstruction, and physeal-sparing reconstruction

Considering Physeal-Sparing Reconstruction

When ACL reconstruction is considered in a pediatric patient, the surgeon must decide if a physeal-sparing method is appropriate. This decision is based upon the patient's skeletal development and anatomic constraints. While patients nearing skeletal maturity may be managed with transphyseal techniques (as indicated in Figure 1), patients with substantial growth remaining (>2 years until skeletal maturity) may be good candidates for physeal-sparing techniques.

Choosing the Right Physeal-Sparing Approach

After choosing physeal-sparing ACL reconstruction, one must decide upon the most appropriate method. Several techniques are described in the literature, but there are two main approaches: the extraphyseal Iliotibial Band Reconstruction (ITBR) and All-Epiphyseal Reconstructions (AERs). While the ITBR uses no bone drilling, AERs use horizontal-oblique bone tunnels or sockets placed wholly within the epiphyses without crossing adjacent growth plates. Each approach has its own risks and benefits.

Although the ITBR is appropriate for any patient with open growth plates and significant growth remaining (Figure 1), we use it most commonly for prepubescent (Tanner Stage 1-2) children with a great amount of skeletal growth remaining. These patients generally have a small amount of epiphyseal bone stock, precluding all-epiphyseal tunnel placement. We use all-epiphyseal reconstruction in prepubescent and pubescent adolescents who have >2 years of skeletal growth and several inches of height growth remaining. Several variables, including provider experience, influence the decision to perform one procedure rather than the other in an adolescent patient where either is reasonable. In patients with less than two years of skeletal growth remaining, we prefer transphyseal reconstruction with care to only place soft tissue (no bone or screw) at the level of the growth plate.

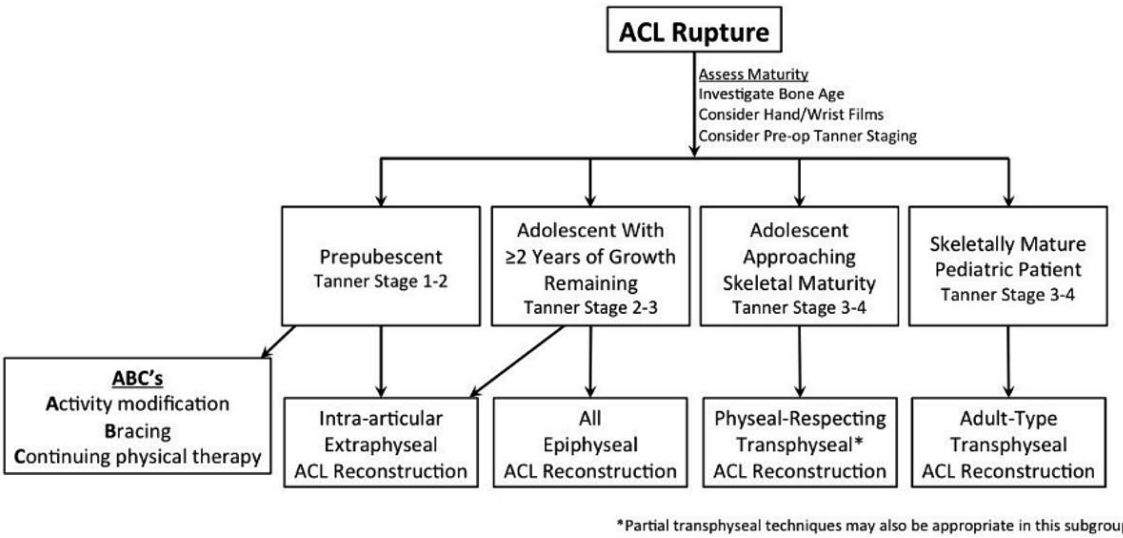

Figure 1. Algorithm for the treatment of ACL tears in pediatric patients. The lower panel illustrates which techniques are appropriate based upon the patient's developmental status.

Physeal-Sparing Surgical Techniques

Iliotibial Band Reconstruction (ITBR)

The combined intra-articular and extra-articular ACL reconstruction using auto genous iliotibial band graft is a tunnel-free reconstruction.[5,6] In this procedure, a mid-substance slip of the iliotibial ban d (ITB) is brought through the "over-the-top" position around the lateral femoral condyle and then through the "over-the-front" position under the intermeniscal ligament to form a new ACL (Figure 2). This non-anatomic reconstruction provides satisfactory knee stability, with the extra-articular portion of the ITB graft providing extra rotational joint stability.[7]

Surgical Technique

1. Examination Under Anesthesia and Diagnostic Arthroscopy

The patient is prepped and draped in the supine position with a tourniquet in place and the lateral thigh generously exposed. It is useful to map anatomic landmarks using a skin marker (Figure 3A-B). After anesthetic induction, an examination is performed to confirm ACL insufficiency. A diagnostic arthroscopy through standard anteromedial and anterolateral portals is performed. The ACL stumps are debrided and meniscal pathology is addressed.

2. Lateral Incision

Next, a longitudinal incision is made over the lateral aspect of the distal thigh, centered over the ITB, beginning at the joint line, and extending proximally 6-8 cm (Figure 3C). The underlying ITB is exposed and a periosteal elevator is used to separate it from the subcutaneous tissues, extending proximal to the skin incision for about 10 cm to free the entire length of the future graft. The ITB's anterior and posterior extents are identified and may be marked (Figure 3D).

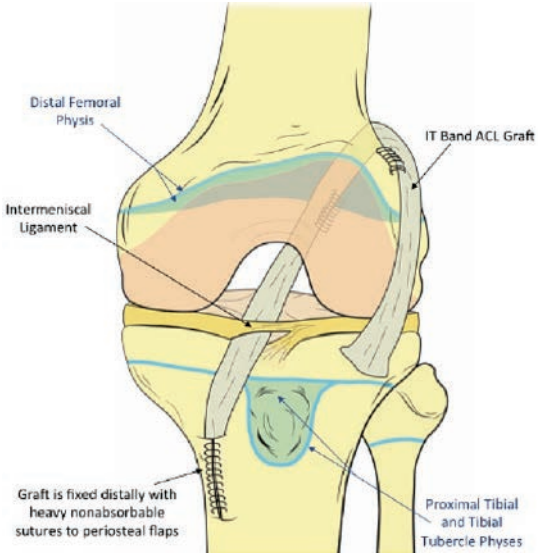

Figure 2. Schematic drawing of the IT band reconstruction technique demonstrating the use of the mid-substance slip of the IT band looped posterolaterally over the lateral femoral condyle, through the joint, and under the intermeniscal ligament to form a new ACL.

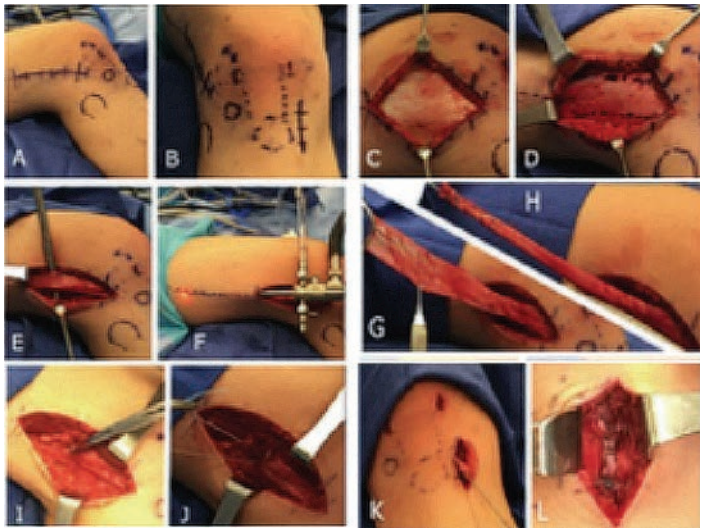

Figure 3. (A-B) Right knee prior to ITBR with anatomic landmarks. **(C-D)** Exposure and identification of the ITB. **(E-F)** Division of the ITB. **(G-H)** Preparation of the ITB graft. **(I-J)** After the graft has been pulled through the joint, it is sutured into the femoral periosteum at the insertion of the intermuscular septum. The graft lies in the "over-the-top" position. **(K-L)** The graft is fixed distally in a metaphyseal trough and sutured to the adjacent periosteum.

3. Prepping the ITB Graft

Parallel anterior and posterior longitudinal incisions are made at the distal ITB to mobilize a central slip of the tendon (Figure 3E). This should constitute 2/3 or more of the ITB's width. Dissection is carried distally to free the slip from the joint capsule and patellar retinaculum. Care must be taken to leave the graft attached to Gerdy's Tubercle. Proximally, the ITB divisions are extended beyond the skin incision using curved meniscotomes. Visualization can be improved using the arthroscope under the subcutaneous flap (Figure 3F). The ITB slip is freed at its proximal end through either the existing incision or a separate 1 to 2 cm counter incision on the lateral thigh. The proximal ITB slip is whip stitched with heavy nonabsorbable suture (Figures 3G-H). At this point, the free slip should measure 15-20 cm (varying with patient size). Suture ends should be cut and left long as tags to assist in graft passing.

4. Initial Passing of the ITB Graft

A curved Kelly-type clamp is extended through the anteromedial portal, through the joint, between the femoral condyles, carefully out through the capsule in a high posterior position, and into the lateral operative field. Arthroscopic viewing through the anterolateral portal can be of assistance in this step. Care should be taken to avoid damaging the perichondral ring when dissecting posteriorly. The ITB graft suture tags are secured with the clamp and carefully pulled out through the anteromedial portal. The clamp is disengaged, leaving the suture tags partially in the joint.

5. Anteromedial Tibial Incision and Final Graft Passing

A longitudinal skin incision of approximately 3 to 4 cm is made at the anteromedial tibia near the pes anserinus.

Dissection here is carried to the periosteum. A rasp may be placed through the incision and used to create a shallow groove in the tibial epiphysis posterior to the intermeniscal ligament. The clamp is then extended through the incision, under the intermeniscal ligament, and into the joint where it is used to secure the suture tags and guide the graft out through the tibial incision. As the graft is pulled into place, it assumes an "over-the-top" position around the lateral femoral condyle (Figure 3I) and an "over-the-front" position as it passes over the anterior tibia under the intermeniscal ligament.

6. Femoral Fixation

The leg is placed in 90° of flexion without lower leg rotation. With slack removed from the graft, mattress sutures are placed to secure its extra-articular portion to the periosteum on the posterior femur where the intermuscular septum attaches (Figure 3J).

7. Tibial Fixation and Closure

At the anteromedial operative site, the periosteum is incised in-line with the skin incision distal to the physis for approximately 3 cm. Some surgeons carry out this step under fluoroscopy to avoid injuring the growth plate. A shallow metaphyseal trough is made beneath the periosteal incision. With the knee in 20° of flexion and the graft extending into the medial tibial operative site, the free end of the graft is trimmed, tensioned, and seated into the trough (Figure 3K). Mattress sutures are used to secure the graft to the adjacent periosteum (Figure 3L). The knee is gently ranged, and skin incisions are closed.

8. Postoperative Management

The patient is initially restricted to 0-90° of knee flexion. They use crutches and are maintained in a hinged knee brace locked in extension for ambulation. Continuous passive motion can be useful in the early postoperative period. The patient is allowed to toe-touch weight-bear. After 2 weeks, full range-of-motion is allowed. At 6 weeks, the knee brace can be removed, and the patient enters a rehabilitation program.

All-Epiphyseal Reconstruction with All-Inside technique

AERs make use of horizontal-oblique tunnels that do not cross physes (Figure 4). The use of low-dose intraoperative fluoroscopy is recommended to ensure all-epiphyseal tunnel placement. Although 8-strand hamstrings autograft is preferred by the senior author, other graft types are used in various circumstances. Graft fixation can be achieved through a variety of approaches. All-epiphyseal cortical button fixation will be discussed here, but alternatives include interference screws and post constructs.

Surgical Technique

1. Examination Under Anesthesia and Diagnostic Arthroscopy

The patient is prepped and draped in the supine position, and an examination under anesthesia is performed. The senior author prefers to outline the lateral femoral condyle using a skin marker as seen in Figure 5A. The resulting circle is bisected into four quadrants, with proper femoral guide placement lying just anterior to the center of the circle. A diagnostic arthroscopy is performed, meniscus tears are addressed, and the ACL footprints are debrided. The graft is acquired, prepared, and placed on looped button constructs under tension using a graft board.

2. Femoral Gui de Placement

A pediatric-specific femoral targeting guide is set to 95° and placed at the femoral ACL footprint. Then, a 1-2 cm incision is made slightly anterior and distal to the lateral femoral epicondyle and dissection is carried to the periosteum. Using the g uide, a pin is placed through the incision, lateral to m edial, completely within the distal femoral epiphysis. The plac ement of the pin is checked via fluoroscopy to ensure that it avoids the undulating distal femoral physis.

3. Tibial Guide Placement

Another targeting guide is set to 25-35° and placed at the tibial ACL footprint. A small anteromedial tibial incision is placed 1-2 cm medial to the tibial tubercle and carried to the periosteum of the proximal tibial epiphysis. Using the guide, a pin is placed through the tibial incision extending to the tibial ACL footprint. Care is taken to ensure that the pin does not violate the physis. Fluoroscopy is again used to confirm proper pin placement.

4. Drilling

Because ACL graft diameter drops with tensioning,[8] post-tensioning graft diameter is measured, and retro drilling tools are accordingly selected. The femoral retrodrill sleeve

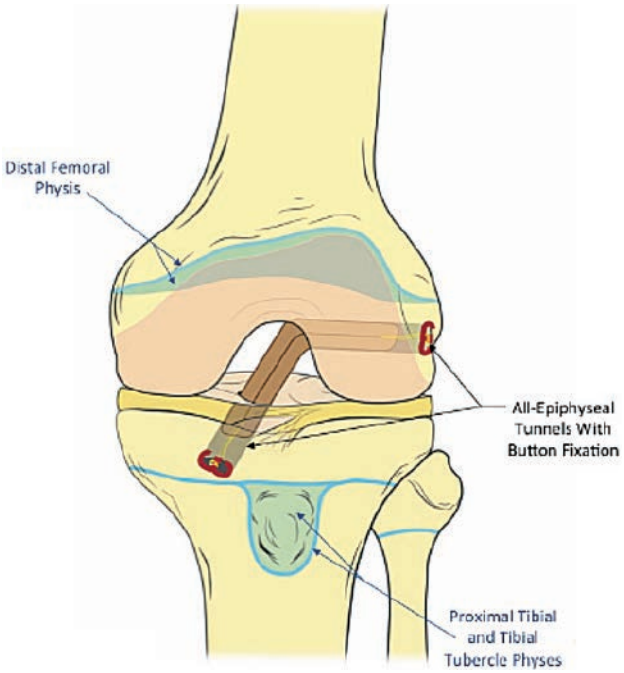

Figure 4. Schematic of an all-epiphyseal reconstruction with cortical button fixation

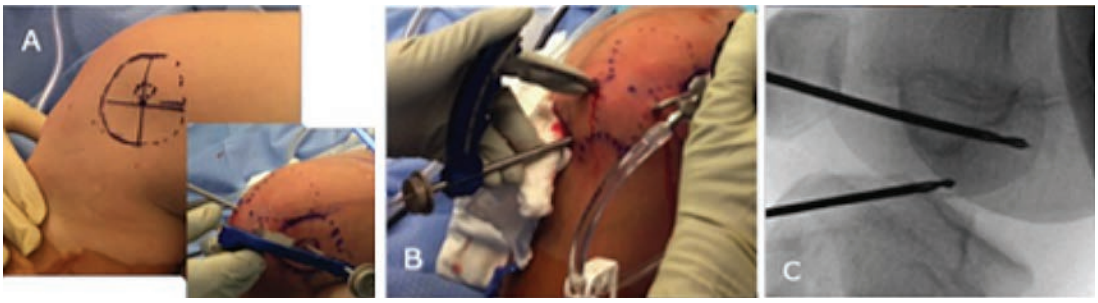

Figure 5. A left knee undergoing all-epiphyseal reconstruction. **(A)** The femoral guide is placed and the femoral guide pin is driven into the proximal ACL footprint. **(B)** The tibial guide is placed and another guide pin is driven into the distal footprint. **(C)** Intraoperative fluoroscopy or CT-scan confirms the epiphyseal placement of the guide pins.

is malleted over the guide pin to a depth-stop of 7-10 mm, and the pin is removed. The appropriate retrodrill is advanced through the sleeve into the joint, deployed, and used to drill a socket of approximately 20-25 mm in length in a retrograde fashion. The position of the retrodrill sleeve ensures that an adequate cortical wall is left intact. Tibial drilling is performed in an analogous fashion to form a socket of approximately 15-20 mm in length. The retrodrill sheaths are carefully removed. Arthroscopy can be used to evaluate the sockets and confirm their all-epiphyseal positioning.

5. Graft Shuttling, Fixation, and Closure

High-strength suture loops (shuttle sutures) are advanced through the guide pin holes. The graft (with attached sutures and femoral cortical button) is placed through the anteromedial portal into the joint. Using the shuttle sutures, the femoral side of the graft is pulled into the femoral tunnel. The femoral cortical button is advanced beyond the femoral cortical bone and flipped to rest on the lateral cortical bone of the distal femur. The tibial shuttle sutures are then used to retrieve the distal graft suture tags through the tibial pin hole. The knee is placed in full extension, and the tibial button is added to the exposed graft sutures. The construct is appropriately tensioned until there is no pathologic laxity in the knee. The tibial suture loop is tied to fix the graft length, and the tibial cortical button is flipped to engage cortical bone. The knee is ranged and checked for stability. The graft is evaluated arthroscopically before incisions are closed.

6. Postoperative Management

Continuous passive motion is used for 3 weeks postoperatively. For ambulation in the first 4 weeks, the patient wears a hinged knee brace locked in full extension and is restricted to toe-touch weight bearing. Physical therapy begins on post-operative day 5. Return to sport is allowed when strength and functional testing for the affected limb is equal to that of the contralateral limb—generally around 9 months postoperatively.

Conclusion

Physeal-sparing ACL reconstruction includes a varied set of operative techniques. The iliotibial band ACL reconstruction is non-anatomic and avoids physeal injury by having no bony tunnels or sockets. All-epiphyseal ACL reconstructions avoid physeal injury by placing bony tunnels wholly within the epiphyses. Both types of ACL reconstruction can provide preadolescent and adolescent children with stable knees, allowing them to participate in healthy fitness activities.

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Trauma Tips & Tricks: Peroneal Nerve Palsy Part II

Tyler Morris, MD
Keith Baldwin, MD, MPH, MSPT

Non-Operative Treatment

The goal of non-operative treatment of peroneal nerve palsy is to provide an ankle position in swing that is compatible with heel-toe gait, that reproduces the first and second rocker to the extent necessary to provide deceleration of the forefoot during early stance to prevent a "foot slap". Additionally, because the ankle everters are also paralyzed, a successful intervention should provide sufficient ankle stability to prevent inversion ankle injuries and sufficiently control the tendancy of the hindfoot to tilt into varus when it is loaded. Finally, non-operative treatment should prevent contracture of the triceps surae, as they are un-checked by denervated pre-tibial muscles.

As such, non-operative therapy will consist of a stretching program of the triceps surae, and an ankle foot orthosis (AFO). For the stretching program, we recommend daily stretching (5 times 30 seconds) of both the gastrocnemius and soleus muscles. For an orthosis, we generally utilize a low resistance carbon fiber AFO which allows some deformation into plantarflexion, but has sufficient elastic recoil which allows the foot to spring back into neutral dorsi/plantarflexion. This brace treatment depends on the stretching program to prevent contracture formation which postitions the foot in equinus. Occasionally, patients will find this brace to be too flexible to sufficiently control the tendancy of the foot to invert. If this is the case, either a brace with a more rigid material, or high top shoes or boots is recommended.

Many patients with peroneal nerve palsy are quite pleased with non-operative therapy. It is our practice to treat this set of patients as such indefinitely assuming the process is not due to a reversible process in which delay would compromise viability of the nerve.

Surgical treatment

Surgical treatment of peroneal nerve palsy consists of four basic types of operations: 1. Nerve decompression, 2. Nerve reconstruction, 3. Tendon transfers, and 4. Ankle fusion. The choice of an operation will depend on the duration of the injury, the type of pathology involved, the patient's lifestyle, and other factors.

Nerve Decompression

Nerve decompression is possible when the nerve palsy is early in the course of pathology, assuming the mechanism of injury is compressive. If a compressive lesion (tumor, hematoma, or surgically induced swelling) has occurred, and the process is relatively new, it can be postulated that the clinical symptoms are due to a compression neuropraxia. If a compression neuropraxia is suspected, then treatment should not be delayed. The nerve should be decompressed; the most common site of compression is as the nerve courses around the fibular neck. However, intra operative EMG/nerve stimulation should be utilized to determine the site of compression and decompress the nerve proximal to this.

Nerve reconstruction

Nerve reconstruction is favored as a next possible procedure if EMG studies at 3-6 months show no recovery. Stretch neuropraxias from knee dislocations, or arthroplasty may be generated. In these cases, no specific compression may be present. Intraoperative EMG and nerve conduction studies may be performed. If action potentials are noted across the nerve, and the nerve is continuous, decompression alone may be performed[4]. In cases in which the nerve is non-conducting, but continuous the decision is more complex. The nerve may either be decompressed and observed, or resected and cable grafted. If cable grafting is selected, most often a sural nerve graft is selected. Recovery rate is strongly associated with graft length. A large series showed poor outcomes with less than 50% recovery rate with grafts longer than 6 cm[4,5]. If the nerve is lacerated or discontinuous, the decision becomes simpler, the injured nerve ends are excised, and the nerve then cable grafted with a sural nerve autograft and nerve tube conduit.

Nerve reconstruction if successful offers a patient the greatest chance of an anatomically normal or near normal result with minimal residua (ankle numbness resultant from sural nerve harvest). However, for many pathologies in which the mechanism of injury is stretch, grafting is less successful owing to the large zone of injury.

Tendon transfers

Tendon transfers are a salvage procedure available to patients in whom decompression is not ideal due to the pathology involved in their injury, and nerve grafting is either not compatible with success due to the mechanism of injury or the duration of symptoms (ie the effector muscles are too atrophied to work even if they had a nerve supply). Many tendon transfers have been described for peroneal nerve palsy. All transfers use the "back to front" idea of transferring a flexor or flexor/ inverter to the dorsum of the foot for replacement of dorsiflexion function at the expense of one or more of the functions of the tendon to flex or invert joints of the foot. As such, tendon transfers are not possible in the case of a full sciatic palsy. EMG can distinguish between a common peroneal palsy and a sciatic nerve palsy.

Posterior tibial tendon transfer through the intraosseous membrane was developed over 100 years ago by Codvilla in 1899 and Putti in 1914[5]. Several authors have subsequently modified the technique to address some of the technical difficulties associated with the procedure. Namely the posterior tibial tendon is of insufficient length which can result in calcaneus position of the foot and difficulties with fixation on the dorsum of the foot. Though these issues with the procedure can be largely addressed with either tendon-tendon interface, interference screw, or indwelling suture button fixation, other issues exist with the technique also. Some authors have observed an acquired flat foot deformity resultant from the harvest of the posterior tibial tendon without replacement of its function[3]. This has led some authors to recommend subtalar fusion at the time of tendon transfer to prevent iatrogenic pes planovalgus. This procedure can be associated with over 80% return to brace free gait. However, it is important to note that the strength is 30% less than the contralateral limb.

Many authors believe that the replacement of function of the pre-tibial muscles is due to a tenodesis effect. Transfer of other posterior muscles such as the flexor digitorum longus and flexor hallucis longus has been discussed and described. These tendon transfers are intrinsically appealing because they remove a deforming force (clawing of the toes after paralysis of the extensor muscles) and potentially restore a lost function (dorsiflexion). These transfers have been described as the so called "Hiroshima" procedure for treatment of spastic equinovarus in cerebral palsy, and recently for flaccid peroneal nerve palsy[5].

Additionally, if tendon transfer is to be considered, the patient must be assessed for an equinus contracture. If an equinus contracture exists, it is our practice to address the equinus contracture during the same surgical episode. We generally perform a silverskold test, in which the equinus contracture is assessed with knee flexion and knee extension. If the examination shows that the contracture is only present during knee flexion but disappears during extension, the gastrocnemius alone is tight and we perform a Strayer type zone III gastrocnemius recession. If the equinus contracture is present in both flexion and extension of the knee, both muscles are tight and we perform a Zone II Baker type recession if the contracture is mild (10-20 degrees), and a Hoke percutaneous zone I tendon lengthening if the contracture is greater than 20 degrees with the knee in extension.

The patient is maintained in a cast for six weeks and a solid brace for an additional six weeks after tendon transfer. If a subtalar fusion is included a non-weight bearing cast is utilized for six weeks followed by a weight bearing cast for six weeks. Following this, retraining of the tendon transfer can take place with physical therapy. Rehabilitation is an integral part of the procedure, and any tendon transfer will fail to produce the desired results without a good therapist. We recommend stretching the triceps surae and imagery based retraining of the tendon transfer, as the patient must retrain the tendon to work in a way it is not accustomed to working. Functional electrical stimulation can be helpful in this regard.

Ankle Fusion

Ankle fusion is reserved for patients who are unable to tolerate bracing, and have either failed all or are ineligible for other modalities (tendon transfer, nerve graft, decompression). The goal of the procedure is to effectively fix the foot in a ninety degree position to the tibia. This may be accomplished through ankle (tibiotalar) fusion or pan talar fusion depending on other pathology involved.

Ankle fusion is a last resort because it takes all motion from the ankle joint, has possible complications of non-union as well as hardware related complications, and adjacent segment arthritis. Additionally, forefoot cavus may still be present and will be poorly compensated by a stiff ankle. A negative heel and a metatarsal rocker may then be necessary to restore the rockers of the foot.

Most peroneal nerve palsy can be treated either operatively or non-operatively without resorting to ankle fusion.

Conclusion

Peroneal nerve palsy is a common lower extremity injury after trauma. It can be successfully managed by non-operative or operative means, but requires a thoughtful approach by the treating clinician.

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Single Leg Spica Casting for Low Energy Pediatric Femur Fractures—Operative Technique

Daniel Miller, MD
Susan Nelson, MD, MPH
Todd Blumberg, MD
Andrew Gambone, MD
Joseph Monteleone

[1]Divison of Orthopaedic Surgery
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Introduction

Femoral shaft fractures are common pediatric injuries, with treatment strategies depending on patient age, weight, skeletal maturity, fracture location, comminution, soft tissue integrity, and associated injuries. The American Academy of Orthopaedic Surgeons (AAOS) Clinical Practice Guidelines suggest early spica casting or traction with delayed spica casting for children aged 6 months to 5 years with a diaphyseal femur fracture with <2 cm of shortening[1]. Historically, spica casting for pediatric femoral shaft fractures consisted of a two or one and a half leg spica with the injured leg in 90° of hip flexion and 90° of knee flexion[2,3]. While this is associated with good long term results, there is a significant burden of care on the patient, family, and community[4]. The single leg "walking spica" is safe and efficacious for treatment of low energy pediatric femoral shaft fractures[2,3,5] that decreases burden of care for the patient and family by facilitating safe mobilization with the well leg free[3,5]. Because of this, single leg spica casting has become the preferred technique at our institution. The purpose of this article is to describe this technique for the treatment of low energy pediatric femoral shaft fracture.

Preoperative Evaluation and Indications

Single leg spica casting is indicated in patients aged 6 months—4 years after low energy trauma (e.g. falling off a bed). Contraindications include high energy injury patterns suggested by significant fracture comminution, fracture shortening > 2 cm, or polytrauma.

All patients should undergo a history and physical and screened for concomitant injuries. Children less than 3 years of age should be evaluated for non-accidental trauma, particularly in those patients who are not yet walking. Families should be warned about the potential for complications including fracture displacement, skin related issues, and need for wedging or additional procedures.

Procedure

Closed reduction and spica casting can be performed in the operating room or emergency department provided that appropriate personnel, materials, and sedation are available (Figure 1)[6]. Muscle relaxation may be requested to facilitate closed reduction. We suggest at least two skilled personnel in addition to the surgeon be present to facilitate cast application. A time out should be performed as per institutional protocol.

After induction of anesthesia, an appropriately sized Gore-tex Pantaloon (W. R. Gore and Associates, Inc., Flagstaff, AZ) is applied to act as a waterproof barrier in the event of soiling. Excess liner is removed from the patient's well leg. Layers of six inch stockinette or folded surgical towels are placed between the patient's abdomen and liner to provide room for abdominal expansion following cast application. While the anesthesiologist controls the airway, the child is carefully lifted onto a spica casting table.

The proximal (box) portion of the spica table should end on the mid thoracic spine, at approximately T7, fully supporting the shoulders. The well-padded distal post of the spica table should be adjusted so that it rests snugly against the patient's perineum, supporting the sacrum. The patient's arms may be secured to the side

Figure 1. (A) Supplies include 2 and 3 inch fiberglass cast tape, soft roll, and stockinette folded to be placed on the stomach **(B)** One variation of hip spica table.

or overhead with cast padding or held in place by an assistant depending on the configuration of the available spica table.

One member of the surgical team should be dedicated to holding the leg in the planned casting position of 45° of hip flexion and 45° of knee flexion with slight abduction (30-45°) and longitudinal traction. The well leg should be flexed and abducted as well to prevent pelvic tilt. Web roll cast padding is circumferentially rolled around the injured leg from just proximal to the malleoli to the xiphoid process with careful attention to padding bony prominences. The foot and ankle are left completely free. Longitudinal strips of 2-inch cast padding are applied anterior to posterior to provide additional padding in the groin and perineal region.

Fiberglass casting material is applied first proximal to distal to create a long leg cast and a valgus mold is applied at the fracture site to prevent varus malalignment (Figure 2). Bi-planar fluoroscopy is used to confirm appropriate length, alignment, rotation and cast molding. Up to 2 cm of shortening, 10 degrees of Varus, and 20 degrees of sagittal displacement are acceptable criteria for reduction. Fiberglass is subsequently applied to reinforce the connection between leg and pelvis. A figure of 8 pattern is useful when circumnavigating the pelvis. Fiberglass struts consisting of 6-8 layers of casting tape are added to provide additional mechanical integrity between the trunk and leg along the anterior thigh, lateral thigh, and medial groin (Figure 3).

The liner is folded back and a final layer of fiberglass is applied. The child should be removed from the casting table and rotated into the lateral position so that all portions of the cast can be inspected for sharp edges that may need to be trimmed. Fluoroscopy is used to confirm acceptable reduction and a radiopaque object should be used to annotate the cast at the fracture location in the event that cast wedging is needed at follow up (Figure 4). The stockinette or towels are removed from the abdomen and two diapers (one small to be placed under the cast edges and one larger overtop) are applied to prevent cast soiling.

Postoperative Protocol

Perioperative management includes pain management, cast care instruction by trained staff, and physical therapy evaluation to ensure safe transport. Follow-up examinations with x-rays are performed at one, two, three, and six weeks post-operatively. Young children will self-restrict weight bearing as comfort allows, with formal clearance for weight bearing when callus is visualized on radiographs. Cast wedging can be performed for coronal or sagittal displacement, typically within the first two weeks following reduction. Loss of reduction may require repeat closed reduction or surgical intervention. Casts are removed after clinical and radiographic evidence of union. Reluctance to walk is common following cast removal and limping may persist for up to a year[7]. Physical therapy is generally not indicated. Additional follow up visits are scheduled for 3 and 12 months post operatively, with subsequent visits on an as needed basis.

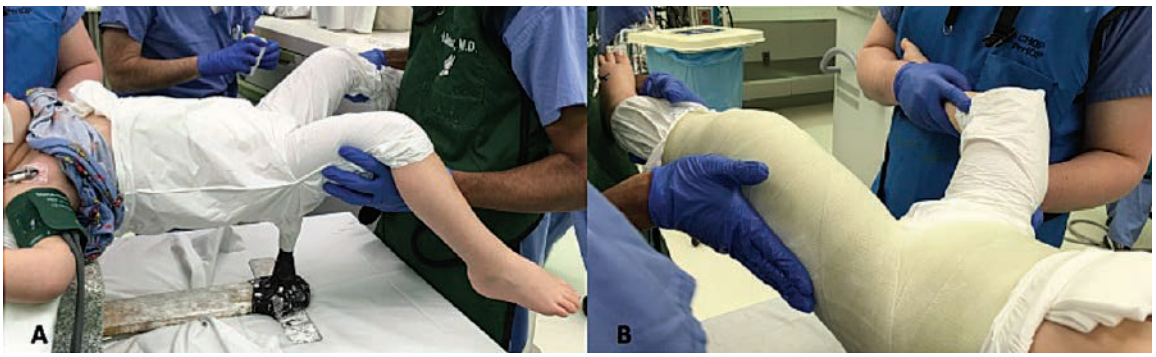

Figure 2. (A) Once the liner is in place the child is lifted onto the spica table and soft roll applied **(B)** Initial layer of cast tape is placed and a valgus mold applied.

Figure 3. (A) 6-8 layer fiberglass struts are added to enhance the mechanical stability between the leg and pelvis portion of the cast and **(B)** overwrapped with one layer of casting tape.

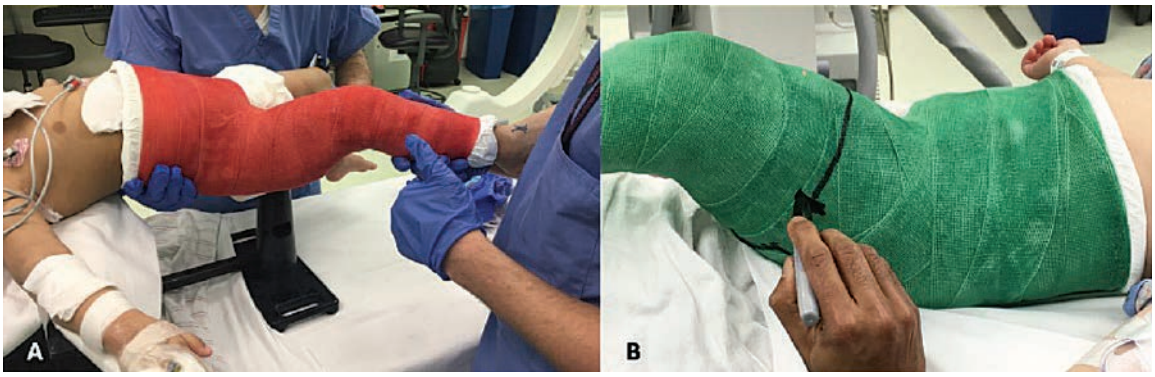

Figure 4. (A) Final casting position. The child can now be removed from the spica table and final fluoroscopy taken **(B)** The cast can be annotated using fluoroscopy to facilitate future wedging.

Discussion

Single leg spica casting provides an attractive alternative to the traditional one and a half leg spica cast when used appropriately. This technique can be used safely in children aged 6 months to 4 years with low energy fractures to obtain satisfactory outcomes while minimizing the treatment burden on the patient and family.

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U·P·O·J

Biomechanical Comparison of Fully-Threaded Solid Cortical versus Partially-Threaded Cannulated Cancellous Screw Fixation for the Treatment of Lisfranc Injuries

Joshua Rozell, MD
Matthew Chin, BS
Derek Donegan, MD
Michael Hast, PhD

Introduction

Lisfranc injuries are a frequent cause of patient morbidity, and if not treated with anatomic reduction and fixation, may lead to substantial pain, chronic instability, and arthritis. Several different screw designs can be readily employed in transarticular screw fixations of Lisfranc injuries, but the biomechanical differences between screws in this application are not well defined. This study sought to investigate the differences between fully-threaded solid cortical (FSC) screws and partially-threaded trabecular (PCT) bone screws in the milieu of a cadaveric model of a Lisfranc injury. The performance of the two screw types was quantified by measuring relative diastasis between surgically fixed bones within the midfoot. We hypothesized that there would be no significant differences in diastasis when comparing PCT and FSC screws.

In an effort to further characterize the biomechanical limits of the two screws, we executed several benchtop experiments to investigate relevant parameters of resistance to bending and pull-out strength. We hypothesized that the PCT screws would have lower ultimate failure and yield strength but higher pullout strength than FSC screws. It was further hypothesized that the loads at which these phenomena occur are substantially lower than those typically experienced during physiological loading in Lisfranc fixation.

Materials and Methods

Ten matched pairs of fresh frozen cadaveric feet were fused in 30° plantarflexion and tested in a universal testing frame (Figure 1A). 3-D locations of midfoot bones were recorded during static loading trials for healthy, injured, reconstructed, and cyclically loaded specimens with either fully-threaded solid cortical (FSC) or partially-threaded cannulated trabecular (PCT) bone screws. Diastasis between the first and second metatarsals and the medial and intermediate cuneiforms was measured and relative bony displacement was normalized to percentages for each specimen. Screws were retrieved after testing and subjected to three-point bending (Figure 1B) and pull-out tests (Figure 1C) to elucidate differences in relevant performance characteristics. One-tailed paired student's t-tests were used to evaluate the injuries applied to the specimens. For all other tests in this study, two-tailed, two-sample, equal variance t-tests were used with significance levels set at p=0.05.

Results

There were no significant differences between screw performances in the cadaveric model (Table 1). The mean normalized diastasis between medial and intermediate cuneiforms after reconstruction was 10.2 ± 11.5% and 6.2 ± 18.2% for FSC and PCT screws respectively ($p = 0.58$), while cycled specimens had mean values of 10.1 ± 17.9 % and 11.8 ± 12.9% ($p = 0.82$). Similarly, mean normalized distance between metatarsals after reconstruction was 2.0 ± 20.3% and 4.5 ± 10.5% for FSC and PCT screws ($p = 0.73$), and −0.7 ± 17.3% and 14.6 ± 24.6% for cycled specimens ($p = 0.15$). No screws were bent or loose when retrieved after

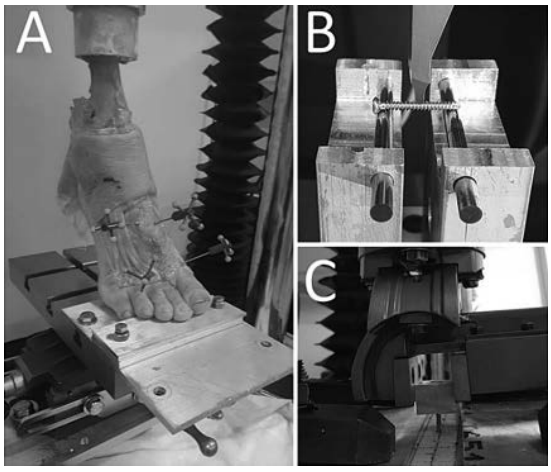

Figure 1. (A) Cadaveric testing positioned specimens in 30° plantarflexion and applied a static compressive load of 343N through the tibia. Relative diastasis of midfoot bones was tracked with 3-D motion tracking techniques. **(B)** Three-point bending tests were conducted to assess resistance to bending. **(C)** Screw pull-out tests were performed to quantify resistance to axial distraction loads.

Table 1. Comparisons of Diastasis Between Bones.

Group	n	Normalized Mean (%)	95% Confidence Interval	P-value
Healthy Cuneiform	20	0	0-0	0.003
Injured Cuneiform	20	12.2	3.7-20.8	
Reconstructed Solid Cuneiform	9	10.2	1.4-19.1	0.58
Reconstructed Cannulated Cuneiform	10	6.2	−6.8-19.2	
100 Cycles Solid Cuneiform	10	10.1	−2.7-23.0	0.82
100 Cycles Cannulated Cuneiform	9	11.8	1.9-21.7	
Healthy Metatarsal	18	0	0-0	0.03
Injured Metatarsal	18	8.4	−0.6-17.4	
Reconstructed Solid Metatarsal	10	2.0	−11.4-17.6	0.73
Reconstructed Cammlated Metatarsal	9	4.5	−2.1-14.I	
100 Cycles Solid Metatarsal	9	−0.7	−15.5-11.1	0.15
100 Cycles Cannulated Metatarsal	9	14.6	−9.7-28.2	

testing. Mean yield loads for FSC and PCT screws were 381.5 ± 15.6 and 375.7 ± 10.6 N ($p = 0.24$), respectively, while mean ultimate strengths were 570 ± 11.9 and 457.4 ± 6.7 N ($p<<0.001$), and ultimate pull-out loads were 121.8 ± 20.1 and 144.3 ± 13.1 N ($p = 0.001$).

Discussion & Conclusion

Results of this study suggest that FSC and PCT screws provide similarly suitable biomechanical stability in the physiologic milieu, despite their differences in failure mechanics. Given the wide variety of bony and or ligamentous patterns of disruption in these injuries, it is important to have multiple techniques in one's armamentarium to provide the patient with the best reconstructive option. In the future, a clinical follow-up study should be performed to confirm the findings of this in vitro investigation.

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U·P·O·J

Well-positioned Calcar Screws Have Decreased Variability in Mechanical Loading Compared to More Distant Screws in Proximal Humerus Fracture Fixation

Samir Mehta, MD
Matthew Chin, BS
Surena Namdari, MS, MD
Michael Hast, PhD

Purpose

Locking plate implants provide an attractive option for proximal humerus fracture fixation, but their clinical success largely relies upon fracture reduction quality and the restoration of the medial calcar support. Placement of a screw inferiorly and parallel to the calcar is a technique that is commonly employed to enhance stability. The locking screws used in these implants have rigidly defined trajectories, and thus, ideal placement of the calcar screws is not always possible in a clinical setting due to plate positioning. The biomechanical consequences of "missing" the calcar in proximal humerus fixation are not well defined. This study sought to elucidate the mechanisms associated with proximal or distal placement of locking plates in two-part proximal humeral fractures. We hypothesized that neutral placement of the plate would provide the best fixation, while distal and proximal plate locations would exhibit significant reductions in fixation strength.

Materials & Methods

Nine pairs of cadaveric humeri specimens (4 M, 5 F, average age 81.2) were used for this study. Specimens were skeletonized and two-part proximal humerus fractures were modeled by creating a 30° wedge osteotomy at the surgical neck of the humerus. Specimens were assigned to one of three groups: idealized calcar screw insertion (NEUT, n = 6), 4mm distal calcar screw insertion (DIST, n = 6), and 4mm proximal calcar screw insertion (PROX, n = 6) (Figure 1). Fractures were stabilized by a single experienced surgeon, using locking proximal humerus plates (DePuy Synthes), per manufacturer guidelines. Specimens underwent a series of biomechanical tests in a universal test frame to quantify the mechanical properties of the repair. Quasi-static torsional stiffness tests and quasi-static axial compression tests at 0, +20, −20 degrees of ab/adductions were conducted prior to a cyclic fatigue protocol consisting of compressive 0 degree axial loads ranging from 50-250N for 5000 cycles at a rate of 1 Hz. A ramp to failure at a rate of 0.1 mm/s was performed after completion of the fatigue test. Measures of initial torsional stiffness, initial axial stiffness, maximum humeral head displacement during fatigue loading, and ultimate load were recorded for each specimen. One-way ANOVAs with alpha = 0.05 were performed to determine differences between groups.

Result

There were no significant biomechanical differences between the DIST, NEUT and PROX groups for internal ($p = 0.178$) and external ($p = 0.710$) torsional stiffness. There were also no significant differences between groups for 0 ($p = 0.744$), +20 ($p = 0.650$), and -20 ($p = 0.278$) degree compression tests. No significant differences were found for maximum displacement ($p = 0.777$) or ultimate load ($p = 0.368$). Full details of results can be found in Table 1.

Discussion and Conclusions

Based on this cadaveric biomechanical model, in well-aligned, well-reduced two-part proximal humerus fractures, position of the calcar screw in the humeral head did not have a significant effect on torsional stiffness, axial stiffness, maximal displacement, or ultimate load. However, variations from the mean in stiffness, load, and displacement were least in the well-positioned calcar screws compared those

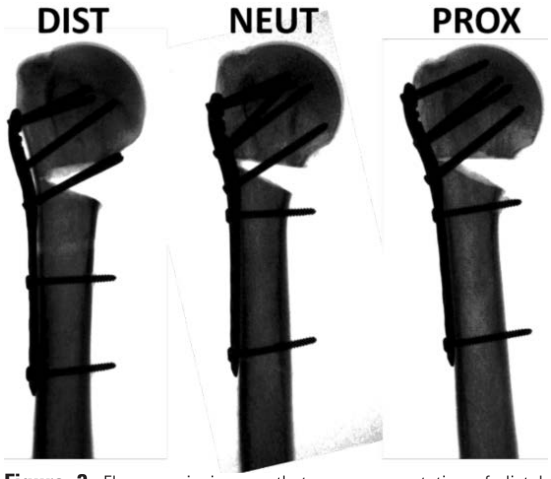

Figure 3. Fluoroscopic images that are representative of distal, neutral, and proximal placements of the locking plates within the study.

Table 1: Summary of Experimental Data (Means ± 1 Standard Deviation).

	DIST	NEUT	PROX	p-value
Int.Rot. Stiff. (Nm/deg)	0.837 (±0.316)	0.764 (±0.276)	0.536 (±0.200)	0.178
Ext. Rot. Stiff. (Nm/deg)	0.702 (±0.29.6)	0.736 (±0.224)	0.599(±0.318)	0.710
00° Anal Stiff. (N/mm)	391.6 (±158.5)	377.6 (±69.5)	337.8 (±127.7)	0.744
+20° Axial Stiff. (N/mm)	207.0 (±117.3)	199.3 (±65.2)	259.6 (±160.3)	0.650
−20° Anal Stiff. (N/mm)	356.57 (±142.2)	404.5 (±93.9)	387.4 (±270.5)	0.278
Max Disp. (mm)	0.936 (±0.486)	0.826 (±0.188)	0.961 (±0.304)	0.777
Ultimate Load (N)	910.8 (±245.6)	912.8 (±183.6)	105-.5 (±167.0)	0.386

screws placed too proximal or distal. Screw position in the well aligned, well-reduced fracture may be less critical than in fractures that are poorly reduced, where greater variability can be limited by screws placed closer to the calcar.

