For 109 years, the Department of Orthopaedics at University Hospitals Case Medical Center has combined first-rate medical care, personalized attention and innovative scientific research with an unwavering sense of purpose – to provide the best possible treatment for patients. The Department of Orthopaedics continues to be one of the top-ranked programs in the nation. This past year, our Pediatric Orthopaedics program was ranked No. 8 by U.S. News & World Report. As we move toward the future, we remain poised to benefit the lives of patients affected by musculoskeletal disorders for generations to come.
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Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

For more information, visit UHhospitals.org/Ortho
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This is the 109th year for the Department of Orthopaedic Surgery at University Hospitals Case Medical Center. We are continuing our mission to provide exceptional patient care, leading basic and clinical research, and top-notch education to our medical students, residents and fellows. This is reflected in our continued NIH funding, primary affiliate relationship with Case Western Reserve University School of Medicine, and consistent ranking among the nation’s leading centers for orthopaedic care according to U.S. News & World Report. In addition, our department continues to provide care to the Cleveland Browns football organization, a partnership that will continue to be mutually beneficial for years to come.

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THE CONSUMMATE TEAM PHYSICIAN

I am proud to introduce the 12th edition of the *Case Orthopaedic Journal*. In keeping with tradition, each year we dedicate the Journal to a faculty member who has not only made a profound impact on the field of orthopedic surgery, but also has played a pivotal role in residency training and enhancing the resident experience during his or her career at Case. It is with great pleasure that this year’s Journal is dedicated to Thomas C. McLaughlin, MD, Associate Professor in the Department of Orthopaedics and Emeritus team physician at Case Western Reserve University.

While not only working with Dr. McLaughlin during my PGY-3 and PGY-5 rotations at the VA Hospital, I had the recent privilege of talking to him about his career at Case, as well as what inspired him to be an orthopaedic surgeon. Interestingly, it wasn’t the surgical aspect of orthopaedics that attracted him to this profession, but rather the desire to be a team physician. Even as a child, he was always interested and involved with athletics, especially since his father was a coach. Dr. McLaughlin was born in Hastings, Nebraska, in 1939 to parents Tom and Charlotte McLaughlin. His dad, better known as Coach “Tiger” Tom McLaughlin, was a standout high school coach before returning to his alma mater, Hastings College, in 1949 as both athletic director and coach. During his 15 years at Hastings College, he coached championship teams in both football and basketball. Most notably, his 1954 football squad went unbeaten and untied. He unexpectedly passed away in 1964 and later that year the Tom McLaughlin Memorial Award was inaugurated. This prestigious award is given annually to the most-outstanding football player. “My dad had over 100 combined seasons as a coach, and only had one losing season. Early on, I thought that I would like to grow up and be a coach, but then I thought to myself ‘How am I supposed to follow in my father’s footsteps. The man only had one losing season! The only person I know that had a better record was Coach [Tom] Osborne, who never had a losing football season during his career at the Nebraska.’”

Despite not pursuing a career in coaching, Dr. McLaughlin wanted to be involved with athletics. One of the things that he observed growing up around the practice fields was that there wasn’t a medical professional designated to take care of the players. “You’ve got to remember,” Dr. McLaughlin says, “back in the 1950’s only a handful of college and professional teams had athletic trainers, and fewer still had designated team physicians.” In those days, the coach addressed and tended to most of the team injuries. “My dad knew a physical therapist that worked at a mental institution of all places. If there were any injuries after a football game, he would take the players to see the physical therapist and use the therapy facilities at the mental institution to allow them to rehab.”

Dr. McLaughlin’s first taste of taking care of players came during high school. He played on the varsity football and golf team, but wasn’t involved in a winter sport, which meant that during his offseason, he would have to take physical education. His high school just built its first athletic training room, and he inquired about being a student trainer for the varsity basketball team. Dr. McLaughlin sarcastically remarked, “I mainly wanted to get out of having to do phys. ed. class! However, it was also a way for me to be involved with sports during the offseason.” Coincidentally, one of the first orthopaedic surgeons recently moved into town, Dr. Yost, and his father quickly recruited him to be the high school’s team physician. He was allowed to be the first student trainer at his high school. He was given a copy of Cramer’s Basic Athletic Training textbook, learned as much anatomy as possible, and mainly taped the players’ ankles before practice and games. If anyone injured themselves then he would call Dr. Yost at his office, who would evaluate the player on his way home from work.

Coach “Tiger” Tom McLaughlin alongside one of his football players at Hastings College.

Dr. McLaughlin served as the Case Western Reserve University varsity athletic team physician for more than 30 years before being named Emeritus team physician.
Dr. McLaughlin’s life was forever changed when he happened to apply to “this big school out east called Harvard” during his senior year. “It was all just happenstance,” remarks Dr. McLaughlin “I was a Merit Finalist and had to list what college I planned on attending in case I received one of the scholarships. I had heard good things about Harvard, but mainly remembered it because Harvard was always in the weekly college football ‘Pick-em’ section of the local newspaper.” As the story goes, he quickly went to the library, found the address to the Admissions Office, and mailed them a letter expressing his interest. “I never expected to hear back,” he says, chuckling to himself, “but about a week later I get a hand-written letter in the mail. It was like Christmas morning!” Apparently the application deadline had recently ended, however, the Admissions Office was willing to make an exception if he completed the application and returned it within a week. Fortunately, he not only completed the application, but also took his mother’s advice and completed the additional scholarship application. As luck would have it, he did not receive the Merit scholarship, but instead received an academic scholarship from Harvard.

After graduating high school, Dr. McLaughlin took the 52 hour bus ride from Hastings, Nebraska to the big city of Boston, Massachusetts. As part of his scholarship, he had to help clean the dorm rooms prior to the start of classes, however, the biggest item on his agenda was applying to be a student trainer. To his dismay, Harvard did not allow student trainers because it was a Massachusetts law that “therapeutic taping could only be performed by a licensed physical therapist.” Initially he was crushed to find out it was not an option to be a student trainer. To console himself, he went to watch the football team practice. “They had a ‘polite’ way of playing football. Even though I wasn’t a physical specimen, I thought that I could compete with those guys.” It turns out he was correct. Tom walked-on to the football team as a freshman and played all four years. Despite being somewhat undersized, he was one of the hardest working players on the team. As a senior, he received the William Paine LaCroix Award for "enthusiasm, loyalty, and team spirit." He was also a co-captain of the junior varsity team and saw varsity action in “The Game” against arch-rival Yale.

After college, Dr. McLaughlin began medical school at the University of Rochester. During his first two years, he also worked as a graduate student trainer for the university’s college football team, and he did such an exceptional job that they offered to pay him a sizeable stipend. It wasn’t until starting his clerkships as a 3rd and 4th year medical student that he decided to pursue a career in orthopaedic surgery. There were a couple of factors that weighed in on his decision. First, his dream job was to be a team physician at either the collegiate or professional level, and the majority of team physicians were orthopaedic surgeons. He figured that since he was not going to be a coach, then the next best thing would be to help the coach and all the players as their physician. Second, he did enjoy the surgical aspect of medicine. His favorite clerkship during medical school was a month elective during his 4th year. He went back to Boston and worked closely with Harvard’s head athletic team physician. After this phenomenal opportunity, his decision to pursue a career in orthopaedics was sealed.

After finishing medical school, Dr. McLaughlin completed his general surgery internship at University Hospitals in 1967, then spent 2 years in the United States Air Force. He completed the remainder of his orthopaedic surgery residency at University Hospitals and graduated in 1973. At the request of Dr. Herndon, he went on to do a Sports Medicine fellowship with Dr. Donald Slocum during the first block of his chief year. This was the most influential period of his surgical training. “Back in those days,” he says “fellowships were very rare and the field of Sports Medicine was in its infancy.” One of the lasting impressions from his fellowship was the emphasis and importance of a thorough history and physical exam. Dr. McLaughlin recounted spending an hour with each patient in order to get an accurate history and physical that would satisfy Dr. Slocum. “At times it was painstaking and
onorous,” jokes Dr. McLaughlin, “but by the end of the exam, I sure as hell could pinpoint exactly what was wrong with each patient. There was no doubt about it.”

Dr. McLaughlin’s dream of becoming a team physician was finally realized when he joined the faculty at University Hospitals and became the head team physician at Case Western Reserve University. In over 34 years of being the head team physician at CWRU, he only missed 2 football games, both home and away. The first was for his father’s induction into the Nebraska Football Hall of Fame, and the second occasion was when he was asked to represent his father at the 50th anniversary of his 1954 team’s undefeated/untied season. “I wanted to be a team physician in its truest sense,” remarks Dr. McLaughlin. “It wasn’t just about showing up to the games in case someone was hurt. I knew everything there was to know about every player, what medical problems they had, where they grew up, what they did during their free time, and how they had been practicing. I wasn’t just there for the games. I went to each practice because I always wanted to be there in case the team needed me. I was determined to give the Case athletes exceptional care that would rival any elite Division-I college or professional team.” Dr. McLaughlin was rewarded for his passion, love, dedication and commitment to Case athletics in 2004, when he was inducted into the CWRU Athletic Hall of Fame. His legacy was further solidified in 2007, when he was made Emeritus team physician at CWRU and the training room was dedicated in his honor.

In addition to his accomplishments as a team physician, Dr. McLaughlin has been an educator of residents and medical students at Case for over 40 years. For many years he passed along his knowledge and expertise to medical students in the art of the physical exam, which he learned during his fellowship with Dr. Slocum. Furthermore, Dr. McLaughlin has been a prominent resident educator and continues to teach the PGY-3 and -5 residents at the VA Hospital. “One of the things that gives me great pride and satisfaction, is witnessing the decision making and operative skills of our chief residents. I have always had the mindset that one of the beauties of the VA system is for the chiefs to be the ‘team captain’ and make the important decisions about patient management, surgical options, and post-operative care.”

Near the end of my interview, Dr. McLaughlin remarked on the final aspect of his career that has given him great contentment. “Aside from my fond memories of being team physician at Case and teaching some of the best residents in the country, I’m very pleased at the advances in the field of Sports Medicine, specifically in the arena of team physicians.” Over his career, Dr. McLaughlin has shared his passion and vision by giving over 50 local, regional and national lectures. In addition, he has taught and trained countless healthcare providers, not just orthopaedic residents, who have gone on to have careers in Sports Medicine. “When I first started, I had little help and I had to manage most team-related issues on my own. There were many high schools that didn’t even have a team physician, let alone trainers. Nowadays, athletes across all levels of competition from high school through college have a true ‘team’ of healthcare professionals at their disposal.”

Dr. McLaughlin, it has been both an honor and a privilege to learn from your clinical and surgical excellence. It is inspiring to see the love, passion, and commitment you have for CWRU, the Case Department of Orthopaedics, and to the field of Sports Medicine. You truly have left a lasting legacy that will be long remembered and cherished. On behalf of the COJ editorial staff, residents, faculty, alumni, and countless athletes you have cared for, I would like to thank you for the legacy you will leave behind and the lasting impression you have had on all of us. As a token of our appreciation, we dedicate this Journal in your honor.

With Gratitude,

Christopher Bechtel, MD
Editor-in-Chief
LETTER FROM THE EDITOR-IN-CHIEF

I am honored to present the 12th edition of the Case Orthopaedic Journal for 2015. The past year has held many exciting developments in our Department that I am pleased to share with you. First and foremost, University Hospitals Case Medical Center formally opened its doors as a Level 1 trauma center on December 1, 2015. Led by Dr. John Sontich, the Division of Orthopaedic Trauma and Post-Traumatic Reconstruction is anchored by Drs. Robert Wetzel and Kevin Malone, who also became the new Chief for the Division of Hand and Upper Extremity. This new addition, coupled with the internationally renowned orthopaedic traumatologists at MetroHealth Medical Center—which welcomed Drs. Jonathan Belding and James Learned onto its staff—make our residency program one of the premier training grounds for orthopaedic trauma in the country.

The Division of Sports Medicine continued to thrive as they are not only the team physicians for the Cleveland Browns, but this year also became the official healthcare partner for the Mid-American Conferences Championship Athletic Events. Furthermore, the clinical and academic excellence of Dr. James Voos was recognized as he became the inaugural Jack and Mary Herrick Endowed Director of Sports Medicine. Finally, this edition of the Case Orthopaedic Journal is proudly dedicated to Dr. Thomas McLaughlin. Dr. McLaughlin, a graduate of the Case Orthopaedic Surgery Residency, joined the faculty at Case in 1973. For over forty years, he has been intimately involved with athletics at Case Western Reserve University as well as residency education and training at UH and the VA hospital.

This year’s Journal features several recently published articles in prominent orthopaedic journals by our current residents, clinical and basic science faculty, and alumni. My hope is that these articles highlight the world-class basic science and clinic research performed at Case. Also included are photos from throughout the year of our residents, faculty, alumni and distinguished visiting professors.

I would like to thank the past and present editorial board—which is comprised of past and present Allen Fellows—for their assistance with this year’s Journal. In addition, I would like to personally thank Dr. Randall Marcus for his continued advice, guidance, and enthusiasm in publishing another “perfect” edition of the Case Orthopaedic Journal. The publication of this periodical is never an easy endeavor, and I could not have done it without everyone’s assistance.

Sincerely,

Christopher Bechtel, MD
Editor-in-Chief
I’m delighted to introduce the 2015 volume of the *Case Orthopaedic Journal*, which highlights the outstanding achievements of the Department of Orthopaedics at Case Western Reserve University School of Medicine (CWRU). The Department continues its ranking as one of the top orthopaedic departments in the United States and we take great pride in the outstanding achievements and excellent work carried out during the past year by our clinicians, scientists, residents and staff.

The Department of Orthopaedics at Case Western Reserve University consists of four medical centers, our research laboratories and, most importantly, the outstanding people who have earned our reputation for excellence. Our medical centers include:

- **University Hospitals Case Medical Center**, which includes Rainbow Babies & Children’s Hospital and the Seidman Cancer Center,
- **MetroHealth Medical Center**
- **Louis Stokes Veterans Administration Medical Center** located on our Case Western campus, and
- **University Hospitals Ahuja Medical Center** and attached orthopaedic musculoskeletal center.

Our basic science laboratories are located:

- in the School of Medicine, with our Molecular Biology division in the Biomedical Research Building,
- in the Case Western Reserve School of Engineering, in the Musculoskeletal Mechanics and Materials Laboratory, and
- at MetroHealth Medical Center and the Veterans Administration Medical Center, where our Functional Electrical Stimulation Laboratories are located. The interdisciplinary Cleveland Advanced Platform Technology (APT) Center of Excellence is based at the Cleveland VA.
- Additionally, our Anatomic Research Laboratory resides in the Cleveland Museum of Natural History, the home of the Hamann-Todd bone collection.

**Medical Center and Medical School Achievements**

University Hospitals Case Medical Center (UHCMC) once again ranks among America’s Best Hospitals for a wide range of advanced care, according to *U.S. News & World Report*. Our flagship academic medical center is among the country’s top 50 in 9 specialties, including orthopaedic surgery. Additionally, UHCMC was ranked in the top 50 for cancer; cardiology and heart surgery; ear, nose and throat; gastroenterology and GI surgery; geriatric; nephrology; neurology and neurosurgery; and urology.
Of the 5,000 hospitals eligible for ranking, only 3 percent are in a top 50 ranking in even 1 specialty. To continually rank among the leading medical centers in multiple specialties year after year is impressive!

_U.S. News & World Report_ also ranked UH Rainbow Babies and Children’s Hospital among America’s Best Children’s Hospital in 8 pediatric specialties, including orthopaedics. Also ranked among the top children’s programs in the country were our cancer; gastroenterology and GI surgery; neonatology; nephrology; neurology and neurosurgery; pulmonology; and urology.

University Hospitals Case Medical Center earned more national recognition for highest quality care from _U.S. News & World Report_ receiving under the publication’s new “Common Care”, “High Performing”, the best ranking in 4 of 5 evaluated areas, including knee replacement. Also ranked was heart bypass surgery, chronic obstructive pulmonary disease and heart failure. No other medical center in our region fared as well.

_Beckers Hospital Review_, an online trade journal, ranked University Hospitals Case Medical Center as one of “100 Great Hospitals in America” in addition to also ranking University Hospital in its list of “World’s Most Ethical Hospitals”.

University Hospitals Case Medical Center is also among the 5 percent of hospitals nationally that received a 2015 Distinguished Hospital Award for “Clinical Excellence” from Health Grades. Recognized hospitals had the lowest risk adjusted mortality and complication rates across 27 common conditions and procedures.

Six graduate medical education residency programs at University Hospitals Case Medical Center rank among the top 10 in the Midwest, according to Doximity, the largest online professional network for U.S. Physicians. UH specialties ranking among the best were orthopaedics (number 7). Rankings were based on research conducted by Doximity with collaboration from _U.S. News & World Report_.

The Department of Orthopaedics at University Hospitals Case Medical Center was selected as one of America’s Best Hospitals for Orthopaedics by the 2015 “Women’s Choice Award”. Our Department was selected based on our comprehensive orthopaedic services, as well as our performance on important CMS measures.

In September, University Hospitals announced its purchase of St. Johns Westshore Medical Center, a 204 bed hospital in Westlake, Ohio. This was followed by an announcement in November, in which University Hospitals acquired Samaritan Regional Health System of Ashland, Ohio. This medical center constitutes our southernmost regional hospital. The University Hospitals Health System now comprises 17 hospitals and more than 26,000 patients and employees.

In December, University Hospitals Case Medical Center became a Level 1 Trauma Center in order to support the significant need for additional trauma care resources in our community. University Hospitals Comprehensive Trauma System also includes our Level 1 Pediatric Trauma Center at Rainbow Babies and Children’s Hospital, as well as our four Level 3 Trauma Centers: UH Geauga, Portage and St. John Medical Center, plus Southwest General Health Center. Dr. John K. Sontich, Associate Professor of Orthopaedics at Case Western Reserve University, was appointed Chief of the Orthopaedic Trauma Service as of August 2015. A graduate of Dartmouth College and the University of Cincinnati Medical School, John did his orthopaedic residency at The Cleveland Clinic Foundation and his trauma fellowship at MetroHealth Medical Center. John is an internationally renowned specialist in orthopaedic trauma and post traumatic deformity correction. He served as president of the Ohio Orthopaedic Society in 2015 and is a former president of the American Limb Lengthening and Reconstruction Society. He has served on the American Academy of Orthopaedic Surgeons Board of Specialty Society since 2009. Dr. Sontich has been invited to present his work internationally, nationally, as well as regionally on over 150 occasions. Dr. Sontich serves as a trauma consultant for the Cleveland Browns and Cleveland Indians.

In September, Dr. Robert J. Wetzel joined our Orthopaedic Trauma Division. Dr. Wetzel, a graduate of the University of Akron (Summa Cum Laude), received his medical degree from Northeastern Ohio Medical University. He completed his orthopaedic residency at Northwestern University in Chicago, Illinois, where he was appointed the Administrative Chief Resident. He completed his trauma fellowship at Indiana University Health Methodist Hospital in Indianapolis. Dr. Wetzel is the author of 6 peer reviewed publications and has been invited to present his work on 7 occasions at international, national and regional meetings. Dr. Wetzel’s sub-specialty is open acetabular and hip joint preservation surgery.
Additionally, on December 1st, UHCMC opened a fully equipped dedicated orthopaedic trauma operating room with 24/7 staffing that was designed by our traumatologists.

As part of our trauma initiative, we appointed Dr. Kevin Malone as Chief of the Division of Hand Surgery, effective October 1, 2015. Dr. Malone received his undergraduate degree from the University of Notre Dame and his medical degree (AOA) from the University of Cincinnati. Following completion of his residency at William Beaumont Hospital, he completed a hand fellowship at the University of Utah. Dr. Guo began her practice at Westchester Medical Center in Valhalla, New York in 2012. Bev has 5 publications and has been invited to present her work on 10 occasions at national and regional meetings. The Department was delighted to welcome her back, having known her during her time as medical student at CWRU.

In 2015, James E. Voos, MD, Associate Professor of Orthopaedics at CWRU and Director of the University Hospitals Sports Medicine Institute was inaugurated as the Jack and Mary Herrick Endowed Director of Sports Medicine at University Hospitals. This honor was made possible by a generous donation from Jack and Mary Herrick, two long-term supporters of University Hospitals. Jack Herrick is the Chairman of the University Hospitals Orthopaedic Leadership Council. Additionally, Jack has been a tremendous business leader and sports enthusiast in Ohio. He has held numerous national and international positions in both the professional and amateur squash associations. Jack has been a great friend to Orthopaedics at University Hospitals for decades and has taken a very hands-on role in our Sports Medicine Institute.

Dr. Voos serves as Head Team Physician for the Cleveland Browns football team. Also leading our sports program is Dr. Sean A. Cupp, the Lead Medical Sports Medicine Physician for the Cleveland Browns and Dr. Michael J. Salata, Associate Team Physician for the Cleveland Browns. Our Sports Medicine Division, which also includes Drs. Donald Goodfellow, Brian Victoroff, Shana Miskovsky, as well as our Medical Sports Medicine Faculty including Drs. Amanda Weiss Kelly, Susannah Briskin and Mary Solomon, currently provides sports coverage to 3 professional teams (Cleveland Browns, Cleveland Gladiators, Lake Erie Monsters); 4 colleges (Case Western Reserve University, Hiram Collage, Lake Erie College and Ursuline College); and 36 high schools. Two of these schools that were previously underserved because of lack of financial resources are now staffed by trainers supported by a partnership between University Hospitals and the Cleveland Browns.

Furthermore, our Sports Medicine Division had 6 research presentations accepted for this year’s NFL Combine Medical Meeting, including 3 podium presentations (the most of any team), in addition to 3 posters.

In 2015, University Hospitals Sports Medicine became the official healthcare partner for the Mid-American Conferences Championship Athletic Events. This effort is being led by Dr. Sean Cupp, who will be working closely with MAC officials to support coaches, trainers and athletes with UH sports medicine experts to help athletes perform to the best of their abilities.

Our Department is extremely grateful to Dr. Stephen Lacey for his outstanding leadership as our Chief of Hand Surgery over the last several decades. He has made numerous contributions to our clinical and educational programs over the years and we look forward to his continued active participation in our Hand Surgical Division.

Joining Drs. Malone and Lacey, as well as Drs. John Shaffer and J. Robert Anderson, in the Hand Division is our newest hand and upper extremity surgeon Bev Y. Guo, MD. Dr. Guo received her medical degree from Case Western Reserve University School of Medicine and completed her residency at New York University Hospital for Joint Diseases. Following a hand fellowship at the University of Utah, Dr. Guo began her practice at Westchester Medical Center in Valhalla, New York in 2012. Bev has 5 publications and has been invited to present her work on 10 occasions at national and regional meetings. The Department was delighted to welcome her back, having known her during her time as medical student at CWRU.

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Departmental Achievements

Our residency received over 750 application for our 6 residency positions in 2015. The Department matched 6 of our top selections. We welcomed to the Department Dr. Jonathan Copp from the University of California San Diego, Dr. Christopher Flanagan from the University of Chicago, Dr. Mark LaBel from Northwestern University, Dr. Alexander Rascoc from Penn State University, Dr. Adam Schell from Emory University and Dr. Joanne Wang from Brown University. Our Trauma Fellow this year, based at MetroHealth Medical Center is Dr. Mai Nguyen from the University of Iowa Orthopaedic Residency.

Maged Hanna, MD, PhD is our Pediatric Orthopaedic Fellow from the University of Toledo Medical Center. The Senior Sports Medicine Fellow this year is Christopher Shaw, MD from the University of Missouri-Kansas City.

Our Dudley P. Allen Fellows this year are Dr. Givenchy Manzano and Dr. Derrick Knapik. Dr. Manzano will work on implant loosening under the mentorship of Dr. Edward Greenfield. Dr. Knapik is working under the mentorship of Drs. Raymond Liu and Ozan Akkus in pediatric anatomic research and biomechanics.

We also welcomed a new faculty member in our Pediatric Orthopaedic Division. Dr. R. Justin Mistovich will be working at both Rainbow Babies and Children’s Hospital and MetroHealth Medical Center. Dr. Mistovich completed his Fellowship in Pediatric Orthopaedics at the Children’s Hospital of Philadelphia. He received his medical degree from Wright State University School of Medicine and completed his residency at Allegheny General Hospital. Dr. Mistovich has 11 publications and has been invited to present his work on 6 occasions at regional and national meetings.

