Discoveries 2009
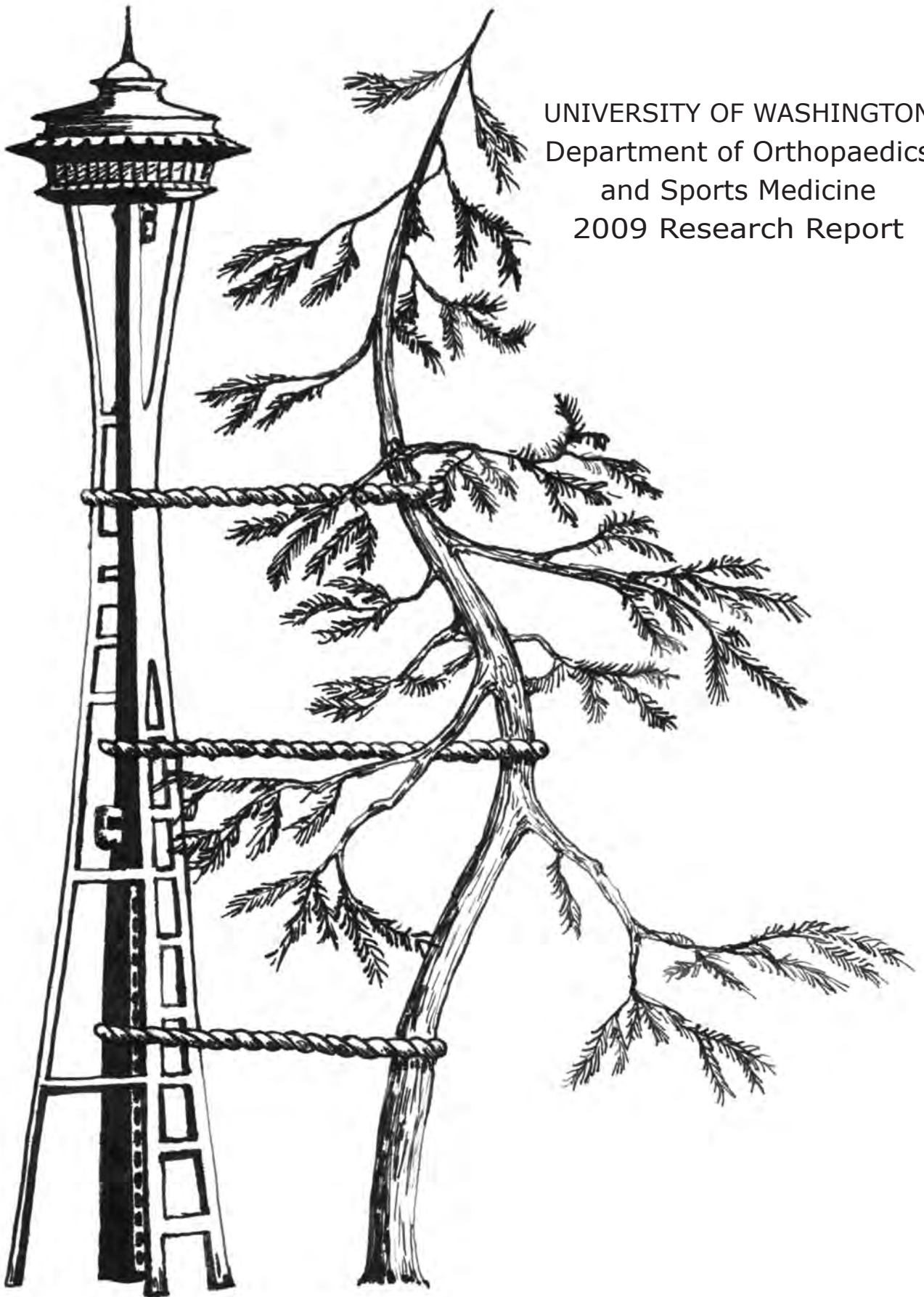
UNIVERSITY OF WASHINGTON
Department of Orthopaedics
and Sports Medicine
2009 Research Report

Contents

Foreword

Orthopaedics is a specialty dedicated to regeneration and renewal. Fortunately our bodies are pretty good at restoring comfort and function after injury. When a bone is broken, stem cells and growth factors surge at the site of injury causing new bone to form, reconnecting broken bone ends. But that's not the end of the story. The newly formed bone then remodels progressively under the influence of mechanical loading to a structure virtually identical to the bone before the injury: regeneration!