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U·P·O·J

Orthopaedic Oncology Tips & Tricks: Prophylactic Femoral Nailing for Metastatic Carcinoma

Andrew Tyler, MD, PhD
Kristy Weber, MD

Introduction

The diagnosis and treatment of carcinoma that has metastasized to bone is an important component of orthopaedic oncologic care. The likelihood of evaluating a metastatic bone lesion, particularly in an orthopaedic oncology practice, is very high. The most common malignant process affecting bone in patients over 40 years old is metastatic disease, and more than 50% of patients with metastatic carcinoma will develop bony metastases[1]. In addition, the skeleton is the third most common target of metastatic disease after the lung and liver. The most common malignancies that metastasize to bone include breast, prostate, lung, thyroid, and kidney carcinomas[2]. Beyond representing a more advanced and aggressive form of disease, bone metastases can destroy the cortical integrity and lead to pathologic fracture. These fractures are associated with a high morbidity, especially those presenting in the lower extremities, as the pain and loss of independent function can be devastating for an already terminally ill patient. Therefore, these lesions should be properly diagnosed and managed to avoid poor functional outcomes and provide improved quality of life. This article will focus on intramedullary nailing of the femur, a common procedure in patient with bone metastases. Many patients present with an actual pathologic fracture, but if a destructive lesion is noted prior to fracture, prophylactic stabilization can be beneficial. By stabilizing the weakened cortex, patients note reduced pain and improved function, allowing them to maintain their independence as they focus on treatment of their primary disease.

Work-up & Diagnosis

The first step in a patient with a suspicious bone lesion is a thorough, well-documented history and physical examination[3]. The importance of this key step should not be underestimated; in up to 27% of patient with skeletal metastases, the history and physical examination alone can identify the location of the primary malignancy[4]. This effort will help determine whether the lesion is occurring in the setting of a known malignancy or if it is an isolated finding, which in turn dictates the need for a biopsy. Basic laboratory studies should be analyzed, and more specific studies can also be ordered if certain diagnoses are presumed; for example, prostate specific antigen should be included if there is concern for metastatic prostate cancer. Furthermore, if the presenting lesion is incompletely assessed on plain films, or if further staging is required, more advanced imaging can be requested. This may include ^{99m}Tc bone scan, computed tomography (CT) scan of the chest, abdomen, and pelvis, and magnetic resonance imaging (MRI). Evaluations using advanced imaging have been shown to identify the primary site of the tumor in at least 85% of patients[5]. Finally, a biopsy should be performed to confirm a tissue diagnosis unless the diagnosis is certain (widespread bone and visceral metastasis).

Indications

Current indications for prophylactic femoral nailing are based on criteria outlined by Mirels', which grades these bone metastases on four different criteria: location, pain, radiographic features, and size (Figure 1), with scores ranging from 4 to 12[6]. A score of 8 or above suggests the need for prophylactic fixation. However, prior to intervention, it is important to consider additional factors, including

- Presence of an actual versus impending pathologic fracture
- Specific location of the bone lesion in the femur
- Underlying diagnosis
- Expected survival

These factors may not only alter the type of fixation that is best for the patient but affects various aspects of intraoperative and perioperative care, such as the need for preoperative radiation of the lesion and the timing of chemotherapy. Additionally, for renal and thyroid carcinomas that metastasize to bone, preoperative embolization may be considered, as these tumor types are highly vascular and can cause brisk bleeding intraoperatively. Furthermore, it is important to establish the correct diagnosis prior to any intramedullary instrumentation of the femur, including the guide rod. While carcinoma is commonly treated with femoral intramedullary nailing, a sarcoma requires wide resection of the lesion. Inappropriate treatment with an intramedullary device can lead to the need for an amputation to

Mirels' Criteria			
	Score		
	1	2	3
Site	Upper limb	Lower limb	Peritrochanteric
Pain	Mild	Moderate	Functional
Lesion	Blastic	Mixed	Lytic
Size	<1/3	1/3-2/3	>2/3

Figure 1. Mirels' Criteria [6]

achieve local control of the disease[7]. In addition, the expected survival of the patient should be on the order of 6 to 12 weeks minimum, to justify the pain and risk of surgery[8].

Operative Technique

In terms of surgical technique, prophylactic nailing of an impending pathologic fracture is similar to intramedullary nailing for an intertrochanteric or femoral shaft nonpathologic fracture, with the primary difference being that the intact cortical bone obviates the need for traction and the oncologic nail has proximal screws into the femoral head and neck. The patient can be placed in the supine position on a radiolucent table with the operative extremity positioned such that adequate AP and lateral fluoroscopic views can be obtained without interference or changes in patient positioning. Full-length, reconstruction type femoral nails are used to provide stability and protect the entire femur[9]. Reamings are often sent during the procedure to confirm the tissue diagnosis. Post-operatively, the patient is made weight bearing as tolerated and is evaluated by physical and occupational therapy. DVT prophylaxis should be tailored to the individual patient, given the elevated risk of thromboembolic disease in the background of cancer. Finally, care should be coordinated with the patient's primary oncology team to ensure that treatment for the primary disease is resumed in a reasonable timeframe; any anti-proliferative medications as well as radiation to the entire femur are delayed until two weeks after surgery to allow the wound time to heal.

Conclusion

Femoral prophylactic nailing for metastatic carcinoma is an important procedure in orthopaedic oncology, not only as a preventative measure to avoid the complications associated with fracture but also as a palliative measure for pain relief in patients with poor prognoses. While most general orthopaedists will not be required to perform prophylactic nailing, it is vital that they understand how to properly evaluate a patient with a destructive bone lesion as well as the treatment options available, to best counsel their patients and ensure that they receive the highest quality of care.

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Rescuing Chondrocyte Hypertrophic Differentiation Potential and Exploring Therapeutic Approaches for Enhancing Bone Formation in Mucopolysaccharidosis VII Dogs

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Caitlin Fitzgerald
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Eileen Shore, PhD
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Introduction

The mucopolysaccharidoses (MPS) are genetic, lysosomal storage diseases characterized by deficient activity of enzymes that degrade glycosaminoglycans (GAGs)[1]. MPS VII is characterized by mutations in the β-glucuronidase gene, leading to incomplete digestion and progressive accumulation of three GAG types[2]. MPS VII patients exhibit severe skeletal abnormalities, especially of the spine[3]. Persistent cartilaginous lesions are present in the vertebrae representing failed cartilage-to-bone conversion during postnatal development, which result in progressive kyphoscoliosis and spinal cord compression[4-7]. Previously, using the naturally-occurring MPS VII canine model, we established that impaired hypertrophic differentiation of epiphyseal chondrocytes contributes to failed bone formation during early postnatal development[8], which in turn is associated with decreased Wnt/β-catenin signaling[9]. We also showed that Wnt pathway activation resulted in normalization of chondrocyte differentiation *in vitro* in MPS VII epiphyseal cartilage[10]. GAGs perform crucial roles in controlling the distribution and availability of Wnts, which are critical positive regulators of chondrocyte differentiation during endochondral ossification. Thus, we hypothesized that aberrant GAG accumulation in MPS VII contributes directly to impaired chondrocyte function and that in the absence of abnormal GAGs, hypertrophic differential potential could be rescued. To test this hypothesis, we undertook *in vitro* studies to compare differentiation potential of MPS VII chondrocytes in the presence and absence of their GAG-rich environment. Furthermore, to explore therapeutic approaches to correct MPS VII bone disease, we undertook a preliminary *in vivo* study in our canine model to establish a dosing regimen and safety profile using lithium, a Wnt pathway agonist, which has been previously shown to enhance bone formation and is approved clinically for other indications[11].

Methods

For this study, we used the naturally-occurring MPS VII canine model that closely mimics the skeletal phenotype of human patients[12].

In Vitro Analysis of GAG Accumulation and Chondrocyte Hypertrophic Differentiation Potential

With IACUC approval, unaffected control and MPS VII dogs (n = 4 for each) were euthanized at 9 days-of-age, and lumbar vertebral epiphyseal cartilage was isolated. For monolayer cultures, cartilage was digested with collagenase until cells were released from the extracellular matrix. Isolated chondrocytes were expanded in basal medium (DMEM, 10% FBS, 1% PSF) then cultured in monolayer in either basal or osteogenic media. For explant cultures, epiphyseal cartilage was cultured as whole tissue explants in basal medium. Media was collected at 3, 7, and 14 days for monolayer cultures and at 5 days for explant cultures. Total media GAG content was measured using the dimethylmethylene blue assay and normalized to total cell count. Cells from monolayer cultures and explants were harvested, RNA extracted, and mRNA expression levels of chondrocyte differentiation markers (Sox9-proliferative; Runx2-prehypertrophic; Col10-hypertrophic) were measured using qPCR. Significant differences between groups ($p < 0.05$) were established using unpaired t-tests.

In Vivo Lithium Treatment

To establish dosage needs of lithium, normal control dogs (n = 2) were treated with twice daily doses of 5 mg/kg of powdered lithium carbonate packaged into gelatin capsules for 1 week for acclimation, then with twice daily doses of 10 mg/kg for 2 weeks, starting at 15 days-of-age. Dogs were monitored for side effects, and serum lithium levels were measured using a commercial assay (Crystal Chem).

Results

In Vitro Analysis of GAG Accumulation and Chondrocyte Hypertrophic Differentiation

In whole explant culture, MPS VII chondrocytes secreted significantly higher amounts of GAGs into the media compared to controls over time,

while isolated chondrocytes showed no differences over 14 days of culture (Figure 1). Likewise, in whole explant culture, MPS VII chondrocytes showed impaired differentiation over time compared to controls, but both control and MPS VII chondrocytes exhibited similar propensity to differentiate over time in isolated cell culture (Figure 2).

In Vivo Lithium Treatment

After the initial 1 week acclimation period, both dogs maintained serum lithium levels within in the desired therapeutic range (0.2-1.5mmol/L) over the following 2 weeks (Figure 3). Dogs exhibited a mild tremor which resolved within a few days. No significant adverse side effects from lithium treatments were observed.

Discussion

The results of this study show that MPS VII chondrocytes regain normal hypertrophic differentiation potential upon removal from their GAG-rich environment. Abnormal GAG accumulation in MPS VII epiphyseal cartilage may disrupt extracellular control of secreted growth factors, such as Wnts, which are necessary to initiate and sustain chondrocyte differentiation. We previously showed that activation of the Wnt pathway with exogenous factors can also normalize chondrocyte differentiation *in vitro*, and taken together, these results indicate that combinatorial therapies that normalize GAG accumulation and activate Wnt signaling may be able to rescue the differentiation potential of resident cells and ultimately normalize bone formation. As a preliminary step, we successfully treated neonatal dogs with lithium, establishing safety and optimizing an oral dosing regimen to sustain therapeutic serum levels. In ongoing *in vivo* studies, we are examining whether GAG reduction via exogenous enzyme replacement therapy (ERT) and Wnt/β-catenin pathway activation via lithium treatment are able to normalize chondrocyte function and bone formation in MPS VII dogs during postnatal growth.

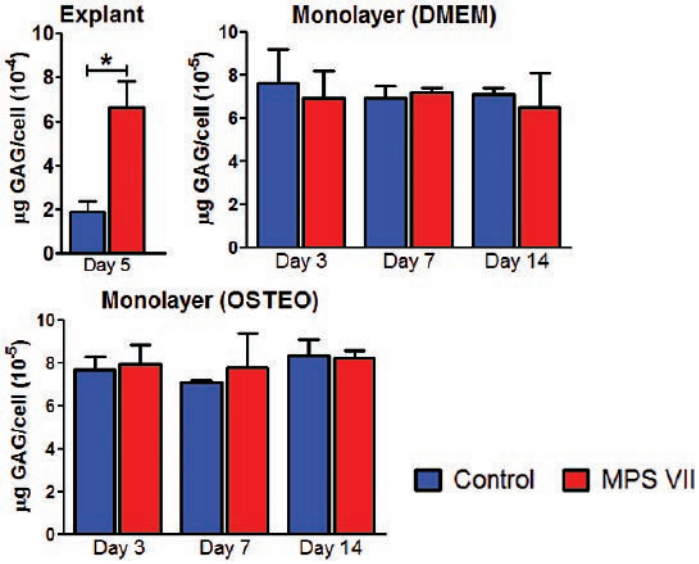

Figure 1. Culture media GAG content. Intact epiphyseal cartilage explants from MPS VII animals exhibited significantly higher GAG content secreted into the media compared to controls. Isolated chondrocytes in monolayer culture showed normalization of secreted GAG content regardless of media conditions. N = 4; *p < 0.05.

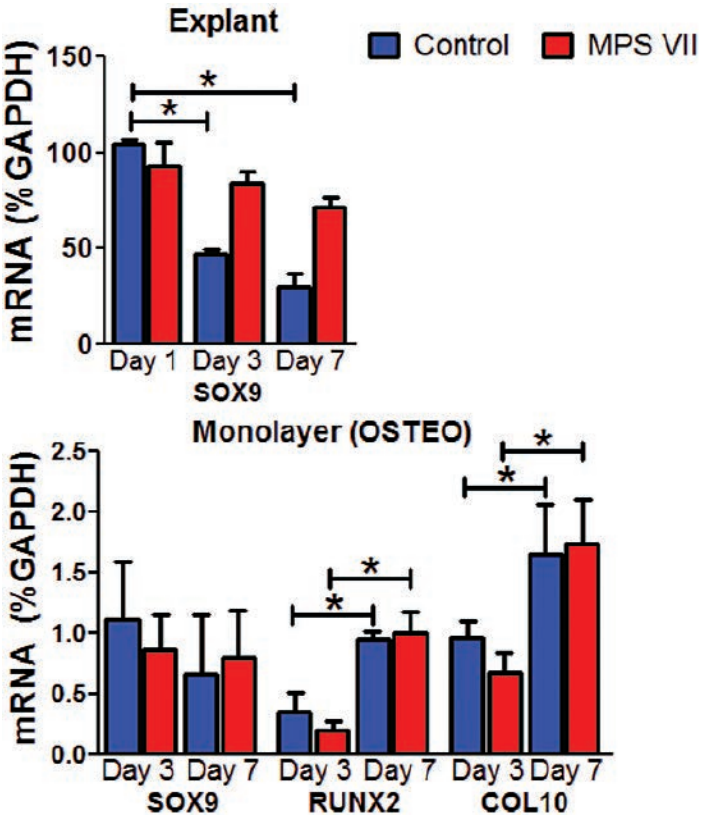

Figure 2. Chondrocyte differentiation potential. In culture, control chondrocytes in intact epiphyseal cartilage explants exhibited propensity to differentiate over time (decreasing SOX9 expression) while MPS VII chondrocytes did not (persistent SOX9 expression). In contrast, both control and MPS VII isolated chondrocytes grown in monolayer culture differentiated normally in the presence of osteogenic conditions. N = 4, *p < 0.05.

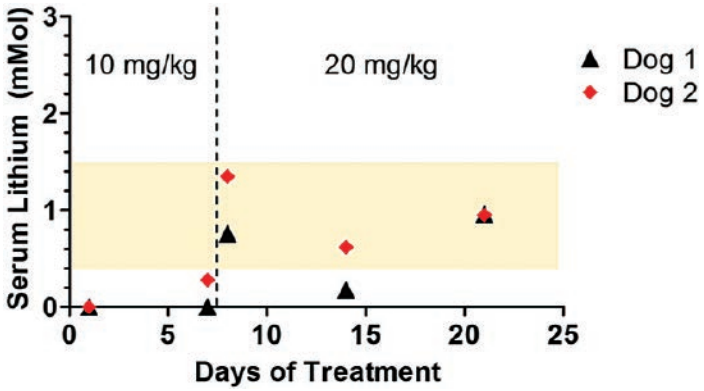

Figure 3. Serum lithium levels in treated dogs. 15-day old normal control animals were treated for 21 days with daily doses of lithium (10 mg/kg daily for 7 days, 20 mg/kg for following 14 days). Dashed line indicates day of increase in lithium dosage. Yellow shaded area indicates target non-toxic, therapeutic range for serum lithium concentration.

Significance

MPS VII is associated with debilitating skeletal disease for which there is no treatment. Our results suggest that therapeutic strategies combining GAG reduction (ERT)

and inducing endochondral bone formation (lithium) may effectively treat skeletal abnormalities in MPS VII patients.

Acknowledgements

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Reproduction-Induced Changes in Maternal Bone Confer Protective Effects against Estrogen Deficiency

Chantal de Bakker, BS
Laurel Leavitt
Casey Krickus
Wei-Ju Tseng, MSE
Tiao Lin, MD
Wei Tong, MD
Ling Qin, PhD
X. Sherry Liu, PhD

Introduction

Pregnancy and lactation induce substantial maternal bone loss, which undergoes a partial recovery post-weaning[1]. However, even after a lengthy post-weaning period, permanent alterations in the maternal skeleton remain[2,3]. At the same time, clinical studies demonstrate that reproduction does not increase future risk of osteoporosis or fracture[4,5]. To explain this paradox, we hypothesized that the permanent skeletal changes induced by reproduction may confer protective effects against postmenopausal bone loss. To test this hypothesis, we tracked changes in bone structure at the proximal tibia following ovariectomy (OVX) in virgin rats and in rats that had undergone 3 cycles of pregnancy and lactation.

Methods

Animal Protocol

All experiments were IACUC approved. Female, Sprague Dawley (SD) rats were assigned to two groups: Reproductive (n = 9) and Virgin (n = 4). Starting at age 3 months, reproductive rats underwent 3 repeated cycles of pregnancy and lactation, with a 6-week post-weaning recovery period between each cycle. At age 12 months, all rats underwent OVX surgery to induce estrogen deficiency, and their proximal tibiae were scanned by *in vivo* μCT prior to surgery, as well as 12 weeks post-OVX (10.5μm, vivaCT 40, Scanco Medical).

μCT Image Analysis

μCT scans made 0 and 12 weeks post-OVX were registered to ensure a consistent trabecular volume of interest (VOI)[6], and trabecular bone volume fraction (BV/TV), connectivity density (Conn.D), trabecular number (Tb.N), and trabecular thickness (Tb.Th) were measured. To evaluate whether variations in baseline microarchitecture can impact the bone loss rate, linear regression analysis was performed, whereby baseline trabecular parameters were correlated to the % decrease in BV/TV following OVX. Individual trabecular dynamics (ITD) analysis[7] was performed to evaluate the rate of structural deterioration (defined as the number of instances of plate perforation and rod disconnection). Cortical bone structure at the proximal tibia, including cortical area (Ct.Area), cortical thickness (Ct.Th), and polar moment of inertia (pMOI) were evaluated, and whole-bone stiffness was estimated through finite element analysis (FEA).

Results

Trabecular Microstructure

Over 12 weeks post-OVX, virgin rats underwent 76%, 86%, and 50% decreases in BV/TV, Conn.D and Tb.N, respectively ($p < 0.05$) with no change in Tb.Th (Figure 1). In contrast, reproductive rats showed a 53% decrease in BV/TV, with no changes in Conn.D, Tb.N, or Tb.Th. Prior to surgery, reproductive rats had 43%, 73%, and 46% lower BV/TV, Conn.D, and Tb.N, respectively, than virgins ($p < 0.05$), but by 12

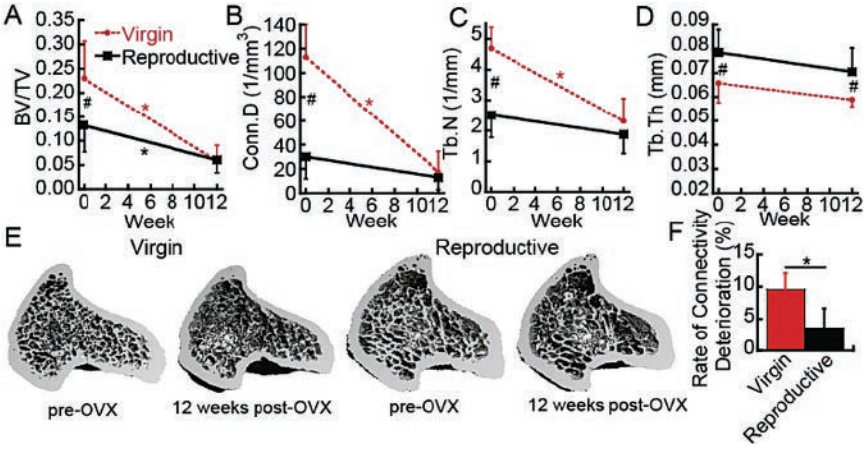

Figure 1. (A-D) Longitudinal changes in BV/TV, Conn.D, Tb.N, and Tb.Th at the proximal tibia. •: wk12 ≠ wk0 ($p < 0.05$); #: Virgin ≠ Reproductive at wk0 or wk12 ($p < 0.05$). **(E)** 3D renderings of the proximal tibia of a virgin (left) and reproductive (right) rat pre- and post-OVX. **(F)** ITD-based rate of connectivity deterioration (defined as the rate of rod disconnections and plate perforations) post-OVX.

weeks post-OVX, these parameters were no longer different between the two groups. Reproductive rats had 20% elevated Tb.Th relative to virgins throughout the study. These results were confirmed by ITD analysis, which illustrated that virgins underwent a 167% higher rate of structural deterioration than reproductive rats.

Correlation of Baseline Structure and Degree of Bone Loss

Linear regression indicated that baseline BV/TV was not significantly correlated to the % reduction in BV/TV post-OVX. However, baseline Conn.D, Tb.N, and Tb.Th were significantly correlated to the degree of OVX bone loss (Figure 2, $r = 0.72\text{-}0.80$; $p < 0.05$). Baseline Conn.D and Tb.N were also both significantly correlated with baseline Tb.Th, and partial correlation analysis indicated that, after adjustment for baseline Tb.Th, baseline Conn.D and Tb.N were no longer correlated with the degree of post-OVX bone loss, suggesting that baseline Tb.Th was the most important factor explaining the degree of post-OVX bone loss.

Cortical Structure and Whole-Bone Stiffness

Both reproductive and virgin rats underwent no changes in Ct.Area, Ct.Th, or pMOI post-OVX (Figure 3). Reproductive rats had greater Ct.Area, Ct.Th, and pMOI (16%, 20%, and 24%, respectively; $p < 0.05$), than virgins throughout the study. Whole-bone stiffness decreased 21% in virgins after OVX ($p < 0.05$), but showed no change in reproductive rats. At 12-weeks post-OVX, virgin rats had 20% reduced whole-bone stiffness compared to the reproductive group.

Discussion

Results from this study confirm the effects of reproduction on maternal bone, as reproductive rats showed inferior trabecular microarchitecture, but increased robustness of cortical bone, prior to OVX. This agrees with previous findings of incomplete recovery of trabecular microarchitecture after reproduction[2,3] as well as a clinical study suggesting that lactation may increase robustness of cortical bone[8]. Furthermore, reproductive history appeared to cause an adaptive response to OVX-induced estrogen deficiency. Reproductive rats showed a lower degree of post-OVX bone loss, resulting in a similar trabecular microstructure between the reproductive and virgin rats at 12-weeks post-OVX, despite differences between the two groups at baseline. Results of our correlation analysis suggest that baseline Tb.Th may be an important determinant of post-OVX bone loss. Thicker trabeculae may be protective against bone loss, as in thinner trabeculae, the elevated rates of bone resorption are more likely to lead to permanent structural damage, whereas in thick trabeculae, increased osteoclast activity may only cause transient resorption cavities which can be refilled through coupled bone formation. However, further studies are required to confirm this hypothesis. Finally, our study indicated a lower degree of whole-bone stiffness deterioration in reproductive rats than in virgins, suggesting that reproductive history may have a protective effect on postmenopausal bone strength. This was likely a result of the lower degree of post-OVX trabecular bone loss, combined with the greater robustness of cortical bone in the reproductive rats.

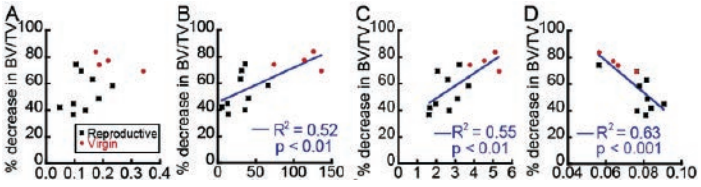

Figure 2. Correlation of the degree of deterioration in BV/TV post-OVX with baseline **(A)** BV/TV, **(B)** Conn.D, **(C)** Tb.N, and **(D)** Tb.Th.

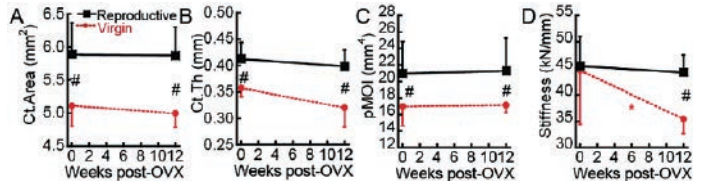

Figure 3. Post-OVX changes in **(A)** Ct. Area, **(B)** Ct.Th, **(C)** pMOI, and **(D)** whole-bone stiffness. •: wk12 ≠ wk0 ($p < 0.05$); #: Virgin ≠ Reproductive at wk0 or wk12 ($p < 0.05$).

Significance

The effects of reproduction on bone health are controversial: reproduction induces irreversible skeletal changes, but does not increase later risk of fracture. This study indicates that the unique phenotype of post-reproductive bone confers protective effects against postmenopausal bone loss.

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U·P·O·J

Relationships Between Peak Bone Microstructure and Rate of Estrogen-Deficiency-Induced Bone Loss

Yihan Li, MSE
Wei-Ju Tseng, MSE
Chantal de Bakker, BS
Hongbo Zhao, BS
X. Sherry Liu, PhD

Introduction

Postmenopausal osteoporosis affects more than 200 million women worldwide[1]. Reduced estrogen levels post-menopause lead to accelerated bone remodeling, resulting in low bone mass and structural trabecular bone deterioration, which cause bone fragility and increased fracture risk[1-3]. Our previous study in rats suggested that variations in trabecular bone microstructure may impact the degree of bone loss following estrogen deficiency induced by ovariectomy (OVX) surgery[4]. We found that the rats that had undergone pregnancy and lactation had significantly thicker trabeculae and attenuated OVX bone loss than age-matched virgin rats. By pooling the data of reproductive and virgin rats together, we found that the percent reduction in bone volume fraction (BV/TV) was significantly correlated with baseline trabecular thickness (Tb.Th), connectivity density (Conn.D), and trabecular number (Tb.N). However, the reproductive history may impact OVX bone loss through other pathways; thus the ultimate relationship between trabecular microstructure and OVX bone loss remains requires further elucidation. Therefore, the objective of the current study is to longitudinally track the bone microstructural changes before and after OVX surgery in a homogeneous population of virgin rats in order to establish the relationship between peak bone microstructure and bone structural changes induced by estrogen deficiency. We hypothesize that the variations in peak bone microstructure can predict the extent of estrogen-deficiency-induced bone loss.

Methods

All animal experiments conducted in this study were approved by IACUC. 51 female Sprague Dawley rats underwent OVX surgery at age of 16-17 weeks and developed osteopenia for 4 weeks.

μCT imaging

μCT scans were performed on right proximal tibiae for all rats at week 0 (before OVX surgery) and week 4 (4 weeks post-OVX) using an in vivo μCT scanner (VivaCT 40, Scanco Medical AG, Brüttisellen Switzerland). A 4-mm region of the proximal tibia was scanned at 10.5 μm voxel size[5]. 3D image registration was conducted to detect a constant trabecular volume of interest (VOI) for each rat to evaluate trabecular microstructure at different time points (Figure 1). Standard trabecular bone structural parameters, such as bone volume/trabecular volume (BV/TV), trabecular thickness (Tb.Th), trabecular number, trabecular spacing (Tb.Sp), structure model index (SMI), and Conn.D were measured. Percent reductions between week 0 and week 4 were calculated for all parameters.

Statistics

Linear correlations and stepwise multiple linear regression analyses were performed to explore the relationship between the baseline (week 0) trabecular microstructural properties and corresponding percent decreases post-OVX. All data were divided into three tertiles, representing groups with Low, Medium, and High relative baseline Tb.Th (adjusted by baseline BV/TV), based on the residuals resulting from the linear correlation of baseline Tb.Th with BV/TV (Figure 2 D). One-way ANOVA with Bonferroni corrections was applied to compare % reductions in trabecular structural parameters among the 3 tertiles.

Results

All rats underwent significant bone loss over 4 weeks post-OVX (55.6±7.8% decrease in BV/TV, Figure 1). Correlation coefficients of linear regressions between baseline parameters and % reduction in trabecular bone microstructural properties are shown in Table 1. % decrease in BV/TV was not predicted by the baseline BV/TV, but it was significantly correlated to baseline Conn.D. Baseline Tb.Th was found to be the best predictor. All baseline structural parameters were significantly correlated to % decrease in Tb.Th. As shown in Table 2, stepwise multiple linear regressions showed that the combination of baseline Tb.Th and Conn.D was correlated with % reductions in BV/TV, Tb.Th, Tb.Sp and

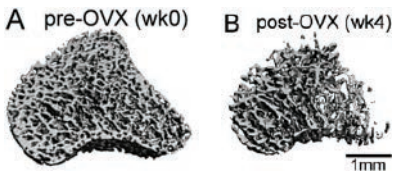

Figure 1. 3D rendering of a registered VOI of trabecular bone pre- and post-OVX.

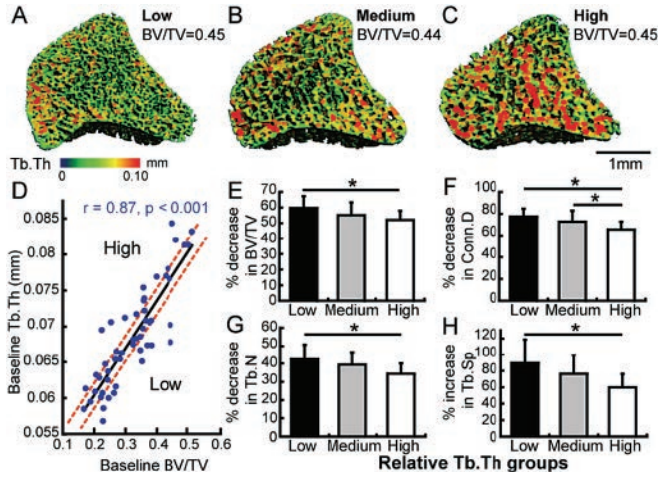

Figure 2. (A-C) Representative trabecular bone images in Low, Medium, and High relative Tb.Th groups. **(D)** Linear regression of baseline Tb.Th and BV/TV. **(E -H)** % changes in microstructural parameters in Low, Medium, and High relative Tb.Th groups. * indicates significant difference ($p < 0.05$).

Conn.D, indicating that baseline Tb.Th and Conn.D were the most important predictors. To further examine the influence of Tb.Th regardless of BV/TV on OVX bone loss, rats were stratified by the relative baseline Tb.Th (adjusted by BV/TV) into 3 groups (Figure 2 A-C). Baseline Tb.Th was significantly correlated to baseline BV/TV ($r=0.87$, $p<0.001$; Figure 2 D), and the corresponding residuals were applied to determine Low, Medium, and High relative Tb.Th groups. % decrease in BV/TV was 13% lower in the High group compared to the Low group (Figure 2 E), and % decrease in Conn.D in the High group was 15% and 10% lower than Low and Medium groups, respectively (Figure 2 F). Moreover, the % decrease in Tb.N and the % increase in Tb.Sp were 19% and 33% lower, respectively, in the High group than the Low group (Figure 2 GH).

Table 1. Correlation coefficients (r) between baseline trabecular parameters and % decrease in trabecular microstructure. Minus sign indicates negative correlation. *: $p < 0.05$, +: $p < 0.01$, #: $p < 0.001$.

% decrease	Baseline Parameters					
	BV/TV	Conn.D	SMI	Tb.N	Tb.Th	Tb.Sp
BV/TV	NS	0.28*	NS	NS	NS	NS
Tb.Th	0.74#	0.59#	−0.72#	0.67#	0.70#	−0.67#
Tb.Sp	NS	−0.31*	NS	NS	NS	NS
Tb.N	NS	NS	NS	NS	NS	NS
SMI	NS	NS	NS	NS	NS	NS
Conn.D	−0.41+	NS	0.44+	NS	−0.60#	NS

Table 2: Correlation coefficients (r) and independent predictors of stepwise multiple linear regression to predict the degree of bone loss by baseline trabecular structural parameters. Minus sign indicates negative correlat ion. *: $p < 0.05$, +: $p < 0.01$, #: $p <$

% decrease	r	Adjusted r	Independent predictors
BV/TV	0.46	0.41	Conn.D+, −Tb.Th+
Tb.Th	0.74	0.68	Conn.D+, Tb.Th#
Tb.Sp	0.51	0.48	−Conn.D#, Tb.Th+
Tb.N	NS		
SMI	NS		
Conn.D	0.68	0.66	−Tb.Th+, Conn.D+

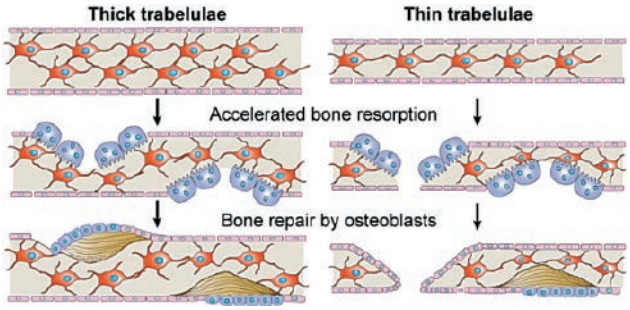

Figure 3. Schematics of accelerated bone resorption followed by osteoblast repair in (Left) a thick and (Right) a thin trabecula.

Discussion

This study investigated the relationship between the peak trabecular bone microstructure and the degree of estrogen-deficiency-induced bone loss. Over 4 weeks post-OVX, estrogen deficiency induced substantial trabecular bone loss and microstructural deterioration. Multilinear regression analysis revealed that the extent of bone loss was influenced by the baseline trabecular microarchitecture, most notably the trabecular thickness and connectivity. A tertile analysis of Tb.Th adjusted for BV/TV suggested that, given the same bone mass (BV/TV), rats with thicker trabeculae had attenuated loss in the volume, number, and connectivity of the trabecular bone network and reduced expansion in the spacing between trabeculae. Our working hypothesis is that the increased bone remodeling in response to estrogen deficiency has variable effects depending on the trabecular thickness. For thick trabeculae, the resorbed bone can be repaired by subsequent osteoblast activities (Figure 3 Left). However, thin trabeculae may be disconnected during remodeling and cannot be repaired (Fig.3 Right). Therefore, trabecular network of low connection but thick trabeculae may be protective against OVX-induced structural deterioration. Future studies with a longer post-OVX duration are necessary to elucidate the effects of peak trabecular bone microstructure on OVX bone loss.

Acknowledgements

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Cyclic Treatment Regime Rescues PTH Withdrawal-Induced Bone Loss and Microarchitecture Deterioration

Wei-Ju Tseng, MSE
Wonsae Lee
Hongbo Zhao, BS
Yang Liu, DDS
Chantal de Bakker, BS
Yihan Li, MSE
Wei Tong, MD
Luqiang Wang, MD
Xiaoyuan Ma, MD
Ling Qin, PhD
X. Sherry Liu, PhD

Introduction

Osteoporosis in postmenopausal women and elderly men is a life-long chronic condition. Intermittent parathyroid hormone (PTH) is currently the only FDA-approved, anabolic agent for osteoporosis. In clinical practice, the recommended duration of PTH treatment is 18-24 months. Despite its potent effect of promoting new bone formation, bone mineral density rapidly decreases upon withdrawal from PTH treatment[1]. It has been recommended that anti-resorptive treatment should be applied upon discontinuation of PTH to prevent bone loss. However, recent reports of atypical subtrochanteric and femoral shaft fractures raised concerns on long-term use of bisphosphonates.

To maximize the efficacy of PTH, the first objective of this study was to uncover the mechanisms behind the adverse effect of PTH withdrawal in an ovariectomized (OVX) rat model. The second objective was to test the efficacy of a cyclic PTH treatment regime[2] on rescuing the PTH withdrawal effect.

Methods

Withdrawal study

27 female Sprague Dawley (SD) rats received bilateral OVX surgery at age 4 months. <u>μCT *Imaging*:</u> 15 rats were assigned to 2 groups: PTH (n = 6, PTH 40μg/kg 5x/wk for 3 weeks followed by saline for 9 weeks) and VEH (n = 9, saline for 12weeks). Sequential scans of proximal tibiae were performed by *in vivo* μCT (Scanco Medical) at 10.5 μm voxel size at weeks -4 (OVX surgery), 0, 3, 4, 5, 6, 8, 10, and 12. 3D image registration[3] was applied to identify the same volume of interest (VOI) in all scans before performing bone microstructure analysis. <u>*Bone histomorphometry:*</u> 12 rats were euthanized after 3 weeks of VEH (V3), 3 weeks of PTH (P3), 3 weeks of PTH followed by 1 week of VEH (P3V1), and 3 weeks of PTH follow by by 2 weeks of VEH (P3V2) treatments (n = 3/group) with the right tibiae harvested for methylmethacrylate (MMA) embedding. Five μm-thick longitudinal sections were stained with Goldner's trichrome to identify osteoblasts, osteoclasts, and bone surface. Osteoclast number and surface per bone surface (Oc.N/BS and Oc.S/BS) were quantified. <u>*Serum TRAP:*</u> In addition to V3, P3, P3V1, and P3V2, blood was collected at P3V9 and V3V9 from rats in the μCT experiment to determine serum TRAP 5b levels.

Cyclic treatment study

6 OVX rats were assigned to (1) cyclic PTH (n = 3, PTH for 3 weeks followed by saline for 3 weeks, 3 cycles) and VEH (n = 3, saline for 18 weeks). Trabecular bone microstructural analysis was applied to registered *in vivo* μCT scans of the proximal tibia at weeks -4, 0, 3, 4, 6, 9, 10, 12, 15, 16, and 18. Longitudinal comparisons were made using 2-way, repeated-measures ANOVA, adjusted for baseline values, and cross-sectional comparisons were made using 1-way ANOVA. Bonferroni corrections were applied to all *post hoc* tests.

Results

Withdrawal study

4 weeks post OVX, bone volume/total volume (BV/TV), trabecular thickness (Tb.Th), and trabecular number (Tb. N) decreased 50%, 13%, and 31% respectively, while structure model index (SMI) increased (all $p < 0.05$, Figure 1 A-D). Bone loss continued in VEH rats for 9 weeks. In contrast, 3 weeks of PTH treatment effectively slowed down the bone loss, causing no changes in BV/TV, Tb.N, or SMI, and a 35% increase in Tb.Th. At week 3, BV/TV and Tb.Th were 97% and 27% greater, and SMI was 30% lower in the PTH- *vs.* VEH-treated animals (all $p < 0.05$). Interestingly, Oc.N/BS and Oc.S/BS were 81% and 83% lower in PTH *vs.* VEH groups. 1 week after the withdrawal (week 4), BV/TV, Tb.Th, and SMI continued to show trends of improvement (Figure 1 ABD). Trends of bone deterioration appeared during the 2nd week of PTH withdrawal (week 5). These are consistent with bone histomorphometry results showing no change in Oc.N/BS and Oc.S/BS 1 week after withdrawal (P3V1, Figure 1 I-J). In contrast, Oc.N/BS and Oc.S/BS became 77% and 82% greater 2 weeks after withdrawal (P3V2) compared to P3 (Figure 1 I-J). Qualitative examination indicated increased number of osteoblasts on the bone surface at P3 compared to V3 (Figure 1 LM). At P3V1, there were no apparent changes in number of osteoblasts or osteoclasts. However, cell height of osteoblasts decreased (Figure 1N).

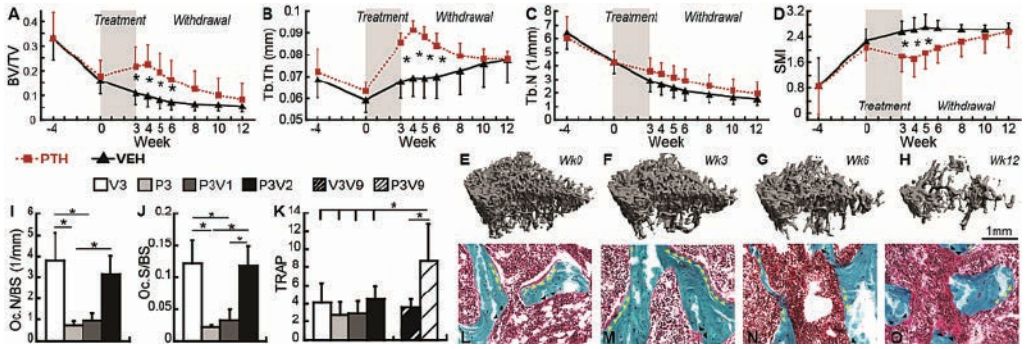

Figure 1. (A-D) % changes in trabecular bone microstructure measurements in PTH and VEH groups. **(E-H)** 3D rendering of trabecular bone microarchitecture at week 0, week 3 (end of PTH treatment). and week 6 and 9 (3 and 6 weeks after discontinuation of PTH) in a same rat. **(I-K)** Osteoclast activities were compared among rats with 3-week VEH (V3) and PTH (P3) treatments, and 3-week PTH treatment followed by 1 and 2 weeks withdrawal (P3V1 and P3V2). Serum TRAP was also measured for PTH rats at 9 week after discontinuation of PTH treatment (P3V9) and for the corresonding VEH rats (V3 V9). **(L-O)** Osteoblasts (yellow arrows) and osteoclasts (black arrows) were shown in Goldner's Trichrome staining of trabecular bone sections at (L) V3, (M) P3, (N) P3V1, and (0) P3V2.
*indicates significant difference between PTH and VEH groups ($p < 0.05$).

At P3V2, cell height of osteoblasts continued to decrease to a similar level as bone lining cells (Figure 1O). 3 weeks after PTH withdrawal (week 6), BV/TV and Tb.Th were still 123% and 20% greater in PTH *vs.* VEH groups, respectively. However, treatment benefit by PTH diminished 5 weeks after withdrawal (week 8). 9 weeks after withdrawal, serum TRAP levels were 59% greater than that in VEH group (Figure 1K).

Cyclic treatment study

Cyclic treatment regime efficiently maintained the benefit of PTH treatment in BV/TV and Tb.N, and further increased Tb.Th (Figure 2). Trends of increase in BV/TV and Tb.Th were observed 1 week after PTH withdrawal in all 3 cycles. Compared to VEH group, BV/TV and Tb.Th were significantly greater in PTH group after 3-week withdrawal in all 3 cycles.

Discussion

Significant bone loss and bone microarchitecture deterioration occurred in OVX animals in response to discontinuation of PTH treatment. Intriguingly, there is a continuous anabolic window during the first week withdrawal from PTH in OVX rats during which no significant change occurred in number of osteoclasts while the height of osteoblasts started to decrease. In contrast, osteoclast number and surface increased 2 weeks after withdrawal from PTH.The morphology of osteoblasts continued to change and became difficult to differentiate from bone lining cells. Changes in bone cells in week 2 after withdrawal led to a decline in bone mass and bone microarchitecture. 9 weeks after withdrawal, the benefits of PTH treatment completely diminished, with no difference in any trabecular bone parameters between PTH and VEH groups. However, serum TRAP analysis indicated more than double the number of active osteoclasts in rats after 9-week withdrawal as compared to VEH rats, potentially leading to more rapid bone loss after long-term PTH withdrawal. Lastly, the continuous anabolic window upon early withdrawal allowed the cyclic treatment regime to efficiently maintain and improve upon the PTH treatment benefit on bone.

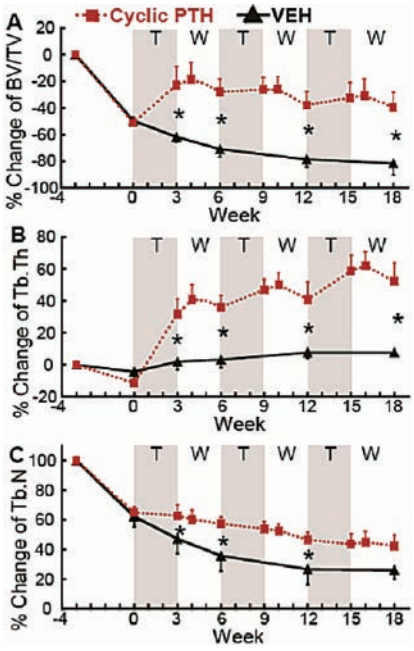

Figure 2. (A-C) % changes in trabecular bone microstructure measurements in cyclic PTH and VEH groups.

Significance

This study demonstrates a continuous anabolic window upon early withdrawal from PTH, which offers a new mechanism in support of the cyclic administration regime of PTH to maximize the total duration and efficacy of treatment.

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U·P·O·J

Engineered Endplates Enhance the In Vivo Performance of a Replacement Disc-Like Angle Ply Structure (DAPS)

Sarah Gullbrand, PhD[1]
John Martin, PhD[1]
Beth Ashinsky, BA[1]
Dong Hwa Kim, PhD[1]
Lachlan Smith, PhD[1]
Dawn Elliott, PhD[2]
Harvey Smith, MD[1]
Robert Mauckm PhD[1]

[1]University of Pennsylvania
Philadelphia, PA and Philadelphia VA
Medical Center
Philadelphia, PA, USA

[2]University of Delaware
Newark, DE, USA

Introduction

Intervertebral disc degeneration involves a progressive cascade of cellular, compositional and structural changes.[1] Surgical treatment of disc degeneration is most commonly achieved via fusion of the degenerated motion segment, which does not restore native disc structure or function, and may exacerbate degeneration of adjacent discs.[2] For the treatment of advanced degeneration, total disc arthroplasty with a cellular, engineered replacement is a promising alternative to fusion; a viable, functional substitute may restore normal mechanics to the degenerated spine. To that end, our lab has created disc-like angle ply structures (DAPS) that mimic the structure and function of the native disc by combining an electrospun nanofibrous annulus fibrosus (AF) with a hydrogel nucleus pulposus (NP).[3] We have previously shown that while the DAPS are mechanically functional following *in vivo* implantation in the rat caudal disc space, the constructs do not integrate with the adjacent vertebral bodies and exhibit progressive reductions in MRI T2 signal and NP proteoglycan content.[4] Here, we report on the *in vivo* performance of an endplate DAPS (eDAPS) implant that was designed to improve construct integration and promote retention of implant composition via the addition of acellular porous polymer endplates.