Congratulations to Faculty Members and Residents

Dr. Robert Gillespie, Director of the Shoulder and Elbow Division at University Hospitals Case Medical Center, received the 2015 Neer Award from the American Shoulder and Elbow Society (ASES) for his study titled, “A Randomized, Prospective Evaluation on the Effectiveness of Tranexamic Acid in Reducing Blood Loss After Total Shoulder Arthroplasty”. This is the most prestigious award granted for clinical research by the ASES. Dr. Gillespie’s co-authors were Drs. Shane Hanzlizik, Yousef Shishani, Jonathan Streit, Reuben Gobezie and Sheeba Joseph.

In March, the Board of Trustees of University Hospitals formally approved the appointment of Dr. Raymond W. Liu as the inaugural holder of the Victor M. Goldberg, MD Master Clinician-Scientist in Orthopaedics. This position was made possible by a generous donation from the late Victor M. Goldberg and his wife Harriet. Additionally, many of Dr. Goldberg’s colleagues, friends, and former patients contributed to this endowment.

At the Case Western Reserve University School of Medicine graduation ceremonies last May, Dr. Nicholas Ahn was awarded the prestigious Kaiser-Permanente Excellence in Teaching Award for his tremendous contributions in clinical education at the School of Medicine.

In September, Dr. Shana Miskovsky and University Hospitals Sports Medicine was recognized by Case Western Reserve University for the “Very Special Relationship” Case Western Reserve University athletics has with UHCMC. Dr. Miskovsky, who sponsored the fireworks at the September 19th CWRU football game, is the CWRU Head Team Physician, assisted by Drs. Amanda Weiss Kelly, Susannah Briskin and Mary Solomon. She follows in the footsteps of Dr. Thomas McLaughlin, who was the Head Team Physician at CWRU for many decades.

Raymond Liu, MD received the Russell A. Hibbs Basic Research Award from the Scoliosis Research Society for his study entitled, “Normal Human Spine Growth and Prediction of Final Spine Height Developed from a Longitudinal Cohort of Children Followed Through Their Grown Until Completion”. His co-authors were Dr. James Sanders at Rochester and Dr. Daniel Cooperman at Yale. Dr. Liu also received the Behrooz A. Akbarnia, M.D. Award for Best Paper at the International Congress on Early Onset Scoliosis meeting in November.

Dr. Matthew Kraay and our total joint replacement surgeons were recognized by CMS for a remarkable decrease in 30 day admission rates to 1.9%. The national and state 30 day admission rates over the same period were 4.9%. Dr. Kraay’s leadership has resulted in considerable efforts to reduce hospital readmissions, as well as length of stay.

Dr. Michael J. Salata, Director of the University Hospitals Joint Preservation and Cartilage Restoration Center, was an invited faculty member for the annual St. Louis University Hip Arthroscopy, Preservation and Replacement Procedures Course.

Dr. Edward Greenfield, the Harry E. Figgie, III, M.D. Professor of Orthopaedics and Director of Orthopaedic Research, was appointed to the Editorial Boards of the Journal of Orthopaedic Research and the Journal of Biologic Chemistry. He also received recognition from Clinical Orthopaedic and Related Research as one of their top scientific manuscript reviewers.
Dr. Ronald Triolo, the Executive Director of the Advanced Platform Technology Center of Excellence at the Louis Stokes Cleveland Veterans Administration Medical Center, received a 5 year renewal as a Center of Excellence from the Rehabilitation, Research and Development Service of the U.S. Department of Veteran’s Affairs. Additionally, Dr. Triolo received a $780,000 grant to support his research in “Natural Sensation for Lower Limb Amputees”.

Dr. Christopher Collier received a $17,740 Orthopaedic Research and Education Foundation Resident Clinical Scientist Training Grant. The grant was awarded for his research in Osteogenic Sarcoma. Dr. William Morris took first place in the Cleveland Orthopaedic Society Resident Essay Contest for his research titled, “Axial Small Molecular Inhibitor, R 428, Reduces Progression of in vitro Models of Osteosarcoma Micrometastasis”. He also received the third place award at the Mt. Sinai Barry Friedman Orthopaedic Resident Research Competition for his work entitled, “Idiopathic Cam Deformity is Not Associated with Conventionally Held Risk Factors for Femoroacetabular Impingement”. Drs. Cynthia Nguyen and Jeremy Gebhart also had their research selected for presentation.

At the 2015 annual meeting of the American Society for Surgery of the Hand, Dr. Mithun Neral had a poster exhibit selected for presentation. His poster was entitled, “Silicone Arthroplasty for Nonrheumatic Proximal Interphalangeal Joint Arthritis: Long Term Clinical Follow Up”. Dr. James C. Kyriakedes was recognized with one of the top 8 presentations at this meeting. His work entitled, “Distal Radius Fractures: Appropriate Use Criteria Versus Actual Management at a Level 1 Trauma Center. His co-authors were Eugene Tsai, MD, Douglas Weinberger, MD, Charles C. Yu, BS, Harry A. Hoyen, MD, Kevin J. Malone, MD, and Blaine T. Bafus, MD.

Dr. Joshua Napora won an award as one of Best Presentations at the International Limb Lengthening Research Society for his study entitled, “Taylor Spatial Frame Stacked Transport for Tibial Infected Nonunions with Bone Loss Analysis of Use of Adjuvant Stability”. Dr. Givenchy Manzano was invited to present his work on, “Salvage Treatment of Failed Surgical Fixation of Hip Fractures” at the American Academy of Orthopaedic Surgeons annual meeting. Dr. Christopher Collier received an AO Trauma of North America Resident Research Award of $10,000 to support his work on, “15-PGDH in Fracture Repair”. Sandra Costello, RN, Clinical Nurse Manager in our Department, authored the “Orthopaedic Care” chapter in the newest edition of Nursing Procedures Made Incredibly Easy! published by Wolters Kluver.

In August, we were notified that our alumni, Alexander J. Ghanayem, MD was selected as Professor and Chair of the Department of Orthopaedic Surgery and Rehabilitation at Loyola University’s Stritch School of Medicine. Dr. Ghanayem, who completed his orthopaedic residency here at Case Western Reserve University in 1994, and his spine fellowship at the University of Wisconsin Madison under another alumni, Dr. Thomas Zdeblick, has had a 20 year career in which he has established himself as an internationally known expert in spine surgery.

In total, over the last year, members of our Department published over 70 peer-reviewed manuscripts and they were invited to present their work on over 200 occasions at national and international meetings. This year’s chief residents who graduated in June, were another outstanding class. They are advancing to fellowships in their sub-specialty areas of choice and we welcome them into the Case Western Reserve / Charles H. Herndon Alumni Association and we wish them all the best in their future careers.

- Kelvin Lim, MD – Hand, University of California, San Francisco
- Stephen Reichard, MD – Foot & Ankle, Stanford University Medical Center
- Jonathan Streit, MD – Shoulder & Elbow, Florida Orthopaedic Institute
- Eugene Tsai, MD – Hand, Tufts
- Ke Xie, MD – Joint Replacement, Florida Orthopaedic Institute
- Ashraf Youssef, MD – Hand, The Cleveland Clinic Foundation

Once again, it has been a privilege to lead this fabulous orthopaedic department in its 109th year. This year’s report highlights the high-quality work that typifies the faculty, residents and staff of this outstanding Department.
AFTER 178 YEARS SINCE ITS FOUNDING AND ALSO 100 YEARS IN ITS CURRENT LOCATION, METROHEALTH IS UNDERGOING AS YET ANOTHER MAJOR "TRANSFORMATION". AGING BUILDINGS AND CHANGING DEMANDS HAVE PROMOTED THE NEED FOR A MAJOR RENOVATION OF THE CAMPUS. THE ULTIMATE LONG TERM GOAL OF A COMPLETELY NEW HOSPITAL WITH COMMUNITY BASED SATELLITES FOCUSED ON INCORPORATING THE NEIGHBORHOODS AND THE PATIENTS’ NEEDS IS SEVERAL YEARS AWAY. THE FIRST PHASE WHICH INCLUDES THE ADDITION OF TWO NEW FLOORS TO THE CRITICAL CARE PAVILION WITH 90 NEW STATE OF THE ART INTENSIVE CARE BEDS IS ON TRACK TO BE COMPLETED THIS COMING JUNE IN TIME FOR THE RNC. WORK ON THE NEW SATELLITE FACILITY IN THE BRECKSVILLE AREA IS ALSO NEAR COMPLETION AND FREE STANDING FULL SERVICE EMERGENCY ROOMS IN CLEVELAND HEIGHTS AND PARMA ARE ALREADY OPEN.

The Department of Orthopaedics at MetroHealth continues to grow and remains highly successful. In the past year we’ve added three new faculty. Jonathan Belding MD, one of our prior residents who completed a spine fellowship at the University of Utah has joined faculty to be part of our orthopaedic spine service. He is truly welcomed by Tim Moore MD who has worked extremely hard over the past years single-handedly running an exceptionally busy spine service, teaching residents and fellows, and doing research. James Learned MD, another prior resident of ours, joined our Orthopaedic Trauma Service after first doing a trauma fellowship at Harborview Medical Center and then an additional pelvic and acetabular reconstructive fellowship with Dr. Keith Mayo at the University of Washington. With the recent loss of John Sontich MD and Kevin Malone MD to University Hospitals’ new trauma service, James and Ari Levine MD stepped in and became exceptionally busy maintaining our trauma service. James is also working with Roger Wilber MD developing the Pelvic and Acetabular Reconstruction service and Ari is expanding his arthroplasty practice. After several years of search in conjunction with Dr. George Thompson at Rainbow Babies & Childrens’ (RB&C) Hospital, we were able to hire a new pediatric orthopaedic surgeon to be based at MetroHealth. R. Justin Mistovich MD who did a pediatric orthopaedic fellowship at Children’s Hospitals of Philadelphia (CHOP) is now helping provide pediatric orthopaedic care at MHMC along with continued help from Drs. Ray Liu and Christine Hardesty. He has a special interest in children’s fractures and sports medicine.
The Orthopaedic Trauma Service remains extremely busy and productive. In addition to our new young faculty including Drs. Ari Levine and James Learned who have added new energy, enthusiasm, and ideas, our senior faculty remain highly involved and productive. Brendan Patterson MD, in addition a busy trauma and reconstructive practice, has taken on new administrative responsibilities as the clinical head of the Medical Specialties Service Line in addition to his role as CFO for the OTA. Dr. Roger Wilber, Chief of Pelvic and Acetabular Injuries and Reconstruction, continues to expand our treatment for complex injuries and problems of this region. In addition, as the Chairperson of AOTrauma North America Education Committee, he has made a significant impact both nationally and internationally on trauma education. Heather Vallier MD, the Chief of Orthopaedic Research and the Clyde Nash Professor of Orthopaedic Research & Education, mixes a busy trauma practice with an exceptionally productive clinical research group. She represented MetroHealth with over ten papers, presentations, and posters at this past year’s Orthopaedic Trauma Association Annual Meeting in addition to being on the board of the OTA.

Our Hand and Upper Extremity Service under the direction of Harry Hoyen MD remains exceptionally busy, taking care of the majority of the complex hand and upper extremity injuries and referrals throughout northeastern Ohio. Harry also travels extensively to teach both national and internationally for the AO. Todd Bafus MD remains busy with his split practice between MetroHealth Medical Center and the VA Medical Center. In addition to taking care of hand trauma, he continues to develop a large shoulder practice. Michael Keith MD still has an active clinical practice but also works extensively with the AAOS developing clinical guidelines and has also increased his research time with the FES program. He has also recently received a joint appointment with the Department of Physical Medicine & Rehabilitation.

Our research activities continue to grow and have been highly productive under the direction of Hunter Peckham PhD. Our FES program has had another highly successful year. With the very active clinical involvement of both Drs. Harry Hoyen and Michael Keith, the first fully implantable neurocontrol system was performed this past year. Dr. Ron Triolo PhD and his group have made significant advances applying a neuroprosthesis for standing balance and trunk control. With the development of the new NeuroMusculoskeletal Service Line with Dr. John Chae as Director, the close association between the Department of Physical Medicine & Rehabilitation, the FES group, the Department of Neurosciences and the Department of Orthopaedics have become even closer. We certainly anticipate that this relationship will lead to even greater advances in the near future.

Our fellowship programs at MetroHealth Medical Center continue to attract and train the very brightest and talented from around the country. This year’s orthopaedic trauma fellow, Dr. Mai Nguyen, came to us from a residency at the University of Iowa and is an integral part of our trauma program. Our rotating hand and upper extremity fellows include Dr. Ashraf Youssef from Case Western Reserve, Dr. Simon Amsdell from University of Rochester, and Dr. Sergio Glait from NYU Medical Center. Our rotating spine fellows include: Colin Haines MD, George Washington University, Assem Sultan MD, Tanta University, Egypt, Elizabeth Bennett MD, Medical College of Wisconsin, Timothy Roberts MD, Albany Medical College, and Kevin Walsh MD, Cleveland Clinic Foundation. We are extremely fortunate to have all of these fellows who are active at all levels of our department including clinical, research, and education and help further expand our network of surgeons throughout the country.

I personally feel extremely privileged and fortunate to be in my current position at this point of my career and to have such an exceptional group of faculty, fellows, residents, and researchers working toward the combined success of our Department, the MetroHealth Medical Center, Case Western Reserve Medical School, and most importantly for the improved health and safety of our patients from Northeastern Ohio. These are very rapidly changing and challenging times but we are well positioned to take on these challenges and prepare the future generations of Orthopedic surgeons.
The orthopaedic surgery section at the Cleveland Veterans Affairs Medical Center (VAMC) has gone through a time of change and transition as we have adjusted our operations to comply with unprecedented clinical, educational, and administrative requirements in patient care. At the same time we have continued to provide excellent orthopaedic care and academic training. As part of this transition we welcomed key new members to the section of orthopaedic surgery and anticipate additional personnel changes in the coming years.

This year I am happy to welcome a new full time faculty member to the staff: John Wood MD (sports medicine and knee surgery). Dr. Wood is a graduate of the University Of Ottawa School Of Medicine. He then completed orthopaedic residency at the University of Western Ontario and completed fellowships in sports medicine at the University of Western Ontario and the University of Rochester. Dr. Wood brings over 21 years of experience as an orthopaedic surgeon as well as senior operations and leadership capability from years of successful practice at the Kaiser and Health Span practices in Cleveland.

I am proud of the contribution provided by our established faculty including Thomas McLaughlin MD (sports medicine, arthroscopy), Patrick Getty MD (orthopaedic oncology), Byron Marsolais MD (orthopaedics and rehabilitation) and Randall Marcus MD (adult reconstruction, foot & ankle) and Mike Vento MD (general orthopaedics). The upper extremity group consisting of: J “Rob” Anderson MD (Hand & Upper Extremity), Blaine “Todd” Bafus MD (upper extremity), Robert Gillespie MD (shoulder & elbow), and Kevin Malone MD (hand surgery) deserves significant recognition for comprehensive expertise ranging from the fingertips to the shoulder. I am pleased to announce that Dr. Bafus will become the director of upper extremity surgery at the Louis Stokes Veterans Affairs Medical Center. His leadership as a surgeon and veteran will enhance coordination of care and patient relations.

We are grateful for ongoing clinical support from our two physician assistants: Greg Field PA-C and Terry Bauer PA-C. This year we are pleased to welcome Susie Ivanov PA-C as a 3rd physician assistant. Susie is a graduate of the Cleveland State University/Tri-C physician assistant program. She holds a BS from the University of Cincinnati in medical imaging and was the recipient of the 2013 Ohio Association of Physician Assistants Past-Presidents Leadership Scholarship. We welcomed Tiffany Chatmon RN MSN who brings 10 years of nursing experience to our group. She has assumed the role of coordinator for adult reconstruction and total joints. Carliss Towns RN-MSN has continued to foster efficiency and patient relations in the specialties of sports medicine and upper extremity surgery. I am happy to announce the promotion of Carliss Towns to full Colonel in the US Army Reserves where she serves as the chief nurse for the 256th combat support hospital.
Professor **Ronald Triolo PhD** guided the Advanced Platform Technology (APT) Center of Excellence and Rehabilitation Research & Development Service of the Department of Veterans Affairs through successful renewal of funding for an additional five year term. The Center focuses primarily in three areas: Prosthetics and Orthotics, Health Monitoring and Maintenance, Neural Interfacing and Emerging/Enabling Technologies. For example, **Umut Gurkan PhD** and **Glenn Wera MD** completed a pilot translational research study on synovial fluid health utilizing a biochip. In Prosthetics and Orthotics, Dr. Triolo’s team collaborates with Mechanical and Aerospace Engineering at Case Western Reserve University in order to refine a prototype robotic exoskeleton that facilitates standing, walking and stair ascent/descent for paralysis. **Michael Keith MD**, **Rob Anderson MD**, and **Dustin Tyler PhD** have also succeeded in restoring natural sensation of touch to upper limb amputees by activating sensory fibers of the radial, median and ulnar nerves with implanted multi-contact electrodes developed by the APT Center. Similarly, they have collaborated with **Harry Hoyen MD** to develop implanted neural prostheses that automatically control seated posture and balance after paralysis by activating the otherwise paralyzed hip and paraspinal muscles. In related work at the Motion Study Laboratory, research on the value of implanted neuroprostheses to improve walking in persons with incomplete spinal cord injuries, stroke, or multiple sclerosis is under investigation. I am pleased to recognize **Kath Bogie DPhil** as a leading researcher in wound prevention and treatment in paralyzed individuals. She was recently awarded an $839,000 grant entitled: “Personalized Pressure Ulcer Care Planning: Development of a Bioinformatics System for Individualized Prioritization of Clinical Practice Guidelines.”

This year the section fondly and respectfully bid farewell to **John Makley MD** (orthopaedic oncology) who staffed a large number of outpatient consults and non-operative care. We wish him good health as he fully retired from the practice of orthopaedics at LSVAMC. I would also like to acknowledge **Victor M Goldberg MD** who passed away unexpectedly over 1 year ago. His contribution of scientific knowledge and clinical expertise will be transmitted through the practice of arthroplasty at this facility indefinitely. We also wanted to acknowledge the hard work of Barb Dennstedt RN-BSN who is now in the section of general surgery. I want to give my personal support and thanks to **Brian Cmolik MD** for his strong unwavering support of veterans orthopaedic care during his tenure as Chief of Surgery.

The current Residency Training Program is divided into two rotations each with a PGY-5 chief resident and PGY-3 resident. Their time is split roughly 50/50 between outpatient clinics and surgical services. In the 2014-15 academic year we performed 7608 outpatient clinic visits and 647 operative cases.
I am delighted that this issue of the COJ is dedicated to Dr. McLaughlin. Tom has always been extremely interested in research and often has great ideas for novel research directions.

Each year, two of our residents are selected as Allen Fellows, who join a research lab for a full-time, year-long, experience. The 2015-2016 Allen Fellows are Derrick Knapik, MD and Givenchy Manzano, MD. Derrick is working with Ray Liu, MD, on a variety of pediatric orthopaedics projects and with Mike Salata, MD and James Voss, MD, on sports medicine projects. Givenchy is working in my lab on projects related to aseptic loosening.

Since last year’s COJ, three talented trainees have joined the CWRU/NIH Musculoskeletal Training Grant. Kathryn Phillippi, DO and Edgardo Rivera-Delgado, PhD, are the new post-doctoral trainees. Kathryn is a Pediatric Rheumatology fellow working with Angela Robinson, MD. Edgardo is working on novel drug delivery systems with Horst von Recum, PhD, in the Biomedical Engineering Department. Greg Learn is the new pre-doctoral trainee. He is working on tendon repair scaffolds with Ozan Akkus, PhD in the Mechanical Engineering Department and is collaborating with Rob Gillespie, MD in our department. We are currently working on the renewal application for the training grant, which, if funded, will provide support for years 31-35 of the training program.

Finally, the CWRU Musculoskeletal Research Day was March 30, 2016. It featured a spectacular talk by Cindy Farach-Carson, PhD our visiting professor from Rice University, as well as outstanding oral and poster presentations by trainees from many of the musculoskeletal research labs at CWRU.
1st Row: Givenchy Manzano, Christina Cheng, Lamere Wang, Evan Dougherty, Eugene Tsai, Ke Li, Stephen Reichard, John Wilber, Randall Marcus, Glenn Wera, Kelvin Lim, Jonathan Streit, Ashraf Youssef, Mark Dwyer, Christina Hardesty, Andrew Chen.

2nd Row: Andrew Tsai, Cynthia Nguyen, Jonathan Copp, James Voos, Derrick Knapik, Leigh-Anne Tu, Christopher Bechtel, Claire Shannon, Sheeba Joseph, Steven Fitzgerald, Thomas McLaughlin, Brian Victoroff, Christopher Flanagan, Mark LaBelle, Harry Hoyen.

3rd Row: Zachary Gordon, Mithun Neral, Michael Reich, Dwight Davy, Raymond Liu, John Shaffer, Patrick Getty, Kevin Malone, James Learned, Nicholas Ahn, Alexander Rascoe, Daniel Quinones, Joshua Napora, Ryan Li.

Trout Club

Will Morris, Chris Collier, Ryan Li, Jamie Kyriakedes, Jeremy Gebhart, Josh Napora and Todd Morrison enjoying the evening’s festivities.

Dr. Ahn uploads another epic presentation while Derrick ensures there aren’t any drinks near the computer.

Hook, Line and Sinker!! Dr. McLaughlin entertains Derrick with a brief story about the evolution of Sports Medicine.
Annual Intern Picnic

Jon and Mark share a friendly embrace during the annual Intern Picnic.

Derrick and Will pose before doing some serious grilling.

Two of our new spine attendings (Drs. Zachary Gordon and Jonathan Belding) discuss interesting cases over an ice cold beverage.

Our gracious host for this year’s event (Dr. Feighan) smiles for the camera with Alex Rascoe and Dr. Learned.

Derrick and Will pose before doing some serious grilling.

New interns Joanne Wang and Adam Schell become fast friends while enjoying Case’s legendary broccoli salad.
METROHEALTH ATTENDINGS

Todd Bafus
Jonathan Belding
John Feighan
Christina Hardesty
Harry Hoyen

Michael Keith
James Learned
Ari Levine
Raymond Liu
Justin Mistovich

Tim Moore
Brendan Patterson
Heather Vallier
John Wilber
Roger Wilber
FACULTY AND RESIDENTS

VAMC ATTENDINGS

Robert Anderson
Todd Bafus
Patrick Getty
Robert Gillespie

Harry Hoyen
Michael Keith
John Makley
Kevin Malone

Randall Marcus
Thomas McLaughlin
BASIC SCIENCE FACULTY

Ozan Akkus
Eben Alsberg
Kath Bogle
Dwight Davy
Edward Greenfield
Umut Gurkan
Shunichi Murakami
P. Hunter Peckham
Clare Rimnac
Ronald Triolo
Guang Zhou
CURRENT RESIDENTS

PGY-5 Residents

Christopher Bechtel, MD  
MD, New York University School of Medicine  
BS, University of Notre Dame

Michael Karns, MD  
MD, University of Cincinnati  
BS, University of Dayton

Cynthia Nguyen, MD  
MD, Baylor University  
BS, UCLA

Michael Reich, MD  
MD, Vanderbilt University School of Medicine  
BA, Washington University

Claire Shannon, MD  
MD, University of Rochester  
BS, University of Western Ontario

PGY-4 Residents

Andrew Chen, MD, MPH  
MD, University of North Carolina  
MPH, Johns Hopkins University  
BS, University of North Carolina

Christina Cheng, MD  
MD, SUNY Buffalo  
BS, Cornell University

Ronak Desai, MD  
MD, Rush University  
BS, Illinois Institute of Technology

Sheeba Joseph, MD  
MD, Case Western Reserve University  
BS, Case Western Reserve University

Sunny Patel, MD  
MD, Case Western Reserve University  
BA, University of Pennsylvania

Andrew Tsai, MD, MSc  
MD, University of Minnesota  
MSc, Carnegie Mellon University  
BS, Carnegie Mellon University
CURRENT RESIDENTS

PGY-3 Residents

Jeremy Gebhart, MD
MD, Case Western Reserve
University
BS, Slippery Rock University

James Kyriakedes, MD
MD, University of Cincinnati
BS, Miami University

Ryan Li, MD
MD, University of Pittsburgh
BA, Case Western Reserve University

William Morris, MD
MD, University of Texas, Southwestern Medical Center
BA, University of Southern California

Todd Morrison, MD
MD, Thomas Jefferson University – Jefferson Medical College
BS, Trinity College

Joshua Napora, MD
MD, Penn State University
BSE, Duke University

PGY-2 Residents

Christopher Collier, MD
MD, University of Chicago
BA, Miami University

Pete McCunniff, MD
MD, University of Iowa
BS, University of Iowa

Mithun Neral, MD
MD, University of Pittsburgh
BSE, University of Michigan

Daniel J. Quinones, MD
MD, Thomas Jefferson University-Jefferson Medical College
BS, University of South Florida

Leigh-Anne Tu, MD
MD, Thomas Jefferson University-Jefferson Medical College
BS, University of Pennsylvania

Douglas Weinberg, MD
MD, Tulane University
BA, Cornell University

Allen Fellows

Derrick M. Knapik, MD
MD, The Ohio State University
BA, University of California, Berkeley

Givenchy Manzano, MD
MD, University of California Irvine
BA, University of California Berkeley
PGY-1 Interns

Jonathan Copp, MD
MD, University of California – San Diego
BS, University of North Carolina

Christopher Flanagan, MD
MD, University of Chicago
BA, Vanderbilt University

Mark LaBelle, MD
MD, Northwestern University
BSe, Northwestern University

Alex Rascoe, MD
MD, Penn State University
BS, Bucknell University

Adam Schell, MD
MD, Emory University
BA, Boston University

Joanne Wang, MD
MD, Brown University
BA Brown University
GRANTS AND AWARDS FOR RESIDENTS

**Dr. Christopher Collier** received a $17,740 Orthopaedic Research and Education Foundation Resident Clinical Scientist Training Grant. The grant was awarded for his research in Osteogenic Sarcoma. Dr. Collier also received an AO Trauma of North America Resident Research Award of $10,000 to support his work on “15-PGDH in Fracture Repair”.