In Orthopaedics we have the opportunity to assist nature in this process of regeneration. We align the bone so that the regenerated structure has the right length and shape. We approximate the torn ends of the rotator cuff so that healing can regenerate a strong and smooth tendon. On occasion, as with a torn anterior cruciate ligament, the body cannot heal the injury; in this situation we have learned to insert a tendon graft in a way that it remodels to a regenerated ligament. When a fracture crushes part of the bone of the knee, we use a bone graft taken from the pelvis that enables the body to regenerate the damaged structure. When the shoulder is damaged by arthritis, we have discovered a way to stimulate the bone of the glenoid socket to regenerate a durable biological joint surface*. These are but a few examples of regenerative orthopaedics. Our faculty are dedicated to the ongoing discovery of many more opportunities to help guide nature's powerful regenerative capacities so that the need for prosthetic 'replacements' made of metal and plastic becomes less while biological solutions become increasingly commonplace.

To represent our dedication to regeneration, we have selected La Gerbe (the sheaf) by Henri Matisse for our cover art. The perpetual regeneration of leaves that have been lost seems nowhere better presented than by Matisse's bold colors and crisp forms. Even Matisse's life speaks for regeneration. In 1941 he was near death from cancer, writing farewell letters to friends and family. After a risky surgery, he regained what he referred to as a 'new life' and took off in the new artistic direction of gouaches découpés (cut out water colors). These works of the last 14 years of his life have been referred to as "the grandest affirmations of the élan vital (the vital force) in Western Art". Like a surgeon, he sought to create by skillful cutting. La Gerbe, multicolored leaves that resemble a spray of flowers, was completed a few months before his death, but it will forever explode with new life. If you like this way of expressing regeneration, I suggest you check out his book *Jazz* published in 1947.

In this report, we provide you with a sampling of our discoveries in the art and science of regenerative orthopaedics. Each day we are learning more and gaining more respect for the regenerative capacities of the human body. Our challenge is to harmonize our efforts with those of nature. We are motivated because we are not content with today's orthopaedics, as good as it is. Today, one in four Americans has an orthopaedic problem needing medical attention; musculoskeletal conditions remain the leading cause of disability in our country (www.boneandjointburden.org). We know that the future holds better regenerative solutions for the conditions that deprive so many millions of individuals each year of their ability to be active and to be able to participate comfortably in their work and play. If you would like to learn more about our efforts in regeneration, I invite you to visit us at www.orthop.washington.edu or to email me at matsen@u.washington.edu.

In conclusion, I would like to thank all the individuals and foundations that have enabled Orthopaedics and Sports Medicine to continue its commitment to ongoing discovery. Look around and see regeneration at work!

Best wishes for good health,

Frederick A. Matsen III, M.D.
University of Washington
Department of Orthopaedics and Sports Medicine
1959 NE Pacific Street, Box 356500
Seattle, WA 98195
Office Phone (206) 543-3690
matsen@u.washington.edu
www.orthop.washington.edu

*On the back cover, please see the preoperative and 10 month postoperative x-rays of the left shoulder of a patient having a successful ream and run procedure (www.orthop.washington.edu/reamandrun).

D. Kay Clawson - A Pioneer in Bringing Regenerative Orthopaedics to the Care of the Injured Patient

by Dick Foley, Bob Clawson, and Rick Matsen

Forty-five years ago, D. Kay Clawson founded the Department of Orthopaedics at the University of Washington. He and his wife Jan continue to be great friends, generous supporters, and much appreciated frequent visitors to the Department. Thus it is a real pleasure to honor Dr. Clawson in the 2009 Report and to take this opportunity to thank him for all his contributions to the University of Washington and to thank his family for establishing the Clawson Family Orthopaedic Library Endowed Fund. Let us tell you a bit about this man.