Methods

eDAPS Fabrication and Culture

DAPS sized for the rat caudal disc space were fabricated by concentrically wrapping aligned, angled strips of electrospun poly(ε-caprolactone) (PCL) nanofibers to form the AF region, and filling the center with a hyaluronic acid hydrogel to form the NP region. Both regions were seeded with bovine disc cells ($2x10^6$ cells/AF and $6x10^5$ cells/NP) and cultured separately for two weeks in chemically defined media containing TGF-β3. After two weeks of culture, the AF and NP regions were combined, and acellular porous PCL endplates, (4 mm diameter, 1.5 mm high) fabricated via salt leaching, were apposed to each side of the DAPS to form the eDAPS construct (acellular construct viewed by μCT, Figure 1A). The eDAPS were cultured for an additional three weeks for a total of 5 weeks preculture.

Implantation Surgery

Athymic male retired breeder rats were anesthetized, and kirschner wires were passed through the C8 and C9 caudal vertebral bodies allowing the placement of a ring-type external fixator.[3] eDAPS were implanted following removal of the C8-C9 disc and a partial corpectomy of the adjacent vertebral bodies. Rats were euthanized at 7 (n = 3), 17 (n = 3) and 35 (n = 7) days.

Magnetic Resonance Imaging

T2 mapping of the eDAPS was performed at 4.7T (16 echoes, TE/TR = 7.84 ms/2,000 ms, FOV = 15×15 mm^2). Average T2 maps were generated for each time point using a custom MATLAB code.[5] Significant differences in eDAPS T2 values at each time point compared to native discs were assessed via a one-way ANOVA, with Tukey's posthoc test.

Mechanical Testing and Biochemistry

Four vertebra-eDAPS-vertebra motion segments 35 days post-implantation, and four native rat tail motion segments, were subjected to mechanical testing (20 cycles, 0 to −3N/~0.3 MPa, 0.05 Hz). Displacement was tracked optically using a high resolution digital camera and a custom texture tracking MATLAB code. The 20th cycle of the force-displacement curve was used to calculate the toe and linear region compressive moduli, and transition and maximum strains via a bilinear fit. Significant differences in biomechanical parameters between native and eDAPS implanted motion segments were assessed via a Student's t-test. Following mechanical testing, the eDAPS were dissected from the motion segment, separated into NP, AF and EP regions, and digested with proteinase-K. Glycosaminoglycan (GAG) content was quantified via the DMMB assay.

Histology

Vertebra-eDAPS-vertebra motion segments were fixed, decalcified and processed through paraffin. Sections were stained with Alcian blue

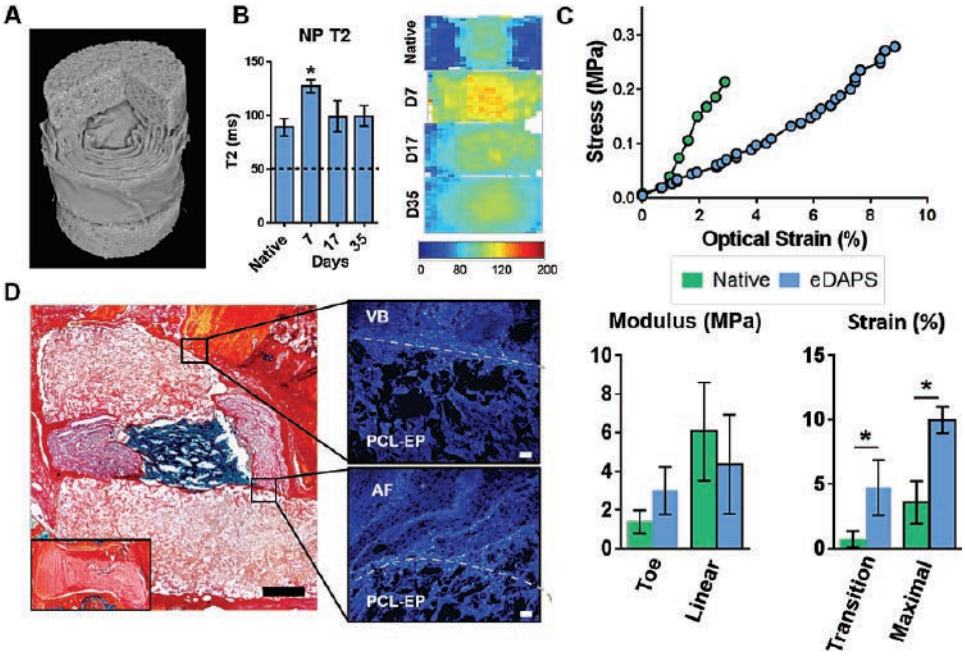

Figure 1. (A) 3D μCT reconstruction of an acellular eDAPS, with cut-away illustrating the lamellar AF structure and porous EP. **(B)** NP T2 values for native rat tail discs and eDAPS from 7 to 35 days in vivo, compared to the NP T2 of DAPS alone (dashed line) at 5 weeks. (* = significantly different from all groups, $p < 0.05$). **(C)** Stress-strain behavior of native rat tail and eDAPS implanted motion segments. **(D)** Representative Alcian blue and picrosirius red stained histology of eDAPS implanted for 35 days; DAPI staining illustrates the cellularity of the vertebral body (VB) and EP interface and the AF and EP interface. Inset illustrates the appearancae of the DAPS alone at 5 weeks in vivo.

(proteoglycans) and picrosirius red (collagen), and the cell nuclei stained with DAPI.

Results

The NP and AF T2 relaxation times of the eDAPS were superphysiologic 7 days after implantation into the rat caudal disc space; the T2 values decreased from 7 to 17 days post-implantation. AF T2 values remained superphysiologic up to 35 days *in vivo* (data not shown), while NP T2 values at 17 and 35 days *in vivo* were not different from the NP T2 of native rat tail discs (Figure 1B). The maintenance of NP T2 signal corresponded with robust Alcian blue staining in the NP region of the eDAPS at 35 days post-implantation. DAPI staining illustrated infiltration of the acellular PCL foam endplate from the AF and NP regions of the eDAPS, in addition to infiltration of native cells from the adjacent vertebral body (Figure 1D). DAPI staining also indicated sustained cellularity of the AF and NP regions of the eDAPS from 7 days to 35 days *in vivo*. After 35 days *in vivo*, GAG content was highest in the NP region of the eDAPS (0.27% ± 0.14%ww), followed by the AF region (0.11% ± 0.01%ww) and EP region (0.03% ± 0.006%ww). The toe and linear region moduli of the eDAPS implanted motion segments were not significantly different from native discs. However, the transition and maximal strains were significantly higher in the eDAPS implanted motion segments compared to native (Figure 1C).

Discussion

Overall, the addition of engineered endplates improved integration and maintenance of DAPS matrix composition *in vivo*. This is in contrast with our previous findings, in which DAPS implanted without endplates were characterized by a lack of integration with adjacent vertebral bodies and progressive loss of NP T2 signal and proteoglycan content.[4] The improved *in vivo* performance of the eDAPS may be due in part to the PCL endplates serving as a barrier to the harsh native environment. eDAPS toe and linear region moduli were similar to that of native tissue, indicating the potential of this engineered implant for functional restoration of motion segment mechanics. Ongoing work will investigate longer durations of *in vivo* implantation, as well as remobilization strategies to further enhance integration and *in vivo* maintenance.

Conclusions

Current surgical strategies for disc degeneration do not restore native structure and function to the spine. A biologic total disc replacement that better integrates with surrounding tissue (while maintaining composition and mechanical function in the native environment) will significantly improve the standard of care for patients with low back pain.

Acknowledgments

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Interposition of a Cell-seeded Slow-Degrading Membrane Generates a Stable Osteochondritis Dissecans-Like Lesion in a Large Animal Model

James Friedman, MD[1,2]
Mackenzie Sennett, BS[1,2]
Marcelo Bonadio, MD[1,3]
Kerry Orji, BS[1]
Blair Ashley, MD[1,2]
Robert Mauck, PhD[1,2]
James Carey, MD[1,2]

[1]University of Pennsylvania
Philadelphia, PA, USA

[2]Philadelphia VA Medical Center
Philadelphia, PA, USA

[3]University of São Paulo
São Paulo Brazil

Introduction

Osteochondritis dissecans (OCD) is a rare but damaging disease that commonly affects skeletally immature individuals and is defined as the separation of an osteochondral fragment (progeny) from surrounding bone (parent bone). There is great interest in identifying the most effective treatment for this disease. However, the rarity and young patient population makes study in humans difficult. A recent pilot study by our group reported successful creation of OCD-like lesions in a porcine model at a two-week time point with the interposition of either collagen (CM) or fenestrated poly(ε-caprolactone) (fenPCL) membranes between a surgically created progeny fragment and parent bone[1]. The purpose of this study was to assess the durability of this non-union between the osteochondral fragment and surrounding subchondral bone at 5 and 10 weeks, as well as the impact of fibrous cell delivery on this process.

Methods

All animal procedures were approved by the Institutional Animal Care and Use Committee (IACUC) in accordance with NIH policy. Osteochondral fragments (progeny) were created bilaterally in the medial femoral condyles (parent bone) of 16 juvenile male Yucatan mini-pigs. Membranes were placed into the defect and the progeny fragment was secured with transchondral sutures (Figure 1). Membranes included CM (5wk: n = 5; 10wk: n = 3), fenPCL (5wk: n = 5; 10wk: n = 3), tenocyte-seeded CM (10wk: n = 2), and tenocyte-seeded fenPCL (10wk: n = 3). Prior to scaffold seeding, allogeneic porcine tenocytes were isolated from excised patellar tendon. Diced tendon fragments were placed in high glucose DMEM supplemented with 10% FBS and 1% Antibiotic-Antimycotic for 1 week before removal of tendon tissue. Isolated tenocytes were expanded through passage 2 before seeding on fenPCL or CM at a density of $1.6x10^5$ cells/cm^2. Tenocyte-seeded membranes were cultured in chemically defined media with 10 ng/ml TGF-β3 for two weeks before implantation. Animals were sacrificed at 5 or 10 weeks after defect creation. Gross inspection, X-ray, micro-computed tomography (μCT), and histology were used to analyze each defect. Experimental groups were compared against control defects with no interposed membrane (5wk: n = 3; 10wk: n = 2). Three blinded scorers assessed the degree of union between the progeny fragment and parent bone on randomly selected μCT slices from all defects. Statistics were performed using one-way ANOVA with Tukey's post-hoc.

Results

Grossly, all defects were visible at the time of euthanasia with a clear demarcation between progeny fragment and parent bone cartilage. Blinded μCT scoring showed no significant difference in bone healing between acellular groups at 5 and 10 weeks. CM and fenPCL showed a trend towards higher levels of non-union at 5 weeks, but had mostly healed by

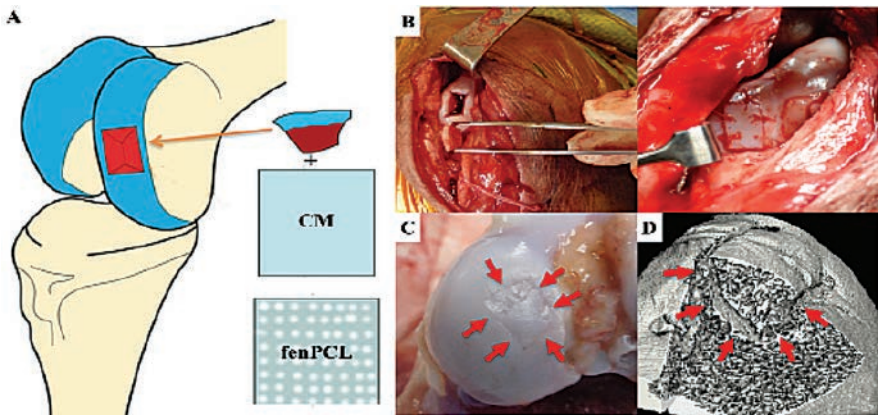

Figure 1. OCD-like lesion creation. **(A)** Schematic showing defect localization on medial femoral condyle as well as collagen and fenestrated PCL membranes. **(B)** Intraoperative views of progeny fragment removal and replacement with transchondral sutures after membrane placement. **(C)** Post-mortem gross view of OCD-like lesion **(D)** Cut-away view of μCT volume-rendering showing perilesional border within the condyle.

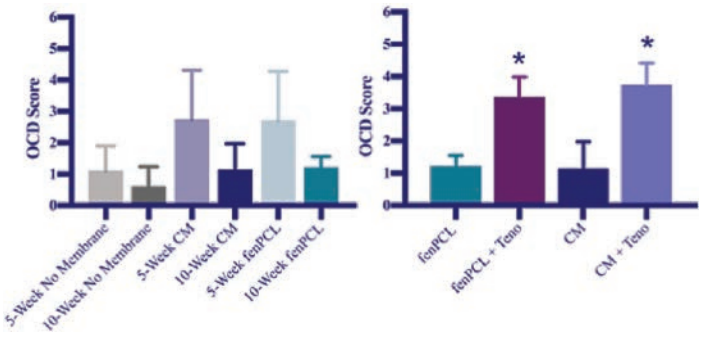

Figure 2. Blinded scoring of μCT images (mean +sd). Three random μCT slices per defect were assigned a score of 0 (complete bone healing) – 6 (complete non-union). No significant differences were found between acellular groups at 5 or 10 weeks (left), but seeded membranes resulted in significantly less healing at 10 weeks (right). (* = $p < 0.05$).

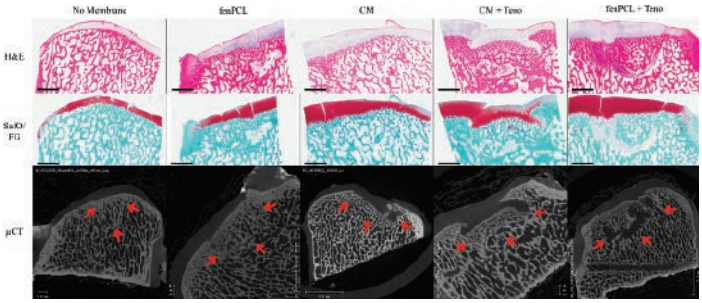

Figure 3. Hematoxylin & Eosin (H&E) and Safranin O/Fast Green (Saf O/FG) staining and μCT images of sections from all groups at 10-weeks post-surgery. Scale bar = 2 mm.

10 weeks. Conversely, tenocyte-seeding of membranes significantly increased the degree of non-union at 10 weeks (Figure 2). Control groups showed nearly complete healing by 10 weeks (Figure 3). Histological analysis confirmed the μCT findings, with all acellular groups showing substantial bone healing and incomplete cartilage healing at 10 weeks (Figure 3). Tenocyte-seeded CM defects showed subsidence of the progeny fragment into the surrounding parent bone. In tenocyte-seeded fenPCL defects, a hypercellular, fibrous border was present around the edge of the progeny fragment.

Discussion

Tenocyte-seeded collagen and fenPCL membranes generated a higher degree of non-union at 10 weeks than acellular membranes. The addition of tenocytes may have resulted in the continuous generation of fibrous matrix that eventually replaced the degradable membranes, allowing for a more persistent fibrous non-union. While CM+teno and fenPCL+teno defects showed similar degrees of non-union, CM+teno progeny fragments subsided into the parent bone whereas fenPCL+teno progeny fragments remained flush with surrounding bone and cartilage. Clinically, OCD lesions are typically flush or slightly proud.The ability of fenPCL+teno membranes to generate non-union while keeping the progeny fragment flush at 10 weeks make it the best candidate for a clinically-relevant animal model of OCD. This animal model will provide a platform to evaluate interventional therapies in future studies.

Significance

This study demonstrates that a tenocyte-seeded fenPCL membrane is capable of generating a stable stage III OCD-like lesion in a Yucatan mini-pig.This animal model will provide a platform in which to evaluate interventional therapies for the treatment of OCD in future studies.

Acknowledgements

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Nuclear Softening Enhances Meniscus Cell Migration into Dense Fiber Networks and Native Tissue

Su-Jin Heo, PhD
Kwang Hoon Song
Breanna Seiber, BS
Feini Qu, BS
Jason Burdick, PhD
Robert Mauck, PhD

Introduction

Cell migration is essential for healing of dense connective tissues[1]. However, the cell nucleus, which is the stiffest organelle in mammalian cells, is an obstacle to efficient migration due to its inability to squeeze through the small pores that typify the dense extracellular matrices (ECM) of these tissues[2]. Modulation of nuclear stiffness is therefore a potential target for enhancing cell mobility. Nuclear mechanics are established in part by the proteins that make up the nuclear lamina, and in part by the packed DNA (chromatin) within[3]. Trichostatin A (TSA) is a histone deacetylase (HDAC) inhibitor that induces hyperacetylation and chromatin relaxation, decreasing nuclear stiffness[3]. We hypothesized that treatment of meniscus cells with TSA would result in more deformable nuclei and thus increase their mobility through both dense fiber networks and the dense ECM of the native tissue. To test these hypotheses, we first developed a novel PDMS/nanofiber membrane cell migration chamber and evaluated whether nuclear softening by TSA pre-treatment improved meniscus cell migration. Next, using sections of adult meniscus, we evaluated whether this same approach could improve meniscus cell migration into native tissue.

Methods

Adult bovine meniscal fibrochondrocytes (MFCs) were seeded on aligned (AL) or non-aligned (NAL) nanofibrous scaffolds (2×105 cells, Passage 1) in basal media (BM: DMEM + 10 % FBS)[3]. A subset of scaffolds was treated with TSA (400 nM) for 3 hours. An image-based edge detection algorithm was used to determine the degree of chromatin condensation (the CCP) in individual DAPI stained nuclei[3] with and without TSA treatment. Additionally, constructs were stretched from 0 to 15% grip-to-grip strain on a custom tensile device and the change in nuclear aspect ratio (NAR) was measured with and without TSA pre-treatment[3]. As an initial assessment of MFC migration, a 96-well transwell migration assay was employed, with pore diameters of 3 or 5 μm (Millipore)[4]. To assess cell contractility with and without TSA pre-treatment, MFCs were seeded onto 10 kPa polyacrylamide gels and traction force was measured[5]. To assess cell migration through dense nanofiber networks, a custom-PDMS 'migration assay chamber' was implemented. The device consisted of a top reservoir containing BM and a bottom reservoir containing BM + 200 ng/mL PDGF as a chemoattractant (Figure 2A). Fluorescently labeled (Cell Tracker Red) aligned (AL) or non-aligned (NAL) nanofibrous PCL scaffolds (thickness: ~ 150 μm) were interposed between the reservoirs, and MFCs (1000 cells, passage 1) were seeded onto the top of each scaffold and cultured in BM with/without TSA for 3 days. At the end of three days, cells were fixed and visualized by actin/DAPI staining. Confocal z-stacks were obtained at 40× magnification and maximum z-stack projections were used to assess cellular morphology. The % of infiltrated cells was quantified, with cells located beneath fibers categorized as 'infiltrated'. To evaluate meniscus cell migration in native tissue, adult meniscus tissue was cryosectioned onto glass slides (~35 μm thick)[4]. To visualize cell invasion, additional living adult meniscal explants (5 mm Φ) were incubated in Cell Tracker™ Green for 1 hour and then placed atop the tissue sections to allow for cell egress onto and invasion into the section[4]. These samples were cultured in BM with/without TSA for 48 hours, at which point maximum z-stack projections were acquired and cell infiltration depth was measured as the distance between the apical tissue surface and the basal cell surface[4]. Statistical analysis was performed using ANOVA (with Tukey's post hoc) or with a Student's t-test ($p < 0.05$).

Results

TSA treatment decreased in the number of visible edges in MFC nuclei (decreased the CCP), indicating efficient relaxation of the chromatin (Figure 1A, B). When TSA-treated cells were deformed, their nuclei increased in NAR to a greater extent than control cells, indicating a softer nucleus (Figure 1C). Treatment with TSA also significantly increased MFC migration through both 3 and 5 μm pores in the transwell assay (Figure 1D). TSA treatment did not, however, alter traction force generation in these cells (data not shown). When MFCs were placed atop scaffolds, the % of cells that had infiltrated was higher in the NAL group than the AL group, and infiltration increased in both groups with TSA treatment (Figure 2B, C). Of note, compared to control

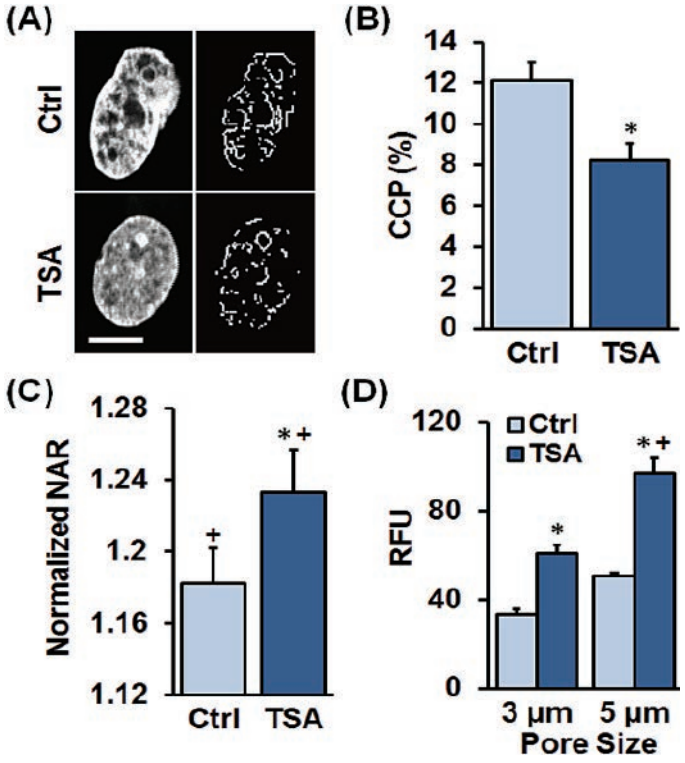

Figure 1. (A) DAPI stained nuclei (left) and corresponding edge detection (right) with/without TSA treatment (Ctrl/TSA, bar = 3 µm), and quantification of chromatin condensation parameter (CCP, right). (B) Quantification of nuclear deformation (NAR) with 15% scaffold stretch (n = ~48, *p < 0.05 vs. Ctrl, +p < 0.05 vs. 0%, normalized 0%). (D) Fluorescence intensity of migrated MFCs in a traditional transwell assay with TSA treatment (n = 5, *p < 0.05 vs. Ctrl, +p < 0.05 vs. 3 µm pore).

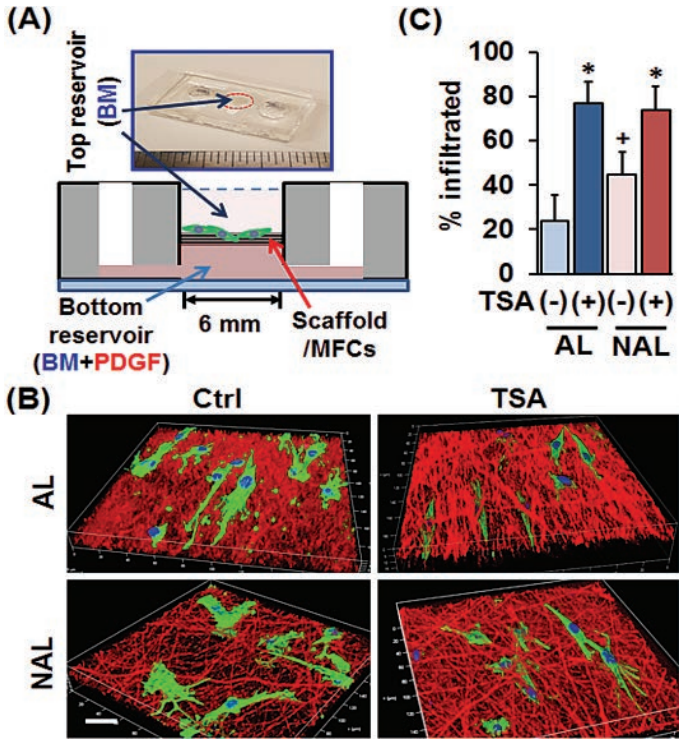

Figure 2. (A) Schematic of PDMS/nanofiber migration chamber. **(B)** Fluorescent images of cells (green), nuclei (blue), and nanofiber scaffolds (red) with/without TSA treatment (Ctrl/TSA, bar = 20 µm). **(C)** Quantification of % infiltrated cells [*p < 0.05 vs. no TSA (−), + p < 0.05 vs. aligned scaffold (AL), n = ~35].

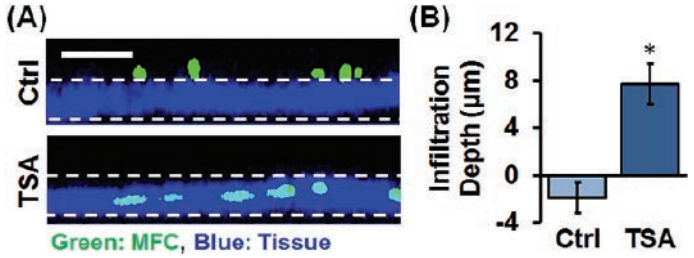

Figure 3. (A) Cross-section view of confocal reconstruction of MFCs (green) migrating through tissue substrates (blue); bar = 50 µm, dashed lines: tissue borders. **(B)** Quantification of cell infiltration depth (n = 45~70 cells, *p < 0.05 vs. Ctrl).

MFCs, TSA treated-cells had more elongated nuclei with higher nuclear aspect ratios (NAR, data not shown). When placed on tissue sections, untreated MFCs (Ctrl) remained primarily on the tissue surface; whereas TSA treated MFCs were found below the tissue surface (Figure 3A). Quantification showed that MFC infiltration depth was significantly greater with TSA treatment compared to controls (Figure 3B).

Discussion

Endogenous cell recruitment is required for healing of injured dense connective tissues. In this study, we demonstrated that nuclear softening via pharmacological decondensation of chromatin in MFCs enhanced their migration through dense fibrous networks and through native tissue. In a previous study, we had shown that partial enzymatic digestion of the ECM also expedites interstitial cell migration[4]. Together, these findings suggest that decreasing the physical impediments to migration (i.e., the properties of the cells themselves and/or the matrix through which they are traveling) can enhance interstitial cell mobility and foster repair.

Significance

Nuclear softening of meniscus cells increased their interstitial migration in dense fiber networks and in native tissue. This approach may improve dense connective tissue repair by enabling more cells to migrate to and colonize the wound site after injury.

Acknowledgements

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U·P·O·J

Mechanical Function of a Composite Nanofibrous Biomaterial Analogue of the Knee Meniscus Inclusive of Radial Inclusive of Radial Tie Fiber-Like Elements

Sonia Bansal, BS
Breanna Seiber, BS
Niobra Keah, MS
Robert Mauck, PhD
Miltiadis Zgonis, MD

Introduction

Menisci are semi-lunar shaped fibrocartilaginous wedges located between the femur and the tibial plateau and support the structure and mechanical function of the knee joint[1,2]. Understanding meniscus structure and function is particularly important given the high incidence of meniscal pathology[3,4]. Circumferentially aligned collagen bundles within the meniscus function to convert compressive forces into tensile hoop stresses[5,6]. In addition, the meniscus contains "radial tie fibers" that originate at the meniscus periphery and interdigitate amongst the circumferential fiber population[5-7]. These radial tie fibers (RTFs) vary in size, spatial distribution, and in their degree of arborization[7], and are thought to bind circumferential fibers together and protect against longitudinal splitting[8,9]. Radial tears interject perpendicularly and sever the circumferential bundles and are thought to compromise mechanical function, though recent studies demonstrated that reduction in load transfer occurs only when these tears reach 90% of the meniscus width[10].This suggests alternative methods for strain transmission in the meniscus. We hypothesize that RTFs play a role in this, particularly in the case of a radial tear. To further this line of inquiry, we quantified RTF density and size in adult menisci as a function of position, and measured the mechanical function of these tissue samples in the context of a radial tear. Additionally, we utilized electrospinning to generate a composite material model of the meniscus, with variable fiber mechanics in each layer, by spinning two polymers with distinct material characteristics.

Methods

Native Tissue Analysis

Medial menisci (n = 14) were harvested from adult (skeletally mature) cows. Six were divided into four equal regions: anterior horn, anterior body (Body-A), posterior body (Body-P), and posterior horn. Each region was cryosectioned in the sagittal plane to 10 μm thickness spanning the cross section and fixed. Three zones were examined: outer, middle, and inner zones. Sections were imaged at 10X via second harmonic generation (SHG, 840 nm excitation). Maximum projections (~5 microns thick) were generated in each zone and the area fraction with positive SHG signal computed as a measure of RTF area fraction (Figure 1A). Fiber thickness was estimated using the FIJI plugin BoneJ[11-13]. Metrics were compared across regions by ANOVA ($p \leq 0.05$) with Tukey's post-hoc tests; data are presented as the mean value for each region and zone (Fig. 1B,C).

Remaining menisci were trimmed as in Figure 2A to yield Anterior, Posterior, and Body segments. These were sectioned transversely into strips (5 × 15 x 0.3mm) with extended tabs for gripping[14]. Samples were preconditioned for 15 cycles (2%-4%) and then evaluated in tension in a ramp to 15% strain (0.5% strain/s). Post-testing, samples were re-equilibrated in PBS for 1 hr, defected with a 50% radial defect at the inner-zone, and retested as above to 50% strain. Stress versus strain data was curve-fit using a custom bilinear fitting program in MATLAB to define the 'toe' and 'linear' moduli[14,15]. Significance (n = 4/group) was analyzed using 1-way ANOVA ($p \leq 0.05$), with Tukey's post hoc; data are presented as mean ± SEM (Figure 2B,C).

Scaffold Fabrication and Mechanical Testing

Nanofibrous 75:25 poly(lactic-co-glycolic acid) (PLGA) and poly(ε-caprolactone) (PCL)

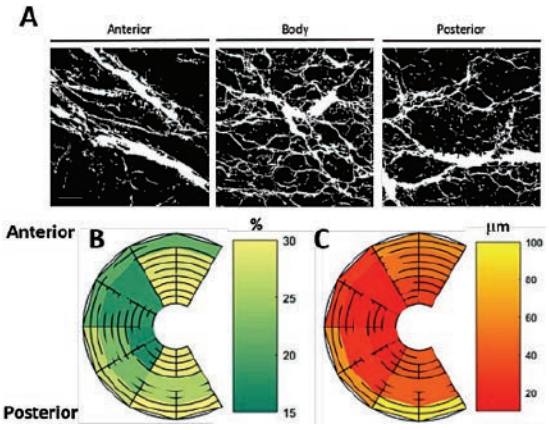

Figure 1. Radial tie fiber (RTF) distribution in adult menisci. **(A)** SHG images of the middle zone of each region, white shows positive SHG indicative of radial tie fiber presence (SB = 200 μm). **(B)** Radial tie fiber density, reported as Area Fraction (%) across the meniscus, and **(C)** Mean fiber thickness (μm).

Correspondence:
McKay Orthopaedic Laboratory
University of Pennsylvania
Philadelphia, PA
soslowsk@upenn.edu

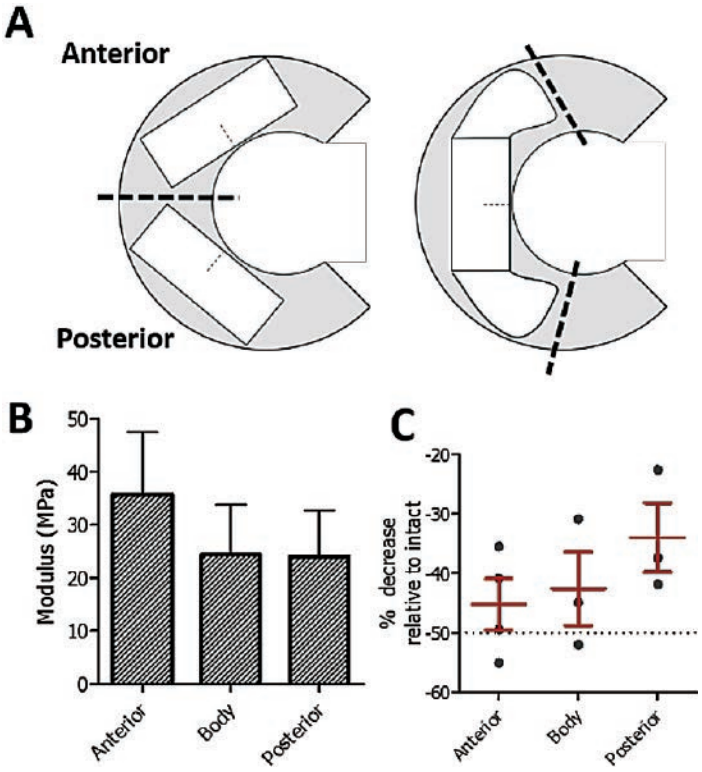

Figure 2. (A) Schematic of native tissue sample preparation **(B)** Linear moduli (LM) of intact tissues by location. **(C)** Change in LM of defected native tissue moduli measured prior to defect creation.

scaffolds were electrospun[7]. For aligned (AL) scaffolds, a mandrel rotating at 10 m/s served as the collector. To form non-aligned (NA) scaffolds, the mandrel was slowed to ~3 m/s. To replicate radial tie elements, AL scaffolds with discrete NA layers were produced by lowering the speed of the mandrel for set periods of time. Composite scaffolds had 7 alternating AL and NA layers (Figure 3A) with 33% distributed NA content overall. The composition of each layer was varied such that scaffolds with softer (PCL) or stiffer (PLGA) intervening NA layers were produced. Scaffolds were trimmed to 40 mm length (in the AL direction) × 5 mm width for testing. Two conditions were tested: intact or defect, with the latter having a radial cut spanning 50% of the width. Samples were evaluated in tension (ramp to 100% strain at 0.5% strain/s) (Figure 3B). Stress versus strain data was curve-fit as above and a custom MATLAB program used to determine the yield and failure strain and toughness. Significance (n = 6/group) was analyzed by 1-way ANOVA ($p \leq 0.05$), with Tukey's post hoc; data are presented as mean ± SEM (Figure 3C-F).

Results

SHG revealed differences in RTF fiber density between zones, with the central body lower than the anterior or posterior horns ($p < 0.05$). RTF thickness varied as a function of region ($p < 0.02$) and zone ($p < 0.005$) (Figure 1B,C). The linear modulus of anterior, body, and posterior sections (35.8 ± 11.8, 24.4 ± 9.5, and 24.0 ± 8.8 MPa) were not different from one another (p= 0.78). However, we noted an attenuation in the decrease in apparent modulus with defect of posterior samples compared to all other regions (Figure 2B,C).

For scaffolds, the linear region modulus of PLGA-only AL scaffolds was ~4x higher than PLGA NA scaffolds (241 ± 13 vs 53 ± 2 MPa, $p < 0.001$) and linear region moduli of AL and NA PLGA scaffolds were ~7 and ~5x higher than AL and NA PCL scaffolds, respectively (34 ± 2 and 11 ± 0 MPa, $p < 0.001$) (Figure 3C). Yield strains for AL and NA PLGA scaffolds (1.5 and 2.4%) were lower than PCL scaffolds (AL: 10% and NA: 6%, $p < 0.001$) (Fig. 3D). The greatest toughness of defected scaffolds was seen in AL PLGA scaffolds (1.1 ± .10 $J \cdot m^{-3} \cdot \mathbf{10}^{4}$, $p < 0.001$). Failure strain ranged from 36% (PLGA, AL) and 46% (PLGA, NA) in single-polymer scaffolds (Figure 3E,F).

Composite scaffolds showed distinct mechanical behavior

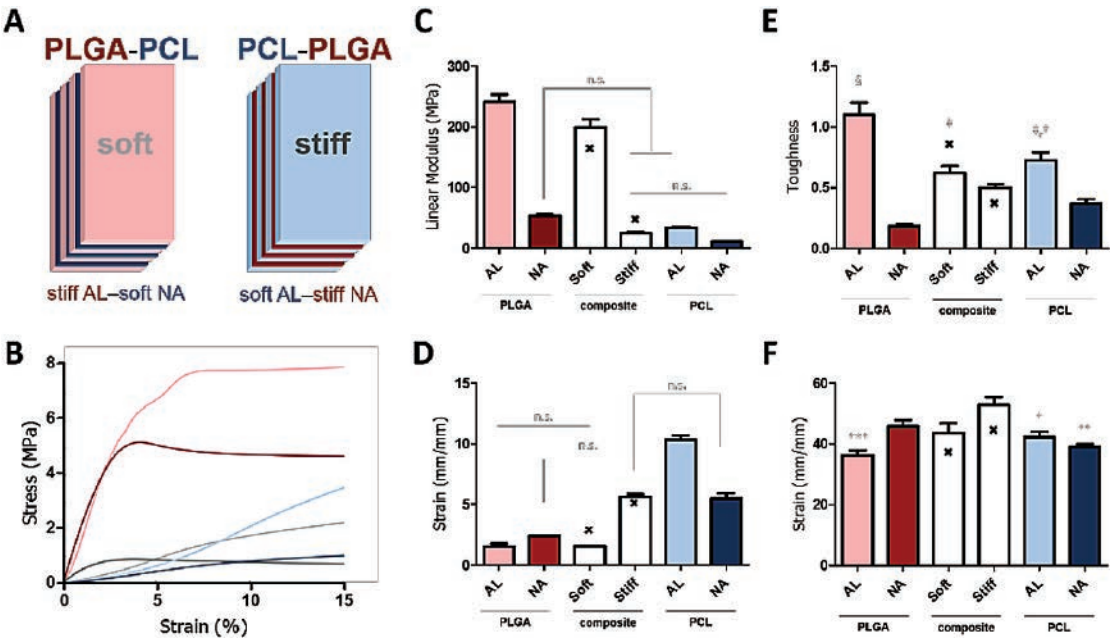

Figure 3. (A) Schematic of composite scaffold preparation **(B)** Stress-strain plots of each group to 15% strain. **(C)** Linear moduli and **(D)** yield strain of intact AL, NA, and composite scaffolds. $P > 0.01$unless otherwise indicated. **(E)** Toughness and **(F)** failure strain of defected AL, NA, and composite scaffolds, § = $p \leq 0.05$ vs. all other groups, Toughness. ‡ = $p \leq 0$ .01 vs. PLGA-NA, Toughness. † = $p \leq 0.01$ vs. PCL-NA, Toughness. * = $p \leq 0.05$ vs. PCL_PLGA, Failure strain. "x" indicates expected outcome from weighted mixture model.

that did not always match expectations, based on a simple weighted mixture model combining the individual components. Expected linear modulus of composites formed from AL PLGA with intervening NA PCL did not match predictions while the reverse configuration exceeded predicted value ($p = 0.0002$, Figure 3C). Toughness of AL PLGA/NA PCL scaffolds was lower than expected ($p = 0.01$) while AL PCL/NA PLGA scaffolds were higher than expected ($p = 0.008$) (Fig. 3D). Similarly, the yield strain of AL PLGA/NA PCL scaffolds was lower than expected values ($p < 0.0001$) while AL PCL/NA PLGA scaffolds were higher ($p = 0.04$) (Figure 3E). Conversely, strain at failure was under predicted for both, with this being significant for AL PCL/NA PLGA scaffolds ($p = 0.03$, Figure 3F).

Discussion

Radial tie fibers (RTFs) form a branched fiber network that interdigitates with circumferential fibers in the meniscus, and may function to stiffen the composite and make it more resistant to crack propagation. This effect would likely be contingent upon RTF density, distribution, and thickness. We found the greatest density of RTFs in the posterior horn, potentially reflecting the more demanding in vivo loading experienced in this region. Our finding of a trend towards a higher apparent modulus in the posterior horn (in the context of a radial defect) supports the hypothesis that RTFs play such a functional role. To study these interactions in a more controlled setting, we developed a biomaterial analog containing RTF-like elements. These distinct disorganized fibrous layers (that were interspersed in an otherwise aligned fiber array) altered scaffold mechanics. The finding of increased failure strain (compared to scaffolds of a single composition) supports the beneficial effects of RTF inclusion in native meniscus. This may act by enabling efficient and prolonged load transfer in the context of tears that interrupt the circumferential fibrous architecture. Understanding of this complex composite behavior will inform engineering design towards the fabrication of functional meniscus replacements, and could alter clinical practice with respect to surgical intervention.

Acknowledgements

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U·P·O·J

Effects of Hypoxia and TGF-β Exposure during Monolayer Expansion on the Survival and Matrix Producing Capacity of Mesenchymal Stem Cells

Sun Peck, PhD[1,2]
Justin Bendigo, BS[1,2]
Sarah Gullbrand, PhD[1,2]
John Tobias, PhD[2]
George Dodge, PhD[1,2]
Robert Mauck, PhD[1,2]
Neil Malhotra, MD[2]
Lachlan Smith, PhD[1,2]

[1]Philadelphia VA Medical Center, Philadelphia, PA

[2]University of Pennsylvania, Philadelphia, PA

Introduction

Degeneration of the intervertebral discs is implicated as a major cause of lower back pain[1]. There is a need for treatment options that not only alleviate symptoms but also reconstitute native tissue structure and mechanical function within the disc. Over the past several years, application of mesenchymal stem cells (MSCs) for disc regeneration, particularly for the nucleus pulposus (NP), has received considerable attention. Previous studies have shown that MSCs are capable of undergoing differentiation into a NP-like phenotype under certain culture conditions[2-4]; however, a key challenge to successful application of MSCs for NP regeneration is the harsh *in vivo* environment. The NP region of the disk, which is characterized by low nutrition and oxygen tension, both of which may negatively impact the survival and biosynthetic properties of MSCs[5]. The objective of this study was to investigate whether exposing MSCs to hypoxia during monolayer expansion enhances subsequent survival and regenerative potential in the nutrient and oxygen poor NP environment. Furthermore, we investigated whether priming MSCs towards an NP-like phenotype by exposing them to TGF-β3 during monolayer expansion enhances subsequent regenerative potential.

Methods

Cell Isolation and Expansion

Bone marrow-derived MSCs were isolated from 3 juvenile bovine femurs and tibia (<6 months of age), pooled, and expanded to confluence through a single initial passage in monolayer in normoxia (21% O_2) and basal medium (DMEM (4.5 g/L glucose) and 10% FBS). The cells were then passaged and expanded in basal medium in one of four different conditions for 1 week: 1. Normoxia (21% O_2; standard MSC expansion conditions); 2. Normoxia + TGF-β3 (10 ng/mL); 3. Hypoxia (2% O_2); 4. Hypoxia + TGF-β3 (10 ng/mL).

Pellet Culture

After the monolayer expansion protocol described above, cells were passaged and cultured in pellets (250,000 cells/pellet) in a simulated NP-like environment (hypoxia (2% O_2) and chemically defined media with low glucose (1 g/L) DMEM and no growth factors)). After 2 weeks of culture, pellets were harvested and either fixed in formalin and processed for paraffin histology (n = 2) or analyzed for biochemical composition (n = 5). For histology, sections were stained with Alcian blue (glycosaminoglycans, GAG) or picrosirius red (collagen). For analysis of biochemical composition, DNA, GAG, and collagen contents were quantified using the PicoGreen (Thermo Fisher), dimethylmethylene blue, or hydroxyproline assays respectively. DNA was analyzed per pellet, and GAG and collagen were normalized to DNA. Significant differences ($p < 0.05$) between groups were established using 2-way ANOVA with Bonferroni post-hoc tests ($p < 0.05$).

Microarray Analysis

Bovine MSCs were isolated and expanded under the four conditions described above, with cells from 3 different donor animals maintained as distinct biological replicates. Cells were harvested, high quality RNA (RIN > 9) was isolated from each sample, and global gene expression was measured using the WTPlus Bovine Gene Chip (Affymetrix GeneChip system). Gene expression data were normalized using Robust Multi-array Average. Significant differences in gene expression were determined using 3-way mixed model ANOVA ($p < 0.05$; adjusted for false discovery rate).

Results

Pellet Culture

DNA content for pellets with MSCs expanded in hypoxia, both with and without TGF-β3, was significantly higher than for those with MSCs expanded in normoxia, both with and without TGF-β3 (Figure 1A). DNA content was lowest for pellets with MSCs expanded in normoxia with TGF-β3, and highest for pellets with MSCs expanded in hypoxia with TGF-β3. There was no significant effect of monolayer expansion condition on pellet GAG content (normalized to DNA, Figure 1B). Collagen content exhibit the opposite trend to DNA, and was highest

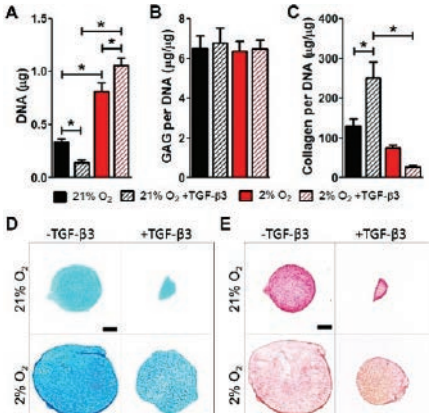

Figure 1. Composition of MSC pellets after monolayer expansion in different oxygen and TGF-β3 conditions. A. DNA content, B. GAG per DNA, and C. Collagen per DNA. D. Alcian blue staining for GAG. E. Picrosirius red staining for collagen. *$p < 0.05$; scale bar = 0.2 mm.

for pellets with MSCs expanded in normoxia with TGF-β3 ($p < 0.05$ vs both normoxia without TGF-β3 and hypoxia with TGF-β3, Figure 1C). Histological results supported these findings (Figs 1D and E), where pellets with MSCs expanded under hypoxia, with and without TGF-β3, were larger than those with MSCs expanded under normoxia, suggesting higher cell numbers.

Microarray Analysis

Principal component analysis (PCA, Figure 2A) indicated significant effects of MSC donor on the global gene expression in response to each expansion condition.The effects of altering oxygen tension alone (without TGF-β3) during monolayer expansion on MSC gene expression were moderate. MSCs expanded under hypoxia exhibited differential expression of genes implicated in the cell stress response (B4GALT56: galactosyltransferase; LPL: lipoprotein lipase; NGF: nerve growth factor; PK: pyruvate kinase) compared to normoxia expanded MSCs (Figure 2B). Exposure to TGF-β3 during monolayer expansion resulted in the greatest effects on global gene expression, irrespective of oxygen tension. In particular, there were significant effects on expression of genes involved in growth and inflammation, including those of the TGF-β, NFκB, and caspase activation pathways (Figure 2C).