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**Dr. Joshua Napora** won an award as one of Best Presentations at the International Limb Lengthening Research Society for his study entitled, “Taylor Spatial Frame Stacked Transport for Tibial Infected Nonunions with Bone Loss Analysis of Use of Adjuvant Stability”.

**Dr. Christopher Bechtel** was nominated to attend the 2015 American Orthopaedics Association Resident Leadership Forum.

Congratulations to **Drs. Alex Rascoe** and **Christopher Flanagan** who have been awarded the Dudley P. Allen Fellowship for 2016-2015. Dr. Rascoe will work on implant loosening under the mentorship of Dr. Edward Greenfield. Dr. Flanagan will work on the induction of osteointegration using PEEK hydroxyapatite composite under the mentorship of Dr. Claire Rimnac.
Percutaneous, Intramedullary Screw Fixation of Unstable Distal Fibula Fractures: a minimally invasive technique.

Robert J. Wetzel MD, Jonathan Twu MD, Nickolas Garbis MD, and Anthony T. Sorkin MD

Abstract
Displaced fractures of the distal fibula are often seen in bi-malleolar and tri-malleolar ankle fractures, tibial shaft or tibial plafond fractures and can lead to post-traumatic arthritis and ankle instability if not properly reduced. While fracture reduction and fixation are usually achieved via open techniques with a plate and screws, this may lead to soft-tissue complications in poor hosts or in patients with skin at-risk. We believe that restoration of ankle mortise stability can be adequately achieved in a soft-tissue friendly manner with a simple, percutaneous 3.5mm intramedullary screw. A retrospective chart review yielded 72 distal fibula fractures treated with a single percutaneous intramedullary screw. Forty-seven were associated with rotational ankle fractures, nineteen with pilon fractures, and six with tibial shaft fractures. There were no deep infections. There was one (1.4%) superficial infection that was successfully treated with dressing changes and oral antibiotics. Radiographic union was achieved in all but one case (1.4%). We have made this technique our standard practice for patients with the potential for wound healing issues and have demonstrated reasonable results with no deep infections and only one case of nonunion. Economically, the IM fibular screw is roughly half as expensive a standard plate and screw construct.

Key words: Percutaneous; Intramedullary Screw; Fixation; Distal Fibula; Ankle Fractures

Background: Ankle fractures are commonly seen in orthopaedics with the bimalleolar type being the most common.1 Ankle fractures have a described incidence of about 187 per 100,0002 with an expected 3-fold incidence increase by 2030 in some areas.3 These injuries can present as an isolated low energy rotational injuries3, or with higher energy injuries such as pilon fractures or tibial shaft fractures.4,5 Restoration of the ankle mortise is crucial in these fractures, and a slight malreduction can lead to changes in ankle contact pressures and joint incongruity which may predispose patients to pain, instability, and post-traumatic arthritis.6 Reduction of the lateral malleolus is crucial as it has been shown to prevent talar translation and joint incongruity in fractured ankles.7,8 It is a commonly accepted tenet of periarticular fracture treatment that restoring anatomical relationships best prevents post-traumatic arthritis in the future9, and open reduction and internal fixation (ORIF) can allow for anatomic restoration of distal fibula fracture using direct visualization. We feel that ORIF should remain the gold standard for achieving an anatomic reduction, but certain clinical scenarios may preclude an open approach due to soft tissue concerns, whether they are due to the energy from the trauma itself or due to patient biology. Alternatively, percutaneous intramedullary (IM) fixation of distal fibula fractures has been previously described with soft-tissue concerns in mind.4,5,10-12

The senior author (ATS) has utilized a percutaneous IM screw technique of the lateral malleolus in his practice for many years in order to preserve the soft-tissue envelope and prevent deep infection. We hypothesized that this percutaneous technique can avoid soft tissue complications and deep infection while still obtaining near anatomic reduction of the distal fibula and ankle mortise and achieve radiographic union with minimal complications. Additionally, we feel that percutaneous fixation with a single 3.5mm solid screw has economic advantages over most standard fixation methods.

Patients and Methods
A retrospective, Institutional Review Board approved review of all distal fibula fractures seen in OTA/AO 44-A, 44-B, and 44-C injuries as well as distal fibula...
fractures associated with OTA/AO 42-A, 42-B, 42-C, 43-A, 43-B, and 43-C injuries was performed. Patients were isolated using a current procedural terminology (CPT) code search through billing data. This group included lateral malleolus fractures associated with low- and high-energy rotational ankle fractures, pilon fractures, and tibial shaft fractures across two institutions over an 8 years period. All patients were treated by a single surgeon (ATS) and received a percutaneously placed IM screw via our technique described below. Clinical follow-up data was analyzed and radiographs were analyzed for union and maintenance of reduction. Medical records were reviewed for return to the operating room and presence of a complication including deep infection, wound dehiscence, and hardware issues among others.

Surgical Indications: Many lateral malleolus fixation techniques, such as Rush rods, Steinmann pins, plate and screws, variable pitch screws, locking nails, and lag screws alone have been previously described in the literature. In our series, we utilized percutaneous fixation with a single 3.5mm screw if the soft tissue envelope was compromised or deemed at-risk. Our indications included patients with lateral malleolus fractures associated with rotational ankle, pilon, or tibial shaft fractures with a tenuous soft tissue envelope. This was apparent by the presence of fracture blisters, significant edema, deep contusion, or skin tenting. Other indications included patients in whom the avoidance of a larger incision is beneficial due poor healing potential, such as those with poor nutritional status, vasculopathy, diabetes mellitus, or other medical comorbidities that significantly effect wound healing. We also use this technique in osteoporotic patients where the quality of fixation with standard hardware can be difficult. Percutaneous fixation with a single solid screw may also have an economic indication in the current era of heightened awareness of the economic burdens in medicine. The use of a single screw as compared to an interlocked intramedullary nail, locking plate, or even a standard plate and screws construct is far less expensive.

Surgical Technique: The patient is positioned supine on a fully radiolucent or standard operating room table (surgeon preference). The limb is prepped and draped in the usual sterile fashion. If additional approaches or incisions are to be made, a nonsterile pneumatic tourniquet can be placed on the proximal thigh out of the operative field if desired, however we do not routinely use a tourniquet if the entirety of the procedure will be percutaneous. Image intensification is brought in from the contralateral side. Appropriate anteroposterior (AP), mortise and lateral views are obtained paying close attention to the medial clear space and overall fibular displacement on multiple views.

The fracture is initially manipulated closed, and is often able to be reduced with gentle traction, inversion, and medially directed pressure over the lateral malleolus. Rotation of the ankle or pronation/supination of the foot may be helpful depending on the fracture type. Provisional reduction is held with finger pressure or with a small pointed reduction clamp and checked with fluoroscopy (figure 1). The small pointed clamp can be used to hold the reduction or even directly manipulate and reduce the fracture. It is applied to the fracture using percutaneous stab incisions, which cause minimal trauma to the surrounding soft tissues (figure 2). It should be noted that blunt dissection with a periosteal elevator or freer elevator should be utilized through the anterior stab incision to avoid potential injury to the superficial peroneal nerve. Alternatively, a slightly larger longitudinal incision can be made directly over the fracture site no longer than the width of the clamp. The clamp can be inserted longitudinally and then rotated 90 degrees so that both tines can be placed through the same incision.

Once satisfied with the reduction, a small stab incision is made 2-5mm distal to the tip of the lateral malleolus (figure 3). The incision should be just large enough to allow clearance for the drill guide and a 3.5mm screw head. A 2.5 mm drill bit with
guide, if needed, is placed just slightly medial to the tip of the lateral malleolus on the mortise view and at the exact tip (which is posterior) on the lateral view (figure 4). As with other intramedullary techniques, obtaining a proper starting point is an essential step, and time should be taken to ensure proper position prior to introducing the drill bit.

The cortex is carefully opened with a 2.5mm drill bit, aiming towards the anteromedial corner of the metaphysis. The drill bit should be advanced to but not passed the fracture site (figure 5), and often times well short of the fracture site in more proximal fractures. A self-tapping 3.5mm cortex screw will easily find the IM canal of the fibula when inserted. Particular care should be taken not to remove excess metaphyseal cancellous bone or to create an oblong cortical hole with the drill, especially in the osteoporotic patient. Clinical pictures of the setup can be seen in figure 6. A standard 3.5 mm fully threaded cortical screw, with lengths from 90mm to 130mm from a pelvic implant tray or an individually sterile wrapped screw, is normally used for final fixation. We routinely use a 130mm screw unless the fibular canal narrows significantly toward its proximal aspect, as it is the longest screw available in our implant set. The screw is inserted into the pilot hole slowly and steadily advanced under image intensification, aiming toward the anteromedial corner of the metaphysis (figure 7). Live fluoroscopy or rapid sequential shots should be utilized to ensure proper screw trajectory and ensure that no malreduction is introduced. The goal is to have the screw touch and “bounce off” the anteromedial metaphysis. Once contact is made, the screw will curve along the intramedullary canal of the fibula (figure 8) gaining purchase on the endosteum. Placement in this manner will help to hold the distal fragment in a well-reduced position when screw is inserted in its final position (figures 9 and 10). As the screw engages the endosteum of the diaphysis, the initial posterolateral to anteromedial trajectory will place a sustained anteromedially directed force on the fragment, preventing the typical lateral and posterior displacement of the initial injury.

If the screw is having difficulty directing up the medullary canal, it may be that the angle of insertion is too aggressive. If not adjusted, the tip of the screw can
Figure 2: Cancer stem cell (CSC) hypothesis model. CSCs divide into two cells: 1) an identical CSC which self-renews and maintains a pool of CSCs (white balls), and 2) a differentiated progenitor cell that continues to proliferate generating heterogeneous cancer cells comprising the bulk of the tumor (grey balls). (adapted from [40])

Figure 8.

Figure 9.

Figure 10.

Figure 11.
penetrate the medial or anterior fibular cortex. In our experience, we have found that the 3.5mm screws are usually flexible enough to conform to the canal of the fibula without difficulty. Larger screws are stiffer and have difficulty bending to an appropriate fit. We feel that the bend is crucial as it applies a dynamic reduction force on the fracture. Screws larger than 3.5mm are also usually too wide in diameter to easily fit in the narrow fibular diaphysis. It is critical to remember to hold the reduction with either a clamp or continual manual pressure until the screw is fully inserted. Care is taken to also look for rotational deformity as the screw is advanced. In right ankles, the tendency is to internally rotate the distal fragment of the fibula, and with left ankles, the tendency is to externally rotate the distal fragment. Keeping the fracture clamped during screw insertion helps to prevent rotational malreduction.

The screw is advanced until the screw head is just flush with the tip of the distal fibula. Screw insertion should be performed using a power screwdriver attachment with continuous screw advancement under slow and constant speed. If inserted with a stop and start technique, this could lead to the screw head shearing off (figure 11). This failure of the screw can also be seen when an extreme trajectory angle of the screw causes an exaggerated bend in the screw during insertion. We suspect this is due to the increased torque that is seen at the head-neck junction of the screw, as it has to overcome a significant amount of static friction force to begin turning again once it has already taken several bends in the canal. This is why we recommend live or rapid sequential fluoroscopic images during insertion to ensure proper depth of placement. If the screw breaks where the screw shaft meets the bone then you have two options. If the screw shaft has spanned the fracture then no further measures need to be taken. If the screw has not spanned the fracture, then abandoning this technique for standard ORIF is recommended. If the screw breaks before completion of insertion then we recommend extending your incision and trimming the prominent portion of the screw and then following the algorithm above depending on if the screw has spanned the fracture.

Results

We identified 72 distal fibula fractures in which IM screw fixation was utilized. The average age was 50 years old. There were 31 male patients and 41 female patients. Three patients were lost to follow-up. Forty-seven injuries were rotational lateral, bi- or tri-malleolar ankle fractures. Nineteen injuries were associated with tibial pilon fractures and six were associated with tibial shaft fractures. The average clinical follow-up time was 6 months (range 1.3–17 months). We recorded a total of 9 complications. These included one superficial infection that was successfully treated with oral antibiotics and local wound care (1.4%). There were no deep infections (0.0%). Two cases had to return to the operating room for secondary procedures (2.8%). One patient who had a high-energy pilon fracture developed post-traumatic arthritis and required a tibiotalar arthrodesis. The second patient had a symptomatic syndesmotic screw (pain over the screw head) that was removed. His fibular IM screw was removed at the same time, but it was not symptomatic. Neither of these secondary procedures was directly related to the IM screw technique. There was one case of nonunion (1.4%). This patient had a high-energy pilon fracture, and the fibular injury was a proximal, Weber C type, fracture with associated bone loss. The nonunion never required a secondary procedure or bone grafting and ultimately resulted in screw breakage at the nonunion site. After his screw broke, this patient’s most recent follow-up X-ray demonstrated abundant callous formation at the nonunion site and clinically he had been back to work with full weight-bearing without an assistive device. There were three cases (4.2%) of hardware issues. There was one case of screw cutout of the anterior fibular diaphysis during insertion. The second was a case of screw prominence from backing out 7mm into a sub-fibular position due to shortening of the fibula as the associated tibial shaft fracture also shortened. The third case had the screw head shear off during insertion. This happened prior to our avoiding the start-and-stop technique of putting in the screw. We subsequently have put the screw in on continuous live fluoroscopy on power and have not had any other cases of the screw head breakage.

This patient healed without any clinical consequence of the screw head breaking. Three cases (4.2%) had less than anatomic (>2mm) reduction of the distal fibula. The first case is the aforementioned case of the fibula shortening causing sub-fibular screw position. Another case was associated with a highly unstable rotational ankle fracture with poor bone quality that required a supplemental external fixator in an obese patient. The last case was associated with a high-energy pilon fracture that was treated with initial staged external fixation and definitive internal fixation. Of these three cases that exhibited malreduction of the distal fibula, none of them demonstrated lateral talar translation or malreduction of the ankle mortise.

We also analyzed the cost of IM screw fixation versus a 1/3 tubular plate and non-locking screw construct based on the pricing information available at our institution. Based on those costs, we found the single IM screw to be half as expensive as a tradition plate and screws construct. Additional alternative constructs such as proprietary IM interlocking fibular nails or locking plates...
are significantly more expensive than a standard plate and screws.

**Conclusions**

Displaced fractures of the distal fibula are seen in isolation, in bi-malleolar, and tri-malleolar ankle fractures, in pilon fractures, and associated with tibial shaft fractures. These injuries can lead to post-traumatic arthritis and ankle instability if not properly reduced. It is a well-accepted principle that unstable ankle injuries with displaced lateral malleolar fractures can be treated with surgical intervention to reduce subluxation or dislocation of the tibial talar joint and restore rotational stability. Many reduction and fixation techniques have been described including antiglide plates, non-locking and locking plates, interlocking nails, variable pitch screws, lag screws, and Knowles pins. IM fixation has also been described using Steinmann pins and Rush Rods, but some concern exists regarding hardware issues or delayed or nonunion.

Evans et al. describe a case series of 27 pilon fractures in which the lateral malleolus was treated with intramedullary fixation. Twenty of 27 were treated with an intramedullary screw and the remaining 7 were treated with a guide wire from a humeral nail in instances where the diameter of the fibular canal was too narrow for a screw. They describe their technique but lack some specifics regarding the starting point, the dynamic screw bend, as well as pearls and pitfalls when compared to our technique. They do address that they did not see any distraction of the fracture site due to the cancellous nature of the metaphyseal bone being less dense than the endosteal purchase of the fibular diaphysis. Their screw lengths were between 70-100mm, slightly shorter than the size of screws used in our series. Their series had minimum of 1-year follow-up, and they had no wound healing issues or delayed or nonunion.

In a case series of 23 patients, Stewart et al. described distal fibula fractures associated with tibial shaft and pilon fractures treated with a 3.5mm distally interlocked retrograde Ender nail (Smith & Nephew, Memphis, TN). The fibulae diaphyses in this series were opened with a 3.5mm drill bit along the entire length of the nail, which we feel may introduce an oblong entry hole in the distal metaphysis due to its size and rigidity of the large drillbit. Similar to Evans et al., this series also had a minimum follow-up of 1 year. They had no wound complications and one return to the operating room for symptomatic hardware directly related to a loose and prominent distal interlocking screw. In their series they had two tibial nonunions but no fibular nonunions.

Ray et al. have published a group of 24 cases that were treated with percutaneous IM screw fixation. Eighteen were rotational ankle fractures, two had associated pilon fractures, and four had associated tibial shaft fractures. They utilized a 4.2mm screw (Zimmer Warsaw, IN) between 2.5 in. (63.5mm) to 4 in. (101.6mm) in their series. Although they state that it was slightly flexible, we feel that a screw diameter larger than 3.5mm may be too stiff to take an adequate bend to apply the appropriate dynamic reduction force without causing cutout, cortical perforation, or malreduction. Good to fair radiographic reductions were obtained in 95.8% of cases. They had no deep infections but did have one superficial wound complication (4.3%) and had one nonunion, a 95.5% radiographic union rate. They obtained functional scores based on subjective levels of pain, range of motion, and return to pre-injury activity level in nineteen patients. They demonstrated 84.2% excellent or good results and 15.8% fair or poor functional results. Bankston et al. published one of the largest series of IM screw fixation in rotational ankle fractures, which was a group of 44 patients who underwent IM screw fixation. They concomitantly performed a biomechanical cadaveric study that compared resistance to torsion between the IM screw and a buttress plate and lag screw. The IM screw actually had a 5% higher resistance to torsion but the difference between the groups was not statistically significant. Their clinical complications consisted of one case of hardware prominence and one case of hardware failure.

Our current series of IM screw fixation is unique in that we have the largest case series to our knowledge in the literature. Our group contains not only lateral malleolar fractures associated with rotational ankle fractures but also those associated with pilon and tibial shaft fractures as well. We demonstrated no cases of deep infection with this technique and only one superficial wound complication, which is consistent with other reports. No secondary procedures occurred in our series that were directly related to the IM screw. We report a 1.4% nonunion rate, which is slightly improved compared to the 4.5% occurrence of nonunion reported by Ray et al. Our malreduction rate of 4.2% was the same as the 4.2% that Ray et al. reported to have a poor radiographic outcome. While Evans et al. and Stewart et al. both reported no cases of wound problems or nonunion, our series had 2.5-3 fold more patients. Our increased sample size may have allowed for a less biased complication rate. Additionally, we have demonstrated, without breaking vendor pricing contracts and listing specific dollar amounts, that the cost of a single 3.5mm IM screw 130mm in length is half as much as a 1/3 tubular plate and screws construct.

There are several limitations to our study. This is a case series from a single surgeon, which introduces inherent biases. Also, this study lacks validated clinical outcomes to correlate with the
radiographic outcomes. Furthermore, our clinical follow-up time is an average of 6 months whereas most similar studies have 1-year minimum follow-up. We do not routinely continue to see patients after radiographic union or the resolution of symptoms, and, because this study was retrospective, we did not expect to have long term clinical follow up times. Moreover, our follow-up times may have been less due to the majority of our patients having rotational ankle fractures, which typically tend to need less follow-up compared to a pilon or tibial shaft fracture.

We feel that IM fixation with a single solid screw is not only adequate for obtaining and maintaining reduction while remaining friendly to the surrounding soft tissues, but also may be the most cost efficient fixation option. Our results are consistent with many other publications in the literature. We do not propose that this technique replace the traditional open reduction and internal fixation, but rather hope that orthopaedic surgeons will consider using this technique in hosts at high-risk for soft tissue compromise.

References
Helical Cervical Spine CT is Sufficient to Exclude Cervical Spine Injury in Adult Blunt Trauma Patients

Augustine M Saiz Jr, MD1; Christina E Martin, BS1; Rishi Lall, MD1; Paul A Anderson, MD2; Daniel K Resnick, MD3; Lee D Faucher, MD1

1Department of Surgery, 2Department of Orthopedics and Rehabilitation, 3Department of Neurosurgery, University of Wisconsin School of Medicine and Public Health

Abstract

Introduction: Cervical spine clearance of adult blunt trauma patients poses difficulty due to the inability to assess symptoms. Most protocols suggest the addition of an MRI to a negative CT scan to rule out any injury. The purpose of this study was to identify whether CT alone was sufficient for cervical spinal clearance.

Methods: The records of all adult blunt trauma patients admitted to our Level 1 Trauma Center who underwent cervical spine CT from August 1, 2006 to December 31, 2009 were retrospectively analyzed. Patients with neurologic deficits on exam were excluded. Demographics, injuries, cervical CT results, mechanism of cervical spine clearance, cervical spine MRI results, and outcome data were collected and analyzed. Sensitivity, specificity, and negative predictive value were calculated.

Results: Of 2683 adult trauma patients with possible cervical spine injury who underwent a cervical spine CT, a total of 2101 (78.3%) patients had a negative CT scan and physical exam confirmed the CT results in 1901 of those patients. Of the remaining 200 patients, 195 patients had MRI confirm the results of the CT. MRI identified 5 patients (1.78%) that had a cervical spine abnormality missed by the initial CT; however, none of these injuries resulted in altered treatment or management. CT had a sensitivity of 94.19% (CI, 86.95, 98.09), a specificity of 100% (CI, 98.13, 100), an accuracy rate of 98.22% (CI, 95.90, 99.42), and a negative predictive value of 99.76%.

Conclusion: Our study supports that CT alone is sufficient to clear the cervical spine in adult blunt trauma patients. Additional MRI imaging is unnecessary. Individual institutions need to assess their capability and potential to apply this approach as it is user and machine dependent. Strength of this study is the institutional focus and size of population. Limitations include the retrospective design.

Introduction

The trauma surgeon faces a difficult challenge in optimal cervical spine management of the adult blunt trauma patient due to absence in protocol and guidelines for management of these patients. While cervical spine clearance in the alert, cooperative patient is well established under National Emergency X-Radiography Utilization Study (NEXUS) and Canadian C-spine Rule criteria, clearance has become more imaging based.1,2 Especially for patients who cannot cooperate with the clinical clearance process, early recognition of injuries remains critical in order to prevent or limit neurological damage and to increase the opportunity for reestablishment of function in the future.3 Guidelines are needed to ensure adequate and timely clearance.

Attempts have been made to produce a standard protocol. Both the Eastern Association for the Surgery of Trauma (EAST) and the American Association of Neurological Surgeons with the Congress of Neurological Surgeons (AANS/CNS) have put forth guidelines. The current standard recommended by EAST and AANS/CNS to Level 1 trauma centers for clearing the cervical spine in obtunded or intubated patients involves a primary screening with computed tomography (CT) imaging but what follows a negative CT is often left to the individualized discretion of the physician and/or institution.4,5 Options include removal of the cervical collar or adjuvant assessment, either via magnetic resonance imaging (MRI) or delaying clearance until a clinical examination can be reliably performed.4,5 This is where the question of clearance method stems.

Physicians and trauma centers struggle to achieve balance between prompt identification of injury and confirmation of absence of injury. On one hand, a missed diagnosis of a cervical spine injury carries possible consequences of neurological deterioration, paralysis, and death.6 On the other hand, the risks posed by prolonged cervical collar use includes increased intracranial pressure, skin ulcers, and respiratory deterioration; furthermore, MRI scanning poses its own risks of secondary brain injury due to
transport, increased intracranial pressure, and lack of ICU monitoring. Modern multi-slice helical CT has become the test of choice for primary screening of cervical spine injuries at many trauma centers because of its accuracy, cost-effectiveness, and efficiency. Yet, MRI has been declared in the literature as the gold standard for clearance of the cervical spine. This is due to the previously cited ability of CT to adequately delineate osseous injuries but its inadequacy in being able to exclude ligamentous and soft tissue injuries. With the literature at odds, the decision-making process remains difficult.

At the center of the decision and debate is whether CT alone is specific and sensitive enough to detect all significant cervical spine injuries and the risk-benefit ratio of obtaining an MRI. Our hypothesis is that current helical CT with 3D reconstruction provides enough information to allow for diagnosis of all unstable cervical spine injuries that require immobilization and that the MRI adds no additional information in adult trauma patients with normal cervical CT findings. We hypothesize that MRI of the cervical spine constitutes an unnecessary examination if the preliminary CT is negative. If this is the case, MRI use in this situation could be eliminated resulting in decreased patient risk, morbidity, and financial cost. Furthermore, cervical spine clearance based solely on the initial CT scan would expedite removal of cervical collars and thus decrease risks of cervical collar complications.

Patients and Methods

With institutional review board approval, we performed a retrospective review of a prospectively collected database. The data collected was from the University of Wisconsin Trauma Center at University of Wisconsin Hospital, an American College of Surgeons verified Level I Trauma Center that provides tertiary care for the metropolitan area of Madison as well as south central Wisconsin and parts of Illinois and Iowa. All adult blunt trauma patients admitted to the UW Trauma Center who underwent cervical spine CT from January 2006 to December 2009 were identified. During the time frame of the study, the Trauma Center admitted 7587 patients. Medical records of adult blunt trauma patients were retrospectively analyzed to determine gender, age, presenting Glasgow Coma Scale (GCS) score, and Injury Severity Score (ISS). Patients with neurologic deficit consistent with spinal cord injury were excluded from the study.

All adult blunt trauma patients underwent helical CT during their initial trauma evaluation in the emergency department. These patients were sorted into the following categories:

1. Whether or not they were cleared based on initial CT results,
2. Whether or not they received an MRI or fluoroscopy after the CT,
3. Whether or not they were diagnosed with a cervical spine injury based on CT results and/or MRI results,
4. Whether or not they were maintained in cervical spine precautions until able to be cleared by physical exam, and
5. Whether or not they were cleared by physical exam or MRI.

Specifically, the ability of CT to detect soft tissue injuries was analyzed within the injured patient population. Special focus was placed on the 281 patients who had an initial CT followed by an MRI and whether that MRI revealed an occult injury or simply agreed with the initial CT.

Cervical spine helical CT scans with 3-D reconstruction were acquired on a 64 detector-row helical CT scanner (Lightspeed™ VCT, GE Medical Systems, Waukesha, WI) in the emergency department. The cervical spine protocol required imaging from the base of the skull to the T2 vertebrae. Multiple thin section (1.25-2.5 mm) axial scans were obtained through the entire cervical spine from the magnum foramen to T2. The 1.25 mm axial images were used to perform multplanar 2-dimensional reconstructions in the sagittal and coronal planes for additional diagnostic evaluation. A CT was considered positive if there was a fracture, other bony malalignments, disc herniation, ligamentous injury, subdural or epidural hematoma, spinal cord contusion or edema, or other soft tissue injury.

Cervical spine MRI studies were performed using a HD Signa HDXT Twin Speed 1.5T (GE Medical Systems, Waukesha, WI). Three-plane localizer, sagittal T2 fat-sat, sagittal STIR, sagittal T1, axial T2 and axial T1 images of the cervical spine were obtained. MRI was considered positive if it met any of the aforementioned criteria. Additionally, the medical record search also analyzed whether any patient subsequently needed surgery or other therapeutic interventions related to their cervical spine injury. All radiographic images were read, interpreted, and received final impressions from attending radiologists at UW Hospital.
Statistics

Sensitivity, specificity, and accuracy were calculated in the normal methods with confidence intervals calculated using $F$ distribution method.

Results

Between January 2006 and December 2009, 7587 patients were admitted to UW Trauma Center and entered into the database. Of these, 2683 were adult trauma patients with possible cervical spine injury who underwent a cervical spine CT (Table 1 and Figure 1). There were 1907 men (71%) and 776 women (29%) with an age range of 18 years to 99 years (mean, 44.78 ± 18.8). 281 of these patients had a MRI performed in addition to the CT, with 201 being male (71%) and 80 being female (29%) with an age range from 18 years to 92 years old (mean, 44.1 ± 19.1).

Cervical spine CT was positive for bony or soft tissue injury in 582 patients (22%). Of those patients, 54 patients had soft tissue or ligament injury discovered by the CT and 26 of those patients had a follow-up MRI that confirmed the CT scan findings. The other 28 patients with soft tissue injuries identified on CT did not have a follow-up MRI and the CT was the definitive assessment. All of these patients were treated in accordance with the soft tissue or ligament injury identified. The CT was negative for any bony or soft tissue injury in 2101 patients (78%). All patients with negative CT (and MRI, if obtained) were considered cleared.

There were no adverse outcomes noted in review of their follow-up.

In the 281 patients undergoing both CT and MRI scans, MRI was positive for an abnormality in 86 patients (31%) and negative in the other 195 patients (69%), whereas, CT was positive for injury in 81 of the patients (29%) and negative in the other 200 patients (71%). Therefore, MRI identified 5 patients (2.5%) that had a cervical spine abnormality in the 200 patients that had negative CT scans.

Of the 5 missed injuries, cervical spine MRI did identify two unstable injuries that were missed by cervical spine CT on review. These two were cranio-cervical injuries were present on CT but were missed by radiology staff and subsequently diagnosed by MRI; however they were not diagnosed as unstable by MRI initially nor altered the treatment plan at the time. The three other cases had abnormal signal in the posterior ligaments (two at C1-2 and one mid cervical spine which were not thought to be significant) and the spines were deemed stable. These patients were maintained in rigid cervical collars and were scheduled for follow-up with orthopedic spine or neurology. None of these patients developed further cervical

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Age N Mean Std</th>
<th>Range</th>
<th>GCS N Mean Std</th>
<th>Range</th>
<th>ISS N Mean Std</th>
<th>Range</th>
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<tr>
<td>CT</td>
<td>2683 44.78 18.79</td>
<td>(18.0-99.8)</td>
<td>2683 13.17 4.05</td>
<td>(-5.0-15.0)</td>
<td>2654 15.48 11.08</td>
<td>(1.0-75.0)</td>
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<tr>
<td>MRI</td>
<td>281 44.05 19.27</td>
<td>(18.1-92.1)</td>
<td>281 11.02 5.21</td>
<td>(-5.0-15.0)</td>
<td>277 21.42 12.49</td>
<td>(1.0-54.0)</td>
</tr>
<tr>
<td>Negative CT and Positive MRI</td>
<td>5 52.60 32.05</td>
<td>(23.8-92.1)</td>
<td>5 10.40 4.67</td>
<td>(3.0-15.0)</td>
<td>5 20.2 17.06</td>
<td>(5.0-45.0)</td>
</tr>
</tbody>
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Table 1: Comparison of patient demographics stratified by those that received a CT scan, those that had an MRI, and those that had an injury detected by MRI that was missed by CT. Glasgow Coma Score (GSC). Injury Severity Score (ISS).

Figure 1: Patient diagnostics
In our study, none of the five missed injuries by CT were classified as unstable at the time of presentation or by MRI. The first missed injury was detected on MRI as a small amount of edema in the region of the apical ligament without subluxation and recorded not as a definite ligamentous injury but only that it could not be ruled out. The second missed injury was described as alar ligamentous injuries, C1-C2 posterior interspinous ligament high-signal, small amount of ventral foramen magnum venous epidural blood, pre-vertebral soft tissue swelling, and tiny superior right lateral mass C1 fracture. The third injury that was detected by MRI was interpreted as signs of extensive dorsal ligamentous and muscle soft tissue injury throughout the cervical spine, especially at C1-C2 and C2-C3 where there was evidence for focal interspinous tears. C6 and C6-C7 disk protrusions were also present. The fourth injury MRI uncovered was via high signal intensity of the posterior superior aspect of the C4, C5, and C6 spinous processes that were concerning for possible supraspinous ligament injury. There was also intermediate T2 signal intensity between the spinous processes that was possibly due to mild interspinous ligament injury. The last injury that was detected only by MRI was an interspinous ligament injury as unstable and based off of the CT and MRI findings identified the atlanto-occipital dislocation injury was simply missed on CT by radiology at the initial time of presentation.

During re-examination of the third injury, the CT showed mild atlanto-occipital dislocation with increased joint space between the occiput-C1 with subluxation of the occiput-C1 joint on the right. Re-examination of the MRI identified mild atlanto-occipital dislocation with increased joint space and fluid in the occiput-C1 joint and C1-C2 joint. Both the CT and MRI confirmed the injury as unstable and the treatment recommended due to either CT or MRI findings was surgery to correct the instability. This atlanto-occipital dislocation injury was simply missed on CT by radiology at the initial time of presentation.

In summary, re-examination of the five CTs found that two significant injuries and one mild injury that should have been identified initially were missed by radiology. Another CT was poor quality, but the edema identified on MRI was insignificant and did not change management. In the one that CT still did not find any abnormalities upon re-examination, the disruption between C1-C2 identified on MRI was stable and did not require treatment. In all cases, CT and MRI agreed on the degree of stability of the injury and the recommended treatments were the same based on either CT or MRI findings.

Overall, when analyzing the actual observations that were made, using MRI as the gold standard and comparing CT to MRI, cervical spine CT had a sensitivity of 0.9419 (CI, 0.8695, 0.9809), a specificity of 1.000 (CI, 0.9813, 1.000), and an accuracy rate of 0.9822 (CI, 0.9590, 0.99942). The cervical spine CT had a negative predictive value of 99.76 percent.

**Discussion**

Exclusion of cervical spine injury remains a significant challenge that still confronts all practitioners in an emergent setting. In awake, alert adult blunt trauma patients there exist clinical protocols for clearing the cervical spine, including simple clinical examination. However, no easy process exists for the trauma practitioner dealing with the obtunded adult blunt trauma patient, and furthermore, imaging has become almost universal in clearing the
cervical spine. Debate surrounds the decision regarding whether the cervical spine can be cleared by CT scan alone or if MRI is necessary for such clearance. Currently at our institution, the protocol for cervical spine clearance relies on MRI for final clearance. Another option is waiting for the patient’s mental status to sufficiently clear so that a reliable physical examination can be performed but this approach risks increased morbidity due to prolonged cervical collar use.

There are multiple facets and consequences related to clearance of the cervical spine. Missed or unrecognized cervical spine injuries can result in neurologic deterioration, paralysis and even death (Marshall et al. 2008). Furthermore, as reported by Lekovic et al, the cost of litigation for a missed cervical spine injury averaged $2.9 million regardless of the outcome. However, the cost of MRI is significant, with an average price of $2,986 at our institution. Additionally, transport to the MRI suite, incompatibility of monitoring equipment with the magnet, and long nature of the study results in nursing personal not being able to monitor the patient. Prolonged cervical collar use can result in skin ulcers and increased intracranial pressure among other morbidities. Therefore, the sooner the cervical spine of a patient can be safely and surely cleared, the better off the patient will be. Our data clearly demonstrates that the cervical spine can be cleared with CT alone with confidence.

As technology has advanced and CT imaging has improved with multidetector scanners, the need for MRI to confirm cervical spine clearance in adult blunt trauma patients has declined. As Stassen et al. in 2006 reported in a study of 52 obtunded adult patients, 25% had a negative CT but a positive MRI for cervical spine ligamentous injury. As such, the study concluded that the use of CT alone for cervical spine injuries was unacceptable as it missed a statistically significant number of cervical spine injuries, using in their study a General Electric CTI Helical scanner (GE Medical Systems, Waukesha, WI). In 2007, Como et al. examining 152 patients at his home institution using a Phillips Brilliance Power 16 multislice detector scanner (Phillips Medical Systems, Best, The Netherlands) stated that MRI may be unnecessary in a negative CT scan population as only 5.2% of patients had an injury subsequently seen by MRI. Similarly to our own findings, none of these patients required new interventions or surgeries, and furthermore, eliminating MRI scans would have decreased health care costs by a quarter of a million dollars at that institution. Three other smaller studies done around the same time also concluded that CT can be used as the initial screening method required for cervical spine clearance; however, two of them only compared the CT to cervical radiographs and not MRI. CT has also been shown to be cost-effective in the trauma setting.

In 2008, Tomycz et al. reviewed 180 obtunded adult blunt trauma patients undergoing both CT and MRI and found that MRI identified 21.1% of patients with acute traumatic findings not seen by the initial CT, yet again none of these patients required surgery or developed delayed instability. Using a 4-slice GE Lightspeed Plus CT scanner (General Electric, Milwaukee, WI) they concluded that MRI was unlikely to uncover an unstable cervical spine injury in this patient population after a negative CT. In a study by Steigelman et al. using multiple different CT scanners, they found that MRI in patients with a normal CT scan did not alter treatment. They examined 122 patients, 7 of whom had an injury discovered by MRI. No operative intervention was performed despite findings on MRI. Interestingly, they also reported that MRI use had climbed from 1% of obtunded patients in 2002 to 18% in 2006. This suggests that perhaps defensive medicine has become the main factor in the ordering of MRI even after a negative CT scan.

In a 2010 meta-analysis by Schoenfeld et al., 1550 patients with a negative CT were reviewed. In this group, 182 (12%) had an injury detected by MRI. Altered treatment was received in 96 patients, including need for operative intervention in 12 patients. The authors concluded that CT imaging alone cannot clear the cervical spine and that the use of MRI in cervical spine clearance is supported. However, the study was done over the time period of 2000-2008 and helical scanning and MDCT, more modern techniques that significantly change CT quality, were not described in the manuscript. Menaker et al. in the same year using a 40-slice Philips Brilliance CT scanner (Philips Medical Systems, Cleveland, OH) also concluded that MRI continues to be necessary for cervical spine clearance as it changed clinical practice in 17.8% of 213 adult blunt trauma patients. The study calls into question whether newer CT technology is adequate for cervical spine clearance solely. Additionally, the American College of Radiology (ACR) recommends that MRI be used to evaluate the cervical spine in patients whose neurologic status cannot be fully described in 48 hours, even among patients who had a negative CT. Como et al. in 2011, using a Philips Brilliance Power 16 or Philips Brilliance Power 64 multislice detector, similar to the one used in our study, concluded in a prospective study that if CT is negative for cervical spine injury then the patient is safe to be cleared without needing a supplemental MRI. Soult et al. in 2012 came to a similar conclusion after reviewing 190 adult blunt trauma...
patients, 24 of whom were obtunded, and MRI finding that 20% of the obtunded subset had a ligamentous injury not seen on CT but none had cervical spine instability nor required surgery. In 2011 Panczykowski in a meta-analysis of 14,327 obtunded adult trauma patients determined that cervical CT had both a sensitivity and specificity greater than 99.9% and a negative predictive value of 100% and therefore concluded that modern CT alone is sufficient to clear the cervical spine in this patient population and adjuvant imaging is unnecessary. It should be noted that these results are similar to the results found in our own study albeit in a smaller population. It was further concluded that the incidence of an unstable cervical spine injury among a negative modern CT approximates to 1 patient every 14 years in the typical US Level I trauma center whereas 325 to 3200 patients would sustain a complication from prolonged cervical collar use in the same time period.

A major weakness of the CT has historically been identification of soft tissue injury. As Tins and Casser-Pullicino state in a report in 2007, the strength of CT is imaging of bony injuries as it does not assess stability and soft tissue trauma is poorly visualized. In our study, we report that CT determined 54 soft tissue injuries and, of those that later received a MRI, 100% reported the same soft tissue injury. As CT technology advances with more and more slices, visualization becomes improved allowing delineation of not only osseous injuries but soft tissue injuries as well.

Our study correlates significantly with previous literature regarding cervical spine clearance based solely on CT. The two studies that suggest that MRI is necessary in addition to CT were done at institutions using less modern CT imaging technology than that used in our study. In this study, MRI provided no clinically relevant information. MRI served only to increase healthcare costs, expose the patient to potential risks, and delay cervical spine clearance. Moreover, as Muchow et al mention in their 2008 study, MRI has poor specificity with many false positives. One potential cause in recumbent patients is that extracellular fluid will layer in the posterior neck which will be seen as increased signal on T2 MRI or STIR sequences. In our patient population, CT was able to correctly identify injuries, including soft tissue injuries, while having a negative predictive value of over 99 percent.

The main problem with CT imaging is inaccurate reading by radiologists which occurred in two of our cases. Our results should be limited to institutions with the same 64-slice CT technology. The quality of a CT image will only be as good as the CT scanner, but more importantly, the value of the CT image will only be as good as the interpretation and the confidence in that interpretation.

Our study explicitly supports the stance that modern CT alone is sufficient to adequately clear the cervical spine in obtunded adult trauma patients. MRI is therefore unnecessary for cervical clearance in obtunded patients with negative CT imaging and actually poses more risks than benefits. Modern CT imaging is the most effective method of cervical spine clearance for adult blunt trauma patients. The current study also presents clear evidence that the cervical collar may be safely and immediately removed following a negative CT scan for acute cervical spine injury. Most importantly, though, this study turns attention to discrepancies across institutions related to cervical spine clearance. Different institutions with different radiologists and equipment will inherently have different capacities to determine cervical spine clearance based solely on a CT. Therefore, we advise all institutions to assess their own capabilities to determine if they are able to clear the cervical spine with CT alone, as our study has for the University of Wisconsin.

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Characterization of Ossification of the Posterior Rim of Acetabulum in the Developing Hip and Its Impact on the Assessment of Femoroacetabular Impingement

William Z. Morris, MD, Jason Y. Chen, AB, Daniel R. Cooperman, MD, and Raymond W. Liu, MD

Investigation performed at Rainbow Babies & Children’s Hospital and Case Western Reserve University, Cleveland, Ohio

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Abstract

Background: Many radiographic indices that are used to assess adolescents for femoroacetabular impingement rely on an ossified posterior acetabular wall. A recent study identified a secondary ossification center in the posterior rim of the acetabulum, the ossification of which may affect perceived acetabular coverage. The purpose of this study was to characterize ossification of the posterior rim of the acetabulum with use of a longitudinal radiographic study and quantify its impact on the radiographic assessment of femoroacetabular impingement.

Methods: In this study, we utilized a historical collection of annual radiographs made in a population of healthy adolescents. Six hundred and twelve anteroposterior radiographs of the left hip of ninety-eight patients were reviewed to identify the appearance, duration, and fusion of the secondary ossification center in the posterior rim of the acetabulum. The center-edge angle was then measured before appearance and after fusion of the secondary ossification center in a subset of ten patients with <5° of rotation on all radiographs.

Results: The secondary ossification center in the posterior rim was identified in seventy-three of the ninety-eight subjects, with no significant difference between the sexes. The mean patient age at the time of radiographic appearance of this secondary ossification center was fourteen years for males and twelve years for females. The mean duration of radiographic appearance was ten months for both sexes. Serial center-edge angles were measured in a subset of ten patients, and they increased during posterior rim ossification by a mean of 4.1°.

Conclusions: The secondary ossification center in the posterior rim of the acetabulum (the posterior rim sign) is a common radiographic finding that reliably appears for ten months around the time of triradiate closure. Posterior rim ossification led to a mean increase of 4° of perceived acetabular coverage through the center-edge angle. Given the narrow margin between normal coverage (33° to 36°) and acetabular overcoverage (>40°), the use of radiographs in adolescents with incompletely ossified hips may lead to misinterpretation of acetabular coverage. In patients with open triradiate cartilage, magnetic resonance imaging may be considered for the assessment of femoroacetabular impingement.

Clinical Relevance: The posterior rim ossification sign is a normal finding in adolescent hip development and has important implications for the proper evaluation of femoroacetabular impingement.

Introduction

Femoroacetabular impingement is an increasingly recognized cause of hip pain in adolescents and young adults, and it may be a causative factor in early osteoarthritis of the hip. With growing focus on diagnosis and early management of femoroacetabular impingement, it becomes critical to understand all aspects of the development of the hip and the final ossification of the acetabulum. Ponseti characterized the gross and histological development of the triradiate cartilage in the developing hip. Subsequent authors have characterized the radiographic development of the acetabulum, but there has been limited information centered on the development of the posterior wall of the acetabulum. Characterization of the development of the posterior rim of the acetabulum is critical, as many radiographic indices for evaluating femoroacetabular impingement (crossover sign, center-edge angle, and posterior wall sign) rely on complete ossification of the posterior wall of the acetabulum for accurate assessment.

Ossification of the acetabulum depends in part on the development of secondary...
ossification centers within the triradiate cartilage. Early studies by Ponseti and Wiberg identified ossa acetabuli in the anterior and posterior rims of the acetabulum. Ponseti described what he termed an *acetabular epiphysis* in the superior rim of the acetabulum in the cadaveric specimen of a single fourteen-year old boy. Wiberg noted the presence of anterior and posterior ossa acetabuli in twenty-three hips of children between one and seventeen years old. Although these studies identified the presence of ossa acetabuli, the power of their conclusions was limited by the small number identified and the use of radiographs. The most exhaustive investigation of secondary acetabular ossification that we are aware of was presented in a recent study by Fabricant et al. The authors utilized magnetic resonance images (MRIs) and limited corresponding radiographs to evaluate the ossification of the posterior wall of the acetabulum. They noted a radiographic sign that corresponded to a secondary ossification center in the posterior rim of the acetabulum termed the *posterior rim sign* (Fig. 1). The use of three-dimensional imaging in each of their patients allowed them to definitively identify this ossification center (which resembled those radiographically by Ponseti and Wiberg) as located in the posterior rim of the acetabulum. While this study provided a valuable characterization of the development of the posterior wall on MRIs, the imaging studies (radiographs and MRIs) appeared to capture only one moment in time for each patient rather than the ongoing development of each individual patient.

The purpose of this study was to characterize the ossification of the posterior rim of the acetabulum and the posterior rim sign as seen on radiographs through the use of a longitudinal study on a large sample of healthy adolescents as well as to quantify the effect of this ossification on perceived femoroacetabular impingement through measurements of the center-edge angle.

**Materials and Methods**

The Brush inquiry is a collection of radiographs made annually in a longitudinal study of more than 4400 healthy children and adolescents from 1926 to 1942. The study population included children and adolescents from the Greater Cleveland (Ohio) area who had received approval from family physicians and/or been selected for enrollment through “health contests” at local schools. The purpose of these events was to confirm that the children participating in the study were free from disease and deformity. Anteroposterior radiographs of the left hip were retrieved for 150 subjects of the study who had attended at least four follow-up visits. Subjects were excluded from the current study if any of the consecutive images were damaged or distorted. Ninety-eight of these subjects (forty-four females and fifty-four males) were included in our study, as they had at least four consecutive annual radiographs and documented closure of the triradiate cartilage. In total, 612 images in ninety-eight patients were evaluated. These consecutive annual images were assessed for the appearance, duration, and fusion of the secondary ossification center in the posterior rim of the acetabulum (Fig. 2). The timing of closure of the triradiate cartilage in relation to the posterior rim of the acetabulum was also documented. Closure of the triradiate cartilage was evaluated according to the Oxford bone age score. An Oxford bone age score of 2 corresponds with the first sign of osseous invasion of the triradiate cartilage and some loss of radiolucency on the radiograph, and an Oxford bone age score of 3 corresponds with total ossification of the triradiate cartilage and complete loss of radiolucency on the radiograph. Three subjects were excluded from this assessment because limited contrast quality of their images near the triradiate cartilage precluded accurate scoring. All images were reviewed by a single author (W.Z.M.). Images associated with any uncertainty regarding the presence of the ossification center or the exact Oxford bone age score were also reviewed by the senior author (R.W.L.).