Discussion

The results of this study suggest that exposure to hypoxia during monolayer expansion leads to improved survival (higher DNA content) when these cells are subsequently cultured in simulated NP-like conditions with limited oxygen and nutrition. Interestingly, exposure to hypoxia during monolayer expansion had no significant impact on the subsequent matrix (GAG or collagen) producing capacity of MSCs in the absence of TGF-β3. In contrast, exposure to TGF-β3 under normoxic conditions during expansion significantly inhibited subsequent MSC survival and boosted collagen production on a per cell basis with no effect on GAG. This may suggest induction of a post-mitotic and pro-fibrotic phenotype, which may be detrimental to the capacity of MSCs

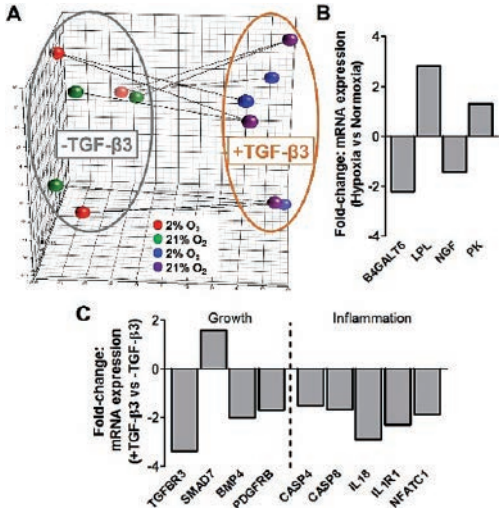

Figure 2. Microarray results. **(A)** Principal component analysis (PCA) plot. Lines connect all samples from a single animal. **(B)** Effects of hypoxia on gene expression in the absence of TGF-β3. **(C)** Effects of TGF-β3 on growth and inflammation pathway gene expression. N = 3; all $p < 0.05$.

to regenerate NP tissue. Microarray results support this view, with TGF-β3 exerting significant effects on signaling pathways that regulate fibrosis and inflammation, which eclipsed any beneficial effects of hypoxia alone. Ongoing work will seek to verify these findings, by determining the type of collagen (I or II) being produced and measuring levels of pro-inflammatory factors in the culture media. Finally, microarray results highlighted the significant effects of donor on the response of MSCs to environmental stimuli, potentially due to variations in age and sex, the impact of which should be considered during future translational studies.

Significance

The results of this study demonstrate that alterations in monolayer expansion environment significantly impact the survival and matrix producing capacity of MSCs and provide a foundation for optimizing the regenerative capacity of these cells in the intervertebral disc.

Acknowledgements

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Structural and In Vivo Functional Measures Predict Achilles Tendon Fatigue Mechanics During Healing

Snehal Shetye, PhD
Benjamin Freedman, PhD
George Fryhofer, MD
Corinne Riggin, BS
Josh Gordon, MD
Stephen Thomas, PhD
Dan Farber, MD
Louis Soslowsky, PhD

Introduction

The Achilles tendon is one of the most commonly injured tendons, affecting approximately 31 in 100,000 people each year[1]. Previous laboratory studies have shown that specific mechanical and material properties of the rat Achilles tendon in the post-injury period may be used to assess healing quality. However, direct clinical measurement of these mechanical properties is not yet possible[2-5]. Further, clinical functional measures, such as the "hop test," are not capable of isolating specific tendon properties[6]. Therefore, the purpose of this study was to use multiple regression analyses to identify clinically measurable functional capable of predicting the mechanical properties of healing Achilles tendon. We hypothesized that tendon properties, including cross sectional area (CSA), echogenicity, collagen fiber alignment, weight-bearing, and ankle range of motion would be strongly predictive of post-injury tendon fatigue mechanical properties.

Materials and Methods

Study Design

Data used in this multiple regression statistical analysis study were obtained from previous studies using rat Achilles tendon blunt transection injury models, which incorporated post-injury immobilization and gradual return to treadmill activity (n = 110). Complete data sets needed for developing a robust regression model were acquired from October to November 2016. Studies #1[2] and #2[3] investigated the role of surgical treatment (repaired [R] vs. non-repaired [NR]) and return to activity timing at 3 and 6 weeks post-injury in male rats. Study #3[5] evaluated tendon healing at 3 and 6 weeks post-injury on injured female and ovariectomized (OVX) rats that underwent NR treatment.

Regression Modeling

The predictor variables were: measures of collagen structure (echogenicity and circular standard deviation (CSD) (*high frequency ultrasound*)); active functional limb assessment (vertical, braking, propulsion, and lateral ground reaction force magnitudes (*gait analysis*)); tendon morphology (CSA (*laser-based measurement*)); and passive functional limb assessment (total ankle ROM, toe, and linear stiffness in dorsiflexion and plantarflexion (*passive ankle manipulation*)). Sex (M = [1,0], F = [0,1], OVX = [0,0]) and surgical treatment (NR = 1, R = 0) were inputted as categorical variables. The response variables were secant stiffness, hysteresis, laxity, secant modulus, and secondary phase slope (fatigue testing). Assumptions required for linear regression analysis were general linearity between single predictor and dependent variables, normality, non-multicollinearity (Durbin-Watson), neutrality of the dependent variables, and lack of outliers. Step-wise backward elimination linear regression analysis was performed to select the best structural and functional variables for predicting mechanical properties. The resulting regression coefficients were then used to predict mechanical properties for all groups.

Statistical Significance Evaluation

Coefficients of determination and two-tailed p-values were calculated for each regression model and significance was set at $p < 0.05$ for all tests (SPSS, IBM, Inc., Version 24, Armonk, NY).

Results

All assumptions for multiple regression were satisfied and Durbin-Watson scores were greater than 1.62 for all models presented (Table 1). The chosen independent variables strongly predicted secant modulus and hysteresis ($R^2 > 0.74$, $p < 0.001$). Secant stiffness and laxity were moderately predicted by the chosen independent variables, with R^2 values of 0.34 and 0.46, respectively. Although statistically significant, the slope of the secondary phase was only weakly predicted by the independent variables. Repair type and plantarflexion linear stiffness were involved in predicting four of the five response variables. Sex was a contributing factor in predicting hysteresis, laxity, and secondary phase slope. Dorsiflexion linear stiffness, plantarflexion toe stiffness, lateral force, echogenicity, and total ankle ROM were not significantly predictive in any regression model.

Discussion

The Achilles tendon typically operates under high and cyclic loading scenarios, which can result

Table 1. Significant coefficient results using multiple regression analysis.

Response variable	R^2	*p*	CSA (mm^2)	CSD (*)	Dorsi.Toe Stiffness (N*mm/deg)	Plantar Lin Stiffness (N*mm/deg)	Vertical Force (%BW)	Propulsion Force (%BW)	Braking Force (%BW)	Ankle ROM(*)	Sex	Repair Type
Secant Stiffness (N/mm)	0.3	<0.001	–	–	–	−34.3	0.1	0.8	–	–	–	–
Hysteresis (MPa mm/mm)	0.74	<0.001	0.0003	–	−0.01	−0.04	–	–	–	−0.00006	0.008	0.002
Laxity (mm/mm)	0.46	<0.001	–	–	−19 .9	2.3	–	–	–	–	2.3	−18.6
Secant Modulus (N/mm)	0.76	<0.001	−2.9	−3.3	–	−53.1	0.3		−0.9	–	–	−5.8
2nd Phase Slope (mm/mm /% fatigue life)	0.11	0.036	–	–	–	–	–	–	–	–	0.017	0.016

in tendinopathy and acute rupture. Following treatment, injured tendons are expected to perform under similar physiologic cyclic loading conditions. Clinical assays such as ultrasound, gait analysis, and passive joint assessment cannot directly evaluate tendon fatigue properties. However, since many of these assays are generally simple to perform, even if not used routinely in clinics, defining their relative importance would be important to clinicians. Our regression results suggest that clinical evaluation of ankle joint stiffness into plantarflexion may serve as a viable metric for estimating and tracking tendon strength after injury. Further, CSA measurements allow clinicians to predict the healing tendon's efficiency in storing elastic energy (hysteresis) and ability in bearing load (secant modulus). Both parameters are crucial for allowing the tendon to withstand cyclic loading. Surprisingly, unlike ankle stiffness and cross-sectional area, ultrasound parameters (echogenicity, CSD) were not predictive of tendon fatigue properties, in contrast to a previous study[7]. Although both studies had similar coefficients of determination between echogenicity and secant stiffness, the other functional measures included in our model were more predictive. Finally, in this study, CSA values were obtained using a laser-based technique not performed in humans; however, transverse plane ultrasound methods are in use clinically, and can provide similar area measurements that correlate very well to laboratory-based measurements[8]. Overall, clinically relevant in vivo functional measures assessed healing tendon quality by accurately predicting tendon fatigue mechanical properties.

Conclusions

This study highlighted specific clinical measurements of tendon properties that reliably and significantly predicted the quality of tendon healing. This was achieved through controlled and rigorous laboratory experiments not generally feasible in the clinical setting.

Acknowledgements

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Biceps Tenotomy in the Presence of a Supraspinatus Tear Alters the Adjacent Intact Tendons and Glenoid Cartilage

Zakary Beach, BS
Jennica Tucker, BS
Stephen Thomas, PhD
Katherine Reuther, PhD
Chancellor Gray, MD
Chang-Soo Lee, MD
David Glaser, MD
Louis Soslowsky, PhD

McKay Orthopaedic Research Laboratory, University of Pennsylvania, Philadelphia, PA

Introduction

A rotator cuff tear is a common injury in athletes and workers who repeatedly perform overhead movements, and it is not uncommon for this demographic to return to activity shortly after treatment. A biceps tenotomy can be performed in the presence of a rotator cuff tear to reduce pain and improve joint function[1]. However, the effect of this procedure on the surrounding tissues in the glenohumeral joint is unknown. Therefore, the purpose of this study was to investigate the effects of a biceps tenotomy in the presence of a supraspinatus rotator cuff tear, followed by overuse activity as well as the mechanical and histologic properties of the remaining rotator cuff tendons and glenohumeral articular cartilage. We hypothesized that a biceps tenotomy in in this context would result in adverse changes in the surrounding tissues demonstrated by a decrease in joint function, as well as decreased mechanics and increased cellular activity in the intact tendons and glenoid cartilage.

Materials and Methods

Experimental Design

46 adult male Sprague–Dawley rats underwent 4 weeks of overuse activity (downhill (10°) treadmill running at 17 m/min for 1h/day, 5 days/week)[2] to create a tendinopathic condition in the supraspinatus tendon. Next, the animals were randomized into two groups: unilateral detachment of the supraspinatus tendon alone (SO) or detachment of the supraspinatus and long head of the biceps tendons (SB), as previously described[3]. After surgery, animals were allowed 1 week of cage activity before returning to the overuse training over 2 weeks. After training, all animals underwent 5 weeks of overuse activity[4].

Ambulatory Measurement

Forelimb gait and ground reaction forces were quantified using an instrumented walkway[4]. Data was collected 1 day prior to tendon detachment to obtain baseline values and also at 3, 7, 14, 28, 42 and 56 days post-surgery.

Tendon Mechanical Testing

Tendon testing was performed as previously described[3]. Briefly, stain lines were used to track optical strain. Cross-sectional area was measured using a custom laser device[5]. Tensile testing was performed as follows: preload to 0.08 N, preconditioning (10 cycles of 0.1-0.5 N at a rate of 1% strain/s), stress relaxation to 5% strain at a rate of 5% strain for 600 seconds, then ramp to failure at 0.3% strain/s.

Cartilage Mechanical Testing

For cartilage thickness measurements[4], specimens were scanned using ultrasound. Each thickness map was divided into six regions, and a mean thickness was computed for each region. Utilizing a 0.5-mm-diameter, nonporous spherical indenter, cartilage indentation testing was performed[4]. Briefly, a preload (0.005 N) was followed by eight stepwise stress relaxation tests (8 μm ramp at 2 μm/second followed by a 300 second hold). Equilibrium elastic modulus was calculated, as described[6], at 20% indentation thickness and assuming Poisson's ratio ($\upsilon = 0.30$).

Histology

Tendon samples were stained with hematoxylin and eosin, while cartilage samples were stained with safranin O, fast green and iron hematoxylin. Tendon sections were graded for cellularity and cell shape[4]. Cartilage sections were graded using a modified Mankin Score[7].

Statistical Design

For ambulation data, significance was assessed using a two-way ANOVA, followed by paired t-tests when appropriate. Multiple imputations for missing data (~15%) were conducted on the ambulatory measures. Tendon and cartilage mechanics were evaluated using t-tests. For histology, median grades were compared between groups using a Mann-Whitney test. Significance was set at $p < 0.05$.

Results

Biceps tenotomy resulted in no differences in ambulatory measurements. The lower subscapularis tendon did not show any midsubstance changes or in its insertion between groups. However, the upper subscapularis tendon increased its insertion area in the presence of the detachment of the long head of the biceps (Figure 1A). Increases in the moduli of infraspinatus and upper subscapularis

tendons (Figure 1B) were also found. An increase in tendon midsubstance elastic modulus was also seen in the upper subscapularis tendon (Figure 2). Biceps tenotomy did not reveal changes in elastic modulus in the insertion of the infraspinatus, lower subscapularis or upper subscapularis tendons. Histology showed a significantly increased score for cell shape in the midsubstance of the infraspinatus tendon, signifying that the cells present may be more metabolically active. Results showed no differences in the lower or upper subscapularis tendons in cellularity or cell shape in any region. The biceps tenotomy group showed a significant decrease in glenoid articular cartilage thickness in the anterior-superior region and a significant increase in the superior region when compared to the intact long head of biceps tendon group (Figure 3A). The biceps tenotomy group also showed significantly greater equilibrium elastic modulus in the center and anterior-superior regions (Figure 3B). Histology showed significant increases in modified Mankin score in the biceps tenotomy group in the center, anterior-superior and posterior-superior regions of the glenoid articular cartilage.

Discussion

Results suggest that the tissues in the surrounding joint are altered when a biceps tenotomy is performed in the presence of a supraspinatus only rotator cuff tear. The alterations seen in the infraspinatus and upper subscapularis tendons in the presence of a biceps tenotomy could be caused by an interruption in the anterior-posterior force balance, which has been shown to be important to joint health and function[8]. The altered mechanical properties of the glenoid articular cartilage, combined with the increased modified Mankin score, suggests that a biceps tenotomy in the presence of a supraspinatus tendon tear alters the loading in the superior half of the glenoid articular cartilage, which could be due to increased humeral head translation in the absence of the long head of the biceps tendon[9]. These findings show that the biceps tenotomy exacerbates the negative effects associated with overuse after a supraspinatus only tear[4]. Results indicate that the properties of the surrounding tendons and glenoid cartilage are altered in the presence of the biceps tenotomy, perhaps due to decreased joint stability. Future studies are needed concerning biceps tenotomy in the presence of a rotator cuff tear in humans to determine whether the short-term pain-relief of the biceps tenotomy results in increased joint damage long-term.

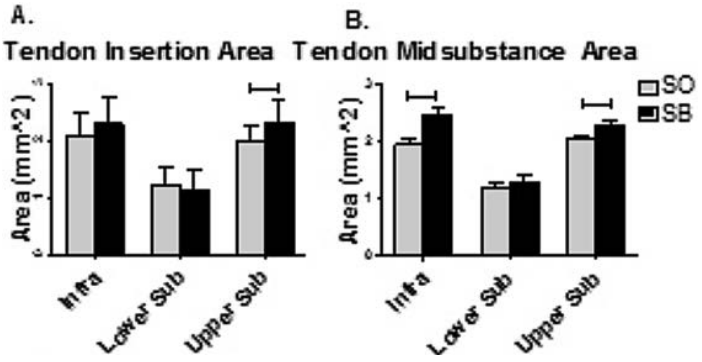

Figure 1. (A) Infra and upper subscap tendon midsubstance area was increased in SB group. **(B)** Upper subscap tendon insertion area was increased in SB group.

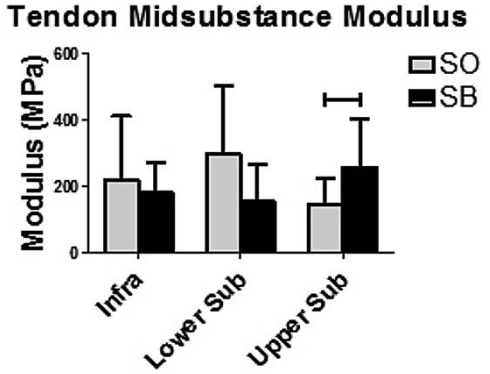

Figure 2. Upper subscap tendon midsubstance elastic modulus was increased in SB group.

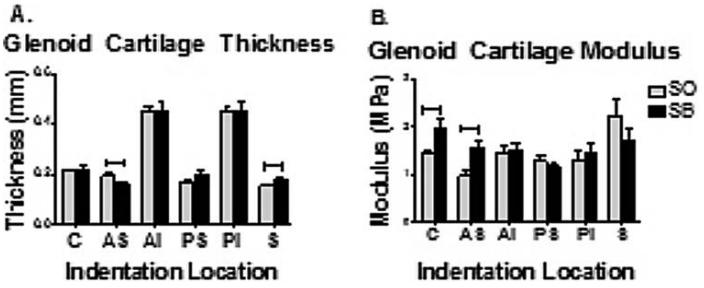

Figure 3. (A) Glenoid cartilage thickness was altered in the anterior-superior and superior regions. **(B)** Glenoid cartilage modulus was increased in the center and anterior-superior regions.

Conclusions

This work demonstrates that a biceps tenotomy in the presence of a supraspinatus tendon rotator cuff tear affects the surrounding tissues in the rotator cuff of a rat model. Therefore, alternative methods of treatment should be explored that aim to address patient-specific problems while preserving long-term joint health.

Acknowledgements

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Achilles Tendon Mechanical and Compositional Properties Differ Drastically in Early Healing Between Repaired and Non-Repaired Tendons

Benjamin Freedman, PhD
Tyler Morris, MD
George Fryhofer, MD
Pankti Bhatt, BS
Nabeel Salka, BS
Daniel Farber, MD
Louis Soslowsky, PhD

McKay Orthopedic Research Laboratory, Philadelphia, PA

Introduction

The decision to surgically repair Achilles tendons following rupture remains controversial[1]. Although operative treatment has been believed to result in superior Achilles function and lower re-rupture rates compared to conservative (non-operative) management[2], there is inadequate scientific evidence to support this belief[3,4]. Recent work has identified superior mechanical properties with conservative management at 3- and 6-weeks post-injury in rodents[5,6]. However, the immediate mechanical, structural, and histological changes during healing that drive these later healing responses remained unknown. Therefore, the purpose of this study was to evaluate the early tendon healing response by directly comparing repaired versus non-repaired Achilles tendons at 1-week post-injury. We hypothesized that non-repaired tendons would have superior mechanical, structural, and histological properties compared to repaired tendons at 1-week post-injury.

Materials and Methods

Study Design

Sprague Dawley rats (n = 36) at 16-weeks of age were used (IACUC approved). Animals received 2 weeks of treadmill exercise training (up to 60 minutes at 10m/min) prior to a complete blunt transection of the right Achilles tendon[5,6]. Animals were then randomized into repaired (Urbaniak variant of the Kessler) and non-repaired groups. Injured hind limbs were immobilized in plantarflexion. *Ex vivo* Assays

1-week post-injury, animals were euthanized and the Achilles tendon-foot complex was carefully removed *en bloc*. Achilles tendons were then finely dissected, cross sectional area measured, and secured in fixtures. Tendons were then loaded at 1N in a PBS bath while a series of sagittal B-mode high frequency ultrasound images (HFUS) were acquired (Vevo 2100, MS550D; VisualSonics) (n =1 0/group)[5]. Tendons (n = 10/group) were then mechanically tested through: stress relaxation (6% strain), a low-load dynamic frequency sweep (0.1 to 10 Hz), and constant strain rate until ultimate failure (Instron Electropuls 3000) [5]. An additional set of tendons was used for histological and immunohistochemical (IHC) analysis (n=8/group). Sagittal sections (7 μm) were collected and stained with Hematoxylin-Eosin (H&E), as well as with Safranin-O and Fast Green (SAF-O). Sections were also stained for collagen types I and III, with proteins visualized using 3,3' Diaminobenzidine.

Analysis

Achilles tendon relaxation, dynamic modulus (|E*|), tanδ, and toe and linear moduli were computed from mechanical data. Echogenicity and collagen fiber alignment were evaluated from the HFUS images at the injury site[7]. Three blinded graders independently evaluated cell density, nuclear shape, and SAF-O staining at the injury site. IHC was analyzed for % area stained with ImageJ (NIH, v1.48). T-tests were used to compare mechanical and structural properties and Mann-Whitney U-tests were used to compare histological scoring ($\alpha = 0.05$).

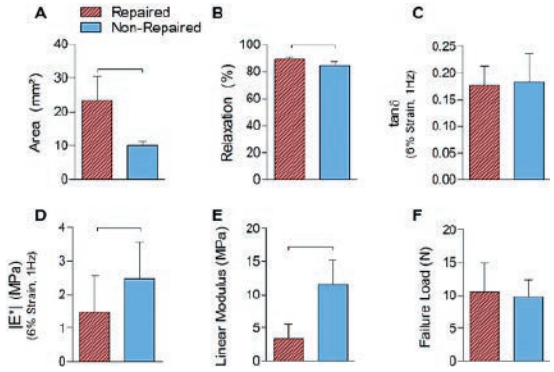

Figure 1. Mechanical Properties. Repaired tendons had elevated **(A)** tendon cross sectional area and **(B)** percent relaxation, but decreased **(D)** IE*I and **(E)** linear modulus compared to non-repaired tendons. No differences in **(C)** tano or **(F)** failure load existed between groups. Data are presented as mean and standard deviation, and statistical significance is indicated with lines ($p < 0.05$).

Results

Repaired tendons had a larger cross sectional area compared to non-repaired tendons (Figure 1A). Low strain viscoelastic testing revealed that percent relaxation (Figure 1B) was greater in repaired compared to non-repaired tendons, but there were no differences in tanδ (Figure 1C). |E*| and linear modulus (Figure 1D,E) were both decreased in repaired tendons compared to

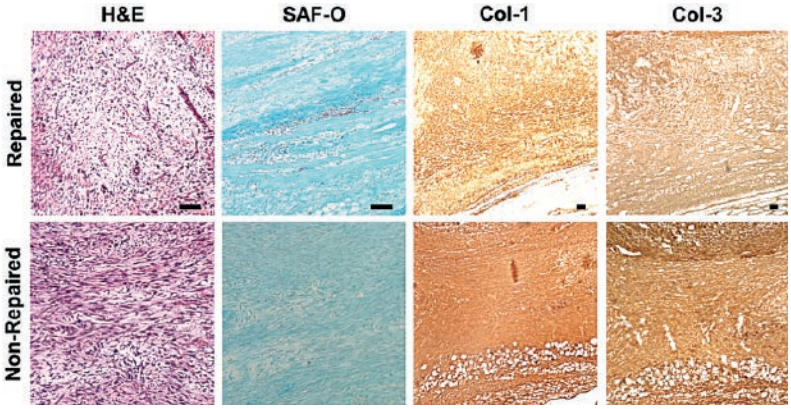

Figure 2. Histological and Immunohistochemical Properties. Repaired and non-repaired tendons were sectioned and stained with H&E, SAF-O, collagen type-I, and collagen type-III. Nuclei in repaired tendons were more round than in non-repaired tendons when assessed at the injury region (midsubstance). Non-repaired tendons had a trend for increased cellularity compared to repaired tendons. No differences in SAF-O, collagen type-I, or collagen type-III staining were observed. Scale bar = 100 μm.

non-repaired tendons, but there were no differences in failure load (Figure 1F). Histological evaluation (Figure 2) found that repaired tendons contained nuclei that were more rounded in shape compared to non-repaired tendons. Additionally, there was a trend for increased cellularity in non-repaired tendons. No differences in SAF-O staining, collagen type-I, or collagen type-III staining were found. No differences in echogenicity or collagen fiber alignment were detected at the injury site (not shown).

Discussion

This study investigated the effects of surgical treatment on Achilles tendon healing at 1-week post-injury in rodents. Overall, we observed large changes in material properties between groups at 1-week post-injury. In contrast, a previous study[8] found no differences in function or mechanics between repaired and non-repaired tendons 15-days post injury. This previous study did not control for the resting position of the ankle, which could reduce the potential mechanical benefits of conservative treatment.The role of mechanical loading has been shown to be a very sensitive factor for Achilles healing[9]. Mild tendon loading protection induced through Botox and limb suspension can modulate tendon material properties. Regarding histological findings, we observed increased cellularity and collagen disorganization at 1-week post-injury, similar to that found at later time points post-injury[5,6]. These changes notably continued later into healing[5,6], suggesting that disorganized matrix rich in collagen types-I and type–III is deposited early and propagates throughout tendon healing. Unlike tenocytes in uninjured tendon that display a spindle-like shape[10], cells in healing tendons had a more round morphology. Although material properties were superior in non-repaired tendons, no differences were observed in collagen staining or fiber alignment, which suggests that other changes in tissue composition may drive these mechanical responses. Future studies will examine additional protein and molecular changes due to surgical treatment.

Conclusions

Given the controversy between surgical or non-surgical treatments for Achilles rupture, well controlled basic science studies are necessary to evaluate tissue healing. This study identified numerous mechanical and cell morphological differences between repaired and non-repaired tendons as early as 1-week post-injury. This data may also provide a foundation for the differential healing response due to surgical treatment observed at later time points.

Acknowledgements

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Tendon Strain Stiffening is Reduced During Healing and High Magnitude Long Duration Dynamic Loading

Benjamin Freedman, PhD[1]
Ashley Rodriguez, BS[1]
Cody Hillin, MD, MS[1]
Stephanie Weiss, BS[1]
Joseph Sarver, PhD[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopedic Research Laboratory, Philadelphia, PA

[2]Department of Biomedical Engineering, Drexel University Philadelphia, PA

Introduction

Tendons transfer stresses and strains from muscle to bone during loading, resulting in multi-scale changes to their extracellular matrix (ECM). For example, tendon stiffness increases with strain, as disorganized ECM at the microscopic level becomes more aligned and less crimped[1]. Previous work has shown that tissue strains correlate with cellular and nuclear strains in uninjured tendons during *quasi-static* tensile loading[2]. However, it remains unknown how ECM stresses are altered in clinically relevant situations, such as high *dynamic* loading and *healing*, which may propagate to alter strain transfer to cellular components. Therefore, the objective of this study was to investigate the role of tendon healing and dynamic loading on mechanical strain stiffening and fiber recruitment. We hypothesized that healing and high magnitude long duration dynamic loading would reduce strain stiffening and fiber recruitment compared to uninjured tendons and low magnitude long duration dynamic loading.

Materials and Methods

Study Design

Female C57BL/6 mice at 150 days of age were randomized into uninjured controls (n=60 mice) and those that received bilateral partial width (60%), full thickness excisional injury (n=120 mice) to their patellar tendons (Figure 1A) (IACUC approved)[3]. Animals injured were randomized into groups euthanized at 2 or 6 weeks post-injury.

Ex vivo Assays

Following sacrifice, tendons were harvested immediately and carefully prepared for mechanical testing under aseptic conditions to maintain cell viability. The patellar tendon was stamped into a "dog-bone" shape to isolate the injury site, and cross sectional area measured at the injury site[4]. To maintain tenocyte viability during loading, tissues were immersed in a bath containing sterile DMEM supplemented with 5% FBS, maintained at 37°C integrated with a tensile testing device (Instron 5848; Norwood, MA). Cell viability was evaluated following each type of testing protocol using an MTT assay. To evaluate the effect of healing on strain stiffening, tendons (n = 10-13/group) were preconditioned and ramped at constant strain rate (0.1% strain/s) until 1% or 10% strain prior to a frequency sweep (Figure 1B). To evaluate the effect of dynamic loading and healing on strain stiffening, tendons were randomized into a zero, low, or high magnitude loading protocol (corresponding to the toe or linear regions of the force-displacement curve) for either 10 or 1000 cycles at 1Hz. During loading, force and displacement data were acquired and analyzed using MATLAB (Mathworks, Natick, MA). ***Analysis***

The change in equilibrium stress (force divided by the cross sectional area) between 1 and 10% strain was used to indicate the amount of strain stiffening, and the dynamic modulus assessed during dynamic loading were computed. Using quasi-static ramp data, we applied a structurally based elastic model [5, 6] to quantify the non-linear force-displacement behavior as fibers uncrimp to their slack length. Data were evaluated with either one-way ANOVAs with post hoc t-tests or with two-way ANOVAs with post hoc Fisher's tests.

Results

Cell viability was maintained throughout mechanical testing. Tendon healing affected strain stiffening, as the change in equilibrium stress was reduced at both 2- and 6-weeks post-injury compared to uninjured control tendons (Figure 2A).This decrease in strain stiffening was

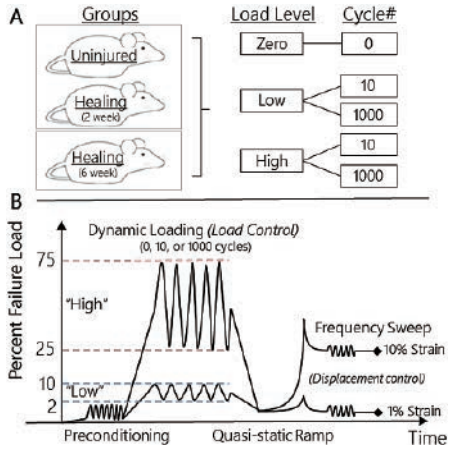

Figure 1. Study Design. **(A)** Mice were randomized into three groups before **(B)** quasi-static and dynamic loading were completed. The dynamic loading protocols varied the magnitude (low or high load) and duration (0, 10, or 1000 cycles) of loading.

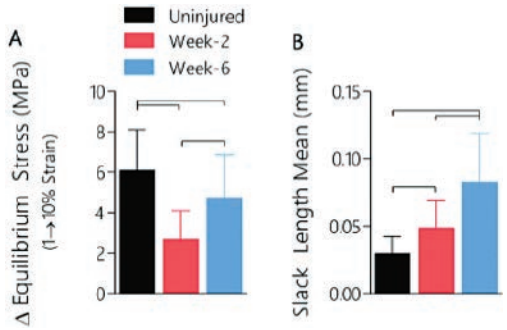

Figure 2. Effect of healing on tendon stress and slack lengths. **(A)** The change in equilibrium stress was reduced in tendons 2- and 6-weeks pos-injury. **(B)** Tendon mean slack length increased in healing tendons. Data shown as mean ± SD. Bars indicate $p < 0.05$.

coupled with increased fiber slack lengths (Figure 2B). Strain stiffening was also reduced due to high magnitude loading in uninjured and 6-week post-injury tendons, but not 2-week post-injury tendons (Figure 3A). Cycle duration only affected strain stiffening for high magnitude loading in uninjured tendons. Although neither loading magnitude nor cycle duration altered the change in equilibrium stress in tendons at 2-weeks post-injury, an increase in these factors increased slack lengths in all groups (Figure 3B). The dependence of slack length on cycle duration in high magnitude loading was mirrored by increases in the secant modulus, which was also affected by cycle duration during high magnitude loading (Figure 3C).

Discussion

This study evaluated stress transfer in uninjured and healing tendons during quasi-static and dynamic loading. Although mechanical properties are well established to be inferior in healing tendon[6], the relationship to strain stiffening and additional effects of dynamic loading are poorly understood. Multi-scale strain transfer (i.e., relationship of strain between structural hierarchies) ultimately affects cell proliferation, differentiation, and matrix production[7]. The stress-strain response was greatly reduced in tendons at 2-weeks post-injury, which suggests that the multi-scale response to loading may be abnormal. Interestingly, although there were no significant differences in the change in stress with varying loading protocols 2-weeks post-injury, tendons exhibited elevated slack lengths, suggesting that the toe region is elongated, but the overall change in stress from 1 to 10% strain remains similar. Slack length data may reveal structural changes responsible for the mechanical response. Additionally, the role of changing material properties with loading may provide insight into the dynamic functional nature of tendons. Future studies will be designed to specifically assess changes in collagen structure due to injury and dynamic loading, and measure strain transfer to cells in these loading paradigms.

Conclusions

Defining the mechanical implications for loading and tendon healing on the ECM may provide important insight into material behavior and ultimate strain transfer to resident cells. This study showed that healing and dynamic loading alters the tendon strain stiffening, which may be due to fiber uncrimping and the change in material modulus during cyclic loading.

Acknowledgements

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Disclosures: Benjamin Freedman (N), Ashley Rodriguez (N), Cody Hillin (N), Stephanie Weiss (N), Joseph Sarver (N), Louis Soslowsky (N)

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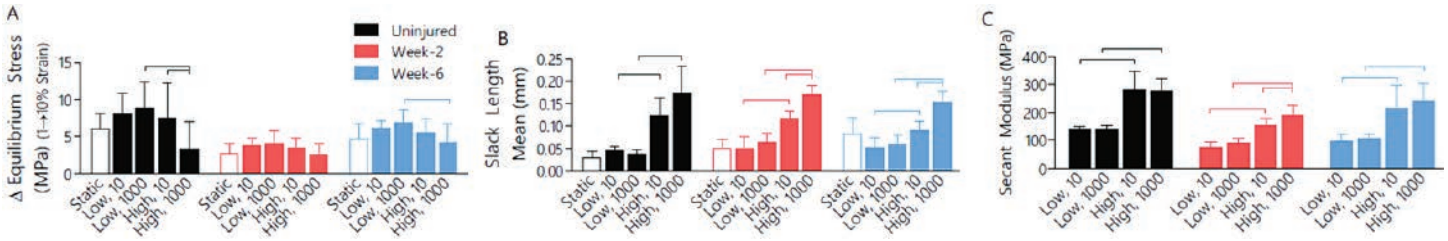

Figure 3. Effect of magnitude and duration of loading on tendon stress, fiber recruitment and macromechancis. **(A)** The change in equilibrium stress with loading was dependent on load magnitude and healing. **(B)** Mean fiber slack length increased following high magnitude, long duration loading. **(C)** The secant modulus increased with long duration loading in 2-week post-injury tendons. Data shown as mean ± SD, with clear columns indicating quasi static loaded tendons. Bars indicate $p < 0.05$.

U·P·O·J

Effects of Pulsed Electromagnetic Field Therapy at Different Frequencies and Durations on Rotator Cuff Tendon-to-Bone Healing in a Rat Model

Julianne Huegel, PhD[1]
Daniel Choi, BS[1]
Courtney Nuss[1]
Molly Minnig[1]
Jennica Tucker, BS[1]
Cody Hillin, MD[1]
Andrew Kuntz, MD[1]
Erik Waldorff, PhD[2]
Nianli Zhang[2]
James Ryaby[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Research Laboratory, Philadelphia, PA

[2]Orthofix Inc., Lewisville, TX

Introduction

Rotator cuff tears affect millions of individuals each year, often requiring surgical intervention. Although advancements in surgical methods and rehabilitation protocols have improved clinical results, rotator cuff repair failure is common[1]. To further improve surgical outcomes, various non-invasive therapeutics have been utilized post-operatively[2,3]. We have previously shown that pulsed electromagnetic field (PEMF) therapy improved tendon-to-bone healing in terms of tendon modulus in a rat rotator cuff model[4]. While it is known that several cell and tissue responses, including osteogenic differentiation of stem cells, are frequency dependent, the effect of frequency has not yet been evaluated in this system[5,6]. Therefore, the objective of this study was to determine the influence of both PEMF frequency and exposure time on rotator cuff healing. We hypothesized that a PEMF signal with a higher fundamental frequency and for a longer duration would lead to further improvements in mechanical properties.

Materials and Methods

210 (including 60 from[4]) adult male Sprague-Dawley rats (400-450 g) were used in an IACUC approved protocol. Animals underwent acute supraspinatus injury and repair[7] followed by either Physio-Stim® PEMF (PS, Orthofix, Inc.) or High Frequency PEMF (HF, similar to PS but with a higher fundamental frequency) for 1, 3, or 6 hours daily. Control animals did not receive PEMF therapy (non-PEMF). Animals were sacrificed at 4, 8, or 16 weeks (n = 10 per group per time point). At sacrifice, right shoulders (n = 7 per group per time point) were dissected and processed for histological analysis, including quantification of fiber alignment circular standard deviation as a measure of collagen organization[8-10]. Left limbs (n = 10 per group per time point) were frozen at −20°C and thawed for dissection prior to tendon cross-sectional area measures and mechanical testing[7,10,11]. Statistical comparisons were made between control animals and all treatment groups at each time point. Mechanical testing and collagen fiber organization comparisons were made using one-way ANOVAs with post-hoc tests. Histological comparisons were made using Mann-Whitney U tests. Significance was set at $p<0.05$.

Results

Mechanical properties

Improvements in mechanical properties were identified for all treatment modalities when compared to non-treated animals (Figure 1A, B). Specifically, one hour of PS treatment led to increased tendon stiffness at all time points, as well as an increase in modulus at 4 weeks. One hour of HF treatment increased stiffness and modulus at 8 weeks. Animals treated with three hours of PS had a decreased cross sectional area (not shown), increased max stress (not shown), and increased stiffness at 4 weeks, as well as increased modulus at 4 and 8 weeks. Three hours of HF PEMF led to increased max load at 4 weeks (not shown), and increased stiffness at 4 and 8 weeks. Treatment with six hours of PS increased modulus substantially at 4 weeks, and increased stiffness and modulus at 8 weeks. Cross-sectional area was also reduced at 4 weeks, but increased at 16 weeks (not shown). The final treatment regimen, 6 hours of HF PEMF, resulted in significant mechanical improvements; including increased stiffness at all time points and a three-fold increase in tendon modulus 8 weeks after repair. Tendon cross sectional area was increased at 16 weeks (not shown). No differences were noted in percent relaxation in any group.

Histological observations

No differences were measured in tendon cell shape or cell density in any treatment group when compared to controls. Collagen organization showed improvements at the tendon insertion at 16 weeks in animals treated with 3 hours of HF PEMF (Figure 2A). This group also showed improved alignment at 8 weeks in the tendon midsubstance (Figure 2B). Additional improvements were identified for 1 hour HF PEMF and 6 hours of PS at 16 weeks in the midsubstance (Figure 2B). Importantly, no adverse effects were identified in any mechanical or histological property.

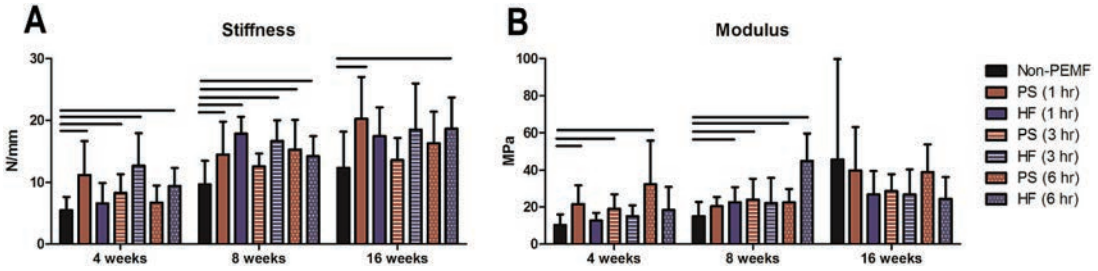

Figure 1. Tendon mechanical properties. **(A)** Tendon stiffness was increased in all groups receiving PEMF treatment, regardless of modality, when compared to non-PEMF controls. **(B)** Modulus was improved in all groups except HF (3 hr) at 4 and/or 8 weeks. By 16 weeks, properties were similar between control and treatment groups. Data displayed as mean ± SD. Bars indicate $p < 0.05$.

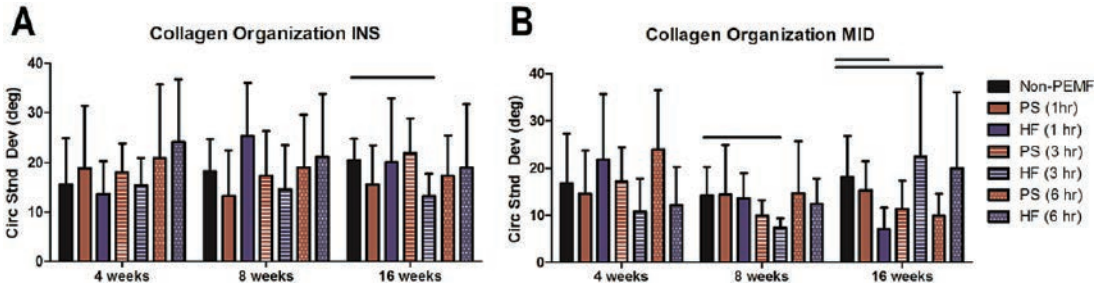

Figure 2. Collagen fiber alignment. **(A)** At 16 weeks, collagen alignment was improved at the injury site (insertion) in animals treated with HF (3 hr). **(B)** Collagen alignment was similarly improved for HF (3 hr) at 8 weeks in the midsubstance. Improvements were also seen at 16 weeks in groups treated with HF (1 hr) and PS (6 hr). Data displayed as mean ± SD. Bars indicate $p < 0.05$.

Discussion

Overall, results suggest that PEMF has a positive effect on rat rotator cuff healing for pulse frequency or treatment duration tested in this study. Tendon mechanical properties, including tendon stiffness and modulus, were significantly improved with all six treatment modalities compared with control. Additionally, collagen fiber organization was improved after treatments, suggesting more organized tissue in PEMF-treated tissues, consistent with the improved mechanical strength seen in treated groups. We suspect that PEMF treatment may increase tendon cell metabolism, which then in turn increases both collagen production and matrix remodeling. These proposed changes are supported by our findings of improved mechanical properties and improved collagen alignment. Our previous work indicates that PEMF treatment does not alter joint function[4]; in conjunction with these current findings, these animal studies promote the evaluation of PEMF to improve rotator cuff healing in the clinical setting.

Conclusions

Non-invasive PEMF therapy improves tendon-to-bone healing in an acute rat supraspinatus detachment and repair model, supporting investigation of this treatment in a clinical scenario of post-operative rotator cuff healing.

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U·P·O·J

Poly-N-Acetyl Glucosamine (sNAG) Enhances Rotator Cuff Tendon Healing in a Rat Model

Courtney Nuss[1]
Daniel Choi, BS[1]
Julianne Huegel, PhD[1]
Stephanie Weiss, BS[1]
John Vournakis[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Research Laboratory, Philadelphia, PA

[2]Marine Polymer Technologies, Inc., Burlington, MA

Introduction

Rotator cuff injuries are a common musculoskeletal problem frequently requiring surgical intervention which, unfortunately, has a high failure rate[1]. Various forms of biological augmentation have been utilized in an attempt to improve tendon repair[2]. Poly-N-acetyl glucosamine (sNAG) polymer containing nanofibers have been shown to increase the rate of healing of venous leg ulcers, with an 86% success rate clinically[3]. However, whether this nanofiber material could improve tendon-to-bone healing is unknown. Therefore, the purpose of this study was to investigate the healing and potential analgesic properties of sNAG containing membranes in a rat rotator cuff tendon injury and repair model. We hypothesized that sNAG would improve tendon-to-bone healing and reduce pain.

Materials & Methods

Study Design

80 adult male Sprague-Dawley rats (400-450g) were used in this IACUC-approved study. All animals underwent a full thickness transection and repair of the left supraspinatus tendon as described[4,5]. Before repairing the supraspinatus in half the animals, a thin membrane of sNAG (4mm diameter) was placed on the "foot print" of the supraspinatus tendon to bone insertion. Animals were further subdivided, receiving only 1 day of analgesics (buprenorphine) on the day of surgery or receiving the standard 3 days of analgesics. Therefore, animals were randomized into one of four groups receiving: 1) only 1 day of analgesics, 2) the standard 3 days of analgesics, 3) 1 day of analgesics with sNAG, and 4) 3 days of analgesics with sNAG. All groups were allowed normal cage activity after surgery. Animals were sacrificed either 2 (n = 4 per group) or 4 weeks (n = 16 per group) post-injury and repair. Animals sacrificed at 4 weeks underwent a longitudinal in vivo ambulatory assessment with measurements 1 day pre-injury and 3,7,14, and 28 days post-injury and repair[6].

Ex-Vivo

The 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 were either immediately dissected and processed for histology (n = 4 per group), or frozen at -20°C and later thawed for dissection at the time of quasistatic mechanical testing[7,8] (n = 12 per group).

Statistics

Mechanical testing and collagen fiber organization data were evaluated using two-tailed t-tests. 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 tests.

Results

Mechanical properties

Mechanical property differences were observed between groups with and without sNAG that received 3 days of analgesics. Specifically, in the presence of analgesics, tendons receiving the sNAG polymer had significantly increased max load and max stress (Figure 1A, B), as compared to tendons without sNAG. No mechanical differences were observed between groups treated with and without sNAG when only 1 day of analgesics was provided. Additionally, the use of analgesics alone did not have an effect on mechanical properties.

Histologic observations

Several differences were seen between groups receiving 3 days of analgesics. At 4 weeks, cellularity was increased at both the insertion and midsubstance in non-sNAG animals compared to those treated with sNAG. Cells were more round at 2 weeks in the midsubstance and at 4 weeks in the insertion in sNAG treated animals compared to the non-sNAG animals. No significant differences were seen in collagen organization or other histological parameters.

Ambulatory Measurements

No differences were observed in ambulatory measurements between groups treated with 1 and 3 days of analgesics in the absence of sNAG. Improvements were observed at 14 days

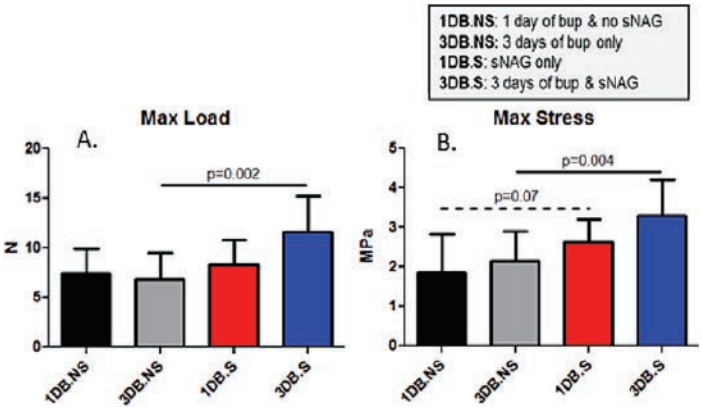

Figure 1. Both max load **(A)** and max stress **(B)** are significantly increased in the supraspinatus of animals treated with sNAG compared to non-sNAG in the presence of the standard 3 days of analgesics (buprenorphine.)