We hypothesized that, given the location of the secondary ossification centers near the lateral edge of the sourcil, the amount of perceived acetabular coverage on radiographs would increase during ossification of the posterior rim. To quantify this change in coverage, we measured the change in center-edge angle before appearance and after fusion of the secondary ossification center (Fig. 3). We identified all subjects within the
sample population in whom a secondary ossification center was visualized. Their radiographs were then rescreened to identify a subpopulation for whom images were available before appearance and after fusion of the secondary ossification center. Because rotation has been shown to affect coxometric indices\textsuperscript{13,14}, images were screened to identify the ones with <5° of pelvic rotation in order to minimize distortion of the center-edge angle measurements. Rotation was determined by measuring the sacrococcygeal joint-pubic symphysis distance, which was standardized with a marker on each image for scale. The literature has shown that a sacrococcygeal joint-pubic symphysis distance of 1 cm corresponds to approximately 5° of pelvic rotation\textsuperscript{13,15} and that rotation of >4° may affect coxometric indices\textsuperscript{16}. Consequently, a sacrococcygeal joint-pubic symphysis distance of <1 cm was used as the cutoff for inclusion in the current study. The center-edge angle was then calculated for each specimen with use of the radiograph made immediately before the appearance of the secondary ossification center and the image made at the time of fusion of the secondary ossification center. The center-edge angle was measured through modification of the original technique as described by Wiberg\textsuperscript{9}. The center-edge angle was then formed by a vertical line through the center of the femoral head and a line from the center of the femoral head to the lateral edge of the sourcil. To account for any pelvic obliquity during imaging, the vertical reference line used for the center-edge angle was drawn in a standardized fashion, perpendicular to a line drawn tangent to the roofs of the first sacral foramina.

**Statistics**
The age of the subjects at the time of appearance of the secondary ossification center and the duration of the secondary ossification center were compared between the sexes with use of the Student t test. The comparison of the rate of appearance of the secondary ossification center by sex was performed with use of a chi-square test. The center-edge angles were analyzed with a paired samples t test to compare the center-edge angle values before and after appearance and closure of the secondary ossification center in the posterior rim of the acetabulum. The center-edge angle of all images was initially measured by a single author (J.Y.C.). The angle was then remeasured by the same author as well as a different author (W.Z.M.) on twenty images. The intraclass correlation coefficient for intraobserver and interobserver reliability was calculated. The values were then interpreted as follows: <0.40 was considered poor, 0.40 to 0.59 was considered fair, 0.60 to 0.74 was considered good, and >0.74 was considered excellent\textsuperscript{16,17}. The mean duration of the posterior rim...
sign was determined by analyzing the presence and duration of the sign as a Poisson distribution. This probability mass function allows for analysis of the mean of an event occurring within a discrete time interval, independently of other events. In this case, the event is the duration of the appearance of the posterior rim sign on radiographs made at discrete annual intervals. The event occurs for each subject of the study, independently of one another. The absence of the radiographic sign was assigned a value of zero for the distribution. The mean, termed \( \gamma \), of the distribution is the mean duration of the radiographic sign. The standard deviation is defined as the square root of the mean.

**Source of Funding**

Internal funding from Case Western Reserve University was received in support of this study. No external funding was received.

**Results**

**Posterior Rim Ossification**

The secondary ossification center in the posterior wall of the acetabulum was noted on the radiographs of seventy-three (74%) of the ninety-eight subjects. The ossification center was noted in thirty-three (75%) of forty-four females and forty (74%) of fifty-four males, with no significant difference between the groups \((p = 1.00)\). The secondary ossification center appeared (as the posterior rim sign) at a mean age (and standard deviation [SD]) of 12.2 ± 0.9 years for females and 14.0 ± 0.8 years for males \((p < 0.001)\). The secondary ossification center was radiographically present for a mean (and SD) of 10.1 ± 3.2 months in females and 10.0 ± 3.2 months in males \((p = 0.95)\). Of the seventy-three subjects in whom the secondary ossification center was visualized, sixty-four (88%) displayed the posterior rim sign on only one annual radiograph, whereas the other nine (12%) demonstrated the radiographic sign on two consecutive annual radiographs.

The appearance and fusion of the posterior rim secondary ossification center corresponded closely with closure of the triradiate cartilage. The triradiate cartilage had begun to ossify (Oxford bone age score, 2) in sixty-three (90%) of seventy subjects on the radiograph made immediately preceding fusion of the posterior rim secondary ossification center. For the remaining seven (10%) of the seventy subjects, the triradiate cartilage was fully fused while the posterior rim secondary ossification center remained open; however, the posterior rim was fused by the following year.

**Center-Edge Angle**

The subjects with identified secondary ossification centers were rescreened to find those with images that had <5° of pelvic rotation and satisfactory contrast to identify the anatomic landmarks necessary for measurement of the center-edge angle. Of the seventy-three subjects, only ten fit these strict criteria, as most had slight rotation of at least one of the needed images. Seven females and three males were evaluated. The mean center-edge angle (and SD) before appearance of the secondary ossification center in the posterior rim of the acetabulum was 28.4° ± 3.3°. The mean center-edge angle (and SD) after fusion of the secondary ossification center was 32.5° ± 2.5°. The mean increase (and SD) in center-edge angle was 4.1° ± 2.8° (range, 1.0° to 9.1°). This difference was significant with use of a paired t test \((p < 0.002)\). Twenty images were remeasured by the initial grader (J.Y.C.) as well as another grader (W.Z.M.) to validate the accuracy of the measurements. The intraclass correlation coefficients for interobserver and intraobserver reliability were 0.93 and 0.88, respectively, which demonstrate excellent agreement.

**Discussion**

The secondary ossification center in the posterior rim of the acetabulum appeared in a reliable fashion near the time of closure of the triradiate cartilage (at a mean age of twelve years in girls and fourteen years in boys). These findings further validate those of Fabricant et al.10, who similarly noted the posterior rim sign around the time of closure of the triradiate cartilage have the sign present on radiographs because the ossification center both appeared and fused between the making of the annual images. This is roughly what our data demonstrated, as approximately one in four subjects did not demonstrate the radiographic sign. Consequently, we suspect that the posterior rim sign is present in most adolescents at some point during
development and that it was not captured in a minority of subjects simply because of its short-lived nature.

The clinical importance of the posterior rim secondary ossification center stems primarily from its impact on the assessment of the posterior wall of the acetabulum. Many of the metrics for the assessment of femoroacetabular impingement involve evaluation of the posterior wall of the acetabulum, including the posterior wall sign, crossover sign, and centeredge angle. These radiographic indices rely on a fully ossified posterior wall for accurate radiographic assessment. Given the location of the secondary ossification center at the lateral edge of the sourcil, we anticipated that we would see a change in the centeredge angle during ossification of the posterior rim. With use of a subset of ten patients from the sample population, we demonstrated a mean increase in the center-edge angle of about 4° (range, 1.0° to 9.1°) before appearance and after fusion of the secondary ossification center (Fig. 4). This broad range reflects the slight variation in superolateral extension of the ossification center. Some centers were located more posteriorly and did not extend to the lateral edge of the sourcil. Consequently, these centers were less likely to impact the centeredge angle than an ossification center extending more superiorly would have.

Given that the mean center-edge angles for normal acetabular coverage (33° to 36°) and acetabular overcoverage (>40°) differ by as little as 4°, there appears to be substantial potential for misinterpretation of radiographs in adolescents with incompletely ossified hips. Prior to closure of the triradiate cartilage, the posterior rim of the acetabulum may be incompletely ossified and appear relatively hypoplastic. This finding could lead surgeons to falsely diagnose relative undercoverage of the hip through misinterpretation of the centeredge angle. In these situations, one could consider the use of MRIs, as they would demonstrate both ossified and cartilaginous zones of the acetabulum and limit errors in interpretation.

The strengths of our study are its longitudinal nature and the widespread use of radiographs. The opportunity to study annual radiographs in healthy adolescents allowed us to identify this secondary ossification center in a much larger proportion of the population than had been previously identified. This also enabled us to directly quantify the impact of the appearance and fusion of this ossification center on perceived acetabular coverage.

There are a few limitations to our study. All of the adolescents included in this study were white, which may limit generalizability of our findings to other ethnicities. This sample population was representative of the study (the subjects of which were 92.2% white) and of the population of the Greater Cleveland area at the time of the original longitudinal study. Although a literature search did not reveal any studies with findings of differences in acetabular development by race, conclusions drawn from this study should be applied cautiously to other ethnic groups. Another limitation of our study is that only unilateral images of the hip were made. Consequently, we are unable to comment on whether the bilateral development of the posterior rim occurs in a synchronous manner. A third limitation is the small sample size of the subgroup used to determine the change in center-edge angles. Despite the relatively small size of this subgroup, the differences in center-edge angle reached significance.

In summary, we have characterized the ossification of the posterior rim of the acetabulum through the use of a historical longitudinal radiographic study. We have also demonstrated the potential for misinterpretation of radiographs in the assessment of femoroacetabular impingement in adolescents with incompletely ossified bone about the hip.

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CHARACTERIZATION OF OSSIFICATION OF THE POSTERIOR RIM OF ACETABULUM


24. Tannast M, Siebenrock KA, Anderson SE. Femoroacetabular impingement: radiographic diagnosis—what the
The Association of Tibia Femur Ratio and Degenerative Disease of the Spine, Hips, and Knees

Douglas S. Weinberg, MD and Raymond W. Liu, MD

From the Division of Pediatric Orthopaedic Surgery, Case Western Reserve University, Rainbow Babies and Children’s Hospital, Cleveland, OH.

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ABSTRACT

Background: When individuals with asymmetric lower extremities present for evaluation of limb-length inequality, correction can occur at the tibia, femur, or in both bones; however, there are limited data available to justify either technique. The aim of this study is to examine the normal ratio of tibia length/femur length (T/F), and to explore the relationship between T/F ratio and osteoarthritis of the spine, hips, and knees.

Methods: Bone lengths of 1152 cadaveric femora and tibiae from the Hamann-Todd osteological collection were measured. Degenerative joint disease was graded in the hip, knee, and spine. Correlations between the ratio of T/F and osteoarthritis were evaluated with multiple regression analysis.

Results: The average ratio of T/F was 0.80±0.03. There was a strong correlation between age and arthritis at all sites, with standardized β ranging from 0.44 to 0.57 (P<0.0005 for all). There was a significant correlation between increasing T/F and hip arthritis (standardized β=0.08, P=0.006), and knee arthritis (standardized β=0.08, P=0.008).

Discussion: Increasing tibia length relative to femur length was found to be a significant predictor of ipsilateral hip and knee arthritis. Therefore, we recommend that when performing limb lengthening, surgical planning should lean toward recreating the normal ratio of 0.80. In circumstances where one bone is to be overlengthened relative to the other, bias should be toward overlengthening the femur. This same principle can be applied to limb-reduction surgery, where in certain circumstances, one may choose to preferentially shorten the tibia.

Clinical Relevance: This is the first study to report long-term consequences of lower extremity segment disproportion.

Key Words: tibia/femur length ratio, segment disproportion, limb-length discrepancy, degenerative joint disease (J Pediatr Orthop 2015;00:000–000)

Limb-length discrepancy is a relatively common condition in orthopaedic clinics. Treatment is considered in patients with >2cm of discrepancy,1 and in patients with persistent symptoms. Options include shoe lifts, epiphysiodesis or acute shortening of the long limb, or lengthening of the short limb.

Limb lengthening and reconstructive surgery techniques have undergone considerable advances in the last 25 years since first being described by Codivilla2 in 1905. Principles pioneered by Ilizarov and others have allowed for the successful lengthening of upper and lower extremities in adults and children.3–5 However, indications and surgical goals for limb lengthening or shortening remain controversial, in part due to the lack of research emphasizing long-term consequences.6

The consideration of tibial-femoral segment disproportion in limb-equalization surgery has been largely ignored in the literature.7 When individuals with asymmetric lower extremities present for evaluation of limb lengthening, correction can occur at the femur, tibia, or in both bones simultaneously. However, to our knowledge, there are limited data available to aid in surgical decision making from the perspective of tibial-femoral length (T/F) ratio.

It would therefore be clinically prudent to determine whether tibial-femoral segment disproportion in adults is associated with eventual degenerative osteoarthritis of the spine, hip, or knee. Accordingly, we designed a study using a large osteological collection to confirm the normal ratio of T/F, and to explore its association with degenerative joint disease of the spine, hip, and knee.

METHODS

Cadaveric Specimens

Cadaveric tibiae and femora from the Hamann-Todd Osteological Collection (Cleveland, OH) were obtained. This collection contains over 3000 complete, disarticulated human skeletons cataloged for age, sex, and ethnicity in a large database that we utilized for our study. We included 625 specimens between the ages of 40 and 79 years at the time of death. Exclusion criteria included any obvious fractures of the femur or tibia (15), obvious rheumatologic disease (13), slipped capital femoral epiphysis (2), suspected Blount disease (1), evidence of infection affecting the joint surfaces (2), incomplete demographic information (2), or incomplete skeletons (14), leaving a total of 576 skeletons (1152 tibiae and femora) for primary study.
Arthritis Grading
Arthritis grading was performed by the study authors using a system for spine, hip, and knee degenerative osteological disease. The two orthopaedic surgeons, each with over 1000 hours of experience studying orthopaedic paleopathology in the Hamann-Todd collection, carefully examined a large number of specimens together to quantify known osteological signs of arthritis. A spine grading system was modified, and a previously validated grading system for the hip and knee was used. Spine osteoarthritis was evaluated with a scale from 0 to 4 at each vertebral joint level, from L1 to L2 through L5 to S1. Measurements from each level were averaged to represent a composite spine arthritis measurement, graded from 0 to 4. Arthritis of the proximal femur and acetabulum were graded from 0 to 3 and combined to form a composite hip measurement, graded 0 to 6. The patella, medial femoral condyle, lateral femoral condyle, patellofemoral articulation, lateral tibial joint surface, and medial tibial joint surface were graded from 0 to 3, and these measurements were combined to represent respective patellofemoral, medial, and lateral knee compartments, each graded 0 to 6. These compartments were averaged to form a composite knee measurement, graded 0 to 6 (Fig. 1). Twenty specimens were measured independently by each author to establish interrelator reliability. Intrarelator reliability was assessed by one of the study authors with a 4-week interval between grading.

Measuring Tibial and Femoral Length
All tibiae were measured by using a digital ruler in millimeters. Measurements were taken from the most superior aspect of the lateral tibial plateau to the most inferior aspect of the lateral tibial plafond. A public database of femoral length measurements was available for the specimens chosen. Using a digital ruler, 100 pairs of femora were measured by the study authors to confirm accuracy of the database, with 25 pairs of femora chosen from each 10-year age increment. Femoral length was measured from the superior aspect of the femoral head to the center of the femoral condyles. Tibia lengths were divided by ipsilateral femur lengths to determine the T/F ratios.

Statistical Analysis
All statistics were performed with the SPSS 22.0 software package (IBM Corporation, Armonk, NY). Interrelator reliabilities for femoral and tibial lengths were evaluated with intraclass correlation coefficient. Intrarelator reliability for arthritis grading at each articulation was compared with the Cohen $\kappa$ statistic. An independent samples t test was used to compare T/F between sexes and races. Multiple regression analyses was used to determine the correlates of arthritis; independent variables were age, race, sex, height, and T/F. Separate analyses were run with the dependent variable set as degenerative arthritis of the spine, hip, and knee. For each dependent variable, a repeat analysis was performed using T/F ratios greater or less than the mean. In the multiple regression analysis, larger standardized $\beta$ indicated a more positive (or negative) correlation based on signage. The multicollinearity was assessed as negative based on VIF<10.
and coefficient tolerance >0.1, normal probability plots of the regression standardized residual were inspected for normality, scatterplots of the standardized residuals were inspected for homoscedasticity, and the lack of any undue influence from outliers was confirmed with a Cook's distance <1. Significance was set at $P<0.05$.

RESULTS

For specimen grading, reliability analysis was assessed for each articulation with the Cohen $k$ statistic and are shown in Table 1. All fell within good (0.60 to 0.79) or excellent (0.81 to 0.99) agreement for categorical variables.

For femoral lengths, reliability analysis was performed comparing 100 sets of bilateral femora measured by the study investigators versus the database, with an intraclass correlation coefficient of 0.999. The average age and SD was 56±10 years (range, 40 to 79 y). There were 78 females (14%) and 498 males. There were 398 whites (69%), 176 African Americans, and 2 other ethnicities. Average height was 1708±81mm (range, 1452 to 1923 mm). Average tibia length was 365±27mm (range, 291 to 448 mm), femoral length was 455±28mm (range, 377 to 556 mm). The mean and SD of T/F was 0.801±0.027 (range, 0.716 to 0.922); the distribution of values is shown in Figure 2. The average T/F was greater in males compared with females (0.802 vs. 0.794, $P=0.002$). T/F was decreased in whites compared with African Americans (0.795 vs. 0.816, $P=0.0005$).

The independent determinants of the T/F ratio are summarized in Table 2. Increasing height, male sex, and African American race were associated with increasing T/F.

Average grades for spine, hip, and knee osteoarthritis were $2.2±0.9, 3.1±1.4$, and $2.7±1.3$, respectively. Arthritis increased linearly with age at each joint (Fig. 3). Multiple regression analysis is summarized in Tables 3 and 4. There was a strong correlation between age and arthritis at all sites, with standardized $\beta$ ranging from 0.44 to 0.57 ($P<0.0005$ for all). There was no correlation between T/F and spine arthritis (standardized $\beta=0.030, P=0.257$). There was a significant correlation between increasing T/F and hip arthritis (standardized $\beta=0.078, P=0.006$) and knee arthritis (standardized $\beta=0.077, P=0.008$). These differences were also apparent for specimens with T/F values greater than the mean, although there were no significant correlations for specimens with T/F values less than the mean (Table 4). A subset of specimens with differences in contralateral T/F ratios $>0.01$ ($n=157$) was analyzed separately, and the conclusions were the same as the entire cohort of patients, with a trend toward increased T/F correlating with increased osteoarthritis of the hip and knee, with standardized $\beta$ values of 0.08 ($P=0.11$) and 0.08 ($P=0.07$), respectively, for the hip and knee. This trend was also true for patients with a difference in T/F ratios $>0.02$.

Table 1. Reliability for arthritis grading, assessed with Cohen’s $k$.

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<tr>
<th>Articulation</th>
<th>Interrelator Reliability</th>
<th>Intrarelator Reliability</th>
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<tr>
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<td>0.88</td>
<td>0.93</td>
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<td>0.75</td>
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<td>0.84</td>
</tr>
<tr>
<td>Lateral tibial joint surface</td>
<td>0.66</td>
<td>0.88</td>
</tr>
<tr>
<td>Medial tibial joint surface</td>
<td>0.60</td>
<td>0.82</td>
</tr>
<tr>
<td>Individual spine levels</td>
<td>0.71</td>
<td>0.63</td>
</tr>
<tr>
<td>Proximal femur</td>
<td>0.60</td>
<td>0.66</td>
</tr>
<tr>
<td>Acetabulum</td>
<td>0.65</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Table 2. Multiple regression results, standardized $\beta$ values for factors predicting increasing tibia length/femur length.

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Standardized $\beta$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.029</td>
<td>0.431</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.134**</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Race</td>
<td>0.371**</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Height</td>
<td>0.080*</td>
<td>0.004</td>
</tr>
</tbody>
</table>

A negative value for sex indicates that male sex is associated with increasing T/F ratio. A positive value for race indicates that African American race is associated with increasing T/F ratio.

$*P<0.05. **P<0.0005$. 

Figure 2. A histogram of tibia length/femur length, clustered in increments of 0.01. The average T/F ratio was 0.80, normally distributed over a small range.
When patients present for surgical correction of lower extremity limb deficiency, the orthopaedic surgeon must decide whether lengthening or shortening of the tibia, femur, or both bones should occur. While other aspects of surgical planning for these complex cases have been thoroughly described, to our knowledge this experiment is the first attempt to quantify the long-term consequences of tibial length-femoral length segment disproportion. Our study of a large osteological database was designed to investigate any correlations to spine, hip, or knee arthritis that may have resulted from natural tibia and femur length. Ultimately, the results will provide important normative data on the ideal T/F ratio to reproduce in limb-equalization surgery, and insight into the potential long-term consequences of failure to do so.

This study confirms the average T/F ratio to be 0.80, which is very narrowly distributed. While there has only been limited research on this topic, Strecker et al.\textsuperscript{13} measured tibia and femur lengths of 511 healthy adults with computed tomography, and reported an average ratio of 0.80; these authors did not provide information on sex or race. Paley et al.\textsuperscript{14} and other authors have distributed measurements for incongruous tibia and femur lengths, indirectly suggesting that the proper ratio should lie between 0.78 and 0.85\textsuperscript{13,14} Our data show male sex and African American race to be independently correlated with increased T/F, suggesting that genetic differences exist in lower extremity bone lengths. This is consistent with earlier anthropologic literature that has also shown differences between the long bones of males, females, whites, and African Americans.\textsuperscript{16–18}

As expected, age was by far the most significant predictor of arthritis at all sites. Male sex was correlated with increased spine arthritis. Related epidemiological studies have shown similar results, and these findings support the validity of the arthritis grading system.
grading systems.\textsuperscript{19,20} T/F ratio was not a significant predictor of spine arthritis, whereas increasing T/F significantly predisposed specimens to hip and knee arthritis. Height was associated with knee arthritis, as has been described previously.\textsuperscript{21} To our knowledge, the functional consequences of T/F segment disproportion have not been reported. This makes it problematic to directly compare our conclusions to the literature.

We are unsure as to the exact mechanism causing increased hip and knee osteoarthritis in these specimens, although we suspect it is related to altered biomechanics of gait. Walking gait is known to be an important predictor of arthritis, and is heavily influenced by limb length and alignment.\textsuperscript{15,22,23} In individuals with increased T/F, the knee joint will be relatively closer to the hip joint. As Norkin and Levangie\textsuperscript{[24]} describe in a biomechanical analysis of the lower extremity, the shorter the lever arm, the longer the distance traveled by the smaller segment. This may increase the amount of motion at the hip and knee to accomplish the same excursion.\textsuperscript{22} Similarly, a relatively shorter femur decreases the lever arm of sagittal plane motion, and necessitates increased motion at the hip and knee joints to “clear” a relatively longer tibia. It has been suggested that this type of kinematic interaction can lead to acceleration of degenerative joint disease. However, it is not possible to validate this proposed mechanism without a thorough biomechanical analysis.\textsuperscript{15,25,26} In addition, a more proximal knee joint would cause the pelvis to increase forward tilt during the heelstrike phase of gait,\textsuperscript{27} an established cause of hip osteoarthritis.\textsuperscript{28–33} Song et al\textsuperscript{15} showed increased mechanical work during gait for patients with limb-length discrepancies >3cm, perhaps by a similar mechanism, decreasing the distance between the knee and hip joint relative to the distance between the knee and ankle joint.

While these results show an increased T/F being associated with arthritis of the hip and knee, decreasing T/F did not show a protective effect. The subcategory analysis for specimens with T/F values above and below average suggest that the strong correlations discussed above are most heavily influenced by specimens with increased T/F values who had a greater degree of arthritis. However, when we separately analyzed groups with differences in right and left T/F ratios >0.01 and >0.02, the results of multiple regression analysis were similar to the population of specimens as a whole; increasing T/F trended toward associations with ipsilateral and contralateral hip and knee osteoarthritis.

In general, the goal of limb equalization is to recreate the ratio of the opposite limb. When an exact match is not desirable, such as when only tibia or femur is lengthened or shortened for shortening in both bones, it is reasonable to lean toward recreating the average ratio of 0.80 or lower. In essence, when one bone is to be longer relative to the other, preference should go toward overlengthening the femur or overshortening the tibia to decrease the ratio and potentially prevent future development of osteoarthritis.

The validity of the arthritis grading

<table>
<thead>
<tr>
<th>Population</th>
<th>Spine Osteoarthritis</th>
<th>Hip Osteoarthritis</th>
<th>Knee Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All specimens (n=1152)</td>
<td>β -0.012 P 0.699</td>
<td>β 0.078 P 0.006</td>
<td>β 0.077 P 0.008</td>
</tr>
<tr>
<td>T/F&gt;0.801 (greater than the mean)</td>
<td>0.064 P 0.078</td>
<td>0.080 P 0.035</td>
<td>0.092 P 0.014</td>
</tr>
<tr>
<td>T/F&lt;0.801 (less than the mean)</td>
<td>β -0.005 P 0.878</td>
<td>-0.048 P 0.199</td>
<td>0.037 P 0.354</td>
</tr>
</tbody>
</table>

*P<0.05.

Table 4. Multiple Regression Results, T/F Independent Variable, Standardized β Values.

![Figure 4](image-url) A histogram of differences in tibia length/femur length ratio between right and left legs. As expected, there was minimal difference in the T/F ratio between contralateral legs.
system used is critical to our conclusions. The two orthopaedic surgeons who performed the grading each had substantial experience examining orthopaedic osteopathology in this collection, and all of the reliability comparisons were in the “good” and “excellent” range.\(^\text{13}\) By defining incremental increases in osteophyte formation and other bony findings, we were able to identify a strong correlation between age and increasing arthritis score at each grading site. This, along with expected high standardized β values between age and degenerative disease, strongly supports the validity of the grading system.

Strengths of the study include a large, randomly selected postmortem population free of the selection bias found in many clinical studies.\(^\text{34}\) The strong relationships between age and arthritis, along with high interobserver and intraobserver reliability, validate the osteoarthritis grading scale; in fact Kettler and Wilke\(^\text{35}\) noted that very few macroscopic grading systems have published reliability measurements. In addition, the use of multiple regression statistics provided a thorough analysis of each covariate, and allowed us to determine the independent effects of T/F and each individual variable after accounting for differences in age, sex, race, and height; the standardized β values presented are representative of the unique effect of each variable. However, our study has important limitations. Without longitudinal data, we cannot confirm a cause and effect relationship between tibia/femur disproportion and hip and knee degenerative disease, although a significant correlation clearly exists. Lindsey et al\(^\text{36}\) showed the significant contributions made by the tibialis anterior and other muscles following limb lengthening. Our analysis cannot account for this or other soft-tissue structures.

The cadaveric skeletons obtained in this study were collected from the unclaimed dead of Cleveland morgues from early 1900s. Little is known about their clinical history, and their lifestyles may not be representative of modern patients. Many are presumed to have worked as manual laborers. We were able to exclude specimens with obvious traumatic, metabolic, and infectious conditions, and our large sample numbers should help reduce the effects of any severe cases. Finally, our recommendations assume that gait and mechanical alignment can be relearned following correction of T/F segment disproportion, which Bhaye et al\(^\text{37}\) have found does occur after limb lengthening in general.

In conclusion, our large osteological review of a random population confirms the existing ratio of T/F is 0.80. This study demonstrates that relative overlengthening of the tibia, or overshortening of the femur may predispose individuals to hip and knee arthritis. When surgeons performing limb equalization do not intend to match the opposite limb, we recommend that they aim toward the average ratio of 0.80, or lower. When one bone is to be lengthened relative to the other, preference should go toward a longer femur. These conclusions should assist limb-lengthening surgeons in surgical planning during these complicated surgeries and potentially improve long-term patient outcomes.

Acknowledgements

The authors thank Yohannes Haile-Selassie, PhD, director of anthropology, and Lyman Jellema, MS, collections manager at the Cleveland Museum of Natural History. The authors acknowledge volunteers Lillian Rubin and Phyllis Evey for developing the femoral length database used in this study.

References


Pelvic Incidence and Acetabular Version in Slipped Capital Femoral Epiphysis

Jeremy J. Gebhart, MD,1 Michael S. Bohl, BA,2 Douglas S. Weinberg, MD,* Daniel R. Cooperman, MD,3 and Raymond W. Liu, MD1

1Department of Orthopaedic Surgery, Rainbow Babies and Children’s Hospitals, Case Western Reserve University School of Medicine, Cleveland, OH; 2The Warren Alpert Medical School of Brown University, Providence, RI; and 3Department of Orthopaedic Surgery, Yale University School of Medicine, New Haven, CT.

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ABSTRACT

Background: The etiology of slipped capital femoral epiphysis (SCFE) is multifactorial, but the role of sagittal balance of the pelvis as a contributing factor to its development has not been well studied. Our primary purpose was to determine whether a smaller pelvic incidence (PI), a position-independent anatomic parameter that regulates pelvic orientation, could be a factor that increases shear stress in the epiphyseal growth plate and potentially contributes to the development of SCFE. We also set out to determine whether acetabular retroversion was associated with SCFE.

Methods: We obtained 14 cadaveric pelvis from the Hamann-Todd Osteological Collection whose femurs showed evidence of post-SCFE deformity. Two hundred age-matched, sex-matched, and race-matched pelvis were used as controls. PI and acetabular version were measured using standardized lateral photographs and goniometers, respectively. T tests were performed to evaluate for differences in measured parameters between groups.

Results: The mean PI was 40.6±6.1 degrees for SCFE specimens and 47.4±9.9 degrees for normal specimens (P=0.01). The mean version of SCFE and normal acetabula was 15±7 and 17±6 degrees, respectively (P=0.39). There was also no significant difference in version between SCFE acetabula and the contralateral, uninvolved acetabular of the same specimen (15±7 vs. 17±8 degrees, P=0.33).

Conclusion: Specimens with SCFE deformity demonstrated a smaller PI than a large cohort of normal control specimens. We found no significant difference between acetabular version of specimens with and without SCFE deformity. Contralateral or unaffected acetabuli of SCFE specimens were not more retroverted than the affected side of the same specimen.

Clinical Relevance: Sagittal balance of the pelvis, and particularly decreased PI, may play an important role in the development of SCFE. The influence of mechanical factors beyond the hip joint in the development of SCFE should be considered by clinicians.

Keywords: slipped capital femoral epiphysis, pelvic incidence, acetabular version

INTRODUCTION

The etiology of slipped capital femoral epiphysis (SCFE) is multifactorial, involving a number of biochemical aspects and mechanical factors that include obesity, the physeal sloping angle, femoral retroversion, and size of the epiphyseal tubercle.1-7 Although these factors, as well as the natural history, epidemiology, and treatment, have all been studied in detail since the original description of SCFE by Paré in 1572, the sagittal balance of the pelvis as a contributing factor to the development of this pathology has not been well studied.

Pelvic incidence (PI), a position-independent anatomic parameter that is one of several factors to determine lumbar lordosis and pelvic orientation, has been studied extensively in relation to spine pathology, and numerous studies have shown that increased PI transmits more mechanical forces to the lumbar spine.8-10 It is defined as the angle between the line perpendicular to the sacral plate at its midpoint and the line connecting this point to the axis of the femoral heads and can be easily obtained from a lateral radiograph of the lumbosacral spine (Fig. 1).11 However, the impact of this anatomic parameter with regard to stresses placed on the femoroacetabular joint is not well understood. Our primary purpose of this study was, therefore, to determine whether a smaller PI could be one of the factors that places amplified forces at the femoroacetabular joint, resulting in increased shear stress in the epiphyseal growth plate and potentially contributing to the development of SCFE.

Recently, there have been a number of studies suggesting that SCFE is also...
associated with acetabular retroversion in the affected and unaffected contralateral hips of SCFE patients.\textsuperscript{12,13} Whether this influences the development of SCFE or simply predisposes the patient to developing a combined or mixed-type femoroacetabular impingement remains unclear. Therefore, secondary aims of this study included assessing whether acetabular retroversion was present in patients with SCFE and whether SCFE hips had more acetabular retroversion than unaffected hips of the same patient.

METHODS

We obtained cadaveric specimens from the Hamann-Todd Osteological Collection at the Cleveland Museum of Natural History (Cleveland, OH) for the purposes of our study. The collection is one of the largest of its kind in the world, and contains 2972 complete, disarticulated human skeletons carefully preserved from the unclaimed dead of Cleveland-area morgues from 1912 to 1938. The sex, ethnic origin, and age at the time of death are known for nearly every specimen in the collection, including every specimen used in this study.

Standardized photographs of all proximal femurs in the collection were available for initial review for changes concerning for the post-SCFE deformities described by Cooperman et al.\textsuperscript{14} in a study involving the same osteological collection. These deformities included a roughened surface of exposed metaphyseal bone anteriorly between the site of the original capital epiphysis and its displaced position. Further physical scrutiny of our initial cohort and review of high retroversion specimens from screening the entire collection demonstrated that 14 showed clear sequelae of SCFE, none of which had been treated surgically (Fig. 2).

Presence of a post-SCFE deformity was first assessed by the first author and verified by a single senior author (R.W.L.). Questionable, or “borderline,” specimens were rejected from both the SCFE group and the control group. One of the 14 skeletons with SCFE had bilateral involvement, giving a total of 15 hips available for the study.

Two hundred age-matched, sex-matched, and racematched specimens were randomly selected to be used as controls in this study. Only healthy pelvis in good condition were used in the control group; degraded specimens or those with evidence of postmortem damage and those with evidence of major anatomic abnormality or disorders, including fracture, were excluded. The method for preparing pelvis specimens was similar to that used in previous osteological studies.\textsuperscript{15,16} The hemipelvis and sacrum of each specimen were assembled using rubber bands and a standardized 12mm piece of foam that replaced the cartilage of the pubic symphysis.\textsuperscript{17} The anterior superior iliac spine and the crest of the pubis were placed in contact with a laboratory table, establishing an anatomic frontal plane.\textsuperscript{16,18,19} Acetabular version was measured at the center of the acetabulum in a vertical plane to the laboratory table (horizontal plane) along the anterior to posterior ridges using a 360-degree, 14-inch plastic goniometer (Prestige Medical, Northridge, CA) marked in 2-degree increments (Fig. 3).

After reconstructing the pelvis and obtaining version measurements, standardized direct lateral digital...
photographs were taken of each pelvis specimen. An Easy Square Jr. (EZ Quilting Tools, West Warren, MA) acrylic 6.5 inch ruler was used to mark the center of the sacral endplate (Fig. 4). The PI angle was obtained by measuring the angle formed between a line perpendicular to the midpoint of the sacral endplate and the center of a best-fit ellipse representing the acetabular rim. For consistency, a single photographer positioned all specimens and took all photographs. ImageJ software (http://imagej.nih.gov/ij/; National Institutes of Health, Bethesda, MD) was used to obtain angle values. A single author (M.S.B.) measured PI and version for all specimens, and 2 additional authors (J.J.G., D.S.W.) performed interobserver reliability measurements.

Data analysis was performed in Minitab 16 software (State College, PA). The mean and SD for PI and acetabular version

<table>
<thead>
<tr>
<th>SCFE (n=14) [n (%)]</th>
<th>Normal (n=200) [n (%)]</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)*</td>
<td>51.9±15.3</td>
<td>53.2±2.9</td>
</tr>
<tr>
<td>Sex</td>
<td>M=13 (93)</td>
<td>M=182 (91)</td>
</tr>
<tr>
<td></td>
<td>F=1 (7)</td>
<td>F=18 (9)</td>
</tr>
<tr>
<td>Race</td>
<td>W=8 (57)</td>
<td>W=148 (74)</td>
</tr>
<tr>
<td></td>
<td>B=6 (43)</td>
<td>B=52 (26)</td>
</tr>
</tbody>
</table>

Table 1. Sample Population Demographics
*Values are expressed as mean±SD. B indicates black; F, female; M, male; SCFE, slipped capital femoral epiphysis; W, white.

<table>
<thead>
<tr>
<th></th>
<th>SCFE</th>
<th>Normal</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic incidence</td>
<td>40.6</td>
<td>47.4</td>
<td>0.01</td>
</tr>
<tr>
<td>SD</td>
<td>6.1</td>
<td>9.9</td>
<td>—</td>
</tr>
<tr>
<td>Range</td>
<td>30.0-52.1</td>
<td>20.7-82.5</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 2. Comparison of Pelvic Incidence in SCFE and Normal Specimens
SCFE indicates slipped capital femoral epiphysis.

<table>
<thead>
<tr>
<th></th>
<th>SCFE (n=13)</th>
<th>Normal (n=400)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version (deg.)</td>
<td>15</td>
<td>17</td>
<td>0.39</td>
</tr>
<tr>
<td>SD</td>
<td>7</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td>Range</td>
<td>5-25</td>
<td>—5 to 38</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Acetabular Version in SCFE and Normal Hips
SCFE indicates slipped capital femoral epiphysis.

Figure 3. The anatomic frontal plane was defined as the anterior superior iliac spines and the crest of the pubis. Acetabular version was measured using a goniometer at the central transverse section of the acetabulum.

Figure 4. Pelvic incidence measurement. Point B represents the center of the sacral endplate. Point C represents the center of the acetabulum as measured from a direct lateral view of the pelvis. Angle ABC represents pelvic incidence.
3. The interobserver ICC was 0.97, and normal acetabular is shown in Table 2. The interobserver ICC was >0.99 for measurement of acetabular version.

Acetabular Version in Involved Versus Uninvolved SCFE Hips
In 8 patients, the left side was slipped; therefore, our study group consisted of 8 "contralateral, uninvolved right" hips and 5 "contralateral, uninvolved left" hips. Once again, the specimen with bilateral involvement was excluded in version analysis. The mean version of the 13 SCFEs, as well as the 13 contralateral, uninvolved acetabular, is shown in Table 4.

RESULTS
Fourteen specimens were identified as having post-SCFE deformity. One of the 14 skeletons with SCFE had bilateral involvement, but for purposes of data analysis was treated as a single specimen. Two hundred agematched, sex-matched, and race-matched specimens were included in the normal group. Sample population demographics are shown in Table 1.

PI in SCFE Patients Versus Normal Controls
The mean PI of the 14 SCFE specimens and 200 normal specimens is shown in Table 2. The interobserver ICC and intraobserver ICC was >0.99 for measurement of PI.

Acetabular Version in SCFE Patients Versus Normal Controls
When reconstructing the pelvis, it was noted that the specimen with bilateral SCFEs had damage to both sides of the ilium and the anterior superior iliac spine was missing. Therefore, a true frontal plane and accurate method of determining acetabular version using our methods was unable to be obtained, and this specimen was excluded from version analysis. The mean version of the 13 SCFES and 400 normal acetabular is shown in Table 3. The interobserver ICC was 0.97, and the intraobserver ICC was 0.96 for measurement of acetabular version.

DISCUSSION
The etiology of SCFE is a multifactorial process that has been studied in detail for many years. It is believed that stresses on the proximal femoral physis may be an important biomechanical contributor to the development of this process. We have performed an osteological study to evaluate for differences in cadaveric specimens with and without post-SCFE deformity. We focused on the measurements of PI and acetabular version, 2 anatomic factors that may contribute to increased amounts of stress across the proximal femoral physis.

Our findings suggest that sagittal balance of the pelvis, and particularly decreased PI, may play an important role in the development of SCFE. In addition, we found no significant difference between acetabular version of specimens with and without SCFE deformity. We also found that the contralateral or unaffected acetabulum of SCFE specimens was not more retroverted than the affected side.

PI is the angle between the line perpendicular to the sacral plate at its midpoint and the line connecting this point to the axis of the femoral heads.11 The measurement of PI was first introduced by Duval-Beaupere et al in 1992.26 It is generally accepted that PI becomes stable around the age of 10 years and then remains unchanged throughout adolescence and adulthood for normal subjects.21 Since its introduction, a number of studies have generally concluded that an increased PI may be one of many predictive factors for spondylolisthesis and other spine pathology, but it is not clear whether it is the cause or effect.8 Although this correlational study also cannot delineate cause and effect, our results support the consideration of abnormal stresses at the femoroacetabular joint when PI varies from normal.

The relationship between the lumbar spine and hip kinematics is well recognized clinically.22–25 Sagittal balance necessitates a postural strategy for mobilizing the lumbar-pelvic-femoral complex in such a way that the body transmits stresses from a single structure, the spine, to the 2-part structure of the lower limbs, and vice versa. Proper sagittal balance ensures that forces are located behind the lumbar spine and the femoral heads.11 The sacrum and pelvis form a semirigid structure (ie, the sacropelvis) that translates and rotates with gait for the necessary compensatory balance around the bicoxofemoral axis,26 which passes through the centers of the left and right femoral heads.8 Consequently, disruption of this stability often results in a misappropriation of load absorption. The resulting transfer of displaced mechanical forces has primarily been studied in relation to the increased load on vertebral endplates and associated disks, but our results suggest that the transfer of forces onto the femoroacetabular joints should also be carefully considered. As described by Yoshimoto et al,27 when a subject has a small PI, the pelvis will often tilt forward to maintain normal lumbar lordosis and balance sagittal alignment of the spine. This anterior pelvic tilt would load the anterior aspect of the hip joint and propagate the stresses across...
the physis of the proximal femur that are experienced in SCFE. This increased stress, combined with the before-mentioned insults experienced as a result of obesity, physeal sloping angle, femoral retroversion, and size of the epiphyseal tubercle, could potentially result in the development of an SCFE.

A number of studies have recently suggested that decreased acetabular version may or may not also be associated with SCFE. Because of these discrepancies in the literature, a secondary goal of our study was to assess the anatomic measurement in our cohort of specimens. A study by Sankar et al. showed an increased rate of the crossover sign and posterior wall sign in SCFE patients in addition to showing that the contralateral acetabulum in patients treated for unilateral SCFE demonstrated significantly more coverage compared with matched controls. More recently, Bauer et al. also showed more radiographic signs of acetabular retroversion in SCFE patients.

However, we found no significant difference between acetabular version of specimens with and without SCFE deformity. We also found that the contralateral or unaffected acetabulum of SCFE specimens was not more retroverted than the affected side. Although our number of SCFE-positive hips used for analysis was relatively low due to the limited availability in the collection of specimens, our results are supported by work done by Stanitski et al. and Kordelle et al., both of which showed no differences in acetabular version between SCFE and normal hips using computed tomography (CT) scans and 3-dimensional CT reconstructions, respectively. Our results, obtained by performing highly accurate measurements directly on the acetabulum, and the support of these 2 CT-based studies, which, unlike standing radiographs, are also able to reliably recreate an anatomic frontal plane of the pelvis, support the conclusion that SCFE is not associated with acetabular retroversion.

This study had several limitations. Despite the use of an osteological collection as large as the Hamann- Todd, we were only able to identify 15 total SCFE femurs, with only 14 of these specimens being considered for analysis. In addition, there were a disproportionate number of male specimens included in our analysis. However, the relative proportions of sexes were similar between groups, and the Hamann-Todd Collection consists of a much greater number of male specimens than female specimens at baseline. Within these limitations, we are confident that our measurements were accurate and repeatable, and that we have identified a true difference in anatomy between the groups we defined.

We were also able to identify an unexpectedly large proportion of SCFE femurs in the collection of 2972 total specimens (15/2972). The incidence of SCFE in the general population of the United States is currently thought to only be around 10.8/100,000 with a 3.94 times higher incidence in black children than in white children, and it is significantly more common in male individuals. However, these reported numbers are likely an underestimate because the disorder may be silent, and many patients are never identified in the clinical setting. It is also difficult to estimate the possible effects of nutrition and disease in our study population that lived during the late 19th and early 20th centuries as influences of nutrition and disease in our study population that lived during the late 19th and early 20th centuries as influences.

In addition, the reported incidence of bilateral SCFE depends on the study, method of radiographic measurement, race and type of measurement, but most studies report an incidence of 18% to 50%. However, our careful examination identified only 1/14 (7%) as having bilateral involvement, and, although we have no explanation for this decreased incidence, we are confident that our methods of identifying specimens with post-SCFE deformity was accurate and reproducible.

Our study examines the differences in 2 common anatomic measurements and their associations with post-SCFE deformity. We report that decreased PI, but not acetabular retroversion, is associated with SCFE in a large cohort of osteological specimens. Further clinical study to determine the extent to which sagittal balance of the pelvis may affect the development of SCFE is necessary to better understand the significance of our findings, which indicate that the development of SCFE may be influenced by mechanical factors beyond the hip joint.

References


Particle-Induced Osteolysis Is Mediated by TIRAP/Mal in Vitro and in Vivo
Dependence on Adherent Pathogen-Associated Molecular Patterns

Christopher P. Bechtel, MD, Jeremy J. Gebhart, MD, Joscelyn M. Tatro, MS, Endre Kiss-Toth, PhD, J. Mark Wilkinson, FRCS(Orth), PhD, and Edward M. Greenfield, PhD

Investigation performed at the Department of Orthopaedics, University Hospitals Case Medical Center, Case Western Reserve University, Cleveland, Ohio, and the Departments of Cardiovascular Science and Human Metabolism, University of Sheffield, Sheffield, United Kingdom

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ABSTRACT

Background: Proinflammatory signaling by toll-like receptors (TLRs) likely contributes to biologic responses to wear particles causing aseptic loosening. We recently reported associations with aseptic loosening in patients with polymorphisms in the locus encoding an adapter protein specific for TLR-2 and TLR-4 known as toll/interleukin-1 receptor domain containing adapter protein/MyD88 adapter-like (TIRAP/Mal). To directly examine the contribution of TIRAP/Mal, we tested the hypothesis that TIRAP/Mal deficiency reduces the activity of wear particles. Signaling by TLR-2 and TLR-4 through TIRAP/Mal can be activated by bacterial pathogen-associated molecular patterns (PAMPs) such as lipopolysaccharide or endogenous alarmins. To distinguish between those possibilities, we tested the hypothesis that the effects of TIRAP/Mal depend on the adherence of bacterial PAMPs to the particles.

Methods: In vitro mRNA levels and secretion of tumor necrosis factor-α, interleukin (IL)-1β, and IL-6 were measured after incubating wild-type and TIRAP/Mal−/− macrophages in the presence or absence of titanium particles with adherent bacterial debris, so-called endotoxin-free particles, or particles with adherent lipopolysaccharide. In vivo osteolysis was measured after implanting titanium particles on the calvaria of wild-type and TIRAP/Mal−/− mice.

Results: TIRAP/Mal deficiency significantly inhibited the activity of titanium particles with adherent bacterial debris to stimulate in vivo osteolysis and in vitro cytokine mRNAs and secretion. Those effects are dependent on adherent PAMPs because removal of >99% of the adherent bacterial debris from the particles significantly reduced their activity and the remaining activity was not dependent on TIRAP/Mal. Moreover, adherence of highly purified lipopolysaccharide to the endotoxin-free particles reconstituted the activity and the dependence on TIRAP/Mal.

Conclusions: TIRAP/Mal deficiency reduces inflammatory responses and osteolysis induced by particles with adherent PAMPs.

Clinical Relevance: Our results, coupled with the genetic associations between aseptic loosening and polymorphisms within the TIRAP/Mal locus, support TLR signaling through TIRAP/Mal as one of the factors that enhances the activity of wear particles and further support the hypothesis that bacterial PAMPs likely contribute to aseptic loosening in a subset of patients.

INTRODUCTION
There are approximately 1 million total hip and knee replacements performed annually in the United States, and this is predicted to increase to 3.5 – 4 million by 2030. Despite excellent outcomes, aseptic loosening due to periprosthetic osteolysis accounts for 40-70% of failures requiring revision arthroplasty. The classic paradigm of periprosthetic osteolysis begins with the generation of wear particles that stimulate macrophages to synthesize pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), which sequentially lead to increased production of RANKL, osteoclast differentiation, and local bone resorption.

Additional factors likely enhance the biologic activity of wear particles and therefore predispose patients to osteolysis and aseptic loosening. For example, genetic association studies have implicated multiple polymorphisms in the development of aseptic loosening. Recent work by our laboratories identified several additional polymorphisms within loci encoding genes regulating inflammatory signaling that may increase the risk of aseptic loosening. For example, two distinct polymorphisms within the locus encoding an adaptor protein known as TIR domain-containing adaptor protein/MyD88-adaptor like (TIRAP/Mal) were associated with increased risk or accelerated development of aseptic loosening. Both of these
polymorphisms were previously reported to associate with other inflammatory conditions or are strongly linked to polymorphisms that do so.