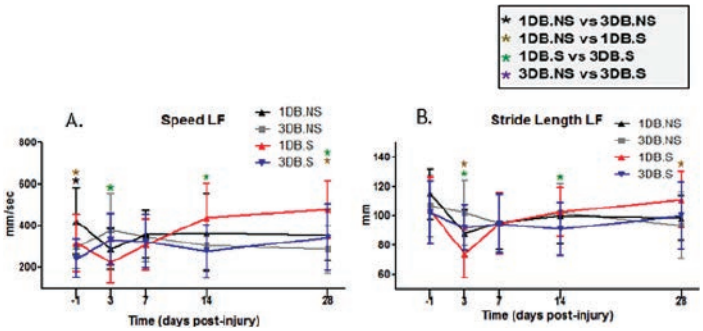

Figure 2. Speed **(A)** and stride length **(B)** of the left front limb (LF) At three days both parameters are significantly decreased in animals treated with sNAG and one day of analgesics (1DB.S) compared to those treated with and three days of analgesics (3DB.S.) However, these parameters are improved at 14 and 28 days (comparison indicated with green asterisk.)

in stride length in animals treated with sNAG compared to animals without sNAG with 1 day of analgesics. Importantly, differences were observed in ambulatory measurements in animals treated with sNAG and receiving either 1 or 3 days of analgesics. Animals receiving only 1 day of analgesics showed decreased speed and stride length at 3 days post-injury and repair, but showed increases in the same parameters at 14 days post-injury and repair (Figure 2A,B).

Discussion

Animals treated with sNAG showed increase in max load and max stress (Figure 1A, B) suggesting that the presence of this polymer improves mechanical strength of the repaired tendon-to-bone healing construct. No other mechanical differences were observed between groups treated with and without sNAG with 1 day of analgesics. Therefore, the observed ambulatory differences in these groups could be associated with pain rather than a structural deficit. For those given 3 days of analgesic, mechanical differences were observed between groups treated with and without sNAG. Therefore, the observed ambulatory differences in these groups could be a result of both pain and structural deficit. When comparing animals treated with sNAG but received differed time courses of analgesics, ambulatory measurements showed decreased speed and stride length at 3 days post injury and repair with only 1 day of analgesic, but improvement in speed and stride length at 14 and 28 days in the same group. This may be explained by the rationale that animals receiving analgesia for a shorter time may experience pain early in healing, limiting weight-bearing on their injured limb. This decreased loading may have led to modest long term functional improvements as well as improved tendon-to-bone healing[10]. Alternatively, those who received the standard 3 days of analgesics supposedly felt less pain, and therefore bore more weight, resulting in delayed improvements in functionality, as seen at 14 and 28 days postop. Because animals in this study were evaluated at relatively early time points, the long-term outcome of the use of sNAG is not fully known. Future studies should evaluate healing at longer time points. Additionally, dosage studies may identify a more effective quantity of sNAG for tendon-to-bone healing. Finally, studies to elucidate the mechanism of action for the changes identified are important.

Conclusions

sNAG improves tendon-to-bone healing in a rat rotator cuff detachment and repair model with the potential of long-term analgesic effects. These results support further study to understand the long-term effects, as well as mechanism of action, of sNAG on tendon healing and analgesia.

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Disclosures

Nuss CA (N), Choi D (N), Huegel J (N), Weiss, SN (N), Vournakis J (3A- Marine Polymer Technologies, Inc.), Soslowsky LJ (5)

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Aging Leads to Inferior Achilles Tendon Mechanics and Altered Ankle Function in Rodents

Adam Pardes, BS
Ashley Rodriguez, BS
Benjamin Freedman, PhD
George Fryhofer, MD
Louis Soslowsky, PhD

McKay Orthopaedic Laboratory
University of Pennsylvania
Philadelphia, PA

Introduction

Achilles tendon injuries are most common in middle-aged men, especially those involved in recreational sports. Increased tendon stiffness, decreased blood flow, and lack of regular physical activity have been suggested as potential causes for the higher incidence of ruptures in this age group, although clinical evidence is conflicting[1-3]. Animal models offer a highly controlled system to study Achilles tendon biomechanics, and have demonstrated a potential explanation for the disparate incidence in Achilles tendon rupture across sex[4]. However, it is unknown if effects of aging could help explain, at least in part, the particularly high frequency of Achilles tendon ruptures in middle-aged men. Therefore, the objective of this study was to identify functional, mechanical, and structural differences among Achilles tendons from young, middle aged, and old male rats. We hypothesized that middle aged and old rats would exhibit increased joint stiffness and decreased Achilles tendon tissue quality as compared to young rats.

Materials and Methods

Design: Young (7 mo), middle aged (18 mo), and old (27 mo) male F344XBN rats, approximating respective human ages of 18, 41, and 60 years, were acquired from the National Institute of Aging (n = 16/group) (IACUC approved) and euthanized three weeks after arriving[5]. *Gait analysis:* Animals (n = 12-16/group) were acclimated to an instrumented walkway, and spatial, temporal, and kinetic parameters were quantified during autonomous locomotion[6]. *Passive joint function:* Ankle range of motion (ROM) and stiffness were measured using a custom device while animals (n = 16/group) were anesthetized[6]. *Sample preparation:* Following euthanasia, Achilles tendon-foot units were harvested and either processed for histological assays or frozen until preparation for structural and mechanical analysis. *High frequency ultrasound (HFUS):* B-mode images of tendons (n = 11-12/group) were captured and analyzed to determine tendon matrix alignment and density[6]. *Mechanical testing:* Samples (n=11-12/group/protocol) were tested to evaluate failure properties (ramp to failure with optical strain tracking) or viscoelastic and fatigue properties (stress relaxation, frequency-sweep, fatigue testing). *Statistics:* One-way ANOVAs were used to compare groups, and significant relationships ($p < 0.05$) were further evaluated using post hoc Student's t-tests with Bonferroni corrections, except for cycles completed (where non-parametric Kruskal-Wallis test with Dunn's post hoc tests were used).

Results

Gait analysis revealed that propulsion force decreased and lateral force increased with increasing age (Figure 1A-B). Animals also took slower, wider, and shorter steps as they aged (not shown). Aging resulted in increased plantarflexion stiffness and decreased range of motion (Figure 1C-D). HFUS analysis showed no differences in tendon organization or density (not shown). Although tendon area was significantly increased in middle aged and old compared to young animals (Figure 2A), stiffness and max load were not different between groups (not shown). Conversely, Achilles tendon max stress and modulus were superior in young animals (Figure 2B-C). Dynamic modulus was greater in the young group as compared to the middle aged and the old animals at all frequencies tested (not shown). Viscoelastic properties (percent relaxation, tan (δ)) were not different between groups, as well as otherfatigue properties (peak strain, laxity, secant stiffness) (not shown). Young animals exhibited decreased fatigue life, but increased hysteresis (trend, 1500 cycles) and secant modulus (50 cycles) (Figure 2D-F).

Discussion

This study identified numerous functional and mechanical differences in the Achilles tendons of young, middle aged, and old rats. Most notably, the young tendons exhibited the greatest mechanical property (max stress, modulus), which could help explain why younger individuals experience fewer Achilles tendon ruptures than middle aged adults. Interestingly, older rats demonstrated impairments in ankle joint function similar to those observed in humans[7-8]. Increased calf muscle activation and metabolic cost of walking during gait in the elderly may be a compensatory mechanism to overcome a tight heel cord that subsequently contributes to the injury of an

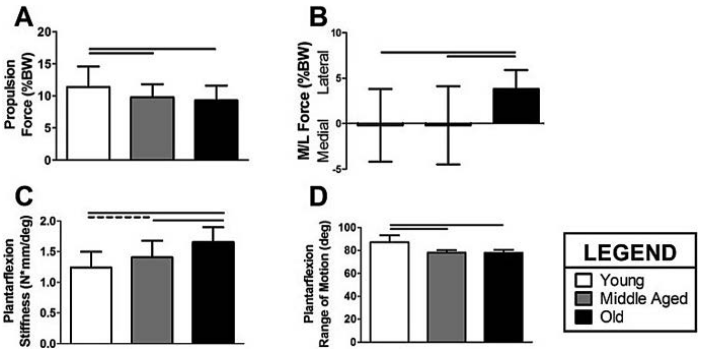

Figure 1. Ankle function. **(A)** Propulsion force decreased and **(B)** lateral force increased with increasing age during gait. Passive motion analysis revealed greater ankle joint **(C)** stiffness and inferior **(D)** range of motion in middle-aged and old rats. Data presented as mean and standard deviation. Solid lines indicate significant differences ($p < 0.017$), dashed lines indicate trends ($p < 0.10$).

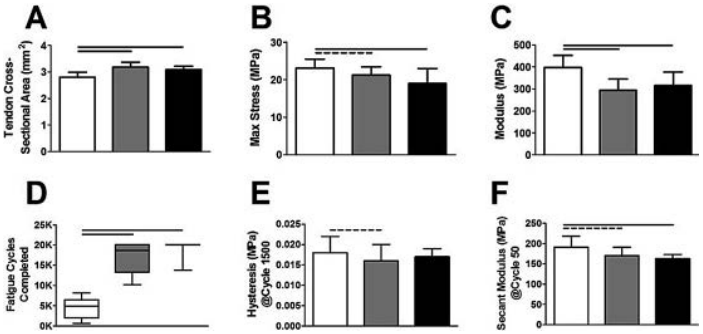

Figure 2. Achilles tendon mechanical properties. Young animals had the smallest **(A)** tendon area and greatest **(B-C)** quasi-static material properties, though they also had the shortest **(D)** fatigue life. Tendons from the young group increased **(E)** hysteresis after 1500 cycles and **(F)** secant modulus after 50 cycles. Data presented as mean and standard deviation, except fatigue cycles completed (five number summary box plot). Solid lines indicate significant differences ($p < 0.017$), dashed lines indicate trends ($p < 0.10$).

already mechanically inferior tendon[9-11]. However, this requires further investigation in a more clinically relevant age group and during more challenging physical activity. We did not detect age-related tendon differences in low-strain viscoelastic properties, although such differences may be present in the entire Achilles tendon-muscle unit[5]. The similar tendon macrostructure observed by HFUS in the current study indicates that age-specific mechanical differences may primarily be the result of altered composition or microstructure, rather than matrix degeneration as a result of increased MMP activity as previously suggested[12]. Lastly, the decreased fatigue life of the younger tendons is likely explained by their decreased cross-sectional area, as they consequently experienced greater peak cyclical stress during load-controlled fatigue testing. We are currently investigating Achilles tendon histological properties and muscle composition in this aging model.

Conclusions

This study supports a potential explanation of the increased incidence of Achilles tendon rupture in the active middle-aged population. Additionally, our results provide a foundation for future studies on Achilles tendon-muscle unit's age-specific responses to loading or injury.

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Effect of Pro- and Anti-Angiogenic Factors on Vascular Response in the Rat Achilles Tendon after Injury

Corinne Riggin, BS[1]
Susan Schultz, RDMS[2]
Chandra Sehgal, PhD[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Research Laboratory, University of Pennsylvania, PA

[2]Department of Radiology, University of Pennsylvania, PA

Introduction

Tendons are hypovascular tissues that become hypervascular after injury. While vascular ingrowth is necessary for tendon healing, hypervascularization following tendon injury is not always believed to be beneficial[1], as degenerated tendons are also highly vascularized[2]. Modulating the vascular response during healing could ultimately improve tendon healing. However, a method for vascular modulation, as well as the optimal vascular response during tendon healing, is unknown. Therefore, the objective of this study was to evaluate the effects of delivery of both pro- and anti-angiogenic factors on the rat Achilles tendon vascular response after injury using in vivo ultrasound imaging and ex vivo histological measures. We hypothesized that vessel properties such as vessel density, vessel size, and blood flow velocity will be increased due to the pro-angiogenic factor and decreased due to the anti-angiogenic factor.

Materials & Methods

Study Design

Under IACUC approval, 56 Sprague Dawley rats were used. All animals underwent a bilateral Achilles incisional injury, followed by injections of VEGF, anti-VEGF, or saline on 3 consecutive days. Ultrasound imaging was performed on days 7, 10, and 14 after injury and photoacoustic imaging was done for the anti-VEGF groups on days 7 and 14. Animals were sacrificed at either day 7 or 14 for histological evaluation.

Surgical Protocol

A 1.5mm scalpel blade created a mid-substance incisional injury in the center of the Achilles tendon width and the tendon was left unrepaired.

Angiogenic Factor Injections

To evaluate pro-angiogenic factor delivery, 5ug VEGF in 20ul saline (or 20ul saline only as control) was injected bilaterally intratendinously on either days 0-2 (early) or 4-6 (late) after surgery. To evaluate anti-angiogenic factor delivery, 50, 250, or 500ug anti-VEGF antibody (B20.4-1-1, Genentech) in 30ul saline was injected bilaterally intratendinously on days 4-6 after surgery (or 30ul saline as control).

Color Doppler Imaging

Imaging (n = 4-8) was performed using a Vevo 2100 ultrasound system (VisualSonics) with a 40 MHz transducer. Animals were anesthetized and positioned with the transducer parallel to the long axis of the tendon. The mean color level (MCL—average blood flow velocity), the fractional area (FA—% area of Doppler signal), and the color weighted fractional area (CWFA—weighted average of blood flow velocity/unit area) were quantified over the tendon area. Data was compared using a 2-way (treatment, time) ANOVA followed by post hoc t-tests.

Photoacoustic Imaging

Photoacoustic imaging (n=6-8) was performed with the Vevo LAZR Photoacoustics Imaging System (VisualSonics) using the same transducer and positioning. Images were taken at two wavelengths (750 and 850 nm) based on the absorption spectrum of oxygenated (HbO_2) and deoxygenated hemoglobin (Hb), respectively. Blood oxygenation (sO_2 Avg), total hemoglobin (Hb Total), and relative tissue oxygenation (sO_2 Tot) were determined. Again, data was compared using a 2-way ANOVA followed by t-tests.

Histological Analysis

After sacrifice, Achilles tendons were dissected and processed. Sections were stained with hematoxylin-eosin (H&E) and graded by 3 blinded, independent graders for cell shape (1 = spindle to 3 = round) and cellularity (1 = less cells to 3 = more cells). Additionally, sections underwent immunohistological staining for CD34, a vascular marker, and graded by 3 blinded, independent graders for vessel density (1 = less dense to 4 = more dense) and vessel size (1 = small diameter to 4 = large diameter). Data was compared using Mann-Whitney t-tests (n=4-8).

Results

VEGF Delivery

There was a significant increase in FA at days 7 and 14 in the late group and a trend towards a decrease in FA at day 14 in the early group when

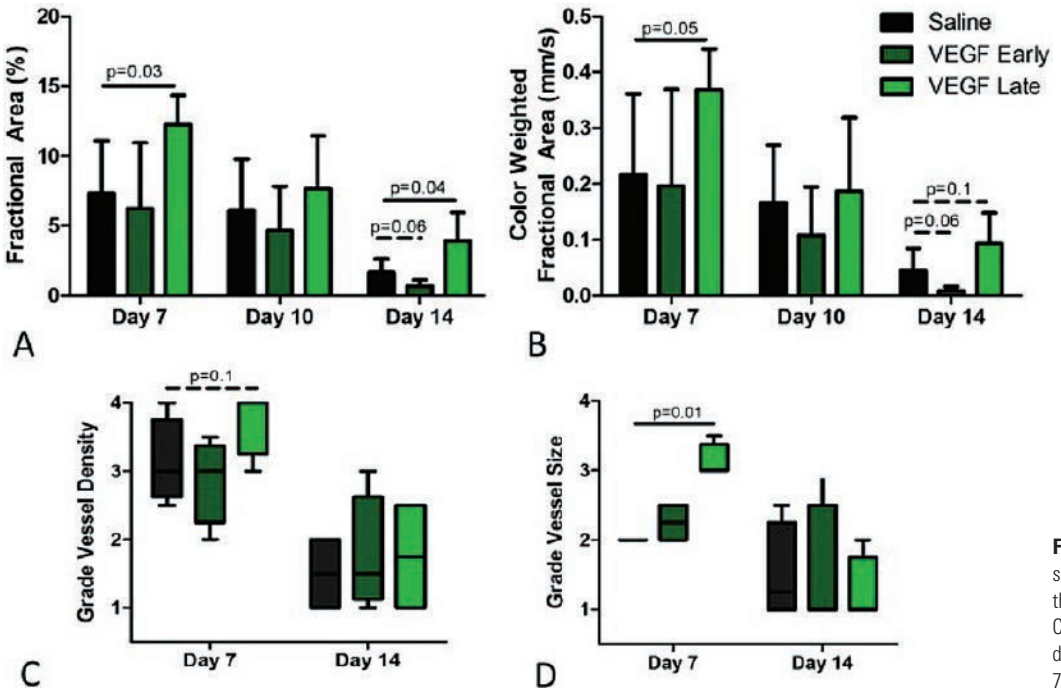

Figure 1. Color Doppler analysis of VEGF delivery showed an increase in **(A)** FA and **(B)** CWFA in the late group at days 7 and 14 compared to saline. CD34 staining showed an increase in **(C)** vessel density and **(D)** vessel size in the late group at day 7 compared to saline.

compared to saline (Figure 1A). There were no changes in MCL (not shown). There was a significant increase in CWFA in the late group at day 7, a trending increase in the late group, and a trending decrease in the early group at day 14 compared to saline (Figure 1B). Histology shows a increasing trend in vessel density (Figure 1C), a significant increase in vessel size (Figure 1D), and significantly more rounded cell shape (not shown) in the late group compared to saline. There were no changes in cellularity (not shown).

Anti-VEGF Delivery

There was a significant decrease in FA on days 7 and 10 in the mid B20 group, and a significant increase in the low B20 group compared to saline (Figure 2A). There were no differences in MCL (not shown). There was a trending decrease in CWFA in the mid B20 group at day 7, a significant decrease in the mid B20 group at day 10, and a significant increase in the low B20 group at day 14 compared to saline (Figure 2B). There were trending and significant decreases in Hb total

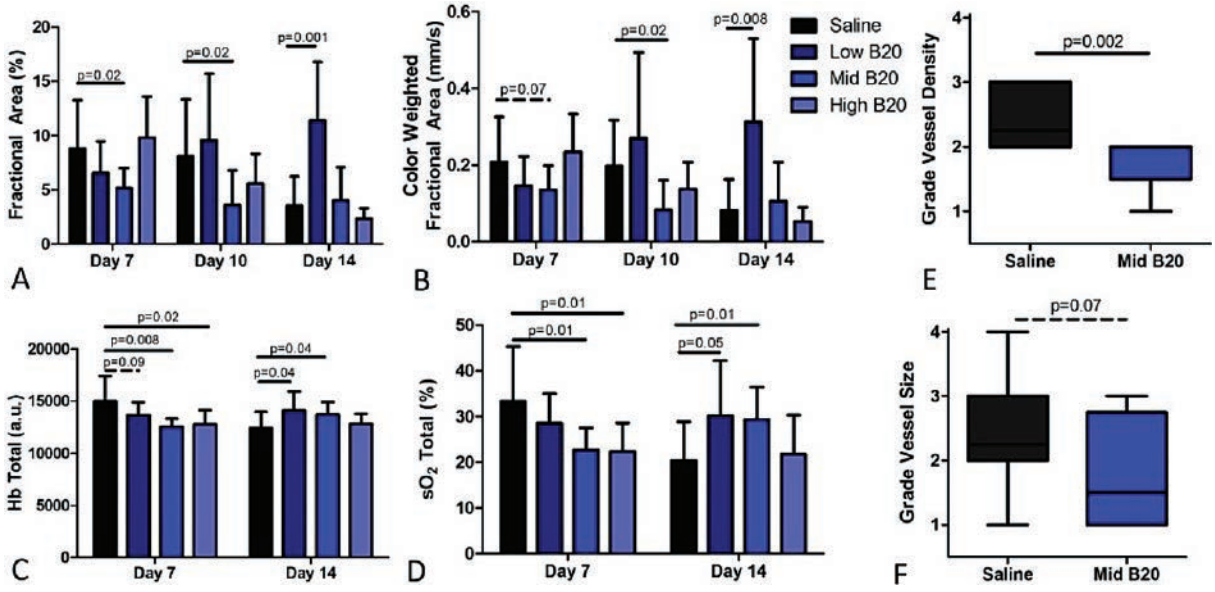

Figure 2. Color Doppler analysis of B20 delivery showed a decrease in **(A)** FA and **(B)** CWFA in the mid B20 group compared to saline on days 7 and 10. Photoacoustic analysis shows a decrease in **(C)** Hb Total and **(D)** sO2 Total in the mid and high B20 groups at day 7 compared to saline. CD34 staining on day 7 demonstrated a decrease in **(E)** vessel density and a trend towards a decrease in **(F)** vessel size in the mid B20 group.

in the B20 groups at day 7, and a significant increase at day 14 in the low and mid B20 groups (Figure 2C). There were no changes in sO_2 avg (not shown). There was a significant decrease in sO_2 total in the mid and high B20 groups on day 7, and a significant increase in the low and mid B20 groups on day 14 (Figure 2D). Finally, there was a significant decrease in vessel density (Figure 2E), and a trending decrease in vessel size (Figure 2F) in the mid B20 group on day 7, with no change in cell shape or cellularity (not shown).

Discussion

This study demonstrated that tendon vascular response after injury could be increased through the delivery of VEGF and decreased through delivery of anti-VEGF. Importantly, both dosage and timing are important factors in regulating the vascular response. The delivery of VEGF was only effective when delivered 4-6 days after injury, during the time when VEGF expression is naturally at a peak[3]. Additionally, the increase in vascularity seen with the delayed VEGF delivery coincided with a more rounded cell shape, suggesting a more active cellular state. When delivered early, vascular response was not increased, and trended toward a decrease at day 14, suggesting that this delivery may have shifted the VEGF expression time period earlier than normal. For delivery of anti-VEGF, the largest reduction in the vascular response was with the mid dosage. The lower dosage caused a compensation effect, with increased vascular measures at later time points. Histological measures of vascular size and density supported the changes seen with ultrasound.

Conclusions

This study establishes a model system for vascular modulation in a rat tendon injury model that can be used to evaluate the role of vascularity in tendon injury or degeneration, and potentially determine therapeutics for improved tendon healing.

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Conditional Deletion of Decorin and Biglycan in Mature Mouse Tendons Results in Inferior Mechanical Properties and Delayed Collagen Fiber Realignment

Kelsey Robinson, MD[1]
Carrie Barnum, MS[1]
Stephanie Weiss, BS[1]
Julianne Huegel, PhD[1]
Snehal Shetye, PhD[1]
Mei Sun[2]
Sheila Adams[2]
David Birk, PhD[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Laboratory, University of Pennsylvania, Philadelphia, PA

[2]Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL

Introduction

Tendon and ligament injuries occur more commonly with increasing age[1] and there is no clear understanding of the mechanisms underlying the pathophysiology of tendon aging. Two small-leucine rich proteoglycans (SLRPs) known as decorin and biglycan, play an important role regulating the assembly and organization of collagen fibrils during development[2-4]. The absence of decorin has been shown to prevent the normal decline in mechanical properties that occurs with aging in conventional knockout mouse models[5]. However, the impact that these SLRPs have on tendon aging and homeostasis independent of their influence on development has yet to be established. Therefore, the objective of this study was to investigate the acute effects of conditional deletion of decorin alone and both decorin and biglycan in mature uninjured tendons. We hypothesize that the loss of decorin or decorin and biglycan will not acutely alter the mechanical properties of mature, uninjured tendons because they will have undergone normal development and minimal aging will have occurred from the time of gene inactivation to sacrifice.

Materials and Methods

Conditional female $Dcn^{flox/flox}/Bgn^{+/+}$($Dcn^{-/-}$) and $Dcn^{flox/flox}/Bgn^{flox/flox}$ (compound decorin/biglycan null) as well as $Dcn^{+/+}/Bgn^{+/+}$control (WT) mice (n = 16/group) with a TM inducible Cre in the Rosa26 locus were utilized (IACUC approved). To induce Cre excision of the conditional alleles, mature 120 day old mice received three consecutive daily IP injections of tamoxifen (9mg/40g body weight). WT mice received tamoxifen injections to control for potential side effects. Mice were euthanized at 150 days old and whole knees were collected. The patellar tendon-bone complex from one limb of each animal was dissected from the knee and prepared for biomechanical testing as described[5]. Tendons were subjected to a viscoelastic testing protocol as well as ramp to failure. Dynamic collagen fiber realignment was quantified using our established cross-polarization imaging technique as described[5]. A bilinear fit was used to describe the toe and linear regions of the load-displacement curve and peak force, equilibrium force, and percent relaxation during stress-relaxation were quantified. Dynamic modulus and phase angle delta were computed during frequency sweeps at multiple strain levels and fiber realignment, failure stress, and failure load were computed during ramp to failure. From the contralateral limb, histological sections of the patellar tendon-bone complex were prepared and stained using standard techniques. Cell shape and cellularity were calculated using commercial software (Bioquant). One way ANOVAs with post-hoc Bonferroni corrections ($p < 0.05/3$) were used to establish significance between genotypes. Kruskal-Wallis tests with post-hoc Dunn's multiple comparisons were used for non-normal data sets.

Results

Compound decorin/biglycan knockouts exhibited increased percent relaxation during the linear region of the test (5% strain) when compared to tendons from WT controls (Figure 1A) and failed at lower loads than both WT and $Dcn^{-/-}$ tendons (Figure 1B). No significant differences in cross-sectional area, modulus, toe or linear stiffness, or transition strain were found between genotypes. The compound knockouts exhibited increased tan(δ) when compared to WT tendons at nearly all frequencies at both toe (not shown) and linear strain levels (Figure 2). However, there were no significant differences in dynamic modulus across groups. In addition, compound knockouts underwent more realignment at the insertion during the linear region of the test than WT tendons (Figure

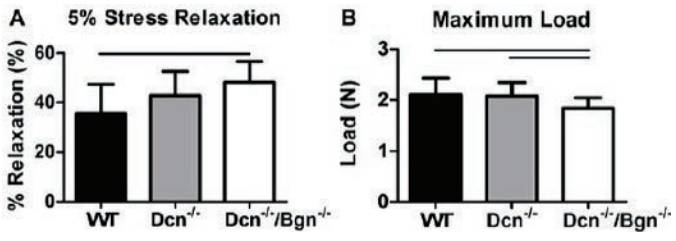

Figure 1. Quasi-static properties of WT, $Dcn^{-/-}$, and $Dcn^{-/-}/Bgn^{-/-}$ patellar tendons. Thirty days after gene inactivation, compound knockouts had increased percent relaxation at 5% strain **(A)** and lower failure loads **(B)**.

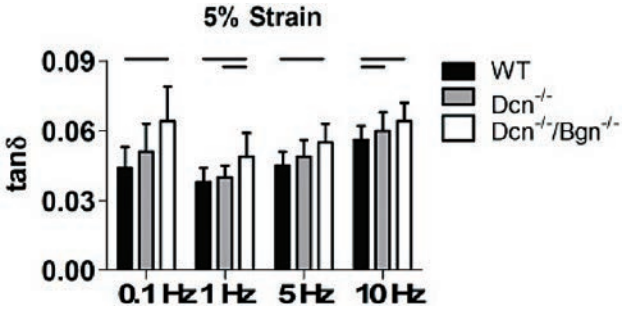

Figure 2. Viscoelastic properties of WT, $Dcn^{-/-}$, and $Dcn^{-/-}/Bgn^{-/-}$ patellar tendons. Compound knockout tendons had significantly increased tan(δ) at 5% strain compared to WT.

3A). The insertion region of WT and $Dcn^{-/-}$ tendons realigned earlier than compound knockout tendons (at 3-5% strain compared to 5-7% strain) (Figure 3B-3D). The midsubstance of WT tendons realigned earlier than both $Dcn^{-/-}$ and $Dcn^{-/-}/Bgn^{-/-}$ tendons (at 1-3% strain compared to 3-5% strain) (not shown). No significant differences in cell density or cell shape were observed across groups (not shown).

Discussion

SLRPs are important for maintaining normal tendon structure and function[5,6]. Contrary to our hypothesis, compound knockout tendons responded inferiorly during dynamic loading compared to WT and $Dcn^{-/-}$ tendons 30 days after gene inactivation. These results suggest that even after a short absence of SLRP expression, tendons deficient in both decorin and biglycan fail at lower loads and are more dissipative of energy during dynamic loading. Furthermore, compound knockout tendons exhibited increased realignment at 5-7% strain, which corresponds to the linear region of the stress-strain curve, consistent with increased fibril sliding during realignment as described previously[7]. Tendons deficient in both SLRPs also realigned at later strains

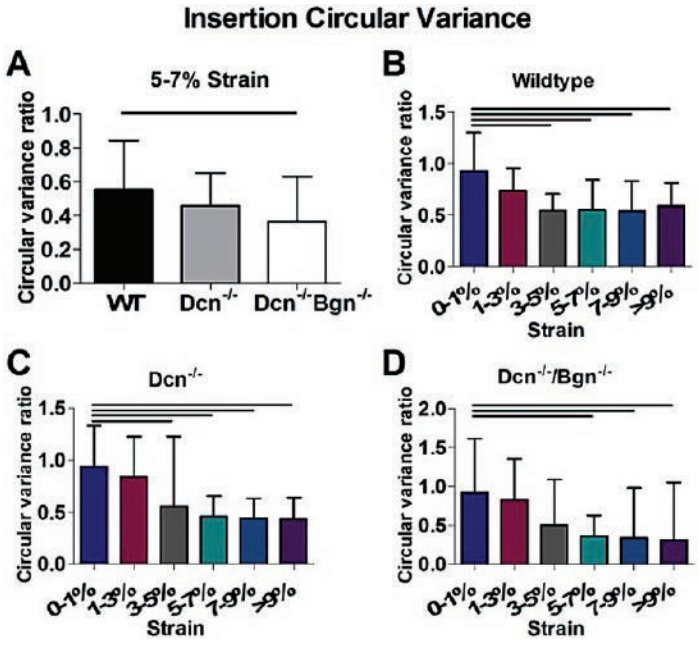

Figure 3. Realignment of WT, $Dcn^{-/-}$, and $Dcn^{-/-}/Bgn^{-/-}$ patellar tendons. $Dcn^{-/-}$/Bgn-/- tendons exhibit increased realignment at 5-7% strain **(A)**. WT **(B)** and $Dcn^{-/-}$ **(C)** tendon insertions realign earlier than $Dcn^{-/-}/Bgn^{-/-}$ **(D)**.

than WT tendons at both the insertion and midsubstance, which may explain their tendency to fail earlier than WT tendons. Previous work found that the normal loss of modulus, increase in tan(δ), and changes in fiber organization that occur in aged mice were prevented in conventional decorin knockout mice while conventional biglycan knockout mice and WT mice aged similarly[5]. The early differences seen in this novel conditional knockout model suggest that the concomitant deletion of both decorin and biglycan after development interferes with the maintenance of the normal tendon response to load at maturity. Therefore, decorin and biglycan may work synergistically to regulate the structure and function of mature tendon. Alternatively, dysfunctional expression of biglycan in $Dcn^{-/-}$ mice may compensate for the absence of decorin and provide protection from some of the changes that occur in the compound knockouts. Future work will focus on the impact that the conditional deletion of decorin and biglycan during maturity has on the mechanical and structural properties of aged tendons.

Conclusions

This study begins to define the interactions between decorin and biglycan in maintaining tendon homeostasis at maturity and will help clarify their role in tendon aging.

Acknowledgements

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Muscle Adapts Dynamically Following Acute Achilles Tendon Rupture in a Rat Model

Nabeel Salka, BS
Pankti Bhatt, BS
Benjamin Freedman, PhD
Tyler Morris, MD
Zakary Beach, BS
Joshua Gordon, MD
Louis Soslowsky, PhD

McKay Orthopedic Research Laboratory, Philadelphia, PA

Introduction

Achilles tendon ruptures are common musculoskeletal injuries with an incidence of 15 to 55 per 100,000 person-years[1]. Although substantial research has evaluated Achilles tendon properties following injury[2], a paucity of data exists on the effects of Achilles surgical repair and return to activity timing on gastrocnemius and soleus muscle properties. Previous studies found that rats experiencing longer immobilization times and surgical treatment exhibit lower muscle TNF-alpha and a higher collagen 1:3 ratio at 3 weeks post injury[3]. However, early changes in muscle that lead to this finding, as well as later changes in muscle architecture, remain unknown. Therefore, the objective of this study was to evaluate muscle fiber size and remodeling for up to 6 weeks post injury. We hypothesized that at early time points, Achilles tendon repair would result in increased muscle MMP activity, and at later time points, delayed return to activity would result in reduced muscle fiber size and increased MMP activity.

Materials and Methods

Male Sprague-Dawley rats (n = 222) at 16-weeks of age were used (IACUC approved). Animals received 2 weeks of treadmill training (up to 60 min at 10 m/min) followed by surgical removal of the right plantaris longus tendon and blunt transection of the right Achilles tendon. Tendons were either repaired (modified Kessler) (R) or non-repaired (NR). All right ankle joints were subsequently immobilized in plantar flexion. Rats experienced immobilization for different lengths of time, returning to activity 1 week (RTA1), 3 weeks (RTA3), or 6 weeks (RTA6) after injury (Figure 1). Animals were sacrificed prior to injury (n = 7), as well as at 1 (n = 33), 3 (n = 74), and 6 weeks (n = 108) post-injury. Upon sacrifice, the right gastrocnemius-soleus muscle complex was harvested, embedded in optimum cutting temperature (OCT) compound, flash frozen, and sectioned transversely at 10 μm. Sections were stained with Laminin and Dapi, imaged, and analyzed for fiber size using the SMASH application[4]. Nuclear number was measured using Image J (NIH, v1.48). Muscle tissue was also excised from the gastrocnemius, flash frozen, and quantitatively evaluated for MMP activity (Sensolyte 520 Generic MMP Assay Kit) using a human MMP-13 standard. Prior to MMP activity quantification, samples were normalized for protein concentration using a bicinchoninic acid (BCA) assay (Pierce BCA Protein Assay, Fisher Scientific). Two-way ANOVAs with Fisher's post-hoc tests were performed for multiple comparisons, while Student's t-tests were performed for pairwise comparisons.

Results

At 1 and 3 weeks post-injury, fiber size was unaffected by repair or RTA. However, at 6 weeks post-injury, delayed return to activity (RTA6) resulted in a significantly smaller muscle fiber size when compared to RTA1 and RTA3 groups (Figure 2). No differences in nuclear number were found. MMP activity was significantly elevated in the muscles of repaired tendons as early as 1 week post-injury (Figure 3A). However, by 3 weeks, no significant effects were seen (Figure 3B). Interestingly, at 6 weeks, RTA1 showed decreased MMP levels regardless of surgical treatment (Figure 3C). Between 1 and 6 weeks post-injury, MMP activity increased significantly more in RTA3 and RTA6 when compared to RTA1, while also increasing more with non-repair in RTA3 (Figure 3D).

Discussion

The decrease in muscle fiber size following 6 weeks of immobilization is consistent with

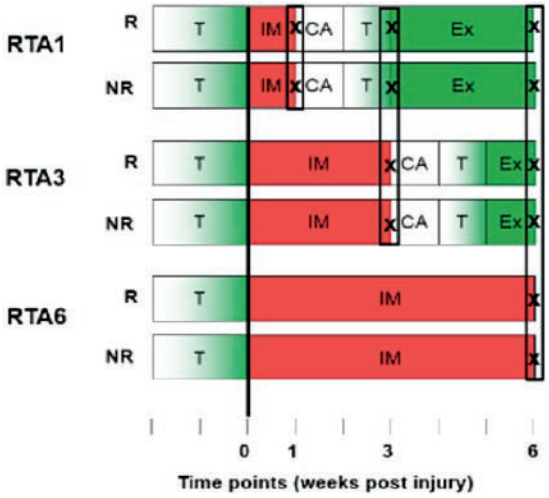

Figure. 1. Study Design. R: Repaired, NR: Non-Repaired, T: Treadmill training, IM: Immobilization, CA: Cage Activity, Ex: Exercise, X: Sacrifice of 18 animals. Boxes indicate the time points post injury evaluated.

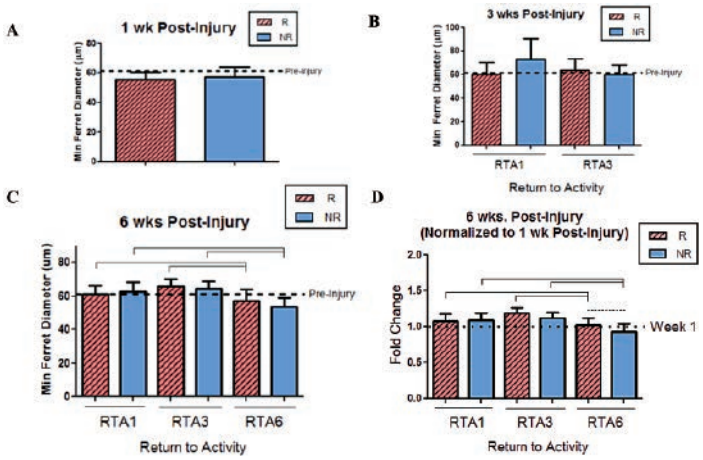

Figure 2. Muscle Fiber Size. R: Repair, NR: Non-Repair, RTA1,3,6: Return to activity after 1,3,6 weeks of cast immobilization respectively. sig. $p < 0.05$, trend $p < 0.1$. Data presented as means and standard deviations.

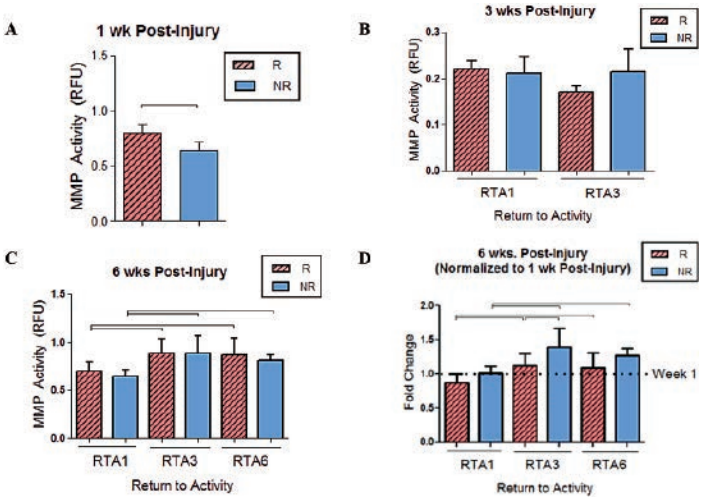

Figure 3. MMP Activity. R: Repair, NR: Non-Repair, RTA1,3,6: Return to activity after 1,3,6 weeks of cast immobilization respectively. sig. $p < 0.05$ Data presented as means and standard deviations.

clinical findings[5]. Prolonged immobilization also resulted in inferior mechanics in NR tendons[6], suggesting that an earlier return to activity provides advantages to both tendon and muscle health. Increased MMP activity in muscle of repaired tendons early in healing highlights the likely dependence of muscle architecture on tendon treatment. However, the absence of differences in muscle collagen content with repair 3 weeks post-injury[3] points to the potential involvement of regulating factors (e.g., TIMPs) and collagen synthesis between 1 and 3 weeks post-injury[7]. Interestingly, the current data suggests that RTA timing can significantly influence MMP activity at later time points. These changes may result from the new loading environment imposed by the injured tendon or additional MMP activity expected from longer periods of immobilization[7]. Either way, the role these differences in MMP activity have in influencing muscle health is unclear, because the extent and nature of matrix turnover caused by higher MMP levels is yet to be identified. Future work will continue to evaluate muscle remodeling by measuring muscle collagen content and uncovering the role of inflammation following Achilles tendon injury.

Conclusions

Although surgical repair initiates MMP activity early in Achilles tendon healing, return to activity time has a stronger effect on muscle properties at later time points by changing fiber size and regulating MMP activity.

Acknowledgements

We acknowledge financial support from NIH/NIAMS R01AR064216 and NIH/NIAMS P30AR050950. We thank Sarah Rooney, Tejvir Khurana, Emmanuel Loro, and Adam Pardes for their assistance.

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FACTS MYTHS

Salto Talaris® Myth Busting

Myth 1:
The Salto Talaris
removes too much bone from the talus.

S.T.A.R.™ removed 51% more talar bone than Salto [1]
INBONE® II removed 47% more talar bone than Salto [1]
Zimmer® Trabecular Metal™ Total Ankle removed 14% more talar bone than Salto [1]

Myth 2:
Mobile Bearing
is superior to the Salto Talaris

"The fixed and mobile bearing prostheses resulted in comparable postoperative outcomes, and the two implant types can be considered equal when choosing the type of implant to use to treat end-stage ankle osteoarthritis." [2]

"This short-term study suggests that Fixed Bearing (Salto Talaris) ankle arthroplasty has results that are equivalent to, if not better than, Mobile Bearing ankle arthroplasty" [3]

Myth 3:
Fixed bearing implants
encourages cyst formation.

Salto 2/103 implants- 1.9% of implants [4]
INBONE 8/293 implants- 2.7% of implants [4]
S.T.A.R. 21/328 implants- 6.4% of implants [4]

Myth 4:
Salto Talaris
doesn't have any clinical supportive evidence.

Salto Talaris: 97.3% at 38.9 months per Oliver et. al. [5]
Salto Talaris: 96% at 2 years per Schweitzer et. al. [6]
Salto Talaris : 97% at 2 years per Gaudot et. al. [3]
Salto Talaris 98% at 43 months per Nodzo et. al. [7]

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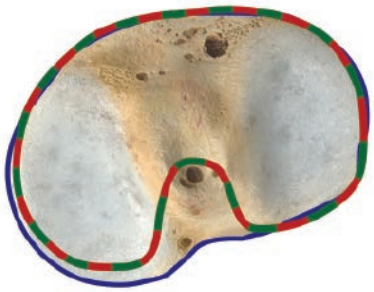

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Letter from the Chairman

L. Scott Levin, MD, FACS

It is an honor and privilege to once again reflect on the accomplishments of our Penn Orthopaedic team this past year. On July 1, 2017, it will mark the completion of my eighth year as Chairman of this vibrant and dynamic department. This past year has been highlighted with many positive changes that reflect well on Penn Orthopaedics. The University of Pennsylvania Health System has expanded its footprint once again by entering into a partnership with Princeton Orthopaedic Associates. By expanding the brand of Penn Medicine farther east, our reach as a health system spans from Lancaster, PA to Princeton, NJ. Penn Orthopaedics has embraced the opportunities to join forces with orthopaedic practitioners in these newly acquired sites. As a result, our core faculty that has historically been based in our downtown hospitals is partnering and collaborating in the areas of quality, patient safety, value-based purchasing, care pathways, clinical research and service line initiatives with a diverse group of regional orthopaedic colleagues. Discussions are ongoing regarding educational opportunities at Virtua in New Jersey. In addition to taking the Penn brand to communities outside of Philadelphia and providing expanding outpatient services at Radnor, Valley Forge and our newest facility at Cherry Hill, NJ, surgeons are now operating at Cape Regional Medical Center, Chester County Hospital, and the Philadelphia Shriners Hospital for Children.

It is said that the only thing constant in life is change. While we have seen many changes occur in healthcare delivery models and reimbursement, we've seen a change in our health system that is trying to stay ahead of the curve with regards to population health, value-based care delivery, and emphasis on patient experience and treatment plans based on patient-reported outcome measurements. There is no doubt that these changes are having a greater impact on how we practice, where we practice and who we will be able to practice on!

Our service line has seen significant expansion of disease team pathways. Cost accounting is making a difference on how we practice medicine. Finnah Pio and Rachel Kleinman should be recognized for their outstanding efforts in coordinating representatives from multiple departments and entities in the health system to integrate service line musculoskeletal care. Special recognition goes to Eric Hume, David Glaser, Samir Mehta, and Brian Sennett for the development of disease team pathways for hip fractures, ACL reconstructions, total hip arthroplasty and total shoulder replacement.

In 2016, I was elected to serve on the American Academy of Orthopaedic Surgeons Nominating Committee to select the presidential line of the AAOS. On ethical grounds, I recused myself from the discussions and deliberations regarding Kristy Weber's candidacy for the Vice President position. Based on her many accomplishments, as well as her service to orthopaedic surgery and to the Academy, Kristy was elected as the first woman President of the AAOS, serving in the presidential year 2019. That same year will be a busy one for Penn Orthopaedics in that I will be serving as the President of the American Society for Surgery of the Hand. Since Dr. Weber's arrival, our department has encouraged diversity in our workforce not only at the resident level but at the faculty level. Our team surely has increased in diversity and this evolution has only made us stronger.

We are very excited to welcome new recruits to our faculty including two spine surgeons, Comron Saifi and Andrew Milby who will be joining Vincent Arlet and Harvey Smith this fall. Stephen Liu is also joining us to represent the hand group at Chester County Hospital and Robert Wilson will help expand our ortho oncology program with Kristy Weber.

On the research side, we have been fortunate to recruit Nat Dyment from the University of Connecticut. He is already funded by the NIH and has settled in nicely to the McKay Research Laboratory. Over the last eight years, we have been fortunate to raise funds for no less than four endowed chairs and I am delighted to report that the W.W. Smith Foundation has contributed another endowed chair to the department. The sole purpose of this chair is to recruit a senior basic scientist to complement our outstanding research faculty.

The department has been spotlighted throughout the University to a large extent based on Lou Soslowsky's promotion as the Vice Dean for Research Integration. I gave a TED talk at this year's TEDxPenn event where our hand transplant program was featured. In addition, our vascularized composite allotransplantation program was portrayed in my keynote lecture to the Penn Academy in Palm Beach in March at the request of the Provost Dr. Vincent Price and University President Amy Gutmann. Fred Kaplan will be honored this year with the 2017 Perelman School of Medicine Distinguished Graduate Award during the Medical Alumni Weekend event on May 12.