As depicted in Figure 1, TIRAP/Mal is an adaptor protein that binds exclusively to the cytoplasmic domains of TLR-2 and TLR-4 and bridges the related adaptor protein, MyD88, to the receptor complex. In response to TLR activation, MyD88 propagates intracellular signal transduction pathways that induce expression of the pro-inflammatory cytokines. Genetic deletion of MyD88 reduces the responses to wear particles.

Those results do not specifically connect TLRs to aseptic loosening because MyD88 is also required for signaling by all members of the IL-1 receptor family. We and other investigators addressed this by showing that deficiency of either TLR-2 or TLR-4 reduces responses to wear particles consisting of titanium, ultra-high molecular weight polyethylene, cobalt-chromium, or hydroxyapatite. Also consistent with a role for the TLRs in aseptic loosening, both TLR-2 and TLR-4 are constitutively expressed by macrophages throughout the body, as well as in periprosthetic tissue. One of the major hypotheses tested in the current study is that TIRAP/Mal deficiency reduces the biologic activity of wear particles both in vitro and in vivo.

TLR-2 and TLR-4 are the receptors respectively for lipoteichoic acid from Gram-positive bacteria and lipopolysaccharide from Gram-negative bacteria. It has been proposed that such bacterial PAMPs contribute to aseptic loosening. For example, considerable evidence exists that the biological activity of wear particles, including ultra-high molecular weight polyethylene, is increased by adherence of PAMPs to the wear particles. One study in particular demonstrated titanium particles isolated from a failed total hip arthroplasty did not evoke pro-inflammatory cytokine production except when lipopolysaccharide was adsorbed onto the particles. Potential sources of PAMPs in aseptic loosening include implant contamination during manufacturing, bacterial translocation from the oral cavity and gastrointestinal tract, and the subclinical bacterial biofilms present on implants retrieved from aseptic loosening patients. In that regard, it has been reported that the bacterial biofilms correlate with osteolysis severity as biofilms were present on 76% of implants from aseptic loosening patients. In that regard, it has been reported that the bacterial biofilms correlate with osteolysis severity as biofilms were present on 76% of implants from aseptic loosening patients. In that regard, it has been reported that the bacterial biofilms correlate with osteolysis severity as biofilms were present on 76% of implants from aseptic loosening patients. In that regard, it has been reported that the bacterial biofilms correlate with osteolysis severity as biofilms were present on 76% of implants from aseptic loosening patients. In that regard, it has been reported that the bacterial biofilms correlate with osteolysis severity as biofilms were present on 76% of implants from aseptic loosening patients.

The major alternative to the PAMP hypothesis is that endogenous molecules known as alarmins or danger-associated molecular patterns activate TLRs during aseptic loosening. However, many of the reported effects of alarmins are now known to be due to contamination with PAMPs and it may be more correct to consider alarmins as working together with PAMPs to activate TLRs. Consistent with that, we found that genetic deletion of TLR-2 and/or TLR-4 inhibits the responses to titanium particles only if cognate PAMPs are adherent to the particles and that alarmins are therefore not sufficient by themselves to activate either TLR-2 or TLR-4. Because TIRAP/Mal functions exclusively with TLR-2 and TLR-4, the second hypothesis tested in this study is that the effects of TIRAP/Mal depend on the adherence of bacterial
**Figure 2.** TIRAP/Mal deficiency inhibits the rapid induction of proinflammatory cytokine mRNAs by titanium (Ti) particles with adherent bacterial debris. TNF-α (Fig. 2-A) and IL-1β (Fig. 2-B) mRNAs were measured in wild-type (WT) and TIRAP/Mal−/− macrophages (Mφs) incubated with the indicated concentrations of titanium particles with adherent bacterial debris for thirty minutes. Results represent the mean (and standard error) of four independent experiments. Each experiment included three culture wells per group, with each well assayed in triplicate. **Compared with wild-type macrophages at the same particle concentration, the difference was significant (p < 0.01).**

**Figure 3.** TIRAP/Mal deficiency does not inhibit induction of proinflammatory cytokines by soluble IL-1β. TNF-α (Fig. 3-A) and IL-1β (Fig. 3-B) mRNAs were measured after incubation with the indicated concentration of IL-1β or titanium particles with adherent bacterial debris (1 · 10⁸ particles/cm²) for thirty minutes. Results represent the mean (and standard error) of four independent experiments. Each experiment included three culture wells per group, with each well assayed in triplicate. Mφs = macrophages, WT = wild-type, and NS = not significant. **P < 0.01.**
PAMPs to the wear particles. The role of TIRAP/Mal in this regard is of special interest because of the genetic association between aseptic loosening and polymorphisms in the TIRAP/Mal locus.

Materials and Methods

Titanium Particle Preparation
As-received titanium particles from the same batch and lot used in prior studies (Johnson Matthey, Ward Hill, MA; catalogue number 00681, lot F06Q16) have substantial adherent bacterial debris (34 endotoxin units/10⁹ particles) as we previously described⁴,⁵. “Endotoxin-free” titanium particles (<0.3 endotoxin units/10⁹ particles) were prepared by five rounds of cycle cleaning as reported previously⁶. Titanium particles with adherent lipopolysaccharide (33 endotoxin units/10⁹ particles) were prepared by incubating “endotoxin-free” titanium particles with 50 µg/mL ultrapure lipopolysaccharide (InvivoGen, San Diego, CA) for four days in phosphate buffered saline containing 1.1 mM calcium chloride⁷. Those particles were then washed ten times in phosphate buffered saline with calcium chloride to remove any unbound, soluble lipopolysaccharide. The final wash was confirmed to be free of endotoxin therefore documenting removal of unbound lipopolysaccharide.

Endotoxin Testing
To determine the endotoxin levels on the particles, high sensitivity spectrophotometric Limulus amebocyte lysate assays (Biowhittaker, Walkersville, MD) were performed as previously described⁸. Particles were resuspended in 25 µL of endotoxin-free water plus 25 µL of B-G Blocker (both from Biowhittaker) to eliminate false positive results due to β-glucans and β-glucan-like molecules⁹. To eliminate false negative results due to assay inhibition, all assays included additional aliquots of particles spiked with known amounts of endotoxin⁴.

In Vitro Experiments
Particle-induced cytokine expression was compared in wild type and TIRAP/Mal⁻/⁻ murine macrophages. Both types of macrophages were from a C57BL/6 background and were immortalized as previously described⁴⁶,⁴⁷. Both cell types were maintained in 5% carbon dioxide at 37°C on tissue culture dishes with Dulbecco’s Modified Eagle’s Medium ([DMEM] Mediatech, Herndon, VA) with 10% heat inactivated fetal bovine serum (HyClone), non-essential amino acids (Mediatech), 2 mM L-glutamine (Mediatech), 100 µg/mL streptomycin (Mediatech), and 100 U/mL penicillin (Mediatech). Macrophages were plated with the above media at a density of 5x10⁴ cells/cm² in 24-well tissue culture plates for mRNA measurements or at 2.5x10⁵ cells/cm² in twelve-well tissue culture plates for cytokine secretion measurements. After twenty-four hours, nonadherent cells were removed by rinsing twice with Dulbecco’s Phosphate Buffered Saline (PBS) without divalent cations (Mediatech). Adherent cells were then incubated in the presence of the indicated concentrations of titanium particles with adherent bacterial debris, “endotoxin-free” titanium particles, titanium particles with adherent LPS, recombinant murine IL-1β, or the vehicle control (DMEM containing 1% heat inactivated bovine serum albumin [R&D Systems, Minneapolis, MN]) as previously described⁴⁶,⁴⁷.

mRNA Experiments
The time-points used for our experiments were based on peak mRNA expression in macrophages incubated with titanium with adherent bacterial debris (Appendix Figure 1) and “endotoxin-free” particles (Appendix Figure 2). After macrophages were incubated for the indicated times with the various stimuli, the media were aspirated, and the macrophages were rinsed twice with PBS. RNA from the adherent cells was isolated using the SV Total RNA Isolation System kit (Promega, Madison, WI) and assessed for concentration and purity by optical density measurement. One hundred nanograms of total cellular RNA were reverse transcribed into cDNA (Invitrogen Gibco, Grand Island, NY). Real time reverse transcription polymerase chain reaction assays were carried out to measure TNFα, IL-1β, and IL-6 mRNAs using standard curves as we previously described⁴⁶,⁴⁷.

ELISA Experiments
Similar to the mRNA experiments, macrophages were incubated for times corresponding to peak cytokine secretion (data not shown) with the various stimuli. After incubation, the media were collected, centrifuged (2300g, 25 minutes), passed through a 0.2 micron µm filter (Gelman Sciences, Ann Arbor, MI), aliquoted, and stored at ~80°C until used. TNFα, IL-1β, and IL-6 concentrations were determined by ELISA using capture and detecting antibodies (R&D Systems).

In Vivo Experiments
To quantify osteolysis, we utilized a validated murine calvarial model of titanium-induced osteolysis⁴⁸. All animal procedures were in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were performed with the approval of our Institutional Animal Care and Use Committee. TIRAP/Mal⁻/⁻ and wild type mice, both on the C57BL/6 background, were matched for age and gender. Mice were randomly assigned to receive titanium particles with adherent bacterial debris, titanium particles with adherent LPS, “endotoxin-free” titanium, or an equal volume of the vehicle control (PBS alone). Thus, 8x10⁷ titanium particles suspended in 40 µL of PBS were implanted on the parietal bones of 6-8 week-old female mice after removal of the periosteum⁴⁹. The mice were euthanized after seven...
Figure 4. TIRAP/Mal deficiency inhibits induction of cytokine expression by titanium particles with adherent bacterial debris. TNF-α (Figs. 4-A and 4-D), IL-1β (Figs. 4-B and 4-E), and IL-6 (Figs. 4-C and 4-F) mRNA (Figs. 4-A, 4-B, and 4-C) and protein (Figs. 4-D, 4-E, and 4-F) levels were measured after incubation with titanium particles with adherent bacterial debris at time points corresponding to peak levels. Results represent the mean (and standard error) of three independent experiments. Each experiment included three culture wells per group, with each well assayed in triplicate. Mφ = macrophages, WT = wild-type, and NS = not significant. *P < 0.05. **P < 0.01. ***P < 0.001.
days, the time of peak osteolysis\textsuperscript{16}, and their parietal bones were harvested and air-dried after removal of all particles and surrounding soft tissues. Microradiographs were prepared and osteolysis was measured in a blinded fashion by computer-assisted histomorphometry over each parietal bone and in a rectangular region 300 pixels wide centered over the central suture and extending the entire length of the suture as previously described\textsuperscript{16,16}.

**Statistical Analysis**

Cytokine mRNA levels were normalized to levels of glyceraldehyde 3-phosphate dehydrogenase (GAPDH) mRNA. Cytokine secretion was expressed by concentration (ng/mL) in the cell culture media. Each experiment included three culture wells per test group, with each culture well assayed in triplicate. All in vitro results are presented as the means ± SE of N = 3-4 independent experiments. An a priori power analysis demonstrated 11 mice (N = 22 parietal bones/group) were needed to detect a decrease in osteolysis of 50% (α = 0.05, power = 0.8). The results of in vivo experiments are reported as the mean percentage osteolysis ± SE of N = 11 mice/group for both the whole parietal bones and suture zones. All of the data sets passed normality and equal variance testing. In vitro results were therefore analyzed by 2-way ANOVA with Bonferroni post-hoc corrections and osteolysis measurements were analyzed by one-way ANOVA with Bonferroni post-hoc tests (StatView 3.0, SPSS). P values less than 0.05 were considered significant.

**Results**

**TIRAP/Mal deficiency reduces the biologic activity of orthopaedic wear particles both in vitro and in vivo.**

Initial experiments focused on the rapid induction of mRNAs encoding the pro-inflammatory cytokines TNFα and IL-1β. Exposure for 30 minutes to titanium particles with adherent bacterial debris potently induced expression of those mRNAs by wild-type macrophages but had little or no effect on TIRAP/Mal\textsuperscript{-/-} macrophages (Figure 2A-B). Of the particle concentrations tested, 1x10\textsuperscript{8} particles/cm\textsuperscript{2} induced the highest cytokine mRNA production and was therefore used for all remaining in vitro experiments (Figure 2A-B).

To determine the specificity of the effect of TIRAP/Mal deletion, we examined stimulation with IL-1β, which signals through MyD88 but independently of TIRAP/Mal.\textsuperscript{16} These experiments showed that TIRAP/Mal\textsuperscript{-/-} macrophages respond robustly to IL-1β (Figure 3A-B). We next determined the periods of maximum cytokine production for titanium particles with adherent debris and based the remainder of the in vitro experiments with those particles on the results shown in Appendix Figure 2. For example, in wild-type macrophages, peak expression of TNFα and IL-1β mRNAs occurred after four hours and levels returned to baseline by twenty-four hours.
PARTICLE-INDUCED OSTEOLYSIS

Figure 6. TIRAP/Mal deficiency does not inhibit induction of cytokine expression by endotoxin-free titanium particles; however, the inhibition is reconstituted by adherence of ultrapure lipopolysaccharide. TNF-α (Figs. 6-A and 6-C), IL-1β (Figs. 6-B and 6-D), and IL-6 (Fig. 6-E) mRNA (Figs. 6-A, 6-C, and 6-E) and protein (Figs. 6-B and 6-D) levels were measured in wild-type (WT) and TIRAP/Mal-/- macrophages (Mφ) incubated with endotoxin-free titanium particles, titanium with adherent bacterial debris, or titanium with adherent lipopolysaccharide (1 x 10^8 particles/cm²) at two hours for mRNA and twenty-four hours for protein. IL-6 mRNA levels are not reported as there is minimal IL-6 transcription after two hours of incubation. Results represent the mean (and standard error) of three independent experiments. Each experiment included three culture wells per group, with each well assayed in triplicate. NS = not significant. *P < 0.05. **P < 0.01. ***P < 0.001. #Compared with wild-type macrophages incubated with either endotoxin-free particles or with the vehicle control, the difference was significant (p < 0.05). $Compared with wild-type macrophages incubated with the vehicle control, the difference was significant (p < 0.05).
Figure 7. TIRAP/Mal deficiency inhibits induction of cytokine expression by titanium particles with adherent lipopolysaccharide. TNF-α (Figs. 7-A and 7-D), IL-1β (Figs. 7-B and 7-E), and IL-6 (Figs. 7-C and 7-F) mRNA (Figs. 7-A, 7-B, and 7-C) and protein (Figs. 7-D, 7-E, and 7-F) levels were measured in wild-type (WT) and TIRAP/Mal-/- macrophages (Mc) incubated with titanium particles with adherent lipopolysaccharide at time points corresponding to peak levels. Results represent the mean (and standard error) of three independent experiments. Each experiment included three culture wells per group, with each well assayed in triplicate. NS = not significant. *P < 0.05. **P < 0.01. ***P < 0.001.
while peak expression of IL-6 mRNA was delayed until 24 hours (Appendix Figure 1 and Figure 4A-C) as were peak levels of all three cytokine proteins in the media (Figure 4D-F).

In contrast, TIRAP/Mal -/- macrophages expressed significantly lower levels of all three cytokines at both the mRNA (Figure 4A-C) and protein levels (Figure 4D-F). In vivo, particles with adherent bacterial debris induced significantly less osteolysis in the calvaria of TIRAP/Mal -/- mice than in wild-type mice (2nd pairs of bars in Figure 5A-B). We therefore concluded that TIRAP/Mal deficiency significantly reduces both in vitro pro-inflammatory cytokine production and in vivo osteolysis in response to titanium particles with adherent bacterial debris.

The effects of TIRAP/Mal depend on the adherence of PAMPs to wear particles.

We previously showed that "endotoxin-free" titanium particles induce substantially less cytokine production in vitro and osteolysis in vivo than the titanium particles with adherent bacterial debris18,19,50,51. Moreover, the residual biological activity of the "endotoxin-free" titanium particles does not depend on TLR-2 or TLR-418,19. We therefore determined the periods of maximum cytokine production for "endotoxin-free" titanium particles (2 hours for mRNA and twenty-four hours for protein) using a particle concentration of 1x10⁸ particles/cm² and based the remainder of our in vitro experiments on this data (Appendix Figure 2 & data not shown). Consistent with our hypothesis that the effects of TIRAP/Mal depend on the adherence of bacterial PAMPs to the wear particles, TIRAP/Mal deficiency did not alter osteolysis or cytokine production induced by "endotoxin-free" titanium particles (3rd pairs of bars in Figures 5A-B and 6A-E). Moreover, the responses induced by "endotoxin-free" titanium particles in wild-type mice were similar to those induced by titanium particles with adherent bacterial debris in TIRAP/Mal -/- mice (Figure 5A-B). The endotoxin removal protocol does not alter the size, shape, or surface chemical composition of the particles42,52. To further determine whether the effects of the endotoxin removal protocol are due to the removal of adherent PAMPs rather than to some other unidentified alteration, we asked whether adherence of ultrapure lipopolysaccharide would reconstitute the biological activity of the particles and the dependence on TIRAP/Mal. Indeed, titanium particles with adherent lipopolysaccharide potently induced osteolysis in wild-type mice and cytokine production by wild-type macrophages and these effects were significantly inhibited by TIRAP/Mal deficiency (4th pairs of bars in Figure 5A-B and 6C-E). Time course experiments were performed to further examine the effects of the particles with adherent lipopolysaccharide. The results of these experiments (Figure 7A-F) closely mirror the results obtained with particles with adherent bacterial debris (Figure 4A-F). We therefore conclude that the effects of TIRAP/Mal are dependent on the adherence of PAMPs to the wear particles, and that the effects of "endotoxin-free" titanium particles are independent of TIRAP/Mal.

Discussion

The primary conclusions of this study are that TIRAP/Mal deficiency reduces the biologic activity of orthopaedic wear particles both in vitro and in vivo and that the effects of TIRAP/Mal depend on the adherence of bacterial PAMPs to the wear particles. Since TIRAP/Mal functions exclusively downstream of TLR-2 and TLR-416, the first conclusion is consistent with prior results that both of those TLRs mediate the biologic activity of the titanium particles18,19. Moreover, those results in combination with the genetic association between polymorphisms within the TIRAP/Mal locus9 support the hypothesis that TIRAP/Mal is a mediator of particle induced osteolysis and aseptic loosening. The genetic association between polymorphisms within the TIRAP/Mal locus9, in combination with the second major conclusion of this study that the effects of TIRAP/Mal depend on the adherence of bacterial PAMPs to the wear particles, also supports the hypothesis that bacterial PAMPs contribute to aseptic loosening. Those results also support our previous conclusion that alarmins are not sufficient by themselves to activate either TLR-2 or TLR-418. Alarmins may nonetheless contribute to aseptic loosening either by acting together with the PAMPs to activate the TLRs or by mechanisms that are independent of the TLRs6. For example, alarmins might contribute to post-translational processing by inflammasomes of pro-IL-1β and pro-IL-1β to the active interleukins7,53,54.

Limitations of the current study include that we only examined one adaptor protein that is specific to two TLRs. In that regard, a polymorphism in a second adaptor protein known as TRIF-related adaptor molecule (TRAM) also associated with accelerated development of aseptic loosening in the discovery cohort of our previous study9. As depicted in Figure 1, TRAM is an adaptor protein that binds exclusively to the cytoplasmic domain of TLR-4 and bridges the related adaptor protein, TRIF, to the receptor complex6. Although additional studies will be required to assess the role of TRAM and TRIF in aseptic loosening, it has been reported that genetic deletion of TRIF does not reduce responses of macrophages to wear particles12. The current study also did not include particles that specifically activate TLR-2. However, TLR-2 signals exclusively through TIRAP/Mal plus MyD8816, in contrast to TLR-4 that can signal
either through TIRAP/Mal plus MyD88 or through TRAM plus TRIF (Figure 1). It is therefore likely that the role of TIRAP/Mal in responses to the titanium particles with adherent bacterial debris documented in the current study include the TLR-2 dependent responses that we previously showed with the same particles. The current study also did not examine wear particles consisting of materials other than titanium. However, other investigators demonstrated that the biologic activity of particles consisting of UHMWPE, cobalt-chromium, and hydroxyapatite also depend on TLR-2 and TLR-4 and therefore also likely involve TIRAP/Mal. Finally, it should also be appreciated that the genetic associations of aseptic loosening with polymorphisms within the TIRAP/Mal locus requires confirmation in larger studies.

In conclusion, this study demonstrated that TLR signaling through TIRAP/Mal in response to wear particles with adherent PAMPs contributes to inflammatory responses in cell culture and murine models of aseptic loosening. Although wear particles are thought to be the primary initiators of aseptic loosening, there is likely to be other factors that modulate the bioactivity of the particles. Evidence is emerging that genetic susceptibility, TLR activation, and bacterial PAMPs are three such factors. Further studies are needed to elucidate the roles of other pathogen recognition receptors and other adaptor proteins and the mechanisms responsible for particle-induced osteolysis in the absence of PAMPs. Detailed understanding of those topics may lead to identification of novel therapeutic targets in the treatment of patients with aseptic loosening.

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Powered Lower-Limb Exoskeletons to Restore Gait for Individuals with Paraplegia – a Review

Sarah R. Chang, BS1,2, Rudi Kobetic, MS1, Musa L. Audu, PhD1, Roger D. Quinn, PhD1,3, Ronald J. Triolo, PhD1,2,4

1Advanced Platform Technology Center, Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Departments of 2Biomedical Engineering, 3Mechanical Engineering and Aerospace Engineering, and 4Orthopaedics, Case Western Reserve University

ABSTRACT
Individuals with paraplegia due to spinal cord injury rank restoration of walking high on the list of priorities to improving their quality of life. Powered lower-limb exoskeleton technology provides the ability to restore standing up, sitting down, and walking movements for individuals with paraplegia. The robotic exoskeletons generally have electrical motors located at the hip and knee joint centers, which move the wearers’ lower limbs through the appropriate range of motion for gait according to control systems using either trajectory control or impedance control. Users of exoskeletons are able to walk at average gait speeds of 0.26 m/s and distances ranging between 121-171 m. However, the achieved gait speeds and distances fall short of those required for full community ambulation (0.8 m/s and at least 230 m), restricting use of the devices to limited community use with stand-by assist or supervised rehabilitation settings. Improvement in the gait speed and distance may be achievable by combining a specially designed powered exoskeleton with neuromuscular stimulation technologies, resulting in a hybrid system that fully engages the user and achieves the necessary requirements to amble in the community environment with benefits of muscle contraction.

Between 270,000 and 1.275 million individuals in the United States are living with spinal cord injury (SCI), where approximately 37% of SCI result in paraplegia12. Among individuals with paraplegia, 38% rank restoration of walking as first or second priorities to improve their quality of life1. Restoring gait can improve overall health including increased cardiovascular fitness, better bone density, improved bladder and bowel function, reduced spasticity, and reduced onset of pressure sores4-6. Gait for individuals with SCI can be restored using neuromuscular stimulation, orthotic braces, robotic exoskeletons, and hybrid neuroprostheses which combine stimulation and orthoses. In this review paper, we will address the existing powered exoskeleton technology that is used to restore gait for individuals with paraplegia and their mobility outcomes.

Several exoskeletons are in the process of being commercialized or are still only found in laboratory research or rehabilitation center environments. Motorized exoskeletal devices developed to aid walking disabilities include ‘Rex’ (Rex Bionics, New Zealand)7-8, ‘ReWalk™’ (ReWalk Robotics Ltd., Israel)9-13, ‘HAL’ (Cyberdyne, Inc., Japan)14-16, ‘Ekso™’ (Ekso™ Bionics, USA)17-18, ‘Indego™’ (Parker Hannifin, USA)19-24 (Figure 1). There is also a research grade powered exoskeleton called the H2 developed to assist individuals post-stroke but also claimed to be capable of assisting individuals with SCI25. Robotic exoskeletons generally use battery-powered electric motors at each hip and knee joint to move the lower extremities through the proper trajectory to produce ambulation. A joystick, control pad, wrist watch, or preprogrammed motions such as a weight shift from forward lean are used to perform the user–selected activity.

Rex
Rex is a robotic walking device that is self-supporting and independently controlled to enable a user to perform basic functions such as stand up, walk, sit down, ascend and descend stairs, and turn without the need for crutches or a walker (Figure 1a)7. During static standing, the hands can be free for the user to perform tasks such as reaching at a counter. The robotic device can be used by individuals with a complete SCI up to the C4/C5 level. Rex has not undergone clinical trials but preliminary research has been performed to combine the Rex robotic device with electroencephalography signals. By combining Rex with the electroencephalography–based brain machine interface capabilities, researchers aim to interpret user intent to assist an impaired individual to walk independently without the need for external control6. There has not been any published research on gait outcomes from the Timed Up and Go (TUG) test, 6-meter walk test (6MWT), or 6-minute walk test (6MWT).