Our educational program continues to evolve with optimization of educational time based on a robust curriculum during our Thursday morning conferences. Our applicant pool continues to amaze me at the quality and depth of our medical school applicants and we again matched outstanding residents this year from a variety of prominent institutions. We continue to have an exceptional Visiting Professor program in Orthopaedic Surgery that is probably one of the most active in the country.

On the administrative front led by Lori Gustave and Fabian Marechal, we continue to attract outstanding health profession interns and many of these individuals such as Rachel Kleinman and recently Amy Schwartz have stayed on to assume greater roles in our clinics and operations.

Our success as a department has been recognized by academic medical centers outside of Penn and we have been requested to consult with these academic medical centers to optimize their operations and department organization of faculty, staff and health systems. Perhaps this is a tribute to our hardwork over the last eight years. In fact, we have been so successful that our Chief Operating Officer Lori Gustave has been promoted to Vice President of Business Operations for the health system. Our collective success has been in large part due to Lori's energy, vision, team building, strategic planning and grit. She will be missed and we are currently searching for a new Chief Operating Officer. We plan to continue to build upon the trajectory that has been set forth with all the progress and accomplishments this year, onward team!

Letter from the Program Director

Craig Israelite, MD

While it may seem difficult to author a Program Director annual update year after year for the UPOJ, in actuality, it is not. The reason is that while under the continuing leadership of Dr. L. Scott Levin, M.D., our program continues to expand at a rapid pace. Every year there continues to be development in all aspects of our program and divisions.

Beginning with intern year, the change has been significant and bold. New rotations have been added to enhance the education of our newest department members. The intern skill year has continued to be refined and has been exceptional. The credit goes primarily to Dr. Nicole Zelenski who has managed to organize and recruit senior residents and faculty for these modules. As a result, the interns are more prepared than ever to ascend to their core resident years.

This year's intern class was as talented and diverse as ever. Our new class includes Dr. Gerald Andah (Penn Medical School), Matthew Counihan (Drexel Medical School), Chelsea Hendow (New York Medical College), Liane Miller (USCF), Christina Nypaver (Loyola University), Christopher Scanlon (Drexel Medical School), Kimberly Stevenson (Georgetown University) and Matthew Webb (Yale). The expectation and observation thus far is that this class will continue the academic and clinical excellence which is expected of our residents.

On the other end of the spectrum are our graduating seniors. A metric of the strength of any program is obviously where the graduates matriculate. Our seniors have once again secured positions at the most premiere fellowship programs in the country. Dr. Jason Anari will be doing a pediatric fellowship at Children's Hospital of Philadelphia. Dr. Joshua Gordon will be doing a hand fellowship at the University of Washington Seattle Harborview. Dr. Philip Saville will be doing a spine fellowship at the Hospital for Special Surgery. Dr. Russell Stitzlein will be doing an oncology fellowship at M.D. Anderson. Dr. Vishal Saxena will be doing a sports medicine fellowship at Massachusetts General Hospital. Dr. Michael Talerico will be doing a trauma fellowship at the University of Washington Seattle Haborview. Dr. Nathan Wigner will be doing a spine fellowship at the University of Washington Seattle Haborview. Dr. Chase Woodward will be doing a spine fellowship at Washington University in St. Louis. We congratulate our seniors who have once again demonstrated that hard work and intellectual curiosity pays off and we have no doubt that they will be leaders in their respective fields.

Once again, I would be remiss not to bestow much of the credit to another outstanding year to our outgoing academic chiefs. Drs. Joshua Gordon, Jason Anari and Michael Talerico have once again provided the stewardship to have one of the most solid and well rounded programs. From one of the most robust visiting professorships to the AM core curriculum conferences, they have contributed outstanding leadership and have positioned our residency once again to be stronger than ever in the upcoming academic year.

Another significant development has been the appointment of Neil Sheth, M.D. as assistant program director and will be joining doctors Ahn and myself. Dr. Sheth brings energy and a specific skill set that will give additional talent to our leadership pool. Of course, we will miss Samir Mehta's, M.D. directorship as he has been promoted to be division leader of clinical research. While not officially an associate program director, I know that no one will doubt the continued effort and value of Dr. Mehta and that he will continue to provide to the residency mission on a daily if not minute by minute basis. Last but not least, is Shana Kurek who keeps the whole program running. Shanna tirelessly handles almost all of the day to day activities and requirements with exceptional skill.

Currently, there are 42 residents within the department. There are 8 new residents who matriculate each year, of which 2 residents spend an entire year doing full time research between post graduate 2 and 3 years. The residents continue to rotate at the University of Pennsylvania Health System locations which include Hospital of the University of Pennsylvania, Penn Presbyterian Medical Center, and Pennsylvania Hospital. Additionally, strong rotations at our VA Hospital, Children's Hospital of Philadelphia and Bay Health Community rotation continues to be very successful. In addition, several of our residents continue to participate and are encouraged to pursue global outreach programs.

While our affiliations are large and diverse, our department continues to strive for balance and well structured core curriculum. The curriculum is run on a 2-year cycle and covers all areas of our specialty. Grand rounds are required and take place every Thursday morning with 4 continuous hours of protected educational time. Additionally, each subspecialty delivers at least one academic didactic conference each week. These morning conferences are comprised of faculty within the division, fellows, residents and students, both from the University of Pennsylvania and visiting from other medical schools throughout the country. These lectures are reviewed, critiqued and discussed with each division chief in order to maintain clinical relevance while updating goals and objectives for each session.

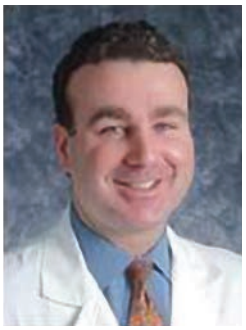
The bottom line is that our highly committed leadership, faculty and staff, our program has continued to not just flourish, but has significant positive growth. More attendings, more courses, more papers, presentations, and awards is the result of what I think has resulted in one of the best programs in the country. It is also one in which I am proud and honored to be associated.

Arthroplasty

Faculty

Charles Nelson, MD

Craig Israelite, MD

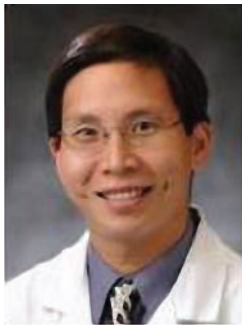


David Nazarian, MD

Eric Hume, MD

Neil Sheth, MD

Atul Kamath, MD



Gwo-Chin Lee, MD

Arthroplasty Division Update: Value Driven Readmission Mitigation for Hip and Knee Arthroplasty at Penn Medicine

Eric Hume, MD, Finnah Pio, Michele Fang, Laura Kosseim, MD

Value is quality compared to cost. American healthcare quality is being measure by frequency of untoward outcomes such as Hospital Acquired Complications (HACS) and readmission rates. American health care is expensive so hurts the public paying for health care and competition in global economy. Cost often drives discussions. Our improvement in readmission rate (Figure 1) show the result of effort so far and fiscal impact of CMS readmission penalties (Figure 2) we face. Gainsharing from bundled payment programs potentially from IBC of $160K and from CMB/Remedy of $740K.

Readmissions are a metric of low quality and are high cost; both contribute to adverse effects on value. Because of this double effect on quality and cost, readmission rates must be a focus for improving value. Readmissions may be preventable, through better patient selection, better preparation preoperatively, better discharge preparation and better post-acute management. Some readmissions can be considered to be "unnecessary", if the care during the admission could have been managed safely as an outpatient.

Readmission mitigation starts in the evaluation done in the outpatient office. First is the decision to proceed with elective surgery. Effective shared decision making utilizing the patient's risks for readmission and complication rates can support the decision for surgery. Our data demonstrate approximately 60% increase of readmission for alcohol use and an almost threefold increase of readmission rate for patients with cirrhosis. But can the effort to minimize risk for safer patient care become restriction of access to health care? As payers and bundle programs apply penalties and offer fiscal rewards for programs to cherry pick and lemon drop, access to care will be adversely affected.

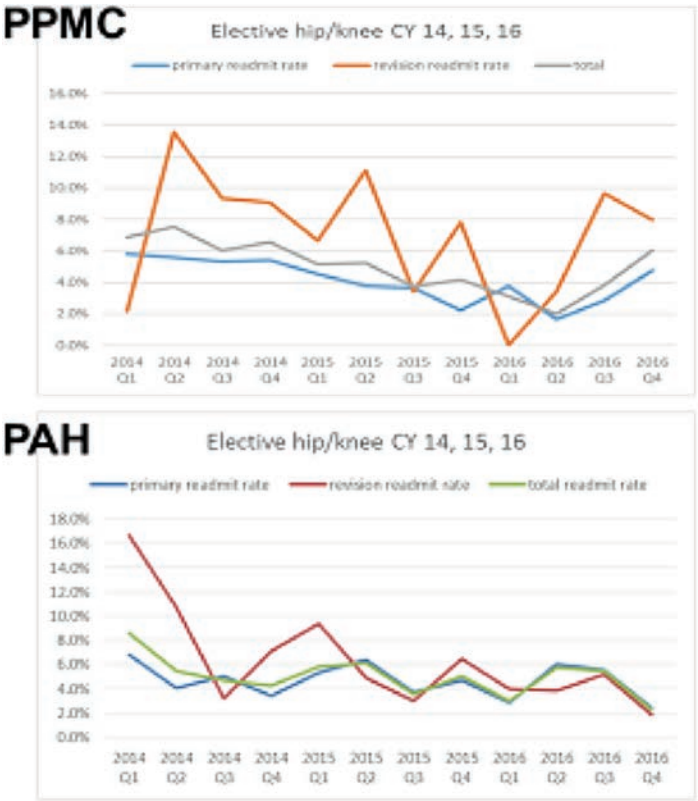


Figure 1.

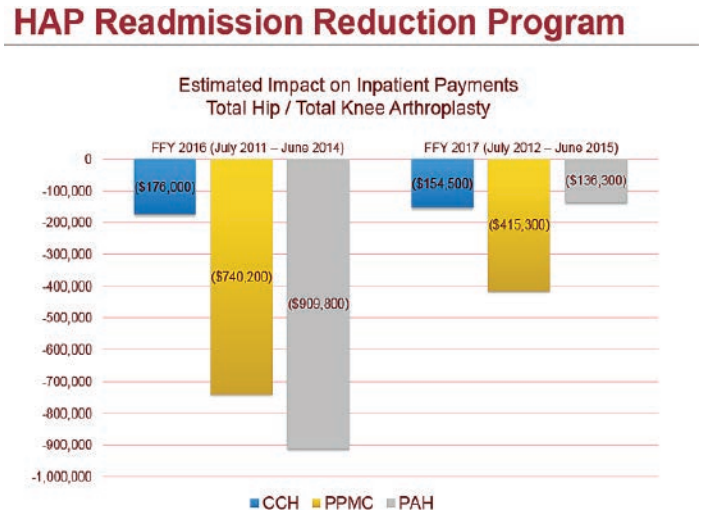


Figure 2.

Our risk stratification has effectively lowered hospital mortality by predicting the right location of care for the postoperative night. Next step is to use risk evaluation to support management before surgical procedure. Patients with A1C of >8 should be managed to a safe glucose level before XXX. Patients with a hemoglobin of <10 predictor and for total hip revisions a hemoglobin of <12, shows higher readmission rate, these patients should be sent to the Center for Transfusion Free Medicine at Pennsylvania Hospital. Nutrition, smoking, excess alcohol intake and chronic opioid users are all important predictors of adverse outcomes. Diligent pre-operative management of these modifiable conditions will further drive down adverse events such as cancellations, complications and readmissions (Figure 3).

Other preventable readmissions fall into orthopaedic and medical categories. The hot joint phone line and advanced practice provider's availability allows urgent conditions to be triaged and managed within a half business day. Our hot joint protocol, based on AAOS and AAHKS periprosthetic joint

Category	PPMC Total Pts	PPMC Readmit N	PPMC Readmit % of category	PAH Total Pts	PAH Readmit N	PAH Readmit % of category
All	3174	90		1,871	48	
Not risk evaled	94	6	6.4%	25	5	20%
ICU	127	6	4.7%	151	5	3.3%
A1c >=8	86	2	2.3%	338	9	2.7%
HB <=12	622	28	4.5%	296	12	4.1%
CHF	144	8	5.6%	40	4	10.0%
CAD	233	8	3.4%	99	5	5.1%
Alcohol Use	139	10	7.2%	16	1	6.3%
Delirium	455	11	2.4%	35	1	2.9%
Cirrhosis	37	2	5.4%	33	2	6.1%
BMI >30	2765	19	0.7%	470	11	2.3%
Complex	2500	81	3.2%	915	25	2.7%

Redcap: primary joints, 1/1/15 to 12/31/16 UHC: primary joints, 1/1/15 to 12/31 /16

Figure 3.

infection guidelines, has allowed us to stop the "unnecessary" readmission for infection. Beyond outpatient care for hot joints, care for the swollen calf can be evaluated in the office and sent for outpatient ultrasound. If negative, the patient is never in an emergency room and never admitted. If there is a DVT at the level of the popliteal fossa or above, collaboration with medical co-management, for an overnight observation unit, to start heparin and bridge to Coumadin or oral agents, can prevent readmission.

A not insignificant number of readmissions occur amongst both our low risk population and our complex patients. Both groups will be addressed using pathways to manage unnecessary medical readmissions with the hospital co-management team. We are working focused management for this group with active navigation. Bounce backs from rehabilitation facilities to emergency rooms are an important source of unnecessary readmissions. Our readmission rate from Skilled Nursing Facilities (SNF) and inpatient rehab facilities (IRF) is approximately twice from home. The Hot Joint protocol (green, yellow, red stoplight) is a resource for SNFs and other post-acute care providers (Figure 4). Communication back to our team for patient care is an important resource for preferred providers.

Complications, rate of periprosthetic joint infection, DVT, PE, are all opportunities for quality improvement and process improvement. Surgical and medical risks both contribute to readmissions. An MI within 90 days for surgery is included in the BPCI bundle cost. While the goal is 0% periprosthetic joint infections and hip dislocations, we cannot completely prevent surgical complications. "Never" events may be best managed by a focus on "always" events in pathways aimed to lower risk of complications.

Quality or cost as driver?

Nationally for hospital systems and surgeons, the concern about bundles has been the apparent drive to the reduce reimbursement, often referred to as "race to the bottom". Because of the delay in getting cost data, our efforts have been aimed at process improvement with clinically pertinent pathways based on clinical reasons for on readmissions. In the two years that we have been managing the CMS Medicare Bundled Payment Care Initiative (BPCI) and Independence Blue Cross bundles for hip and knee arthroplasty for primary joints and for revision joints, high quality and safe care has led to cost savings. We have realized that better safety and better

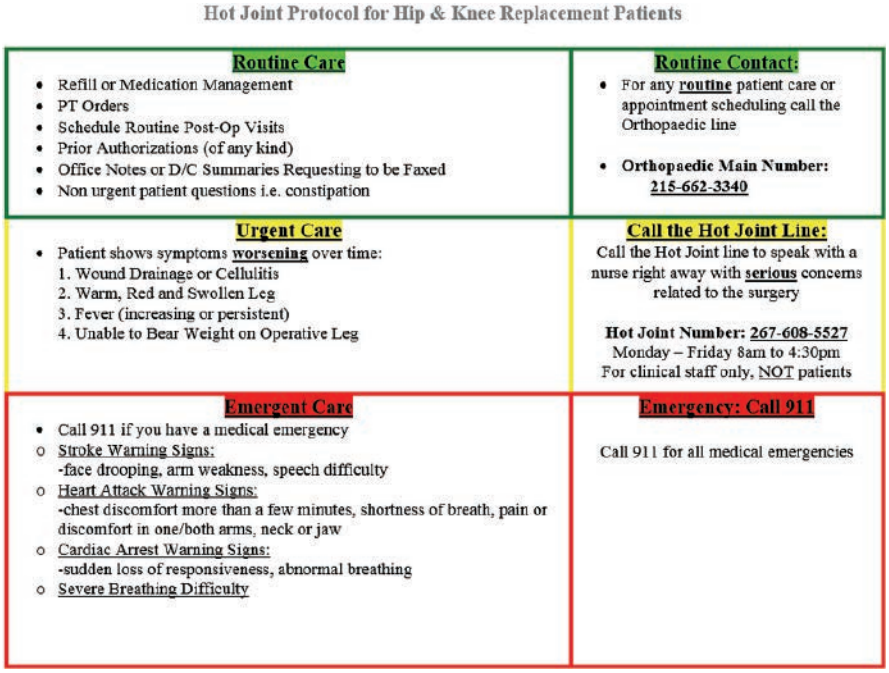


Figure 4.

safer patient care will drop to the bottom line, and has been a reassuring realization.

The "race to the bottom" cost is an important concern. Under the BPCI methodology, the present year's fiscal performance must beat the moving average of the last three years, but the average drifts down with success. Chasing the lowering moving average is not sustainable in the long-term because there is no lower limit for reimbursement. The "race to the bottom" cannot be sustained below the cost line where cost efficient care has been maximized. The line is, at the present, not defined.

In summary, our group is focused on managing readmission rates for all of our hip and knee, primary and revision, arthroplasty patients. Preventable readmissions occur among complex patients whose comorbidities can be mitigated. We continue to work in four time periods: in preop, in acute care, in discharge planning and during post discharge care. For both complex and low risk patients , supporting better home preparation, using preferred home health, SNFs and developing ER/OBS clinical pathways should lower the rate of "unnecessary" readmits. Data from the bundles have informed us as to the cost saving opportunities. While we learn within the bundle structure, we apply the lessons across our whole patient population with the ultimate goal of developing high value population management processes for hip and knee arthroplasty.

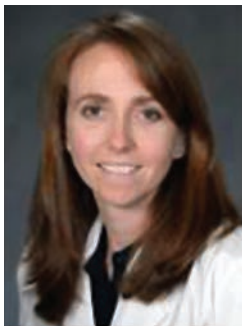
Foot & Ankle

Faculty

Keith Wapner, MD

Wen Chao, MD

Daniel Farber, MD



Kathryn O'Connor, MD, MSPT

Foot & Ankle Division Update

Daniel Farber, MD

The Foot and Ankle Division has had a productive year. Our faculty includes Keith Wapner, Wen Chao, Kate O'Connor, and Daniel Farber. Collectively the division has seen XX patients and performed YY surgical procedures over the past year. We now serve Center City and beyond with locations at the Farm Journal Building, PMUC, Cherry Hill, Radnor, and Exton and perform surgical procedures at Pennsylvania Hospital, Penn Presbyterian, the surgery center at PMUC, and at Chester County Hospital.

Internationally, Dr. Keith Wapner continues to travel the world representing Penn Orthopaedics with presentations in Switzerland, Dubai, and Beijing as well as multiple national talks. He also serves a member of the managerial board of the Foot and Ankle International journal. Dr. Daniel Farber completed his term on the AAOS Board of Directors and now serves on the AOFAS Education committee. He is spearheading a task force to develop an accreditation pathway for foot and ankle fellowships in a cooperative venture between the AOFAS and AAOS. Dr. Farber is the also Associate Editor for Review Articles for the new Foot and Ankle Online Journal of the AOFAS. He continues to direct Penn's Foot and Ankle Fellowship. Locally, Dr. Wen Chao is an Orthopaedic Consultant to the Pennsylvania Ballet. Our newest faculty member, Dr. Kate O'Connor, continues to grow her practice while managing the new foot and ankle education curriculum for the residents and serving on the AOFAS Evidence Based Medicine Committee.

From a research perspective, the division is now part of several national studies. These include an ongoing study of the STAR ankle replacement, a prospective study of a new bone graft substitute and an investigation of the use of bone stimulators for acute operatively treated ankle fractures. Other investigations include collaborations with Penn's Human Motion Laboratory exploring long term follow up of long harvest transfer of the flexor hallucis longus muscle for treatment of chronic Achilles pathology as well as short term follow up of acute Achilles ruptures. We continue to explore insights gained from weight-bearing CT scanning in investigations of ankle and hindfoot arthritis as well as in bunion deformities. An ongoing study looks at the role Orthopaedic surgeons play in influencing patients' choice of footwear. We are collaborating with the Biedermann lab and Mike Hast, PhD to explore the compression properties of a new plate for fusions of the forefoot, midfoot and hindfoot.

The division continues our collaboration with the McKay Lab and Lou Soslowsky, PhD investigating early return to activity after repaired and non-repaired Achilles ruptures. We have also begun to explore treatment options for simulated chronic Achilles ruptures in the rat model and will begin an investigation into the effect of smoking on Achilles rupture healing.

Penn's Orthopaedic Foot and Ankle Division is poised for another exciting year of excellent patient care, service to the orthopaedic community and active research.

Hand

Faculty

David Bozentka, MD

David Steinberg, MD

L. Scott Levin, MD, FACS

Benjamin Gray, MD

Robert Carrigan, MD

Apurva Shah, MD, MBA

Hand Division Update

David Bozentka, MD

It has been another banner year for the Hand Surgical Service in the Department of Orthopaedic Surgery. The program continues to expand the clinical and research efforts.

It is with great pleasure that we welcome back Dr. Stephen Liu to join the hand surgery section. Dr. Liu completed his undergraduate and medical school training at Tufts University. He graduated from the Orthopaedic Surgery Residency at the University of Pennsylvania in 2016. He is currently finishing his year of hand surgery fellowship training at the University of Pittsburgh with an exemplary performance. He will concentrate his hand surgical practice at Chester County Hospital.

Under the leadership of Dr. David R. Steinberg, director of the hand and microsurgical fellowship, two new hand surgery fellows started their year of training. The highly competitive program received over 100 applications for the two positions. Dr. Erwin Kruger, studied at Harvard University and University of Chicago, prior to completing his plastic surgery residency at UCLA.After his fellowship, Dr. Kruger plans to join a private practice group in Scottsdale, Arizona. Dr. Oded Ben-Amotz, completed a plastic surgery residency at Tel Aviv Sourasky Medical Center, Israel, as well as a one-year hand surgery research fellowship at UT Southwestern Medical Center in Dallas, Texas. Dr. Ben-Amotz has been accepted for a second year of hand fellowship training with the Christine M. Kleinert Institute in conjunction with the University of Louisville.

Benjamin Gray MD has established a strong hand surgery practice at Pennsylvania Hospital while completing his Masters of Science in Clinical Epidemiology. In addition to his exceptional clinical work, Dr. Gray has been invaluable to the service in his research efforts. Accordingly, Dr. Gray has been appointed Director of Clinical Research for the Hand Surgery Section. He will lead the direction of the robust clinical research effort within the division. The program has benefited from the extensive research experience of Annamarie Horan PhD as Director of Research for the Department of Orthopaedic Surgery and Kim Lacy RN, BSN as the research coordinator. The group continues to enroll 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. In addition, enrollment is being completed for the blinded randomized control trial to compare Tylenol 3 versus Ibuprofen/Acetaminophen with Dr. David Steinberg as principle investigator. Dr. Steinberg has also continued his productive basic science research in collaboration with the McKay Orthopaedic Research Laboratory.

This past year, Dr. David J. Bozentka was elected to the Academy of Master Clinicians at the Perelman School of Medicine at the University of Pennsylvania. The Academy of Master Clinicians is the highest clinical honor for a Penn Medicine physician. The Academy recognizes outstanding physicians that exemplify the highest standards in patient care and professionalism.

Another successful Penn Flap course for hand and microsurgery fellows and residents was held at the Penn Orthopaedic Human Tissue lab. Local, regional and free tissue transfers were reviewed during the two-day course. The internationally renowned faculty also reviewed nerve transfers and brachial plexus procedures with didactic lectures combined with cadaveric dissection.

The third successful double hand transplant was performed by the Penn Hand Transplant Service on August 22, 2016 at the Hospital of the University of Pennsylvania. Ms. Laura Nataf, a 29 year old quadrimembral amputee due to sepsis, underwent the eight and a half hour procedure by the 30 member team of surgeons, nurses and anesthesiologists. She has since returned to her home in Paris, France where she is continuing her treatment.

It is an exciting time for the hand surgery section with continued expansion of the academic and clinical programs as we look forward to another successful year.

Paris to Penn Medicine: The First Trans-Atlantic Bilateral Hand Transplant

Erwin Kruger, MD, Oded Ben-Amotz, MD, and L. Scott Levin, MD, FACS

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

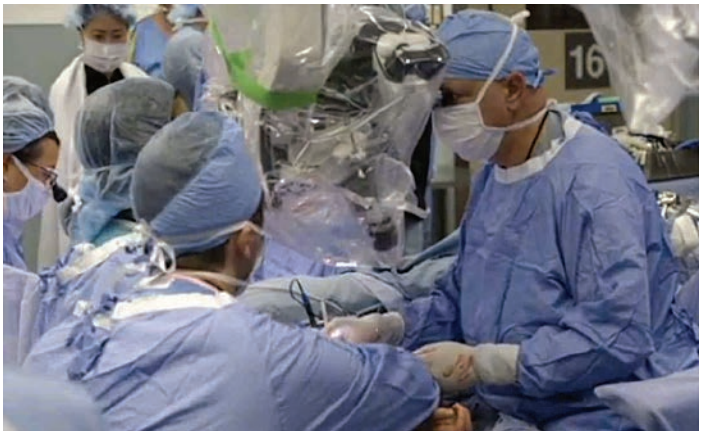
In 2007, 19-year old Laura Nataf, a French university student studying hospitality became septic, leading to multisystem organ failure. Both her arms and legs were amputated due to irreversible peripheral tissue damage from ischemia. Once Laura recovered, she began adjusting to her life as a quadruple amputee patient, and using prosthetics to perform her activities of daily living. Two years went by, and she began asking her care team about hand transplantation, and sought experts in the field in France to evaluate her case.

Laurent Lantieri, MD chief of the department of Plastic Surgery at Hôpital Europèen Georges Pompidou at Paris Descartes University took on her case and became her advocate. Dr. Lantieri had previously performed seven face transplants including one combined face and double hand transplant. He spent 7 years evaluating Laura for hand transplantation and achieved listing her as a candidate. However, problems within the healthcare system in France made it clear it would not be possible to perform Laura's operation in her native country. Dr. Lantieri turned to his colleague, and an equally passionate pioneer of hand transplantation—Dr. L. Scott Levin, MD, FACS, Chair of Orthopaedic Surgery at Penn Medicine and the director of Penn's Hand Transplant Program—for a unique collaboration to list Laura in the United States.

"I first met Laura in 2010 at the American Society of Reconstructive Transplantation meeting in Chicago," Dr. Levin remembers. "I was impressed with Laura's determination; she had her mind set on becoming a bilateral hand transplant recipient. She and I kept in touch through Laurent, and with our first adult bilateral hand transplant a year later, our program was building momentum and wound continue to do so."

Dr. Levin and Lantieri then led a long-term commitment to the Laura as a patient, and what would be a first for all the collaborating institutions: Paris Descartes University, Penn Medicine, and the Gift of Life Donor Program, to prepare an international patient for a bilateral hand transplant. Months of detailed planning and preparation began simulating the bilateral hand transplant at Penn's Human Tissue Lab, with precise roles of the surgical personnel involved. Gift of Life initiated locating suitable organs for transplantation. Laura Nataf was actively listed for bilateral hand transplantation at Penn Medicine in May 2016. In August 2016, the call came in to Dr. Levin from Gift of Life—donor hands were available. It was time.

What happened next was one of the most challenging logistical case preparations to date for a bilateral hand transplant. Laura Nataf was vacationing in Corsica, France, 730 miles from Paris, when she received the call to come to Penn immediately. Over the next 36 hours, Laura took a police escort and two plane rides to travel the 4,400 miles from France to Penn Medicine. All the while, the Penn Hand Transplant team of more than 30 members and three surgical specialties (Orthopaedic surgery led by Dr. L. Scott Levin, Plastic Surgery led by Drs. Benjamin Chang and Stephen Kovach, and Anesthesia led by Dr. Michael Hall) were mobilized. Laura arrived, the donor hands were procured, and nearly 9 hours of surgery later the first trans-Atlantic bilateral hand transplant was completed successfully.



Laura recovered for several weeks at the Hospital of University of Pennsylvania before returning home to Paris under the close care of Dr. Lantieri. She continues to show remarkable progress in her strength and motor function, and keeps in close contact with Dr. Levin and his team. The Penn Hand Transplant program has performed an adult bilateral hand transplant, the first pediatric bilateral hand transplant, and now with Laura the first international patient to receive a bilateral hand transplant in the United States. Laura Nataf's case was an international team effort, a very special case in all aspects, and because of the dedication of all involved, Penn Medicine is gaining experience as an epicenter of international limb transplantation and salvage.

Pediatrics

Faculty


John Flynn, MD


Alexandre Arkader, MD


Keith Baldwin, MD, MPH, MSPT

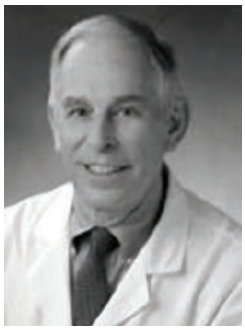

Patrick Cahill, MD


Robert Campbell, MD


Robert Carrigan, MD


Richard Davidson, MD


Theodore Ganley, MD


Malcolm Ecker, MD

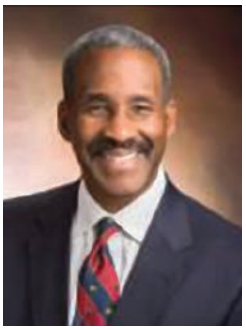

David Horn, MD


John Lawrence, MD


Wudbhav Sankar, MD


Apurva Shah, MD, MBA


David Spiegel, MD


Lawrence Wells, MD


Jennifer Winell, MD

The Children's Hospital of Philadelhpia Division Update

Divya Talwar, PhD, MPH and John (Jack) Flynn, MD

Introduction

The Division of Orthopaedic Surgery at the Children's Hospital of Philadelphia (CHOP) enjoyed another year of significant growth, accomplishment, and innovation. Upholding our mission to provide the most comprehensive care to patients, we have continued to expand our clinical, research, and teaching programs. In 2016, *US News and World Report* ranked the Division of Orthopaedic Surgery 2nd in the nation in pediatric orthopaedic surgery.

In 2016, CHOP Orthopaedics hired one non-operative surgeon, renovated the Nicholson Visiting Professorship, appointed a new manager of Clinical Research, awarded Chair's research grants to four winners totaling $40,000, received the prestigious CHOP Frontier grant of $4.5M, obtained significant extramural funding from major funding agencies such as National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), National Science Foundation (NSF), renovated the Fellowship recruitment and interviewing process, and continued our partnership with CHOP Office of Clinical Quality Improvement on two major projects (Sports and Spine) to improve the efficiency, safety and value of orthopaedic surgery.

Clinical Program

Our orthopaedic faculty continues to expand and is currently comprised of thirty total providers, including nineteen specially-trained pediatric orthopaedic surgeons (sixteen operative and five non-operative), six pediatricians with sports medicine training, and three transition-to-adult care faculty. CHOP Orthopaedics is pleased to announce the addition of a new provider: Dr. Vincent Deeney. Dr. Vincent Deeney (Figure 1). Dr. Deeney joins our team as a non-operative orthopaedic surgeon focusing on spine. In 2016, the department also saw significant growth in the mid-level provider staff. There are currently 24 nurse practitioners and physician assistants, and six athletic trainers who evaluate, diagnose, and treat a full range of musculoskeletal disorders.

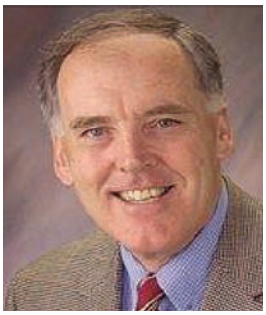


Figure 1. Dr. Vincent Deeney

Education Program

CHOP Orthopaedics currently funds four one-year clinical fellowships and one one-year research fellowship. The 2016-2017 clinical fellows are Daniel Miller, MD; Todd Blumberg, MD; Andrew Gambone, MD; and Susan Nelson, MD (Figure 2). This year's research fellow is Mahmoud El-Magd, MD from Egypt (Figure 3). While at CHOP Dr. El-Magd has focused his research efforts on trauma and lower limb deformities.

Figure 2. (From left to right) Dr. Daniel Miller, Dr. Todd Blumberg, Dr. Andrew Gambone, Dr. Susan Nelson.

Figure 3. Dr. Mahmoud El-Magd

We held our inaugural Drummond Rising Star Visiting Professorship in October 2016. The nominees are rising stars in pediatric orthopaedics that completed their fellowship here at the Children's Hospital of Philadelphia, Department of Orthopaedics. The 2016 Drummond Rising Star Visiting Professor was Michelle S Caird, MD (Figure 4), who is an Associate Professor of Orthopaedic Surgery at the University of Michigan in the Division of Pediatric Orthopaedics and serves as Program Director for the Orthopaedic Surgery Residency. Dr. Caird is one of ten 2015 American Academy of Orthopaedic Surgery Leadership Fellows.

The Division also continues to host visiting scholars to provide them with an opportunity to observe clinical care of pediatric patients in a high volume, academic setting. Over the past year, the Division hosted Dr. Kunbo Park, Assistant Professor of Pediatric Orthopaedic Surgery at Inje University Haeundae Paik Hospital in Busan South Korea.

Figure 4. Michelle S. Caird

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 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, one Department of Defense (DOD) grant and one Veterans Administration (VA) grant.

Our clinical division remains a major national and international center of diagnosis, care and surgical treatment for children affected by MHE. Our scientists are closely collaborating with our clinicians and clinicians-scientists, in particular Dr. Alexandre Arkader, to further examine the genetics of MHE, identify second hits needed to cause tumor formation, and eventually obtain insights into genotype-phenotype correlations that could be used for diagnostic and prognostic purposes. Our faculty member, Dr. Eiki Koyama, joined forces with Dr. Hyun-Duck Nah in the CHOP Division of Plastic and Reconstructive Surgery to study the development and growth of the temporomandibular joint (TMJ) and to identify possible therapeutic means to treat TMJ osteoarthritis, a debilitating condition particularly common in women.

Our basic research work on FOP has led to a current phase 2 double-blind clinical trial sponsored by the Canadian-based pharmaceutical company Clementia. The clinical trial was launched in July 2014 in close collaboration with our colleagues at the Penn FOP Research Center—Drs. Fred Kaplan, Bob Pignolo and Eileen Shore. The results of the phase 2 trial were disclosed for the first time in October 2016 and are exceedingly promising. The drug was well tolerated by the patients and there was a considerable decrease in their HO and improved skeletal function. This work is a major milestone achievement for our basic research division and shows that years of basic research can and do translate into possible new treatments for severe pediatric skeletal disorders.

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

In 2016 CHOP awarded three-year funding support of 4.5 million dollars in the Frontier Program funding to the Division's Center for Thoracic Insufficiency Syndrome (CTIS) to encourage innovation in translational research.

The CTIS Basic Science Research Lab, established with funding from the Frontier Program, is developing a rabbit model of thoracic insufficiency syndrome. Dr. Casey Olson, a bioengineer, leads this lab. It is expected that this model will improve understanding of the biomechanics and the pathobiology of thoracic insufficiency syndrome to help generate new medical and surgical treatments that can be pioneered at CHOP.

The CTIS Advanced Imaging Research Program has now been active for 5 years with collaboration from the University of Pennsylvania Department of Radiology Medical Image Processing Group (MIPG), led by Dr. Jay Udupa, and Dr. Sriram Balasubramanian in the Department of Bioengineering at Drexel University. The CHOP/MIPG collaboration has focused on dynamic lung MRI (dMRI) image analysis of thoracic insufficiency patients to understand the biomechanics of TIS and quantify the degree of dysfunction of the rib cage and diaphragm as a new metric to define thoracic performance. Refinement of the software for the quantification technique along with analysis of dMRIs of CTIS patients are now being supported by a NIH R21 grant. Future work will focus on creating a large database of normative data and standard subjects through an R01 grant-funded initiative. The Drexel University Bioengineering/CTIS relationship is also a long-standing collaboration which centers on detailed software analysis of CT scans and EOS® biplanar radiographs of TIS patients. Recent funding will strengthen this collaboration with many new research efforts.

Genetic Research

CHOP Orthopaedics continues to work in collaboration with the Center for Applied Genomics (CAG), led by Dr. Hakon Hakonarson and Dr. Struan Grant, to compile a registry of DNA and RNA samples. These samples are obtained from patients and families with a variety of orthopaedic conditions including adolescent idiopathic scoliosis (AIS), osteochondritis dissecans (OCD) of the knee, and multiple hereditary exostoses (MHE). This past year, in conjunction with colleagues in genetics and basic science at CHOP, preliminary results from a study of genetic predispositions for MHE were published in *Bone*. To further investigate genetic characterizations of the EXT1/EXT2 mutations harbored by each exostosis and identify second hit(s) across exostoses from the same patient, Dr. Arkader was awarded a competitive faculty award from Division of Orthopaedics. This pilot project represents the first biomedical research focused on MHE.

Orthopaedic Engineering

Dr. Saba Pasha, Director of Orthopedic Engineering, continues her research on application of 3D imaging and computer simulation in surgical planning, use of predictive models in surgical decision-making, and exploring gait and motion analysis for a more personalized treatment. In 2016, Xochitl Mellor joined our team as research technician. Dr. Pasha's work utilizes advanced imaging and motion analysis to collect data on a range of conditions and patient populations. These tools will help us to visualize and determine the best treatment options for patients.

Clinical Research

The Division of Orthopaedic Surgery is currently conducting 158 IRB-approved clinical research projects. This includes 70 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), The Fox Pediatric Spinal Deformity Study (Fox PSDS), PLUTO (Pediatric ACL: Understanding Treatment Operations, and International Hip Dysplasia Institute (IHDI). In 2016, the Division published over 114 articles in major orthopaedic journals, including JBJS, JAMA Pediatrics, JPO, and CORR. Members across our division presented 123 presentations at

Figure 5. (From left to right) Christopher DeFrancesco, Taylor Jackson, and Brendan Striano.

international and national conferences last year alone. Our attending surgeons presented 47 invited presentations.

The Division 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 June, Christopher DeFrancesco (Perelman School of Medicine at the University of Pennsylvania), Taylor Jackson (University of Texas Southwestern Medical Center) and Brendan Striano (Rutgers Robert Wood Johnson Medical School), were awarded with the fellowship (Figure 5).

Recognition and Achievements

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

Alexandre Arkader, MD co-directed the 5th Combined SLOATI/POSNA/EPOS/ meeting, Sao Paulo Brazil Oct 2017. He also served as an International Faculty at the Salzburg Medical Seminar in Pediatric Orthopedics in Salzburg, Austria. Dr. Arkader continues to serve as a reviewer for *Current Orthopaedic Practice, Journal of Bone and Joint Surgery, Clinical Orthopaedics and Related Research and Journal of Pediatric Orthopaedics.* He was invited as a visiting professor at Saint Peter's University Hospital, NJ.

Keith Baldwin, MD, MSPT, MPH is the current Director of Clinical Research and Associate Director of Orthopaedic Trauma in the Division of Orthopedic Surgery. This past year he earned the Jacqueline Perry Award Paper from the Orthopaedic Rehabilitation Organization. Dr. Baldwin was elected as the president of the Orthopaedic Rehabilitation Association and also served as course director for the 2016 Orthopaedic Rehabilitation Association Annual Meeting. Dr. Baldwin currently serves as a reviewer for a number of journals including the *BMC Medical Education*, *BMC Musculoskeletal Disorders, Journal of Bone and Joint Surgery—American*, and *the American Academy of Pediatrics*. He also serves as associate editor for *Journal of Orthopedic Trauma* and an editorial board member of the *American Journal of Orthopedics, Current Orthopaedic Practice* and *World Journal of Orthopedics*.

Patrick Cahill, MD was selected to serve as the program chair at Penn's Rare Disease course on SMA and the SMA course at IPOS. In addition, he served as the director of an ICL course on complications in pediatric spine deformity. Dr. Cahill also serves as chair of the SRS research grants committee and is a member of POSNA's Quality, Safety, Value Initiative Committee. He continues to serve as an Associate Editor for *Spine Deformity Journal* and as a reviewer for the *Journal of Bone and Joint Surgery—American* and the Thrasher Research Fund. Dr. Cahill is an active member in the Harms Study Group, Children's Spine Study Group, and Fox Pediatric Spine Deformity study group.

Robert Campbell, MD continues to expand and develop the Center for Thoracic Insufficiency at CHOP and was awarded the prestigious CHOP Frontier Grant. Dr. Campbell and Dr. Udupa (Perelman School of Medicine) continued their work on the NIH R21 Grant. He continues to serve as a member of the Early Onset Scoliosis Task Force, FDA Grants for National Non-Profit Pediatric Device Consortia, and FDA Office of Orphan Product Development

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

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

B. David Horn, MD is the current chair of the AAOS Pediatric Evaluation Committee and is a member of the Board of Directors for Philadelphia Orthopaedic Society. He 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 Orthopaedic Surgery, continues to serve his 10-year term as a Director of the American Board of Orthopaedic Surgery and his 4-year term as AAOS Chair of Continuing Medical Education. He also co-chairs the sold-out Spine Surgery Safety Summit. Dr. Flynn is co-editors of two textbooks: *Rockwood and Wilkins': Fractures in Children* and *Operative Techniques in Orthopaedic Surgery—Pediatrics*. He is President of the Children's Spine Study Group and is active in the Harms Study Group, a multicenter collaboration of researchers studying care improvements for pediatric spine deformity surgery. In the past year, Dr. Flynn also was invited as a visiting professor at Columbia University, Harvard University and Northwestern University.

Theodore Ganley, MD is the Sports Medicine Director at CHOP, supporting the continued growth of clinical, research, and outreach initiatives. Dr. Ganley has continued in several leadership roles, 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 vice president for the Philadelphia Orthopaedic Society.

John Todd Lawrence, MD, PhD, was awarded the National Science Foundation grant through collaborative research with

the PI at Drexel University, Dr. Leo Han, to conduct in vitro studies for a novel cartilage repair strategy. He also served as an international faculty member at the Salzburg Medical Seminar in Pediatric Orthopedics in Salzburg, Austria. He continues to serve as a reviewer for the *American Journal of Sports Medicine (AJSM)* and *Journal of Shoulder and Elbow Surgery (JSES)*.

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

Apurva Shah, MD, MBA continues to serve as co-PI on a POSNA Directed Research Grant. Dr. Shah also received the Peter F. Armstrong, MD Shriners Hospitals for Children Award, Best Quality, Safety, Value Paper for his research presentation at POSNA, "Determining the Prevalence and Costs of Unnecessary Referrals in Adolescent Idiopathic Scoliosis." In October 2016, Dr. Shah served as team leader and traveled to Sigua Tepeque, Honduras for a pediatric hand surgery medical mission.

David Spiegel, MD continued his work with the Children's Hospital of Philadelphia Global Health Pilot Grant. In collaboration with Dr. Bibek Banskota in Nepal, Dr. Spiegel is conducting the longest follow-up in the world's literature of patients treated by the Ponseti method in a low-middle income country. Dr. Spiegel continued to be an active academic internationally, giving lectures in Iraq, Nepal and Canada. For his international work, the Scoliosis Research Society's (SRS) awarded Dr. Spiegel the prestigious Walter P. Blount Humanitarian Award and John E. Lonstein, MD and Harry L. Shufflebarger, MD Lifetime Achievement Award.

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.

Shoulder & Elbow

Faculty

David Glaser, MD

G. Russell Huffman, MD, MPH

Andrew Kuntz, MD

Shoulder & Elbow Division

David Glaser, MD

It has been another outstanding year for the Shoulder and Elbow division of the Department of Orthopaedic Surgery in the Perelman School of Medicine at the University of Pennsylvania. With continued commitment to manage the most complex cases, the section's tertiary referral network has dramatically increased along with the complexity of cases. In 2016, the group performed over 10,000 visits and performed over 1000 surgical cases.

New to our program and in collaboration with our French colleagues, our fellowship has added an international component which will provide our fellow an opportunity to work with world leaders in shoulder surgery. As Director of our Fellowship, Russell Huffman continues to coordinate the next generation of academic surgeons, with our last several fellows joining teaching programs. Chad Myeroff (F'17) is headed to an academic practice in Minnesota. Russ has completed his 40th Tommy John with his novel technique using 2 cortical buttons, including having a patient 3 years out drafted by the Cincinnati Reds.

As Director of research, Andy Kuntz is leading our research effort, with close collaboration with Louis Soslowsky and others in the McKay Research Laboratory. Together, we help form one of the largest, shoulder research laboratories in the world. The Shoulder and Elbow clinicians have 5 refereed research grants in 2016/17, including NIH, Veterans Affairs, and the industry grants. Andy received an ASES research grant for study titled "Effects of Aging on Tendon Cell Metabolism". He is continuing a funded study investigating "Effect of Scaffold-Delivered Growth Factors in Rotator Cuff Repair". Along with his collaborators, his success has been recognized with 10 abstract acceptances and two papers.

Clinical studies include outcomes using multimodal pain control, outpatient shoulder arthroplasty, long term outcomes of prosthetic implants and cost efficiency in delivering health care. The Penn shoulder and elbow faculty presented 14 abstracts at national meetings, gave 13 talks at international, national, regional and local meetings in 2016/17.

Spine

Faculty

Vincent Arlet, MD

Harvey Smith, MD

Spine Division Update

Vincent Arlet, MD and Harvey Smith, MD

The Spine Division continues with its successful pathway

The Division continues to expand with the addition to new spine surgeons. Dr. Andrew Milby who is a former resident from Penn Orthopaedics will join PPMC after a fellowship at Emory. Dr. Milby will join focus his clinical practice at Penn Presbyterian Medical Center, Valley Forge and Radnor locations, and will also work to support the clinical service at the VA Medical Center. Dr. Saifi completed his residency at Columbia and did a fellowship at Rush. He will join Penn Orthopedics and will be based at PAH and will develop a spine deformity practice.

The PAH Spine Deformity Center was recently equipped with the EOS machine. This x-ray machine allows scoliosis films with five times less radiation than conventional x-rays. It also enables the planning of reconstructive surgery that is tailored to the patient anatomy and needs.