ReWalk™
ReWalk™ is a powered exoskeleton that
can restore independent gait with the use of forearm crutches for individuals with thoracic-level (T7) to lumbar-level (L5) SCI (Figure 1b). ReWalk™ is the only exoskeleton currently approved by the FDA for use at home and in the community with a trained companion, and one of the two exoskeletons approved by the FDA for therapeutic purposes in medical settings under close supervision. The exoskeleton includes motors at each hip and knee joint, a battery unit, computer-based closed-loop controller, and various sensors to measure upper-body tilt angle and joint angles. The hip and knee joints are hinged and the ankle joints are articulated with a spring-assisted dorsiflexion. Activity modes of stand, sit, or start walking can be selected with a wristwatch controller by the user. During walking, the user initiates a step with the forward upper-body movement detected by a tilt sensor, at which point the joint motors will move through a predefined joint trajectory to complete the step.

Clinical trials have evaluated the mobility outcomes such as gait speed, maximum walking distance, Timed Up and Go (TUG) test, 10-meter walk test (10MWT), and 6-minute walk test (6MWT) when using the ReWalk™. Ten male participants with injury levels ranging from cervical level 8 (C8) to lumbar level 1 (L1) have been trained to walk with the ReWalk™ exoskeleton. After one hour of exoskeleton training session twice a week, for a 10-week training period, the majority of participants were able to walk at gait speeds ranging from 0.25-0.48 m/s, walk longer distances ranging from 91-170 m (increased by an approximate average of 23 m from mid-training), and be quicker in standing up, rotating and sitting down (decreased TUG test time by an approximate average of 9s). Twelve individuals with SCI have been trained to walk without human assistance using the ReWalk™ and evaluated with the mobility measures. Gait speeds ranged from 0.03 to 0.45 m/s (average of 0.25 m/s) and walking distances during the 6MWT ranged from 10.8 to 150.4 m [12-13].
HAL
The Hybrid Assistive Limb (HAL) is a powered exoskeleton that was designed to augment nondisabled individuals in their activities, physically support users performing heavy work, and assist gait for individuals with incomplete SCI or who have paralysis due to a stroke (Figure 1c)14. The robot suit HAL includes motors at each hip and knee joint, a passive spring at each ankle for dorsiflexion bias, controller computer unit, batteries, bioelectrical sensors, angular sensors, acceleration sensors, and floor reaction force sensors. The bioelectrical sensors detect minimal electromyography signals from the extensor and flexor muscles of the hip and knee, which can be used to indicate a user’s intent to take a step when walking with HAL.

For users who have impaired walking, HAL uses an autonomous controller based on healthy walking to provide the necessary assistance at the hip and knee joints to move the lower extremities through the appropriate trajectory for ambulation. There is also a cable connection between the exoskeleton and the user, which would allow voluntary robotic supported range of motion. HAL has been evaluated as a tool for rehabilitation for those with chronic incomplete SCI15. Eight participants (injury levels ranging from T7–L3) were trained with the exoskeleton HAL for body weight supported treadmill walking at variable gait speeds and with varying levels of body weight support. After 90 days (five days a week) of training, individuals with incomplete SCI walked at an average speed of 0.50 ± 0.34 m/s with the device as compared to 0.28 ± 0.28 m/s before the training. Walking distances achieved using HAL in the 6MWT before the training was 70.1 ± 130 m and after the training was 163.3 ± 160.6 m, where the distance after training was significantly different from the distance before training15.

Ekso™ Bionics
The Ekso™ Bionics exoskeleton enables individuals with weakened or impaired lower extremities to stand up and walk over ground using an assistive device such as forearm crutches or a walker (Figure 1d)16. The Ekso™ is the second of the two exoskeletons approved by the FDA for therapeutic purposes in medical settings under close supervision. The exoskeleton has battery-powered motors at each hip and knee joint that drives the legs through the proper step pattern and a passive spring for dorsiflexion at the ankle joint, which can provide rehabilitation, over ground gait training, and upright, weight-bearing exercise. Walking is initiated by the user appropriately shifting the upper body. After 24 weekly sessions of training, seven participants with SCI (two with tetraplegia and five with motor-complete injuries) were able to stand, walk, and sit using the Ekso™18. The participants were able to walk with average speeds ranging from 0.11 to 0.21 m/s and were able to walk for times ranging from 28 to 94 minutes.

Indego®
Indego® is a powered lower extremity orthosis that uses motors at the hip and knee joints to move the user’s joints through a prescribed range of motion for walking based on a set of normal biomechanical walking trajectories (Figure 1e)19. The knee motors have electrically controllable normally locked brakes that will lock the knee joints in the event of a power failure. Standard ankle–foot orthoses can be worn with the Indego® exoskeleton. An assistive device, like forearm crutches or a walker, is used for balance and stability. Joint angle sensors are included at the hip and knee joints, and accelerometers are located in each thigh segment. A tilt sensor in the thoracic piece determines whether the user wants to stand up, sit down, or initiate walking by leaning forward or leaning backward. The Indego® is currently undergoing clinical trials.

Participants trained in walking with the Indego® exoskeleton have been shown to have a mean walking speed of 0.22 m/s, with speeds ranging from 0.22–0.45 m/s depending on the participants’ level of injury20–22. Based on the 6MWT, individuals using the Indego® have been shown to have walking distances ranging from 64–121 m depending on the participants’ level of injury, where participants with higher levels of injury walked the shorter distances and participants with lower levels of injury walked the longer distances20. Indego® also estimates that a user would be able to walk a range of 800 m if walking at 0.22 m/s, based on the electrical power measurements of the batteries21–22. TUG test measures have not been reported for the Indego®.

The Indego® has been evaluated for stair ascent and descent with one individual with paraplegia (T10 complete injury level), who was able to successfully ascend and descend a set of steps while using upper body effort on handrails23. Research has also been performed on cooperative control of neuromuscular stimulation with the Indego® powered exoskeleton24. Three subjects with paraplegia (T6–T10 complete) walked with stimulation of the hip and knee extensors while the exoskeleton motors generated hip and knee flexion at the appropriate time during the gait cycle. The cooperative control of neuromuscular stimulation with the powered exoskeleton showed consistent and repeatable gait trajectories, as well as reduced the required torque and power output of the motors compared to walking without neuromuscular stimulation.

H2
H2 is a lower limb exoskeleton that can be used for over ground gait rehabilitation training with an assistive device such as forearm crutches (Figure 1f)25. The
device weighs 12kg and has six actuated joints, with the hip, knee, and ankle joints all fitted with electric motors, a battery pack, joint angle and velocity sensors, and sensors to measure force and torque interaction between the user’s limbs and the exoskeleton, and foot switches to measure contact between the user’s feet and the ground. Unlike the other exoskeletons that use trajectory control for the strategy to restore the user’s gait, the H2 algorithm uses a combination of trajectory control and an interaction torque between the subject and the exoskeleton to generate an adaptive reference for the gait assistance that only assists as needed\(^{25}\). The H2 system has been tested with three participants with post-stroke, though the researchers claim that the system can also be used for individuals with incomplete SCI. Two of the three subjects showed slight improvements in the 6MWT and TUG test.

**CHALLENGES**

While these commercially available and research grade powered exoskeletons are able to restore walking motion at speeds effective for household ambulation, walking speeds and distances when using these devices are still less than what is defined as community ambulation. A full community ambulator is defined as someone able to maintain a speed of 0.8 m/s, while a limited community ambulator is able to walk a speed of 0.4 m/s\(^{26}\). The required velocity to cross a road safely is considered to be approximately 1.06 m/s\(^{-1}\).\(^{27,28}\) It is estimated that the walking distance of 230–342 m for some activities such as supermarket shopping is necessary for full community ambulation\(^{29}\).

The walking speeds reported for Ekso\(^{\text{TM}}\) (0.11–0.21 m/s), ReWalk\(^{\text{TM}}\) (0.25–0.48 m/s), HAL (0.50 ± 0.34 m/s), and Indego\(^{\circledR}\) (0.22–0.51 m/s) are all on average (0.26 m/s) less than half the established and commonly accepted threshold of 0.8 m/s for full community ambulation\(^{26,29}\). Based on the 6MWT, ReWalk\(^{\text{TM}}\) has been shown to have walking distances ranging from 10.8–170 m\(^{10,11}\). Indego\(^{\circledR}\) has been shown to have walking distances ranging from 64–121 m depending on the participants’ level of injury\(^{29}\). Indego\(^{\circledR}\) also estimates that a user would be able to walk a range of 800m if walking at 0.22 m/s, based on the electrical power measurements of the batteries\(^{21,22}\). Ekso\(^{\text{TM}}\) does not report any walking distances. Indego\(^{\circledR}\) has the potential to achieve the 342.0 m for community ambulation because of the battery life and assuming the user is conditioned to complete the distance. Maximum walking distances reported for these powered exoskeletons range from 121 to 171 m, approximately half the distances assumed to be functional in the community, where functional distances can be over 500 m for certain tasks\(^{27,28}\). The robotic exoskeletons can be effective at helping “non-ambulators” become “household ambulators”, but are inadequate for unstructured community environments that involve other pedestrians or automobile traffic.

**ALTERNATIVE APPROACHES**

An alternative approach taken to restore walking for individuals with paraplegia is neuromuscular stimulation. Stimulation can produce a majority of the torque required to move or stabilize the lower extremities against collapse, enabling most users of a surface stimulation system or an implanted neuroprosthesis to stand and initiate stepping. There have been anecdotal and subjective improvements in pain, spasticity, and bowel and bladder function when assuming an upright posture, passively moving the joints, and exercising the arms and torso with the powered exoskeletons\(^{30–31}\). However, this does not take advantage of the individual’s own muscle power and the added exercise benefits that can be gained by stimulating the paralyzed muscles. Use of a stimulation system (Parastep\(^{\circledR}\)) has been shown to reduce muscle spasticity, increase muscle mass and blood flow in the lower extremities, and result in psychological benefits such as enhanced self-image and decreased incidence of depression\(^{6,6,32}\). With the implanted neuroprostheses developed in our laboratory applying neuromuscular stimulation to the appropriate lower extremity muscles, gait speeds can range from 0.5 to 0.9 m/s over maximal distances of 300–400 m\(^{33–35}\). Gait speeds and distances vary between subjects, but approach the accepted benchmark for unrestricted community ambulation of 0.8 m/s\(^{36}\) and the 1.06 m/s gait speed considered necessary to safely cross an intersection, as well as the 230–342 m distance for activities such as supermarket shopping\(^{27,28}\).

Even though walking with neuromuscular stimulation approaches the accepted gait speeds and distances required for full community ambulation, the lower extremity muscles of the neuroprosthesis users can rapidly fatigue. Implanted neuromuscular stimulation that actively generates joint moments by contracting the otherwise paralyzed muscles has been successfully integrated with passive hydraulic exoskeleton orthotic constraints to mechanically support the user’s body weight in a hybrid neuroprosthesis (HNP) that enables individuals with SCI to stand, walk, negotiate stairs, and perform a controlled stand-to-sit transition (Figure 2). In one design, a variable hip constraint mechanism can lock, free, or reciprocally couple the hips, while a dual state knee mechanism locks the knee during stance and frees the knee during swing phase\(^{36–38}\). State-based control of the mechanisms and modulation of neuromuscular stimulation patterns targeting hip and knee muscles during gait have been developed that use pressure and position sensors to implement real-time control of the HNP\(^{39}\).
Combination of neuromuscular stimulation and orthotic constraints increased walking speed by almost 15% compared to conventional reciprocal gait orthoses. The hybrid approach also reduced stimulation duty cycle by more than two thirds as compared to walking with stimulation only, potentially delaying the onset of fatigue and extending walking distance. A variable impedance knee mechanism combined a fluid damper with a linkage transmission to provide sufficient knee stiffness to support a user and substitute for eccentric contractions of the knee extensor muscles during stance phase of gait, while minimizing knee impedance during swing. Damping the knee during stance phase reduces impact at loading and maintains forward progression during gait.

When negotiating stairs, the damper assisted in regulating lowering speeds during descent and reduced the reliance on upper limbs to approximately 40-45% body weight as compared to 70% body weight measured when descending stairs with stimulation alone. Control of the knee during the stand-to-sit transition for individuals with paraplegia has been improved with the implementation of kinematic and kinetic orthotic constraints. A coupling mechanism was designed to coordinate the hip and knee joints, and a damping mechanism was designed to keep a constant knee angular velocity during the transition. Use of these orthotic mechanisms improved the overall coordination between the hip and knee joints for individuals with paraplegia, causing the joints to approach the 1:1 coupling ratio seen in nondisabled individuals. The upper limb forces on the walker were reduced by 70% when sitting down with both the coupling and damping mechanisms as compared to sitting with only stimulation. Similarly, the impact force when making contact with the seating surface was reduced by half for individuals with SCI sitting down with the coupling and damping mechanisms as compared to sitting with stimulation alone. By reducing upper limb and impact forces with the orthotic mechanisms, the potential for injuries during the stand-to-sit transition can be decreased.

**CONCLUSION**

The ability to restore gait for individuals with paraplegia has improved with progress in various powered exoskeletons and neuromuscular stimulation technologies. The powered exoskeletons are able to restore the stand up, sit down, and walking motions. However, they have limits in achievable gait speeds and distances. Neuromuscular stimulation has been shown to allow users to approach the gait speeds and distances for full community ambulation. As advancements through research in these technologies continue to be made, the intersection of powered exoskeletons and neuromuscular stimulation is foreseeable in the next steps to creating a commercial-grade ambulatory assist system that requires less effort of the user and provides more consistent results, while capable of interacting in the home and community environments and at the same time providing tremendous health benefits to the user.

**Acknowledgements**

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**References**

POWERED LOWER-LIMB EXOSKELETONS TO RESTORE GAIT


RAINBOW VISITING PROFESSOR 2015

April 21-22, 2015

Daniel R. Cooperman, MD
Professor, Orthopaedic Surgery and Rehabilitation, Yale University

Grand Rounds: "Hip Shape and Prognosis"

Dr. Cooperman comes home to Case as the 2015 Rainbow Visiting Professor. Here he is alongside two of his longtime partners, friends, and colleagues Drs. Randall Marcus and George Thompson.

BOHLMAN VISITING PROFESSOR 2015

May 12-13, 2015

Paul Anderson, MD, MS
Professor, Orthopaedic Surgery and Rehabilitation, University of Wisconsin

Grand Rounds: "Prevention of Surgical Site Infection"

Dr. Paul Anderson (second from the right) alongside members of our spine faculty Drs. Zachary Gordon, Chris Furey, and Tim Moore.
SCOTT INKLEY VISITING PROFESSOR 2015

June 2-3, 2015

John G. Seiler III, MD
Clinical Professor, Orthopaedics,
Emory University

Grand Rounds: “It’s Just a Stinger”

Dr. Seiler with the graduating chief residents: Drs. Ke Xie, Kelvin Lim, Jonathan Streit, Ashraf Youssef, Eugene Tsai, and Stephen Reichard.

DR. GOLDBERG VISITING PROFESSOR 2015

October 6-7, 2015

C. Lowry Barnes, MD
Professor, Orthopaedic Surgery
Carl L. Nelson MD Chair in Orthopaedic Surgery, University of Arkansas for Medical Sciences

Grand Rounds: “Decision Making in Total Knee Replacements”

Dr. C. Lowry Barnes (3rd from the left) alongside Drs. Matthew Kraay, Claire Rimnac, Christopher Bechtel, Douglas Weinberg, and Randall Marcus.
CARTER–MAKLEY–THEROS LECTURE 2015

November 3–4, 2015

Terrance D. Peabody, MD
Professor, Orthopaedic Surgery
Edwin Warner Ryerson Professor and Chair of Orthopaedic Surgery,
Northwestern University

“Educating the Next Generation of Orthopaedic Surgeons”

Dr. Terry Peabody (center) stands alongside former resident and now Residency Program Director, Dr. Patrick Getty, and our Department Chairman, Dr. Randall Marcus.
OBITUARIES

Dr. Kingsbury G. Heiple

We received the unfortunate news about the passing of one of the “Kings” of our department right as the journal was about to go to press. It is with great sadness that we announce the passing of Dr. Kingsbury G. Heiple on Sunday, March 13, 2016.

Kingsbury Heiple was the Charles H. Herndon Professor and Chairman of the Department of Orthopaedics at Case Western Reserve University (CWRU) School of Medicine and University Hospitals (UH) from 1982 – 1988. Dr. Heiple was an internationally prominent orthopaedic surgeon who made major contributions to the clinical, educational and research missions of our profession.

Dr. Heiple served in the United States Navy during World War II. He was a graduate of the University of Chicago School of Medicine and completed his orthopaedic residency at UH in the CWRU Residency Program. Dr. Heiple joined CWRU and the UH faculty in 1958 and became the Herndon Professor and Chairman in 1982. He retired from practice and became Emeritus Professor in 1993. Kingsbury Heiple was a member of the American Academy of Orthopaedic Surgeons, American Society for Surgery of the Hand, the Orthopaedic Research Society, and the American Orthopaedic Association. He was a Director of the American Board of Orthopaedic Surgery from 1979-1985 and served as its President 1984-1985. He served as an Associate Editor for the Journal of Bone and Joint Surgery from 1969-1980.

Dr. Heiple’s research ranged from seminal work in the mechanical properties of bone to the design of hand, hip and knee implants. His research was funded continuously by the National Institutions of Health (NIH) from 1959-1985. His work resulted in 79 peer reviewed publications and 6 book chapters. In 1985, the American Academy of Orthopaedic Surgeons awarded Dr. Heiple the Kappa Delta Award, the most prestigious award for orthopedic research. In 1993, The University of Chicago Pritzger School of Medicine awarded Dr. Heiple their Distinguished Service Award.

Kingsbury G. Heiple, M.D. greatly contributed to the education and training of over 200 orthopaedic residents. After the announcement of his passing, there was an outpouring of letters and emails to our department from for Case alums expressing their condolences to his family and the privilege to have trained under one of the greats in orthopaedics. As simply stated by one of our alums, “He was a fine gentleman, a gentle man, a scholar, and a simply marvelous teacher of surgical technique.” He will be sadly missed, but fondly remembered by all those who knew him.

Dr. Henry Stein

Dr. Henry George Stein passed away peacefully on May 22, 2015 in Las Vegas, NV. Dr. Stein was born in Bayonne, NY, but grew up in Barberton, OH. He graduated medical school from The Ohio State University and did his residency at Case Western. He became a much loved surgeon in Dayton, OH, where he treated numerous patients during his career. He and his wife, Rita, retired to Las Vegas. Among his many accomplishments, he served as a physician during the first Iraq War in a medical unit in Saudi Arabia, which gave him immense pride. While not only having a passion for WWII history, he also loved cars, flying, big band and classical music, and his dogs: Eli, Daisy and Mac. Furthermore, after retiring to Las Vegas, he became an accomplished pipe maker, which gave him great pleasure. He will be remembered not only for his surgical prowess, but also for his numerous acts of kindness and boundless generosity to all who knew him.
Dr. Barry L. Samson
Dr. Barry L. Samson died July 2, 2015 after a 13 year battle with multiple myeloma. Dr. Samson was an excellent orthopedic spine surgeon. After being diagnosed with cancer, Dr. Samson provided non-surgical care for patients for many years. He was widely recognized by his colleagues and patients for his outstanding knowledge, compassion, wit and character. Dr. Samson graduated from Washington University Medical School in 1974. He completed his fellowship training in spine surgery at the University Hospitals/Case Medical Center in 1979. He practiced orthopedics in the St. Louis Metropolitan area until 2014. He was tremendous supporter of the Multiple Myeloma Research Foundation locally and nationally. Dr. Samson was a respected physician, colleague, and friend to many. He will be greatly missed by all that knew him.

Dr. Karl S. Alfred
Dr. Karl S. Alfred peacefully passed away July 9, 2015 at the age of 97 in Naples, FL. He was born in Stavanger, Norway on July 10, 1917 to Alfred and Thora Abrahamsen. At the age of 6, he immigrated to the United States with his mother. He graduated medical school from Downstate Medical College in Brooklyn, NY. Following medical school, Karl served in the United States Navy as a Medical Lieutenant Commander during WWII. After completing this service to his country, he moved to Cleveland, OH in 1947 and completed his residency in orthopaedic surgery at University Hospitals. He then established a flourishing practice in Cleveland that spanned over half a century. He received both national and international acclaim as an award-winning orthopaedic surgeon, teacher and mentor to scores of orthopaedic surgeons and residents. During his career he served as Chief of Staff at Charity Hospital and also established the Alfred Orthopaedic Lecture at the Cleveland Clinic. Dr. Alfred will be remembered not only for his outstanding career in orthopaedic surgery, but as a caring husband, father, grandfather and great grandfather.

Dr. Howard Geist
Dr. Howard James Geist of Portland died peacefully March 21, 2016, at the age of 86. He was born Aug. 13, 1929 in Madison, WI, to Dr. Frederick and Alice Geist. Howie attended Dartmouth College in preparation for his M.D. at Harvard Medical School. He then had the great fortune to intern at Barnes Hospital in St. Louis, MO, where he met the love of his life, Sally Ray Haase, and they were married in 1956. After two years as a flight surgeon in the U.S. Air Force, he entered and completed an orthopaedic surgery residency at University Hospital in Cleveland and later was on the faculty at Case Western Reserve University. After his time at Case Western, he and Sally explored the country for opportunity and decided on Portland to move their young family. He started an orthopedic practice that helped ease the pain and injuries of thousands of Portland residents for nearly 30 years. Portland was a central part of his life, and he and Sally could often be found on weekends with friends fishing, hiking or at the beach. Howie not only loved the outdoors, fishing, and hunting, but he was an avid skier and squash player. In the second half of his life, he and Sally became dedicated travelers, visiting all seven continents. He will be missed not only by his beloved family, but by all who had the pleasure of knowing him.
Congratulations to the five graduating chiefs of the class of 2016. All five will be completing a fellowship in the 2016-2017 academic year.

**CLASS OF 2016 FELLOWSHIP MATCH**

Christopher Bechtel, MD  
Adult Reconstruction,  
Rothman Institute-Thomas Jefferson University

Michael Reich, MD  
Adult Reconstruction,  
Scripps Clinic

Michael Karns, MD  
Sports Medicine,  
University of Utah

Claire Shannon, MD  
Pediatric Orthopaedics,  
The Hospital for Sick Children,  
University of Toronto

Cynthia Nguyen, MD  
Pediatric Orthopaedics,  
University of Utah
INSTRUCTIONS FOR AUTHORS

1. Manuscript submissions are accepted in electronic format only. All submissions should be sent to caseorthojournal@yahoo.com and have “COJ SUBMISSION” as the subject heading. All submissions should be in Microsoft WORD format. Photos, figures and tables should be submitted in separate jpeg, tiff, or PDF files not embedded within the Word Document.

2. Title should include author’s name, degree achieved, institutional affiliation, and the order of authors in which they should appear.

3. Manuscript
   a. Abstract – Limit to 325 words
   b. Body –
      i. Introduction - State the problem that led to the study, including a concise review of only the relevant literature. State your hypothesis and the purpose of the study.
      ii. Methods - Describe the study design in detail using standard methodological terms. All study designs should include information about how the sample was identified including sample size, inclusions and exclusions. The statistical section should be described in detail with particular emphasis on the statistical strategy used to analyze the data.
      iii. Results – Provide a detailed report on the data obtained during the study.
      iv. Conclusion - Be succinct in this section. Discuss what your study shows. Discuss the importance of the article with regard to the relevant published literature. Discuss the strengths, weakness and limitations of your study.

4. References
   a. The references should be numbered according to the order of citation in the text (not alphabetically) and should be in PubMed/Index Medicus format (go to the NCBI web site for examples (www.ncbi.nlm.nih.gov/entrez/query.fcgi).
   b. All references must be cited in the text.

5. Figures and Tables should be submitted separate from the manuscript text (i.e. Word Document).

6. Scientific Manuscripts – Limit total word count to 4000.

7. Case Reports – Limit total word count to 1500.

CALL FOR ABSTRACTS 2016

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