Drs. Smith and Arlet have been invited to numerous Spine societies and National Visiting Professorships. The division remains active in both clinical and basic science research. Dr. Smith and Dr. Mauck are co-Investigators on a recently awarded a VA Merit Grant based on their work with tissue-engineered disc replacement. As well, the division has been awarded further grants and prizes for its research. Clinical papers on the treatment of Spinal deformities have been published in top Peer reviews journals.

The division of spine surgery is looking at the future with bright perspectives and growth

Sports

Faculty

Brian Sennett, MD

James Carey, MD, MPH

John Kelly, MD

Miltiadis Zgonis, MD

Kevin McHale, MD

Sports Division Update: Dream Team Continues to Add Depth Across All Fields

Daniel Gittings, MD, John Kelly IV, MD, Brian Sennett, MD

The Sports Medicine Division at Penn Orthopaedics has continued to add talent to its depth. Dr. Kevin McHale (Figure 1) was recruited to join the faculty as a Clinical Assistant Professor after completing an Orthopaedic Surgery Residency at Penn and a fellowship in Sports Medicine at Harvard / Massachusetts General Hospital, where he served as an Assistant Team Physician for the New England Patriots, Boston Red Sox, and Boston Bruins. Dr. McHale joined the Cape Regional Physicians Associates group where he now serves the community he grew up in. In addition expanding the team, the Sports Medicine Division continued to provide educational opportunities for the community at large.

In January 2017, the team assembled to host the third annual Throwing Symposium. The audience was treated to several quality lectures including those from Steve Lemos, M.D., Ph.D., team physician for the Detroit Tigers. Dr. Lemos delivered a lecture,'what the Detroit tigers have taught me'and captivated attendees with the hard earned wisdom he accrued through caring for professional players. In addition, Tim Uhl, Ph.D., P.T. enthralled registrants with his talk on 'training techniques to improve velocity'. Other faculty, including revered Phillies baseball therapist, Phil Donley (A.T.C., P.T.) and Craig Morgan, M.D., consultant to Kansas City Royals, conveyed to attendees the most contemporary knowledge on injury prevention and performance optimization of the throwing athlete. The next symposium will be held Jan. 27, 2018. The symposium serves as one of the educational cornerstones of the Penn Throwing Clinic which is directed by John Kelly, MD. In 2017, Drs. Kelly and Sennett will be teaching Instructional Course Lectures at both the American Academy of Orthopaedic Surgeons and the Arthroscopy Association of North America annual meetings, focusing on Advances in the Thrower's Shoulder. These lectures will highlight work performed at the Penn Throwing Clinic, located within the Penn Human Performance Center.

Penn Sports Medicine is currently involved in the development of the Penn Center for the Female Athlete. Drs. Kate Temme and Ellen Casey are directing these efforts with focus on developing an interdisciplinary approach to the female athlete. This center will be the first full academic center in the area with an emphasis on patient care, education, and research. Many educational and research initiatives are currently underway with the most prestigious being Dr. Casey's NIH grant focusing on "Exploring the Modulatory Role of Sex Hormones along the Neuromechanical axis in females". Dr. Casey joined the Penn Sports Medicine faculty in 2016.

The athletic community continues to be served by the Penn Sports Medicine team. The running population was served by Penn Sports Medicine as John Vasudevan, M.D., served as medical director for the Tri-rock Philly Triathlon held in June, 2016, Rahul Kapur, M.D., continues to serve as the medical director for the Penn Relays and Dr. Alexis Tingan will serve as the medical director for this year's Philadelphia Love Run Half-Marathon. Dr. Tingan, completed his sports medicine fellowship at Penn this year and was recruited to join the sports medicine faculty in August 2016. Dr. Sennett continues to serve as a medical advisor to the Philadelphia 76ers.

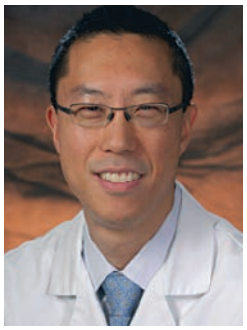
The Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment has continued to grow annually. The center is now recognized as one of the pre-eminent cartilage restoration centers nationally as it has become the #3 center in the nation with respect to volume of autologous chondrocyte implantation surgeries. From a research standpoint, Drs. James Carey, Robert Mauck and Jason Burdick have been awarded the AOSSM Biologics II Research Grant. This $250,000 grant will focus on the "Acellular Bioactive and Dynamic Nanofibrous Scaffolds to Promote Cartilage Repair." The Penn Center for Cartilage Symposium has also continued to grow annually. It has become an international course organized and run by Course Directors James L. Carey, M.D., M.P.H., and Robert L. Mauck, Ph.D. The course in 2016 was attended by a record 197 participants, including physicians, scientists, mid-level providers, nurses, veterinarians, physical therapists, athletic trainers, and students. This years' course will be held on April 28-29, 2017 and is titled "Advances in Biological Joint Replacement".

Dr. Kevin McHale returns to Penn Orthopaedics at Cape Regional Medical Commons.

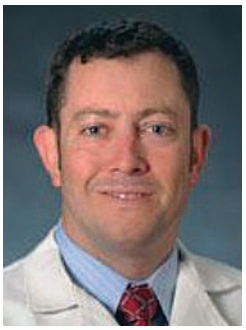
Trauma

Faculty

Samir Mehta, MD



Jaimo Ahn, MD, PhD



Derek Donegan, MD

L. Scott Levin, MD, FACS

Trauma Division Update

Blair Ashley, MD, Samir Mehta, MD, Jaimo Ahn, MD, PhD,
Derek Donegan, MD

The Division of Orthopaedic Trauma & Fracture Surgery continues to be an exceptionally busy and dynamic subset of Penn Orthopaedics. The orthopaedic traumatologists practice at the highest volume Level 1 trauma center in the Delaware Valley. The center is now in its third year at its new home at Penn-Presbyterian Medical Center, with over 1500 cases each year. 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. The chief of the division, Samir Mehta, was recently promoted to Associate Professor and works alongside Jaimo Ahn and Derek Donegan to care for some of the greater Philadelphia's most complex and challenging orthopaedic trauma patients.

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 care, as well as run an outpatient fracture clinic multiple days per week 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. The life-blood of the orthopaedic trauma program is the resident complement, who continues to support the service line through tireless efforts. 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 (Figure 1). 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 facilitates the ability of the trauma service to function at a high-level at all times.

Innovation in patient care occurs contemporaneously with upholding longstanding division traditions. For example, the trauma division has worked closely with geriatric and emergency medicine teams 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. The implementation and evaluation of Penn's program has largely been spearheaded by one of our rising chief residents, Dr. Keith Connolly, in conjunction with Drs. Ahn, Donegan and Mehta from orthopaedics and Dr. Alyssa Krain, from geriatric medicine. Programs like the geriatric hip fracture pathway cannot be a reality without health system support thanks to Rachel Kleinman and Lori Gustave. Additionally, all three attendings are actively involved in research. Dr. Ahn, the quintessential clinician scientist, was awarded the Career Development Grant from the OREF and continues his basic science and translational research in his laboratory at the McKay Laboratory. Dr. Mehta was recently named the head of the Clinical Research Department, alongside Dr. Annamarie Horan, in addition to being actively involved in prospective studies and translational biomechanics research at the Biedermann Lab. Similarly, Dr. Donegan is engaged in biomechanics research within the Biedermann Lab in addition to clinical research projects, with recent publications in Injury, Journal of Orthopaedic Trauma and Clinical Orthopaedics and Related Research.

The division's presence extends beyond the region and beyond medicine, at large. All three attendings are deeply involved with the AO Foundation, an international foundation geared towards advancements in fracture care. By December 2017, all three Penn traumatologists will have chaired a national AO North America course which attracts hundreds of

Figure 1. A trauma team assembled for traditional end of rotation team photograph (from left to right: Dr. Chia Wu, Dr. Michael Eby, Dr. Jenna Bernstein, Dr. Max Courtney, Dr. Blair Ashley, and Dr. Joshua Gordon.)

residents and faculty to learn and to teach the principles of basic and advanced fracture care. Additionally, Drs. Mehta and Ahn have both been involved in international outreach, with Dr. Ahn actively striving to implement a lasting presence in Botswana. Dr. Donegan is extending his influence into the field of business, as he works towards his MBA in the Executive MBA program at Temple's Fox School of Business. He is scheduled to graduate in May 2018 and will undoubtedly bring a fresh perspective and a unique expertise to the department.

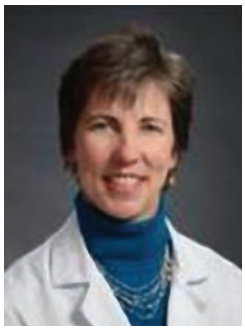
Clinically, the Division continues to extend its areas of expertise focusing on "elective" orthopaedic trauma care. The Division has a distinct interest in peri-prosthetic fractures, infection (osteomyelitis), malunions, and non-unions. The division utilizes advanced technology to facilitate the care 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 performed several cases utilizing 3D printing of implants in an effort to salvage extremities in patients with severe injuries.

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. Ahn, Donegan and Mehta all participate in resident morning lectures, Department Grand Rounds, as well as the General Medical Education Committee (GMEC). Dr. Ahn is also heavily involved in the residency as an Associate Program Director. The department hosts biannual courses provided by the Foundation of Orthopaedic Trauma (FOT), which residents are encouraged to attend. The attendings also lead every trauma team in a trauma cadaver lab prior to their rotation to engender team unity as well as to practice common procedures and exposures.

In conclusion, the expertise and diversity of the Trauma Division continues to grow, and we are looking forward to another momentous year of patient care, innovation, outreach and education.

Tumor

Faculty



Kristy Weber, MD

Orthopaedic Oncology Division Update

Kristy Weber, MD

Abramson Family Professor in Sarcoma Care Excellence, Chief, Orthopaedic Oncology, Director, Penn Sarcoma Program at the Abramson Cancer Center

The Orthopaedic Oncology service at Penn is part of a multidisciplinary team of caregivers that is focused on patients of all ages with bone and soft tissue tumors. This includes the care of patients with benign and malignant primary tumors as well as patients with metastatic bone disease. The Penn Orthopaedic Oncology core team involves Dr. Kristy Weber, Bethany Sterling, CRNP, and Sarah Borgia, MHA, Administrative Coordinator along with an R4 orthopaedic resident. An R2 orthopaedic resident also participates on the service in addition to managing their primary role of evaluating and treating the HUP inpatient and ER consults. Patients are seen during 2 days each week in PCAM clinic, and surgeries are performed 1-2 days per week at HUP. Patients are also managed in the clinic and OR at CHOP along with Dr. Alex Arkader (orthopaedic oncology/pediatric orthopaedics) and Amy Rapino, NP. Bethany Sterling, NP runs a weekly Bone Metastasis Clinic at our Valley Forge location. A new formal connection with the Philadelphia Shriners Hospital to evaluate patients with bone or soft tissue tumors has been forged this year. Our Penn Orthopaedic Oncology Visiting Professor for 2017 is Dr. Ted Parsons, Chair of the Department of Orthopaedic Surgery at Henry Ford Hospital in Detroit.

The multidisciplinary clinical team that treats patients with bone or soft tissue sarcomas meets weekly on PCAM South 12 for a clinical care conference to discuss the presentation and differential diagnosis of new patients as well as the ongoing multimodal therapy for existing patients. Our musculoskeletal radiology team leads the conference under the direction of Ronnie Sebro, MD, PhD. Our musculoskeletal pathology team members provide expertise reading the tumor biopsies and teach all of us about the histologic and molecular appearances of these rare tumors. A new faculty member, Dr. John Wojcik will join the sarcoma pathology team with particular expertise in molecular evaluation of tumors and a strong basic science interest. The medical oncology team is led by Drs. Chip Staddon and Lee Hartner who practice at Pennsylvania Hospital and have provided high level care for sarcoma patients for many years in the Penn community. Dr. William Levin is the lead radiation oncologist at PCAM/HUP who utilizes proton radiation and IMRT for patients with sarcoma, and he works with a network of radiation oncology colleagues throughout the Penn hospital system. Dr. Jacob Shabason will join the faculty in radiation oncology with a particular interest in developing new clinical trials combining immunologic treatments and radiation for sarcoma. Dr. Giorgos Karakousis is a surgical oncologist who treats patients with melanoma as well as retroperitoneal, abdominal and extremity sarcoma. In addition, we have a large surgical team including neurosurgery, plastic surgery, colorectal surgery, urology, and gynecologic oncology surgery that collaborate to surgically resect complex tumors about the spine and pelvis and reconstruct the defects to allow maximal function. Finally, there is a large supportive care team at Pennsylvania Hospital and HUP/PCAM to who assist patients with bone and soft tissue cancers including nurse practitioners, nurses, social workers, nutrition specialists, physical/occupational therapists, prosthetic/orthotic specialists and others focused on alternative therapies. Active marketing efforts are ongoing at both Penn and CHOP to expand the reach of the orthopaedic oncology program in the region

All of the members of our clinical Sarcoma team prioritize seeing patients expediently and efficiently to make an accurate diagnosis and provide expert treatment. A Sarcoma leadership group meets monthly to work on quality initiatives and clinical pathways to improve the overall delivery of care to our patients.

An exciting development for Penn Orthopaedics and the Division of Orthopaedic Oncology is the successful recruitment of Dr. Robert Wilson who will start work in September 2017. Dr. Wilson is completing an orthopaedic oncology fellowship at Vanderbilt and will be joining the Penn community along with his wife, Dr. Jessica Wilson, an endocrinologist and physician-scientist. We are thrilled to have him join the division, and he will take a lead in clinical research and education. He will expand our reach to Radnor and will also initially spend time at the Philadelphia VA hospital performing both tumor surgery and hip/knee arthroplasty.

One of the features that stands out about the Penn Sarcoma program is the presence of a collaborative scientific team focused on new discoveries in sarcoma. Over the past year, the cohesive team of clinicians and scientists from Penn Med, Penn Vet and CHOP have worked together to apply for team science grants. In addition to the monthly Sarcoma research meetings, the smaller team meets regularly to develop a multi-pronged approach to the prediction, prevention, and treatment of sarcoma metastasis to the lung. The core sarcoma research team includes Karin Eisinger, PhD, Malay Haldar, MD, PhD, Celeste Simon, PhD, Margaret Chou, PhD (CHOP), and Nicola Mason, PhD, BVetMed. These investigators utilize sophisticated murine and canine spontaneous sarcoma models to study these diseases. They are focused on immunology, hypoxia, and epigenetics among other areas of study in both bone and soft tissue sarcomas and are collaborating in a translational way with our musculoskeletal radiology and pathology teams and Kristy Weber, MD. Our Sarcoma Visiting Professor this year was David Kirsch, MD, PhD, Vice-Chair of Radiation Oncology at Duke who gave an outstanding talk about the use of genetic mouse models of sarcoma during his visit.

CPL Michael J. Crescenz Veterans Affairs Medical Center Update

Marlene DeMaio, MD, Capt

Medical Corps, U.S. Navy (retired), Chief of Orthopaedics and Spine Surgery, GME Site Director

In last year's edition of the UPOJ, Dr. John Esterhai provided an eloquent and thorough "Health System Update", reviewing our scope and strengths[1]. Dr. Esterhai, a former U.S. Air Force flight surgeon, is the previous and, long-serving, Chief of the service and GME site director who built our strong foundation of patient care and orthopaedic education. I will focus on several transitions since Dr. Esterhai retired.

Staff

Until June 2016, Dr. Joseph Bernstein was the Acting Chief. I then succeeded Dr. Esterhai and became the first full time service chief with a university appointment. Also in June, we saw the departure of Drs. Daniel Farber, Neil Sheth, and Milton Zgonis. Our active surgical staff includes Drs. Jaimo Ahn, Joseph Bernstein, Malcolm Ecker, Ernest Gentchos, Eric Hume, John Kelly, Andrew Kuntz, Harvey Smith, and David Steinberg. All surgeons provide the general and specialty orthopaedic care critical to our patient needs, ranging from uncomplicated (some) to complex (most). Dr. L. Scott Levin continues to volunteer his time. For each resident rotation, he now attends case-based teaching rounds at the VA. Each of the four residents presents a case that is then discussed in detail. All staff are dedicated to resident education and directly supervise in clinic and the operating room. Our diligent and knowledgeable physician's assistants, Mitchell "Chip" Staska and John Wheeler, provide daily consistent care to our patients. We are looking forward to Dr. Katherine O'Connor joining us soon.

Research

Drs. Bernstein, Kuntz, Smith, and Steinberg continue with their VA funded and approved grants. Dr. Smith earned a Merit Grant and will be able to continue his Career Development Award. We are developing a clinical research initiative, to be integrated with the university's clinical research program lead by Dr. Samir Mehta. Dr. Annamarie Horan will be joining us as a research volunteer.

Patient Care

During the 2016 annual year, the orthopaedic general service saw 4957 patients in clinic and the spine service 290. We had 381 cases in the main operating room, of which 15 were spine cases. The loss of main operating room staff and surgeons did impact our caseload. One hundred and fifty-five patients were admitted.

Improving care is critical to our mission; we have targeted several areas for the coming months. At the close of 2016, we had initiated policies for tranexamic acid, opioids, and pre-operative education for total joints. The new Hospitalist-Surgical Co-Management Team has enhanced our ward care. Many of our total joint patients transfer to the facility's Rehabilitation Medicine Service who also work closely with us.

While the current conflict is the longest in our nation's history, our largest patient demographic is from the Vietnam Conflict. With this in mind, I direct you to the Medal of Honor Citation for our facility's namesake, CPL Michael J. Crescenz, U.S. Army, who was only 19 years old when he single handedly overtook three bunkers under direct and unrelenting fire in Hiep Duc Valley, Vietnam on Nov. 20, 1968[2]. The Corporal was attempting to take the fourth bunker when shielded his company's medic and the wounded. This selfless act resulted in his death but saved his squad. CPL Crescenz grew up in West Oak Lane, enjoyed Sea Isle City in the summers, and graduated from Cardinal Dougherty High School. He is the only person from Pennsylvania bestowed The Medal of Honor.

References:

1. Esterhai, J. Health System Update: Philadelphia Veterans Affairs Medical Center Update. *UPOJ*, Volume 26, June 2016, 184-185.

2. http://www.arlingtoncemetery.net/mjcrescenz.htm

Council of Research Laboratories Established within Penn Orthopaedics

Michael Hast, PhD

The Department of Orthopaedic Surgery is proud to announce a new initiative intended to create synergy and collaboration between orthopaedic research entities at the University of Pennsylvania. Dubbed the "Council of Research Laboratories," the team was assembled in January of 2017 and consists of directors from labs located throughout the Penn campus. Topics such as resource sharing, establishing cohesive research themes, and uniformly promoting Penn's steadfast research mission have been recurring themes during the meetings. The Council meets on a monthly basis and comprises the following representatives:

- Biedermann Lab for Orthopaedic Research- Michael Hast, PhD
- Center for Research In FOP and Related Disorders- Eileen Shore, PhD
- Clinical Research Program- Annamarie Horan, PhD; Samir Mehta, MD
- Human Motion Lab- Josh Baxter, PhD
- Human Tissue Lab- L. Scott Levin, MD
- McKay Orthopaedic Research Lab- Robert Mauck, PhD
- Penn Center for Musculoskeletal Disorders- Louis Soslowsky, PhD
- Translational Musculoskeletal Research Center (VA)- George Dodge, PhD; Robert Mauck, PhD
- Translational Research Program in Pediatric Orthopaedics (CHOP)- Maurizio Pacifici, PhD

If you would like to know more about the Council, feel free to contact any one of the members listed above.

Penn Center for Musculoskeletal Disorders

Louis 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 proposal (P30 AR050950) 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.

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 micro-CT Imaging, Biomechanics, and Histology, 2) Developing a pilot and feasibility grant program for investigators, with direct mentorship, whereby new approaches, ideas, and collaborations can be developed prior to seeking extramural funding, and 3) Developing educational and research enrichment programs spanning tissue types, research approaches, and paradigms, through which members can learn from national leaders and from each other.

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

The Center currently has a membership of more than 135 faculty across five schools at Penn (Perelman School of Medicine, School of Engineering and Applied Science, School of Veterinary Medicine, School of Dental Medicine, and School of Arts and Sciences). We also now have faculty members for 10 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 Mauck, PhD and Louis 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 just over 16,000 sq. ft. of space on the 3rd, 4th and 5th Floors of Stemmler Hall. There are over 100 full- and part-time staff and trainees now in the labs. McKay is an active, thriving research and educational environment.

The McKay labs are also undergoing a transformation both in terms of physical space and faculty. Our home, Stemmler Hall, is in the midst of an over a $100 million dollar renovation, which will culminate in 2018 in a fully modernized and aesthetically pleasing facility in which to grow our laboratory space, faculty, and research and training endeavors. In terms of recruitment, we were delighted to welcome Dr. Nathaniel Dyment, PhD, an expert in tendon development and bioengineering, as our newest tenure track faculty member. We are also now actively recruiting for two additional faculty positions, and hope to grow our ranks further in the very near future.

Currently, the lab has an annual research budget from extramural grants, gifts, and endowments of over $13,800,000 and continues to rank within the top five orthopaedic programs in the country in terms of funding from the National Institutes of Health (NIH) with a 2015 ranking of #4. This past year has seen a very impressive and continued rise in new grant activity amongst the faculty.

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

- Dr. Jaimo Ahn—"Modulation of vascularity to enhance geriatric fracture healing"
- Dr. Jaimo Ahn—"Coupling role of osteoclast Notch signaling in physiology and fracture healing"
- Dr. John Esterhai and Dr. Robert Mauck—"Engineered Multi-Functional Nanofibrous Meniscus Implants"
- Dr. Robert Mauck, Dr. Jim Carey, and Dr. Jason Burdick—"Acellular Bioactive and Dynamic Nanofibrous Scaffolds to Promote Cartilage Repair"
- Dr. Lachlan Smith—"Therapeutic Targeting of Wnt/β-Catenin Signaling to Improve Bone Formation in MPS VII"
- Dr. Lachlan Smith—"Enzyme Replacement Therapy for Treatment of Bone Disease in Mucopolysaccharidosis VII Dogs"
- Dr. Louis Soslowsky—"Stimulation of Tendon Repair by Metabolic Modifiers"
- Dr. Spencer Szczesny—"Role of Mechanical Loading and Stem Cell Mechanotransduction in Tendon Degeneration"

In addition, we are delighted to report that the NIH P30 grant supporting our Penn Center for Musculoskeletal Disorders, led by Dr. Lou Soslowsky and entitled "Resource-based Center for Musculoskeletal Disorders Research", has been extended for another five years! This is as a testament to the excellent core facilities in McKay and the widespread impact of our department on the University, as a whole.

In addition to the above-mentioned new grants this year, each of the McKay Laboratory faculty remains well-funded through existing research grants not identified in this new grants list. Further, there were several new industry grants and clinical trials (>$25,000) initiated by both basic science and surgeon faculty this year. These are:

- Dr. Ben Gray—"Protect Neuro Trial Post Marketing Surveillance Prospective Cohort Evaluation of Neurocap® In The Treatment of Symptomatic Neuroma"
- Dr. Eileen Shore—"Sponsored Research Agreement on FOP/MMB" from Gilead Sciences
- Dr. Gwo-Chin Lee "An Open-Label, Non-Randomized, Single-Arm Multi-Center Study to Evaluate Oral Sodium Fusidate (CEM-102) for the Treatment of staphylococcal Bone or Joint Infections in Subjects for whom Chronic Antibiotic Suppressive Therapy is Indicated"

Growing musculoskeletal research in the Department of Orthopaedic Surgery and across the Penn campus has been a primary objective for our program, and this effort has been particularly fruitful in the past year.We look forward to another exciting year of continued growth and success.

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

George Dodge, PhD and Robert Mauck, PhD

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

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

The goal of the TMRC is to develop a focused, internationally recognized research center at the CMCVAMC and to emerge

Table 1. Current Funding at the TMRC.

Type	IP	Amount & Duration	Title
Merit	D. Steinberg	$275,000 per year for four years (2012-17)	Cartilage Repair with Stem Cell Seeded Hyaluronic Acid Hydrogels
Merit	J. Bernstein	$275,000 per year for four years (2013-17)	The Role of Local NSAID Administration and Inflammation on Tendon Healing
Merit	G. Dodge	$275,000 per year for four years (2014-18)	Cartilage Response to Compressive Injury: A Platform for Therapeutic Discovery
Merit	R. Mauck/ L. Smith	$275,000 per year years (2014-18) for four	Bioactive Injectable Implants for Functional Intervertebral Disc Regeneration
Merit	J. Esterhai/ R. Mauck	$275,000 per year years for four (2014-18)	Engineered Multi-Functional Nanofibrous Meniscus Implants
CDA2	H. Smith	$400,000 per year for five years (2014-19)	Tissue-Engineered Constructs for Treatment of Intervertebral Disc Degeneration
SPiRE	R. Mauck	$100,000 per year for two years (2014-17)	Cartilage Repair with Synovial Joint Precursors
SPiRE	C. Scanzello G Dodge	$100,000 per year for two years (2015-17)	The Impact of CC-Chemokine Receptor 7 (CCR7) on Synovitis and Osteoarthritis
SPiRE	A. Kuntz	$100,000 per year for two years (2015-17)	Effect of Scaffold-Delivered Growth Factors on Rotator Cuff Repair
Merit	H. Smith/R. Mauck	$275,000 per year for four years (2017-2012)	Tissue Engineered Total Disc Rep lacement in a Large Animal Model

as a VA Center of Excellence, bringing new resources and regenerative technologies to all service members, past and present. To date, more than 30 VA-based physicians, scientists, bioengineers, and research staff have co-localized to the newly renovated, state-of-the-art research space at the CMCVAMC Medical Research Building. Current VA funding to these investigators has increased to >$2.2 million in direct costs per year (see table below). In addition, the VA has committed more than $4 million in equipment to outfit this new facility, including state-of-the-art devices such as vivo micro-CT, fluoroscopy, atomic force microscopy, super-resolution confocal, and multiphoton imaging. Over the past year, the TMRC has continued to grow, with a new Merit Award (R01 equivalent) issued to Dr. Harvey Smith and Dr. Robert Mauck. Additionally, TMRC postdoctoral fellow Dr. Sarah Gullbrand received an excellent score on her CDA 1 Award application—a two year career development award that will fund her transition into an independent investigator. Finally, Drs. Mauck and Dodge, along with the entire team, were awarded a Shared Equipment Grant to support the acquisition of a new high resolution microCT specimen scanner and associated computing resources (at a cost of ~$500,000). This new system is now in place and being used by TMRC investigators and their collaborators across the Penn community. Overall, the TMRC is on an upward trajectory, with a vibrant multi-disciplinary team of investigators and significant new funding directed towards making possible new discoveries in musculoskeletal repair and regeneration. The TMRC is committed to our goal of translating this research into life changing improvements in patient care and quality of life for both Veterans and the general population.

The Center for Research in FOP and Related Disorders

Eileen Shore, PhD, and Frederick Kaplan, MD

Our collaborative work is to identify the cause of fibrodysplasia ossificans progressiva (FOP) and to use that knowledge to advance the treatment and cure for this debilitating disease. We began with the founding of our research program focused on this rare disorder of heterotopic ossification at Penn in 1991; we became the Center for Research in FOP and Related Disorders in 1998 with a generous gift from the Cali Family. Our critically important discovery in 2006 of the genetic mutation that causes FOP has allowed us to rapidly expand our research efforts. These efforts have led to discovery of new drug targets for FOP and to take the first steps into clinical trials, as well as to successfully promote interest in FOP research and drug development by scientists and researchers from around the world.

At Penn, work at the Center for Research in FOP & Related Disorders is broad, comprehensive, and evolving as research advances are made and clinical treatments are developed; some of our activities during the past year are highlighted:

Clinical Care and Consultation

The Center is the largest clinic and referral center for FOP worldwide, and provides guidance to physicians, families, and patients living with FOP. Furthermore, the Center coordinates the medical management of FOP patients with physicians from around the world.

Clinical Research and Infrastructure Development

Important recent advances that support current and future clinical trials include a global survey of FOP patient disease flare-ups, the first patient-reported longitudinal natural history study for FOP, and development of a Cumulative Analogue Joint Involvement Scale (CAJIS) to rapidly and informatively evaluate FOP disease progression.

Basic Research

The goals of our basic laboratory research are to understand the effects of the FOP mutation in promoting disease and to identify druggable pathways and targets for therapeutic intervention. Our work includes developing *in vitro* and *in vivo* models for investigational and pre-clinical studies and using these systems to understanding how the FOP mutation alters tissues, cell functions, and molecular pathways to initiate and support the progression of heterotopic bone formation. Over the past year, areas of focus have included: defining changes in immune cells in response to the FOP mutation and identifying the cellular response to tissue hypoxia and inflammation; examining changes to the tissue microenvironment and the molecular mechanisms by which the mutant FOP gene alters biomechanical signaling in response to the physical environment; initiating genome wide approaches to identify genetic modifiers of FOP clinical progression and investigating the molecular mechanisms by which ultra-rare FOP variants trigger promiscuous BMP signaling and subsequent heterotopic ossification. Our work has been highly recognized within the bone and musculoskeletal field; of the five 'most talked about articles in The Journal of Bone & Mineral Research (JBMR) in 2016', two were research publications from our laboratory.

Translational Research

These studies focus on pre-clinical testing of potential treatments for FOP in animal models and investigation of biomarkers for FOP that could be used to inform diagnosis and disease onset and progression. A key, recently published study investigated the effects of a small molecule currently used in clinical trials for effects on growth plate chondrogenesis, providing valuable insight for use of this drug in children.

Developmental Research Grants Program

This outreach program encourages investigators working in fields related to FOP research to apply their knowledge and perspectives to FOP and establishes collaborative interactions with the Center. During the past year, the Center supported three innovative projects: "Molecular Basis of Pathogenic Signaling and High Throughput Testing of FOP Therapies in a Zebrafish Model System" (Mary Mullins, PhD at Penn); "Identifying Alternative Therapeutic Targets and Genetic Interactors in FOP" (Dr. Ed Hsiao, MD at UCSF); "Novel Allosteric Destabilizers as Therapeutics for FOP" (Jay Groppe, PhD at Texas A&M).

Clinical Trials

The FOP Center at the University of Pennsylvania is the principle clinical site for the first clinical trial for FOP. We have enrolled and followed patients in two sponsored interventional clinical trials and in a sponsored longitudinal natural history study. We have additionally consulted with pharmaceutical/biotech companies on the study design for pending clinical trials, and have advised 30 pharmaceutical and biotech companies on the development of novel drugs for clinical trials in children and adults with FOP.

Education

The Center continues to mentor the next generations of physicians and scientists in the classroom, clinic, and laboratory. Postdoctoral researchers and graduate, undergraduate, and high school students work on research projects in our laboratory. We annually present FOP patients cases to first

year medical students. Additionally we educate physicians, scientists, researchers, and regulators at medical and scientific forums, meetings, and conferences worldwide.

Although FOP is the founding and primary focus of the Center, we additionally investigate a second rare genetic disorder of heterotopic ossification, progressive osseous heteroplasia (POH). Work in POH during the past year has continued to advance our understanding of how the underlying genetic mutations lead to induction of ectopic osteogenesis and how these mutations impact the formation and maintenance of the skeleton.

Update on the Biedermann Lab for Orthopaedic Research

Michael Hast, PhD

Director, Biedermann Lab for Orthopaedic Research

The Biedermann Lab is specifically designed to execute clinically relevant research projects focused on orthopaedic implant performance. This goal is achieved by partnering engineers with active clinicians– creating academic environments that foster collaborative investigations of clinical problems. The 3,200 square foot lab is located on the 10th floor at Penn Medicine University City, which provides consummate proximity for surgeons and staff of the Lab to develop and execute research projects.

Over the last year, the Lab has been working on over a dozen biomechanical research projects that are in various stages of development, execution, or publication. Ongoing projects have a wide scope of interests and employ a variety of techniques including in silico modeling, cyclic testing of implants, 3-D motion capture, measurement of articulating joint forces, and in vitro simulations of activities of daily living. To date, the Lab has developed several full-length manuscripts that have been accepted for publication at *The Journal of the American Academy of Orthopaedic Surgeons* and *The Journal of Orthopaedic Trauma*. The Biedermann Lab has also obtained external funding from several sources. Specifically, the Lab has been awarded a University of Pennsylvania McCabe Pilot Grant, two sponsored research agreements with DePuy Synthes, and two sponsored research agreements with Integra Orthopedics.

The Lab recently conducted an experiment in alliance with Dr. Derek Donegan focusing on screw biomechanics in Lisfranc injury reconstruction. Additionally, a project was performed in collaboration with Dr. Samir Mehta and Dr. Surena Namdari investigating implant placement during proximal humerus fracture repair. These projects have been submitted as abstracts to the annual meeting of the Orthopaedic Trauma Association and will be developed into full-length manuscripts. Copies of these abstracts can be found within this journal.

These studies illustrate the continuous goal of the Biedermann Lab: to perform research that is relevant and translatable so that the standard of care and quality of life for patients can be improved. In order to continually achieve this objective, a steady flow of research ideas and scientific collaborations is essential. Going forward, the Biedermann Lab will continue to develop and foster academic relationships at Penn and throughout the world. If you have a research interest that may be suitably addressed with the research competencies of the Biedermann Lab, you are encouraged to contact Michael Hast directly. For contact details and more information about the Biedermann Lab, please visit the Biedermann Lab's website: www.med.upenn.edu/biedermann/




Human Tissue Laboratory

Lorianne Kish

The University of Pennsylvania Perelman School of Medicine Human Tissue Laboratory, "HTL" opened its doors in August of 2012 under the direction of Dr. L.Scott Levin. The mission of the lab was to provide an opportunity for residents and surgeons to practice and explore all areas of surgery, review anatomy through dissection and practice approaches and techniques for upcoming surgeries that ultimately result in better patient outcome.

Since 2012, the human tissue lab has hosted hundreds of courses, comprised of internal training, resident training as per the set curriculum and industry partnered events. Departments from all areas of Penn Medicine have consistently used the facility. The benefit of this training is highly valued by the Penn Faculty. It is a teaching tool that is rivaled by none other. Many improvements have occurred since its beginning and Penn is proud to be able to offer the same quality experience as is available in a commercial lab setting. The 14 station HTL offers a high definition overhead camera for the lead surgeon, Stryker surgical lights at each station, live streaming capabilities, flat screens for participant viewing and presentations, Lavalier microphones, arthroscopy towers, specimen holders, a full complement of arthroscopic trays, a full size C Arm, radiolucent table, peg board positioners, gel bumps, blocks, hand held power saws and drills, quick connect attachments, ancillary instrumentation, latex injection capability and a sterilizing dishwasher.

Most recently, the lab has built a private locker room/changing area dedicated to lab attendees, a fully A/V equipped conference room and an adjacent break room. Each year the HTL has grown in the volume of educational events and will continue to reinvest in equipment to enhance the experience of attendees.

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The Research Year: Looking Back

James Friedman, MD and Cody Hillin, MD, MS

Each year, two orthopedic residents leave their second post-graduate year and enter the basic science laboratory. Although projects were planned in advance, the year in the lab allowed us to learn and work in unexpected ways. Looking back on this time, now a year later, provides a broader perspective regarding the projects that we worked on and the mentoring that we received.

Although we both worked on projects that involved live animals, the two experiences could not have been more different. Whether it was working with Drs. Mauck and Dodge on cartilage repair in the Yucatan mini-pig, or using Sprague-Dawley rats and C57BL6 mice to understand tendon repair, we both learned how to translate our early surgical skills to animals. Many long hours were spent with our lab colleagues exchanging our surgical knowledge for their expertise on how to perform laboratory tests and use equipment. Both of us formed friendships that continue to this day, and we were even able to mentor a few that have since matriculated to medical school.

These efforts were not without success. Collectively we had the opportunity to participate in over 10 projects. To date, we have received authorship on nine posters, three published papers, and a podium presentation. In addition, there are a handful of ongoing projects and papers that will continue on with future generations of lab residents. Additionally, during our year we were able to work with Dr. Peck to organize a fundraiser with the cooperation of Drs. Mauck, Soslowsky and Dodge, which generated over $2000 for future ORS grants.

Ultimately, our success from the year spent in the lab came from the assistance of the graduate students and lab staff as well as the direction of Drs. Soslowsky, Mauck and Dodge. We spent innumerable hours in the lab, alongside all of them, and truly appreciate their efforts not only for us, but also for all of the future residents that will have the honor of working with them.

Where Are They Now? 10 Years After Graduating From Penn Orthopaedic Surgery Residency

Daniel Gittings, MD and Blair Ashley, MD

Dr. Isaac Newton once exclaimed that "we stand on the shoulder of giants". Undoubtedly, our Department's success would not be possible without the hard-work, dedication, and mentorship of our predecessors. This year, we would like to highlight alumni that are now a decade out from the Penn Orthopaedic Surgery Residency Program. We hope that their insights are helpful for the next generation of Orthopaedic Surgeons that are currently in the midst of their training.

David Pedowitz

Fellowship: Foot & Ankle at Roger A. Mann, Oakland CA
Current employment: Rothman Institute, Philadelphia, PA

How has training at Penn impacted your practice?

Penn provided me with a supremely well rounded orthopedic education, and specifically emphasized to me the importance of having a critical eye when evaluating new techniques and technology.

What have you learned in your first decade of practice?

On a personal level, humility is very important in medicine—and you need to remember that none of us have perfect results all of the time. Additionally, the bureaucracy of running a practice in the last decade has become burdensome on many levels. At the end of the day, however, this job continues to provide us with exceptional personal fulfillment and satisfaction.

Advice to residents?

Persevere to achieve clinical excellence, get involved in your society and read constantly. If you don't make a habit of staying, not only abreast, but at the top of your field NOW, you never will in the future.

Wudbhav Sankar

Fellowship: Pediatric Orthopaedic Surgery at Children's Hospital of Los Angeles & Shriners Hospitals for Children in LA; Children's Hospital of Boston
Current employment: Children's Hospital of Philadelphia

How has training at Penn impacted your practice?

The Penn residency has profoundly impacted my practice not just by providing the basic foundation of my orthopaedic knowledge, but also by exposing me to a number of outstanding mentors and role-models who showed me the grand possibilities of being an orthopaedic surgeon. Getting a chance to learn from folks like Malcolm Ecker, Denis Drummond, Jack Flynn, and others through my Penn training ignited my passion for pediatric orthopaedics and showed me what it means to really care for children.

What have you learned in your first decade of practice?

The biggest thing I've learned in my first years of practice is the benefit of staying humble and having clear communication with the patient. Things don't always work out perfectly, but you can have satisfied patients if you stick with them through the hard times and try not to sugarcoat anything. Although patients may want to hear best case scenarios, in the end I think they appreciate the honesty and the willingness to tell them what you know for certain and what you don't.

Advice to residents?

My biggest advice for residents is to try to learn from every experience. Too often these days, trainees shy away from experiences where they aren't first assist, or don't like a particular staff member. I would argue that you can learn something from everyone and every scenario. The most successful residents are those who hang around and are eager to jump in as a second assist or just to see what's going on regardless of whether it's their favorite service. Orthobullets will help you on a test, but it's the (extra) hours in the OR and the clinic that will make you a successful doctor.

Richard Scarlett

Fellowship: Sports Medicine at New England Baptist Hospital
Current employment: The Hospital of Central Connecticut

How has training at Penn impacted your practice?

The Penn name gives you automatic credibility. Patients

who do their research and look at your credentials recognize the superior training that you receive at an institution like Penn.

What have you learned in your first decade of practice?

I learned that you are the "talent" that the patient chooses to treat them. However, you wouldn't be able to accomplish your goal of administering excellent care without an extensive supporting cast. You form a team with your office and operating room staff. You need to be the leader of that team. Even as a newly minted surgeon you must be cognizant that your words, actions, body language and tone are constantly being observed and set the mood in your work environment.

Advise to residents?

Take time to exercise. The job of an orthopaedic surgeon is physically demanding. To have a long fulfilling career you need to stay physically fit. Additionally, you serve as a role model for your patients. You'll realize that a large portion of your patients have conditions related to obesity and a sedentary lifestyle. It's beneficial to be in good physical shape to counsel and motivate these patients to make the necessary lifestyle changes.

Brent Wiesel

Fellowship: Shoulder and Elbow, Rothman Institute, Philadelphia, PA
Current employment: MedStar Georgetown University Hospital

How has training at Penn impacted your practice?

While the training I received at Penn was excellent and did a great job of preparing me for practice, the biggest benefit is being part of the Penn Orthopedic alumni community, I continue to be amazed at how frequently I interact with Penn graduates and some of the remarkable things that they have accomplished in their careers.

What have you learned in your first decade of practice?

That Dr. Lackman was right- the 3 most important things to establishing a good practice are affability, availability and ability- in that order.

Advise to residents?

There are 3 rules that I try to teach our Georgetown residents. It often takes them all 5 years to learn them, but most of the time, they understand them by the time they leave. They are: 1) Don't say (or post on line) anything that you would not be comfortable seeing published on the front page of the Washington Post. 2) Only get married once- there is no need or hurry to get married, but once you do it needs to be permanent. 3) Stay in shape and always take the stairs- once you graduate you will have more control over your schedule but between running a practice and having kids you are likely to actually be busier and it is very important that you set aside time every day, even if it is at 4 in the morning or 11 at night, to work out and take care of yourself.

Gregory Carolan

Fellowship: Shoulder and Sports Medicine at San Diego Arthroscopy & Sports Medicine Center
Current employment: St. Luke's Orthopaedic Specialists

Brett Gibson

Fellowship: Shoulder and Sports Medicine at University of Colorado Health Science Center
Current employment: St. Luke's Orthopaedic Specialists

Sharat Kusuma

Fellowship: Arthroplasty at Rush
Current employment: McKinsey & Company—Associate

Armen Martirosian

Fellowship: Orthopaedic Trauma at Florida Orthopaedic Institute
Current employment: University of California San Francisco

Home Town Heroes, International Outreach

Daniel Gittings, MD

"Please give me the coat-hanger." I was shocked as Dr. Azharuddin, an attending Orthoapedic Surgeon in Banda Aceh, Indonesia, fashioned an external fixator from a wire resembling a coat-hanger and PMMA to stabilize a mid-shaft tibia fracture. He remarked that this device costs pennies on the dollar compared to the frames we use in the United States. These innovative solutions in a resources scarce environment are common in the developing world. There is much to learn from our colleagues in these regions. Over the past several years, Penn Orthopaedic Surgery Department has been at the forefront international collaborations.

This past November, Dr. Vincent Arlet traveled to Trinidad celebrate the ten year anniversary of the outreach mission. Over the past ten years, Dr. Arlet has led a team that has cared for over eighty patients with severe spinal deformities. Furthermore, his team has had fifteen residents and fellows that have assisted Dr. Arlet in his efforts.

December 2, 2016 marked the 2nd annual Penn Global Surgery symposium, entitled, "Multidisciplinary Approaches to Sustainable Global Surgery." Penn Orthopaedic's own Dr. James Friedman and Dr. David Spiegel spearheaded the event. The venue was packed with students, nurses, resident and attending physicians. Dr. Mark Shrime, Assistant Professor of Otolaryngology and of Global Health and Social Medicine at Harvard Medical School, provided a keynote presentation that detailed the feasibility of delivering low cost and sustainable surgical care to the five billion people across the world that currently lack access. Other featured speakers included Dr. Georges Azzie, Pediatric Surgeon at University of Toronto's Hospital for Sick Children, Dr. David Spiegel, Pediatric Orthopaedic Surgeon at Children's Hospital of Philadelphia (CHOP), Dr. Kassa Darge, Chairman of Pediatric Radiology at CHOP, Dr. Joshua Atkins, Associate Professor of Anethesia and Critical Care at the University of Pennsylvania, and Dr. Mark Morgan, Chief of Gynecologic Oncology at the University of Pennsylvania. Combined, not only have their global surgery efforts reached Nepal, China, Eritrea, Botswana, Ethiopia, and Rwanda but also their actions have also inspired the next generation of leaders in global health.

Dr. David Spiegel traveled to Iraq, Nepal, and Pakistan over the course of the past year to collaborate with other orthopedists in caring for pediatric patients. Dr. Spiegel received a grant from CHOP to carryon this important work for a minimum of ten years of follow up in Nepal. Notably, Dr. Spiegel was awarded the Walter P. Blount Humanitarian Award from the Scoliosis Research Society and the Humanitarian Award from the American Academy of Orthopaedic Surgeons.

In collaboration with the University of Botswana, Penn's Dr. Jaimo Ahn with the support of the Biedermann family, set the stage to establish another international collaboration called the Botswanna UPenn Partnership (BUP). This region is ridden with orthopaedic trauma from motor vehicle collisions. Trauma has surpassed the morbidity and mortality of the burden of HIV in the region. Additionally, long term problems such as degenerative joint disease have wait lists as long as six months to receive needed surgery. Dr. Ahn hopes that this partnership will blossom of the years to become a robust educational, clinical, and research collaboration.

In Tanzania, Dr. Neil Sheth has continued to lead a team to develop a novel and sustainable venue for orthopaedic care in East Africa. The team has proposed to build an Orthopaedic Center of Excellence at Kilamanjaro Christian Medical Center in Moshi, Tanzania. Surgical teams from Penn and twenty-five partner institutions will coordinate a rotating schedule of two week blocks to ensure year round surgical center staffing. The center will act as a collaborative training center for local health care providers including surgeons, residents, nurses, and therapists. Dr. Sheth traveled with his team including Physician Assistant Kevin Zakielarz and Clinical Research Assistant Mack Hardaker in February 2017 to meet with leaders in the region to set up fund raising efforts.

In conclusion, Penn Orthopaedics has lead in multiple outlets for international collaboration and outreach. These efforts enhance the Department's academic mission for clinical, educational, and research excellence. Their work will benefit many generations to come.

The Implementation of an Intern Surgical Curriculum at Penn

Nicole Zelenski, MD[1] and Nicholas Pulos, MD[2]

[1]University of Pennsylvania. Philadelphia, PA
[2]Mayo Clinic. Rochester, MN

Mandated change

Historically, general surgery rotations during intern year provided orthopaedic trainees with instruction in basic skills including soft tissue handling and knot tying. Changes in surgical education over the last fifteen years have limited the amount of hours residents are permitted to spend in the hospital. Additionally, increased supervision in the operating room and the shift from open to laparoscopic general surgery procedures has limited the utility of these rotations. As such, early exposure to surgical training has decreased. Though no studies have concluded that changes in work hour restrictions have affected case volumes or in training exam scores[5,6], orthopaedic program directors have demonstrated concern that residents will not be adequately prepared for independent practice[7]. This prompted the Accreditation Council for Graduate Medical Education (ACGME) and American Board of Orthopaedic surgery (ABOS) to have 6 months of orthopaedic surgery rotations in their intern year as well as to complete a mandatory surgical skills curriculum[1,2,3].

Current requirements

On July 1, 2013, the ACGME mandated that orthopaedic surgery PGY-1 residents receive a surgical skills curriculum. The basic surgical skills training was designed to integrate with skills training in subsequent postgraduate years and prepare the PGY-1 resident to participate in orthopaedic surgery cases[1,2]. Suggested modules are published online with the goal to acquire and improve skills such as splinting, casting, and application of traction devices as well as basic operating skills such as soft tissue management, suturing, bone management, arthroscopy and use of basic orthopaedic equipment[4]. After an approximately two-year integration period, programs are now required to report the progress and implementation of the program to the ACGME.

The Penn Experience

The Orthopaedic skills month may be implemented in a dedicated month long block or longitudinally and does not count against the current allowance for 6 months of orthopaedic service during the intern year. As such, we have worked with our general surgery, emergency medicine and anesthesia colleagues to try several iterations of the "Month" on their non-Orthopaedic blocks. This included a one-month block in October and April versus dedicating every Thursday after Grand Rounds to intern education. Residents underwent at least 30 three-hour sessions staffed by topic and expertise appropriate attending physicians, fellows, or chief-level residents. This included 14 sessions in the human tissue lab and several guest lectures from physicians in the radiology, plastic surgery, and anesthesia departments.

Both the longitudinal, semester-long curriculum and the dedicated one-month curriculum have merit and the choice between the two was initially limited by the logistics of the year it was implemented. The longitudinal program was easier to facilitate with our non-orthopaedic colleagues and offered more sessions for the interns to meet to review the required modules. However two substantial scheduling difficulties arose: 1. topic and expertise appropriate staffing of the sessions could not always be achieved; 2. continuity of clinical care sometimes prevented interns from leaving for a single day in the middle of a standard week. A well-structured month-long curriculum allows interns to focus on the fundamentals of orthopaedic surgery without being overwhelmed by clinical duties on other services, while giving them time to adequately prepare for the sessions. It also offers the chance to build strong relationships among their class and with senior residents and junior faculty.

Effect on OITE scores

There is significant improvement of OITE scores among interns who have undergone the Intern Skills Month. The in-training scores of interns who started on a non-orthopaedic block of rotations (GS) in the two years prior to the implementation of intern skills were compared to scores from interns who underwent the same rotations after the implementation of intern skills. These interns had directed

OITE preparation and question review led by senior residents as well as dedicated time for independent study. The OITE percentile scores increased nearly twofold for GS interns after initiation of the Intern Skills Month in the fall of 2015. Interns who began the year on the orthopaedic block and did not undergo the skills rotation had similar scores before and after the implementation of skills.

Future of Intern skills at Penn

The mandates set forth by the ACGME and ABOS were designed to enhance the intern year and provide early exposure to orthopaedic surgery. The addition of the skills month has effectively increased the amount of specifically orthopaedic-relevant education during the intern year. The inevitable decrease in less orthapaedically relevant clinical time, which could be seen as a detriment by some, should be valued as an increase in educational efficiency and effectiveness; indeed, learner feedback has been positive and the program has been well received by the interns. In our program, there has also been a secondary benefit of increasing OITE scores among the intern class—nearly doubling the average percentile. After trialing both the longitudinal model as well as a month-long block, the Department of Orthopaedic Surgery will use the Intern Skills Month model going forward. This will allow for a well-structured basic science, clinical and applied curriculum to supplement our residency program. Further study will hopefully demonstrate this to be a worthwhile endeavor, better preparing trainees for independent practice in a changing healthcare environment.

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Leadership Training: A Critical Aspect of Education

John Kelly IV, MD

It has been stated: 'leaders are born, not made.' This is a falsehood which may discourage many from seeking leadership development.

In truth, there are many skills and much knowledge required for effective leadership. To some, many leadership qualities are indeed innate or may come easily; however, ***everyone*** can benefit from training in the principles, methods and skills necessary to lead others.

Simply stated, exemplary leaders convert vision to reality, create exemplary cultures and guide others to sustained excellence. Leadership may be operative at work, at home or in the community. There seems to always be a need for improvement in every arena in life—improvement that only effective leadership can provide.

Leadership is not management. Managers do things right. Leaders do the right thing and can help others morph from 'good to great'[5].

Why Become a Leader?

The great psychiatrist, Victor Frankl[1], noted that everyone has an inner calling that needs to be 'uncovered'. Frankl writes: "Everyone has his own vocation or mission in life to carry out a concrete assignment, which demands fulfillment[1]." Which is to say, Frankl believed that a distinct vocation lies *within* each and every one of us. The recognition of this inner calling is to be revealed through self-discernment while taking note of one's passions and enthusiasm. Combining our bliss with a service orientation will lead us to our life's purpose. Once one's vocation is determined, it naturally follows that the more people engage in a service pursuit, the more good one can render in one's life.

For example, many of our residents have a profound passion for global health and ensuring the wellbeing of those less fortunate. Thus, the formation of 'Global Health Clubs' and 'Global Health Conferences' is extreme leadership in action. One person's passion combined with heroic leadership can help engage countless others to effect real and meaningful change[2]. Indeed, strong leadership can literally transform an enthusiastic vision into quantum service to the world.

Furthermore, each of us will be confronted with challenges at home and in our communities which will demand effective leadership in order to realize success. In fact, in *every* event or arena in life lies a call for leadership and an enactment of essential core values including humility, selflessness, benevolence, discipline and consensus building.

Whether providing direction to one's family, place of worship or community, leadership needs will always be omnipresent.

Orthopedic Surgery

Orthopedic surgeons are called to be leaders of the musculoskeletal care team in clinic, the operating room and the research arena.

Clinically they are often called to the helm of patient care as many treatment decisions are dependent on the surgeon's judgment. It is incumbent upon the surgeon to recognize effective means in leading health care teams toward the singular goal of improved musculoskeletal care. Often medical management of a patient does in fact lead to a surgical solution. The surgeon leader recognizes his or her role as merely another responsible member of health care team who happens to be able to provide an effective means of treatment. Surgeons are not 'heroes'; they are merely 'healers'. In the example of a sepsis of unknown origin which culminates in a surgical 'I and D' of a joint, the leader surgeon is obliged to convey the results of the surgery to the entire team in a courteous and timely fashion so that proper follow up is ensured. If the diagnosis was perhaps delayed due to a missed diagnosis, the leader surgeon is obliged to instruct, not blame, so that future care of other patients is enhanced. *Leaders focus on solutions and do not devote energies to finding fault.*

In surgery, Orthopedists are indeed the 'Captain of the Ship' when executing a procedure. The Surgeon Leader determines the 'culture' of the operating room. The exemplary surgeon treats staff with kindness and dignity while never losing their sense of purpose.

The same can be said of one's overall practice. If the 'culture' at work is less than desirable, there is a leadership issue. Leaders create safe and secure environments where workers can let their God given talents flourish. Fairness and honesty are the order of the day and every worker knows that they will be treated justly and compassionately.

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

Life Skills

In his masterpiece, *Seven Habits of Highly Effective People*, Steven Covey emphasizes that self-mastery must precede the ability to truly influence others[2]. That is, how can one lead

others when one cannot manage their own lives? Once a life dedicated to timeless moral principles is attained, one has gained control over one's life and then can proceed to truly influence others.

When the 'habits' of proactivity, adherence to a mission statement (begin with the end in mind) and adoption of executing around priorities (putting first things first) are mastered, then real ability to influence others is finally gained. Implicit in Steven Covey's seven habits is the adherence to a changeless and principle based core set of values. These include honesty, integrity and faithfulness to commitments.

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

In addition, one must 'walk the talk' to lead. No one will commit to follow one who is duplicitous and not of sound moral constitution. It has been said that 'leadership is merely *who* you are'. How we conduct our lives communicates volumes more than what we say! When we become our best selves, we are simultaneously growing as leaders.

The study and incorporation of effective leadership skills and traits will lead each of us further into lasting and meaningful self-growth.

Penn Leadership Forum

The Penn Leadership Forum was conceived as an effort to convey tried and true principles of real leadership to residents, students, junior faculty and all interested members of the health care team.

A consortium of leaders from the Wharton School of Business, the Penn Perelman School of Medicine, industry, and sports will convey to attendees key principles necessary to lead others to a common good. Chief elements of exemplary leadership such as integrity, selflessness, decisiveness, organization, benevolence, vision, ingenuity and heroism will be discussed in detail[4]. A unique feature of the forum includes 'case discussions' whereupon real life situations will be presented to a panel of experts so that the audience will learn how proven leaders negotiate common challenges. The responsible practice of orthopedic surgery as well as effective living requires consistent leadership. It behooves every surgeon to study what makes great leaders great and enact these skills in daily practice.

In conclusion, leadership is a way of life and requires an ongoing process of self-development. The Penn Leadership Forum will provide future leaders meaningful insights regarding this journey and hopefully help many realize, as Jim Collins would call 'Level 5 leadership'—the highest level of executive function.

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Penn Orthopedics and Penn MERT Team Up for Success

Daniel Klyde, EMT-B, Jaimo Ahn, MD,PhD, Derek Donegan, MD, Samir Mehta, MD

On February 27th, 2017, Penn Orthopedics and Penn Medical Emergency Response Team (MERT), the University of Pennsylvania's student run emergency medical service, partnered together for a continuing education session focused on pre-hospital orthopedic trauma care as a quality improvement initiative. Dr. Daniel Gittings, a third-year orthopedic surgery resident in the Penn Medicine system, traveled to the information session to offer his medical advice and expertise to the members of MERT, a group of approximately 60 Pennsylvania certified Emergency Medical Technicians (EMT) first responders and EMT students.

Dr. Gittings focused his presentation on orthopedic trauma that MERT sees on a day to day basis in their emergency response role. Through case based scenarios, there was discussion on how to evaluate and stabilize orthopedic injuries. MERT EMTs also had the opportunity to participate in splinting demonstrations. Following the lecture, there was a question and answer session.

The quality improvement initiative between MERT and Penn Orthopedics was a successful collaboration between both departments that aided in bringing high quality education to our first responders. Educational lectures like these will continue to raise the bar in patient care throughout our community.

MERT
more than ems

The University of Pennsylvania Orthopaedic Residency Curriculum

Joshua Gordon, MD, Michael Talerico, MD, Jason Anari, MD, Jonathan Dattilo, MD

The Department of Orthopaedic Surgery at the University of Pennsylvania, the first such department in the nation, has a proud and long-standing tradition of rigorous training and education in orthopaedics. This tradition has produced many thought leaders in our field and provides the foundation for each academic year. Forward momentum is a principal tenet of this tradition, and the department seeks to continually improve the educational experience and offer innovative and effective programs. This year has been no different with the addition of several new aspects to our didactic curriculum.

Perhaps the most profound change is in the morning conference schedule; this has taken several years and required the cooperation and coordination of the entire faculty and resident compliment. In prior years, subspecialty morning conferences occurred simultaneously on any given morning and were often distributed throughout the five hospitals through which our residents rotate. Residents and faculty alike observed that due to variation in schedule order and a predilection to spend a large amount of time on topics of particular interest to those giving conferences, breadth of education sometimes suffered. Similarly, when schedule conflicts arose, the number of residents benefiting from the time of the subspecialists could be limited. Lastly, the topics of conferences were not always given with adequate notice for the residents to prepare and optimize their participation. The revised morning conference structure addresses these concerns. We designed a curriculum that integrates one lecture from most sub-specialties every other week. This decreases the hours of lecture given by the attendings, while increasing the number of residents present. Specifically, on Mondays we concentrate on adult reconstruction and trauma, on Tuesdays the focus is on spine and foot and ankle, on Wednesdays we examine sports injuries and hand, Thursday is dedicated to grand rounds and on Fridays we discuss tumor and shoulder and elbow with the addition of chiefs' conference. Chiefs' conferences occur intermittently and allow the chief class to cover practical information associated with planning for surgical cases. In order to structure the morning conferences, we use Miller's Review of Orthopaedics as an outline, thus guaranteeing adequate breadth while providing a primer for each conference. The calendar, with associated recommended readings, was released at the start of this academic year. Since that original calendar was set, early in the year, the conference has taken organic shape with each subdivision figuring out how the conference works best for them.

Along with many other orthopaedic departments across the country, we have also started to integrate the Orthobullets online exams into our curriculum. This allows residents to get an idea of their strengths and weaknesses in terms of their individual knowledge base so that they can best direct their study efforts. Orthobullets has also provided our residents with an expanded question bank, allowing them to optimally prepare for the annual in-service examination and by extension the board examination. We have prioritized this aspect of the curriculum, as it provides the carefully monitored performance data we need to improve our educational program; previously we lacked such feedback. This element should improve our precision in making future modifications to the curriculum.

In developing the current revised curriculum, we looked at the knowledge base as a complement to our surgical skills. With an eye to increasing these skills, we have continued to make excellent use of the University of Pennsylvania Orthopaedic Human Tissue Lab (HTL). This year we continued to use the Sawbones modules to provide our residents with exposure to the use of hardware in a simulated fashion. We also added guided dissections for the residents to increase our hands-on time with cadaveric specimens. We now include guided dissections of the hand, elbow and forearm, shoulder, foot and ankle, leg with a focus on compartment releases, hip and pelvis as well as spine; covering all areas of the body allows our residents the opportunity to dissect free of the concerns that exist during surgery and prepares us to take better advantage of surgical opportunities as they arise. It is important to acknowledge our former chiefs Ryan M. Taylor MD, John G. Horneff III MD and Christos D. Photopoulos MD, who worked hard to secure the protected time necessary for these high-quality education sessions in the HTL. Further the residents collectively appreciate the, often herculean, efforts of Lorianne Kish the director of the HTL who works hard to ensure lab and resource availability.

The quality improvement curriculum is a highly innovative addition to our program this year; it is covered more extensively in a separate piece in this publication of UPOJ, and I would encourage those interested to take a look at that article.

As we look forward to what these many changes will mean for the enhancement of our residency experience, we also look back to recent and equally innovative contributions to the curriculum, asking ourselves how we can best integrate some of these disparate parts. The iTunes U curriculum previously led by Mara Schenker MD is a wonderful resource, but it has not yet been incorporated into the current curriculum. Several approaches are being considered as to how best to reconcile this. One thought is that after the residents have participated in several full cycles of the morning conference curriculum, the readings from Miller's Orthopaedic Review will likely need to be expanded; the iTunes U readings could provide just such enrichment, creating a healthy marriage between the morning conference curriculum and the iTunes U curriculum.

Beyond this, we have begun to explore the use of video to compliment the written steps of the attendings' surgical methods. This addition is still a work-in-progress; issues with quality and clarity have hindered a full-scale roll out of this aspect of our curriculum. Ultimately, we envision a rotation folder created specifically for each service that will contain all of the details pertinent to the work done on that service. Such a folder would include call responsibilities, preferences regarding patient care, videos and written steps describing common procedures, and iTunes U material and other background information relevant to the common conditions seen while on service. Such integration is a monumental undertaking, but as the Department of Orthopaedic Surgery at the University of Pennsylvania has continued to produce the highest quality residents, we must strive to continue to push the edge of excellence in education.

Quality Improvement in the Department of Orthopaedic Surgery in the University of Pennsylvania Health System

Joshua Gordon, MD, Finnah Pio, Alex Neuwirth, MD, Eric Hume, MD

With the works of Berwick, Deming, Porter, Teisberg, Donabedian and many others there has been an increasing focus on quality in medicine, not only as an important means to improving the delivery of care, but potentially as a metric dictating much of what we, as physicians, do. This past academic year Penn Orthopaedics has taken significant steps to strengthen the department's already robust quality improvement program. The department has targeted multiple facets of quality improvement with several key initiatives on the clinical front including reducing postoperative complications and readmissions while simultaneously attempting to integrate these directly into resident education, departmental procedures and the culture of our department.

This year marked the creation of the Penn Orthopaedic Quality Improvement Council and a concomitant formal curriculum focused on quality improvement to complement our ongoing morbidity and mortality conference. The aim of this curriculum is to develop resident expertise in quality improvement beyond a basic understanding, while continuing to foster a culture in which stepwise and continual progress is actualized. The Quality Improvement Council is responsible for organizing and improving the quality improvement curriculum and implementing a quarterly review of clinical progress. The associated conferences are structured to cover principles of the improvement process, expose the department to leaders in the field of quality improvement and generate discussion surrounding specific and ongoing improvement projects. We have already begun to observe significant cross-pollination of ideas within the department from different sub-divisions and individuals with varying areas of expertise.

Perhaps the most innovative portion of the conference involves having residents propose projects; these proposals are then opened to the conference floor for discussion. This process allows those on the front lines of care, including the department leaders, to discuss how projects can best be analyzed, evaluated and implemented, a method that leads to a detailed and organic instruction in project design. We are in the process of measuring the impact of this conference, but anticipate an associated cultural shift and an improvement in quality of the departmental output. To date we have had proposals including improved C-arm use efficiency, improvement in timing of consult execution in the emergency department, improvement in communication between our department and other care providers, and improvements in discharge planning. Some of the proposals have continued on to more robust process improvement projects, while others have simply served as instructive exercises for the younger residents.

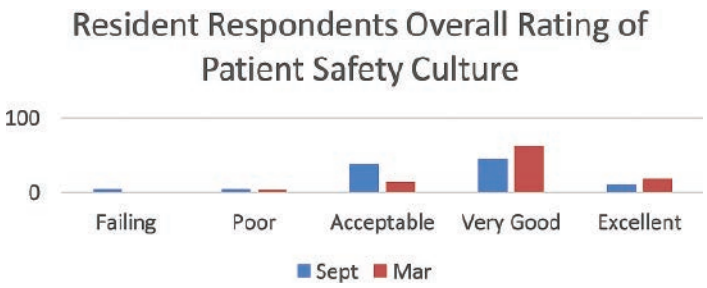

Figure 1. Overall rating given to the department of Orthopaedic Surgery regarding patient safety as measured by a survey given once in September prior to institution of the quality improvement conference and after the first academic year of conference participation.

Upon completion of the first academic year of these quality improvement conferences we took the opportunity to survey the residents regarding their perceptions of quality improvement in the department. Although results are preliminary and require more thorough evaluation we found a general improvement in understanding of quality improvement processes, the perceived involvement of our department in quality improvement exercises, and our perceived overall grade on patient safety (see fig 1). As an extension of our conference we anticipate continuing to monitor the impact of our conference and apply the same quality improvement processes we are teaching to improving the quality of the conference itself.

We are thankful for the work of the founding members of the Quality Improvement Council; Joshua Steere, Joshua Rozell, Ryan Charette, Blair Ashley and Alex Neuwirth have all made significant contributions to realizing some of these changes over the past year. We are also very grateful to Dr. Eric Hume, our superb faculty leader, and Finnah Pio, an expert in quality improvement, who has helped guide many of these changes across the department. As a group, we are all eager to continue work on this fledgling effort, and have been extremely excited to see it take flight while looking forward to seeing what progress it can foster.

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Visiting Professor Lecture Series
Guest Lecturer: Joseph Hsu

Chelsea Hendow, MD

The University of Pennsylvania Department of Orthopaedic Surgery was honored to host Dr. Joseph R. Hsu as a guest lecturer on July 28th, 2016, as part of its visiting professor lecture series. Dr. Hsu is not only a renowned surgeon and an extremely accomplished academic, with several grants from the NIH, but is also a veteran of the United States armed services.

Originally from Baton Rouge, Louisiana, Dr. Hsu went on to become an Honor Graduate from the United States Military Academy. He then completed his medical education and training at Tulane University School of Medicine and Charity Hospital in New Orleans, Louisiana, emerging as an orthopedic surgeon dually fellowship-trained in both orthopedic trauma and adult reconstruction. Finally, in pursuit of expertise in limb salvage and reconstruction, he completed fellowships in the Ilizarov Method in Lecco, Italy, and at the Kurgan Ilizarov Center in Kurgan, Russia.

In 2006, Dr. Hsu was deployed to Baghdad, Iraq, with the 10th Combat Support Hospital at Ibn Sina Hospital, where he fully utilized his expertise. He is now a part of the Carolinas Medical Center, balancing an active clinical practice with his very fruitful research pursuits. He is an investigator in the Major Extremity Trauma Consortium, as well as a member of the Orthopaedic Trauma Association, the American Orthopaedic Association, the Limb Lengthening and Reconstruction Society, and the Society of Military Orthopaedic Surgeons.

Dr. Hsu was introduced on July 28th by the Department of Orthopaedic Surgery's chairman, Dr. L. Scott Levin, who has known Dr. Hsu both personally and professionally for many years, and took the opportunity to highlight his many incredible contributions in his roles as both orthopedic surgeon, and as United States veteran. Dr. Hsu then proceeded to give two captivating lectures, entitled "The Opioid Epidemic: Leading the Solutions," and "Optimizing Outcomes in Lower Extremity Trauma."

In the former lecture, Dr. Hsu delivered a comprehensive review of the current status of the opioid epidemic, the historical use of opioid medications, and the quality literature on the efficacy and harm of utilizing these medications. He used statistics to put our opiate use in perspective, perhaps most poignantly that as five percent of the world's population, the United States consumes over 80 percent of the global supply of opiate medications. He then highlighted the development of opiate use to treat pain, alongside the progression of pain management as a medical and political issue. He pointed out some important fallacies and commonly referenced statistics used to support opiate use, and supplied quality evidence to support the use of a multimodal pain strategy that minimizes opiate use. Finally, he outlined an initiative being currently utilized by the Carolinas Healthcare System, whereby the electronic medical record alerts prescribers to patients at risk for opiate abuse or overdose at the point of care, offering them the information to make an educated decision about whether to prescribe these high risk medications.

His second presentation focused on a unique, multi-disciplinary approach to addressing the high levels of disability and deteriorating function in patients with limb salvage for high-energy lower extremity trauma (HELET). Ten such soldiers were treated with his "Return to Run" program of rigorous physical therapy combined with an energy-storing ankle-foot orthosis, and as a result eight were able to run 2 miles without stopping. This landmark program sheds light on the importance of rehabilitation for such patients, on the pathway for return to function for patients with limb salvage, and on the possible applications for ankle-foot orthoses.

Finally, Dr. Hsu lead a literature review, featuring classic orthopaedic trauma articles presented by University of Pennsylvania orthopaedic residents, beginning with one authored by Dr. Hsu, entitled "What to Read and How to Read It." This article provided a scaffold on which to base the proceeding discussions, and gave the residents a valuable overview on how to efficiently narrow down and glean significant information from the tremendous resources available to physicians.

All in all, it was a privilege to host Dr. Joseph Hsu, and the day was one that will certainly impact the practice of orthopedic surgery at the University of Pennsylvania. Dr. Hsu is clearly dedicated to the practice of evidence-based medicine, and leads by example in this regard, and the University of Pennsylvania can only hope for the opportunity to collaborate with him further in the future.

Guest Lecturer: Kevin Chung

Liane Miller, MD

The University of Pennsylvania Department of Orthopedic Surgery was honored to welcome Dr. Kevin Chung, Charles B. G. de Nancrede Professor of Surgery, Plastic Surgery and Orthopedic Surgery and Chief of Hand Surgery at the University of Michigan Health System, as the 2016-2017 Leo Leung Lectureship Visiting Professor on October 13th, 2016. Dr. Chung received his master's degree in Public Health at the University of Michigan as a Robert Wood Johnson Clinical Scholar and obtained his general surgery training from the University of Texas in San Antonio, his plastic surgery training from the University of Michigan and his hand surgery training from the Curtis National Hand Center in Baltimore. Dr. Chung has served as a Director for the American Board of Plastic Surgery and the American Board of Surgery and was past Chairman of the AO North America Hand Education Committee, where he oversaw hand surgery educational programs for the US and Canada. At the University of Michigan School of Medicine, he serves as the Assistant Dean for Faculty Affairs, Director of the hand fellowship program, and Associate Director of the medical school global health program, Global REACH.

Dr. Chung has been highly praised for his research and teaching accomplishments, receiving the Dean›s award from the University of Michigan Medical School for Clinical and Health Services Research as well as the Dean's award for Outstanding Clinician Award recognizing the exemplary performance of a practicing clinician. He has published over 480 peer-reviewed manuscripts, 300+ book chapters, 20 textbooks, and is the Editor-in-Chief of Grabb and Smith's Plastic Surgery, 8th Edition, the preeminent textbook in the field of Plastic Surgery.

Dr. Chung delivered two lectures during the Grand Rounds session. In line with his research interest focusing on the structuring of evidence-based practice in plastic and hand surgery, his first lecture examined how to define value in healthcare and discussed quality assessment instruments to better delineate and understand patients' perceptions of outcomes for the treatments they receive. For his second presentation, Dr. Chung described the clinical and biomechanics implications of flexor tendon repair, providing preferred core suture techniques to obtain the strongest repair and outlined post-operative therapy guidelines to maintain range of motion without threatening the integrity of the repair. He provided case examples from his practice and encouraged discussion amongst the faculty in attendance.

After the completion of the morning lecture session, Dr. Chung graciously demonstrated a few of his clinical techniques in the department's state of the art Human Tissue lab. Students, residents, and faculty observed as Dr. Chung performed a variety of beautifully intricate dissections to illustrate tendon transfer procedures for radial, median, and ulnar nerve injuries.

The time Dr. Chung spent show-casing his surgical techniques and promoting a rich discussion regarding quality within our field was invaluable to all of those in attendance. The University of Pennsylvania Department of Orthopedics was honored to have Dr. Chung the 2016-2017 Leo Leung Lectureship Visiting Professor.

Guest Lecturer: Judy Baumhauer

Matthew Webb, MD, MHS

On January 12th, 2017 Dr. Judith F. Baumhauer MD MPH visited the Department of Orthopaedic Surgery at the Hospital of the University of Pennsylvania for the annual June C. Wapner Memorial Lectureship. Dr. Baumhauer is a Professor of Orthopaedics and Associate Chair of Academic Affairs at the University of Rochester Medical Center. The first annual June Wapner Endowed Lectureship was held on May 24th, 2012 and hosted Dr. Roger Mann, professor of orthopaedic surgery and director of the foot and ankle fellowship program at Oakland Bone & Joint Specialists, and the lectureship has since hosted some of the many leaders in foot and ankle surgery including James A. Nunley, MD in 2014 the former Chair of the Department of Orthopaedics at Duke University and former president of the American Orthopaedic Foot and Ankle Society (AOFAS).

Dr. Judith F. Baumhauer earned her medical degree at the University of Vermont College of Medicine where she was elected to the Alpha Omega Alpha honor society. She then completed her residency in orthopaedic surgery there at the Medical Center Hospital of Vermont. Dr. Baumhauer went on to complete her fellowship in foot and ankle surgery at the Medical College of Wisconsin. She then earned a Masters in Public Health from the University of Rochester School of Medicine and Dentistry. Dr. Baumhauer is currently the director the Foot and Ankle Institute at the University of Rochester Medical Center, a joint venture in clinical care and research between the University of Rochester Medical Center Department of Orthopaedics and Rehabilitation and the Ithaca College Department of Physical Therapy.

Dr. Baumhauer is the recipient of numerous research grants and author of many articles in the scientific literature and she has made numerous academic contributions to the field of foot and ankle surgery on many foot and ankle topics such as the diabetic foot, foot and ankle biomechanics, and gender disparities in foot and ankle surgery[1,2]. Dr. Baumhauer has also published extensively on the reliability and validity clinical measurements in foot and ankle surgery[3-6], and she has also collaborated on projects with our own faculty at Penn[1,7]. She has authored multiple contributions to textbooks in the field including the foreward and rheumatoid chapter in the first edition of Gould's *The Handbook of Foot and Ankle Surgery* and the chapter on plantar heel pain in the ninth edition of Mann's *Surgery of the Foot and Ankle.* Dr. Baumhauer served as course faculty for more than 30 national, international and regional courses. She is a reviewer for several scientific

journals including *Journal of Bone and Joint Surgery*, *Journal of Orthopaedic Research*, *Techniques in Foot and Ankle Surgery* and *American Journal of Orthopaedics*.

Dr. Baumhauer is involved in national leadership in the field and has served on the AOFAS Board of Directors in various roles. She served as AOFAS Board Vice President and Secretary, and Editor of the AOFAS member newsletter, prior to becoming President. Dr. Baumhauer also sits on the Board of Directors of the Orthopaedic Foot & Ankle Education Foundation; is a member of the AOFAS Finance Committee and a reviewer for the scientific journal, Foot & Ankle International (FAI). In 2010 she traveled on the AOFAS Overseas Outreach Project to Vietnam as a surgical volunteer and is the recipient of both the prestigious Roger Mann Award and J. Leonard Goldner Awards. She has received the J. Leonard Goldner Award which recognizes authorship on the most outstanding basic science paper presented at the AOFAS annual meeting twice, most recently in 2016. The only person to win this award more than twice is none other than James A. Nunley (2003, 2010, 2011). In 2008, Dr. Baumhauer was elected the first woman president of the Eastern Orthopaedic Association and in 2011 she was installed as the first woman president of the AOFAS.

On January 12th, 2017 the faculty and residents of the Department of Orthoapedic Surgery at the Hospital of the University of Pennsylvania were delighted to welcome Dr. Baumhauer for three lectures entitled "Patient Reported Outcomes: How They Influence the Care We Give Our Patient," "Great Toe Surgery for Arthritis," and "Cheilectomy, Fusion, and Synthetic Cartilage Implant." Her lectures sparked discussion about patient reported outcome measures, in particular the PROMIS system. Following her lectures, she demonstrated modern techniques in foot and ankle surgery in our Human Tissue Laboratory. We hope to integrate innovations that Dr. Baumhauer presented during her visit into our department in the future.

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Guest Lecturer: Todd Albert

Christina Nypaver, MD

The University of Pennsylvania Department of Orthopaedic Surgery had the great privilege of welcoming Dr. Todd J. Albert as a guest lecturer to Grand Rounds this past February. Currently serving as the Surgeon-in-Chief at the renowned Hospital for Special Surgery (HSS) in New York City since 2014, Dr. Albert needs no formal introduction as many if not all are familiar with his tremendous contributions to the academic Orthopaedic world. Dr. Albert graduated from the University of Virginia School of Medicine and completed his residency in Orthopaedic Surgery at Thomas Jefferson University Hospital, where he would sometime later serve as Chairman of the Department of Orthopaedics and President of the Rothman Institute, before accepting his current position at HSS. He completed his fellowship in spinal surgery at the Minnesota Spine Center and currently specializes in disorders of the cervical spine.

Dr. Albert has a particular interest in cervical spinal deformity conditions such as ankylosing spondylitis, kyphosis, herniated discs, scoliosis, spinal cord injuries, and post-op spinal infections. Over the course of his career, Dr. Albert has written about 300 papers, seven books, and forty book chapters. His research has been overwhelmingly funded by both the National Institute of Health (NIH) and the National Institute of Arthritis and Musculoskeletal Research, awarding him the opportunity to be a co-primary investigator in the National Spine Patient Outcomes Research Trial. He also serves on the boards of several Spine related scholarly journals and as a leader for several Research Spine societies. His research has been presented and acknowledged on both a national and international scale. It is therefore no surprise that he was awarded the Arthritis Foundation's Charley Award for his contributions to orthopaedics.

Dr. Albert presented two lectures during Grand Rounds. The first was titled *Measuring Value: How to Deal with the New Healthcare Paradigm: High Value Orthopaedic Care at HSS*. His lecture described the challenge of current health care systems and providers in the United States to provide the best quality care at a reasonable value, an issue that has been very relevant given recent political events. He pointed out that the United States is, in fact, not the best at achieving this goal despite spending more of its GDP towards health care than any other country in the world. Dr. Albert noticeably caught the audience's attention by sharing that musculoskeletal complaints are the largest drivers of both direct and indirect health care costs in the country, i.e. orthopaedic surgeons are by no means innocent bystanders.

HSS has long served as a leader institution for Orthopaedic Surgery on all fronts. Dr. Albert characterized HSS as constantly striving to "reach the above", which includes providing the best quality care in the most cost efficient way to their primary focus: their patients. He went on to describe the infrastructure and algorithms that HSS has installed in order to achieve the latter, giving interesting examples of pathways that have already been implemented.

Dr. Albert humbly acknowledged that being at HSS has its certain advantages that other academic centers do not share. Their institution has a unique patient population and is entirely devoted to musculoskeletal care; therefore its practitioners and providers of all subspecialties and trades are well versed in caring for patients for orthopaedic issues.

His talk sparked constructive conversation with regards to the very real challenges that other institutions, including Penn, face in providing the same level of care that HSS strives to deliver, and how to go about tackling those challenges in a concrete way. Perhaps the most memorable line from his lecture was about the tendency of academic centers to constantly desire expansion, stating for patients "Bigger is not better…better is better".

His second lecture entitled *Cervical Deformity: Principles and Treatment*s focused on how he first became interested in cervical spine pathology, with a particular emphasis on the importance of respecting the life-altering complications that can occur after cervical spine surgery.

He also defined the mechanics and anatomy of the cervical spine, which must be clearly understood before a deformity can be defined. He noted that the "the conus of economy" or the ability to maintain an upright posture and a horizontal gaze needed to perform day to day activities, varies from patient to patient and is critical to understanding and treating cervical spine deformities. Deformities depend on a host factors, he mentioned, all of which must be acknowledged in order to provide the correct treatment for the certain patient. Finally, he went on to show pictorial demonstrations of his own remarkable challenges and success stories of treating patients who had previously had significant, incapacitating deformities.

Dr. Albert concluded his visit by offering his invaluable knowledge and time to the residents in the Human Tissue Lab, teaching approaches and methods for cervical spine ACDF and PSF. The University of Pennsylvania Department of Orthopedics was honored to have Dr. Todd J. Albert as a visiting professor on February23, 2017.

Chief Residents

Jason Anari

Hometown: Yardville, NJ
Undergraduate School: The College of New Jersey
Medical School: Robert Wood Johnson Medical School at Rutgers University (UMDNJ)
Residency Highlights: Some of my best memories of residency include: the first day I met my 7 fantastic co-residents and the surgery program director referred to us as the Eagles offensive line, match day for my wife and I for our respective fellowships, and lastly fixing a Pipkin 4 as the trauma chief this past August.
Future Directions: I will be at CHOP in 2017-2018 pursuing a Pediatric Orthopaedic Surgery Fellowship. I hope to spend a career in academic pediatric orthopaedics focusing on scoliosis and pediatric trauma.

Joshua Gordon

Hometown: San Francisco, CA
Undergraduate School: Pitzer College
Medical School: David Geffen School of Medicine at UCLA
Residency Highlights: Friends, mentors and team work—I am deeply appreciative for my time at UPenn.
Future Directions: I am headed to University of Washington, in the only city, perhaps more sunny than Philadelphia... Seattle. Looking forward to a lifetime of hand and micro surgery in which I hope to do all I can to provide and improve patient care!

Phillip Saville

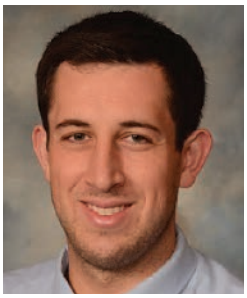
Hometown: Winchester, England
Undergraduate School: University of Leicester
Medical School: University of Leicester (England, UK)
Residency Highlights: My first day and my last day.
Future Directions: Hospital Special Surgery for Spine fellowship, followed by private practice in MIS Spine.

Vishal Saxena

Hometown: Fairfax, VA
Undergraduate School: Northwestern University
Medical School: Pritzker School of Medicine at the University of Chicago
Residency Highlights: Lab year with Dr. Robert Mauck, serving as co-Editor-in-Chief of UPOJ, forming what will be lifelong relationships with my attendings and co-residents.
Future Directions: Sports Medicine fellowship at Massachusetts General Hospital, busy practice with a focus on cartilage repair.

Russell Stitzlein

Hometown: Grove City, OH
Undergraduate School: Miami University
Medical School: Cleveland Clinic Lerner College of Medicine
Residency Highlights: Learning from my senior residents and then having the opportunity to pass along that knowledge and mentor future classes; developing lifelong friendships with my co-residents; and, most importantly, the birth of my first child (Cesar) and spending time with him and my wife and sharing many fond memories with my co-residents and their families!
Future Directions: Musculoskeletal Oncology Fellowship at MD Anderson Cancer Center and then plan to work in academic orthopaedic oncology



Michael Talerico

Hometown: Wildwood, MO
Undergraduate School: University of Notre Dame
Medical School: Saint Louis University School of Medicine
Residency Highlights: Co-scrubbing cases with my classmates during PGY 2-5. Learning how to not only operate for attendings, but with attendings. Teaching juniors the same way chiefs once taught me, and realizing how rewarding it is.
Future Directions: Fellowship at Harborview Medical Center in Seattle, WA. Plan to be an orthopaedic traumatologist in the Midwest/Southeast area of the country at a level one trauma center.

Nathan Wigner

Hometown: Colonial Heights, VA
Undergraduate School: North Carolina State University
Medical School: Boston University School of Medicine
Residency Highlights: Graduating with my class.
Future Directions: Spine Fellowship at University of Washington, Seattle. Plan to pursue a career practicing spine and orthopaedic trauma at a level one trauma center.

Chase Woodward

Hometown: Omaha, NE
Undergraduate School: Northwestern University
Medical School: Feinberg School of Medicine at Northwestern University
Residency Highlights: Meeting, courting, and marrying my wife, Allison. Being *genuinely mentored* by dedicated professors. Time spent in the trenches with my fellow residents.
Future Directions: Spine surgery fellowship at Washington University in St. Louis, running an efficient practice with satisfied patients, starting a family.

Current Residents

Clinical Year 4

Keith P. Connolly, MD

Undergraduate:
Michigan State University

Medical School:
University of
Central Florida
College of Medicine

Daniel P. Lim, MD

Undergraduate:
University of
Southern California

Medical School:
Keck School of Medicine
at USC

Tyler R. Morris, MD*

Undergraduate:
The University of
Pennsylvania

Medical School:
Drexel University
College of Medicine

Alexander L. Neuwirth, MD*

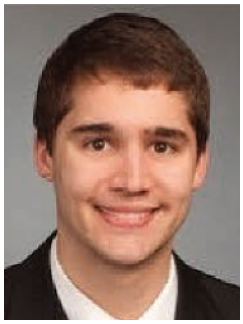
Undergraduate:
Rutgers University

Medical School:
Robert Wood Johnson Medical
School at
Rutgers University (UMDNJ)

Joshua C. Rozell, MD

Undergraduate:
Emory University

Medical School:
Drexel University
College of Medicine



Joshua T. Steere, MD

Undergraduate:
Creighton University

Medical School:
Stritch School of Medicine at
Loyola University Chicago

Chia H. Wu, MD, MBA

Undergraduate:
University of Pennsylvania

Medical School:
Perelman
School of Medicine at the
University of Pennsylvania

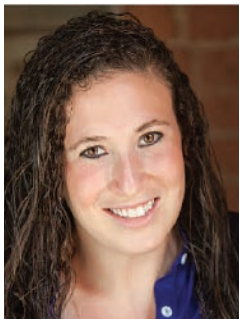
Zachary R. Zimmer, MD

Undergraduate:
Colgate University

Medical School:
Stony Brook University
School of Medicine

*Indicates Resident is in the 6-year Research Track

Clinical Year 3



Jenna A. Bernstein, MD

Undergraduate:
Cornell University

Medical School:
University of Connecticut School of Medicine

Kristin Buterbaugh, MD

Undergraduate:
Northwestern University

Medical School:
Icahn School of Medicine at Mount Sinai

Jose A. Canseco, MD, PhD

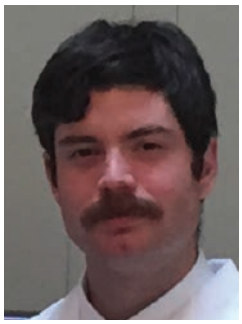
Undergraduate:
Massachusetts Institute of Technology

Medical School:
Harvard Medical School

Jonathan R. Dattilo, MD

Undergraduate:
Northwestern University

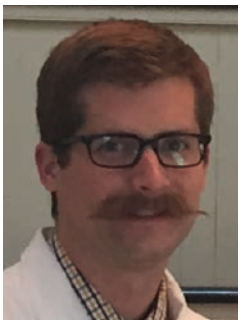
Medical School:
Johns Hopkins University School of Medicine



James M. Friedman, MD*

Undergraduate:
Duke University

Medical School:
Duke University School of Medicine



Cody D. Hillin, MD, MS*

Undergraduate:
University of Rochester

Medical School:
Baylor College of Medicine

Luke A. Lopas, MD

Undergraduate:
University of Wisconsin-Madison

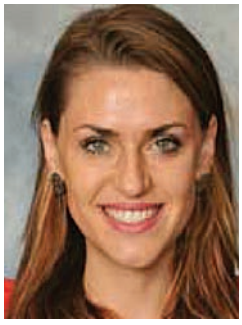
Medical School:
University of Wisconsin School of Medicine & Public Health

Nicole A. Zelenski, MD

Undergraduate:
Bryn Mawr College

Medical School:
Duke University School of Medicine

Research Year



Blair S. Ashley, MD*

Undergraduate:
The College of William and Mary

Medical School:
University of Pittsburgh School of Medicine

Daniel Gittings, MD*

Undergraduate:
Providence College

Medical School:
Boston University School of Medicine

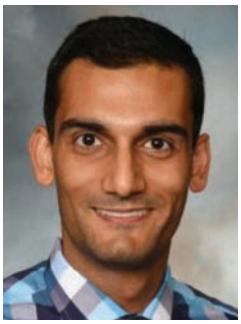
*Indicates Resident is in the 6-year Research Track

Clinical Year 2

Ryan Charette, MD

Undergraduate:
University of Connecticut

Medical School:
University of Connecticut
School of Medicine



Adnan Cheema, MD*

Undergraduate:
University of Missouri-Kansas

Medical School:
University of Missouri-Kansas
School of Medicine

Michael Eby, MD, MS*

Undergraduate:
University of Pennsylvania

Medical School:
Georgetown University
School of Medicine

Rikesh Gandhi, MD

Undergraduate:
Boston College

Medical School:
Duke University School of
Medicine

Mark Hasenauer, MD

Undergraduate:
Boston College

Medical School:
New York Medical College

Matthew Sloan, MD, MS

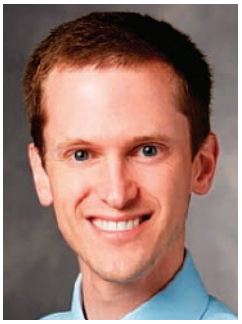
Undergraduate:
University of Massachusetts

Medical School:
University of Massachusetts
Medical School

Andrew Tyler, MD, PhD

Undergraduate:
Harvard University

Medical School:
University of Texas at Dallas
Southwestern Medical School



Matthew Winterton, MD

Undergraduate:
Brigham Young University

Medical School:
Perelman School of Medicine
University of Pennsylvania

*Indicates Resident is in the 6-year Research Track

Clinical Year 1

Gerald Andah, MD

Undergraduate:
University of Pennsylvania

Medical School:
Perelman School of Medicine University of Pennsylvania

Matthew Counihan, MD, MS*

Undergraduate:
Univ. of Richmond

Medical School:
Drexel University College of Medicine

Chelsea Hendow, MD, MS

Undergraduate:
Univ. of CA—Los Angeles

Medical School:
New York Medical College

Liane Miller, MD*

Undergraduate:
Univ. of CA—Santa Barbara

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

Christina Nypaver, MD

Undergraduate:
Univ. of Notre Dame

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

Christopher Scanlon, MD, MS

Undergraduate:
Univ. of So. Carolina—Columbia

Medical School:
Drexel University College of Medicine

Kimberly Stevenson, MD, MS

Undergraduate:
Univ. of Delaware

Medical School:
Georgetown University School of Medicine

Matthew Webb, MD

Undergraduate:
Harvard College

Medical School:
Yale School of Medicine

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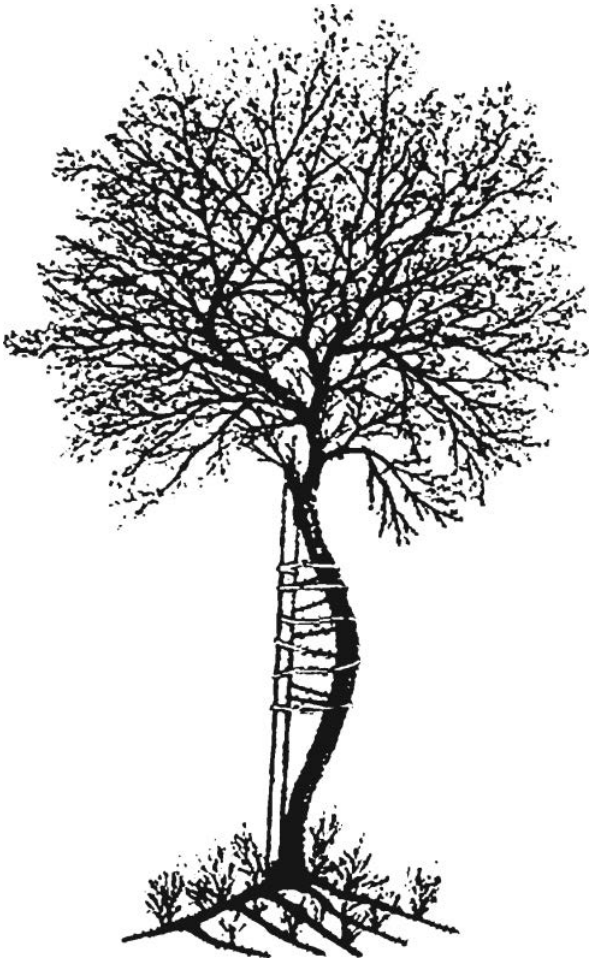

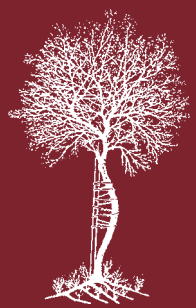

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