Twentieth century American History has recorded many stories of unique individuals born between the World Wars, raised in the time of the Great Depression, and who served in the Second World War. On returning to civilian life they went on to remarkable achievement. The life of Dr. D. Kay Clawson is an example of this "American Story". The only child of older parents, he was born August 8, 1927 in Salt Lake City, Utah. Growing up as a "spoiled child" in a secure middle class home his life was altered sharply by the death of his father at age 14. The tragedy of this loss unleashed an industriousness and resolve in him that led to a series of jobs including working in the Salt Lake Clinic, a multi-specialty medical clinic, as a receptionist and telephone operator. An early fascination with medicine after visiting the San Francisco World's Fair in 1939, led to a position as a Navy corpsman during service in World War II. The physician contacts made at the Salt Lake City Clinic resulted in support through the local chapter of The Harvard Club in applying to Harvard for medical training after spending three years at the University of Utah following the war. At Harvard Medical School, where he met his future bride, Janet Dorothy Smith. Dr. Clawson received his medical degree from Harvard in 1952 and married Janet on June 1 that year. They subsequently had two children: Kim Clawson Rosenstein, M.D., and David Roger Clawson, M.D.

Cadet Col. Kay Clawson, Salt Lake City Regiment, 1944

The drive to succeed through those years is best exemplified by always holding not one, but two part-time jobs, to finance his education. Deciding on Orthopedic Surgery as his specialty, he entered the Resident Training Program at Stanford University in 1953. He expanded upon this training through a fellowship in advanced orthopaedics at the National Foundation for Infantile Paralysis from 1955–1958, and as a first assistant to Professor H. J. Seddon, honorary senior registrar at the Royal National Orthopaedic Hospital at the University of London from 1957–1958.

Dr. Clawson's abilities impressed his teachers, particularly Don King, M.D. and Sterling Bunnell, M.D. They encouraged his career in Academic Orthopedics. After six weeks as an assistant professor at the UCLA, he was asked to head the Division of Orthopaedic Surgery at the University of Washington – truly a "fast track."

During his years at the University of Washington he was recognized for his contribution to fracture care with his development of the sliding hip screw for fractures of the upper femur and the thoughtful application of closed

intramedullary nailing for fractures of the femoral shaft. In that the theme of this issue is 'regeneration' it is critical to point out that both of these techniques allow for the individual to get up on their feet and bear weight on the injured leg. The load of this weight bearing is shared between the metal implant and the bone itself, resulting in a stimulation of bone regeneration at the fracture site. At the time, these were revolutionary ideas and highly controversial. It required great strength and resolve to resist the rampant criticism of orthopaedic surgeons who felt that 'conservative care' meant leaving patients in bed in traction until their factures were healed enough for a body cast. Clawson's introduction of these two devices were major factors in the establishment of the University of Washington and Harborview Medical Center as the birthplace of modern trauma care and for establishing what is now the standards for fracture care. They led directly to our current philosophy so nicely expressed by Ted Hansen: "fix all the fractures and get 'em out of bed!" Check out the exciting "the Harborview Story" prepared by Bob Clawson and Dick Foley; you can see it at www.traumastory.com.

Clawson's department was the first in the country to recognize sports medicine as unique part of Orthopaedics; he was a founding member of the American Association of Orthopaedic Sports Medicine. He brought the care of the varsity athletes to the faculty of the Department. In recognition, we are now the Department of Orthopaedics and Sports Medicine.

He was a vigorous chairman, a great surgeon and an authoritarian educator. He was concerned that medical students had insufficient education in the bone and joint conditions commonly encountered in the practice of primary care; his action was to establish a musculoskeletal core course – today this course remains as a cardinal example of the 'systems' curriculum. He developed the 'party line' – a practical guide to many of the common problems encountered in orthopaedics. Residents that deviated from the party line ran the risk of a seismic event! Lessons learned from him are never forgotten. Perhaps most important is the way he advocated for each of his faculty, residents and students. Everyone knew he was there for them 100%.

In 1975, Dr. Clawson left the UW to become the Dean of the University of Kentucky Medical School and then to Kansas City as Executive Vice-Chancellor of the University of Kansas Medical Center in 1983. At each institution he left a legacy of excellence and support for faculty and students. While he is now 'retired' he remains as vigorous as ever, still thoughtful, provocative and supportive.

Dr. Clawson's professional activities, memberships on committees and in associations, commissions, and appointments are too numerous to list here, as are his hundreds of published journal articles, books, and book chapters. However, thanks to the generosity of the Clawson family, many of these resources, along with his autobiography, *My Journey: Genes or Environment*, will be available to future leaders in orthopaedic surgery in the Clawson Library at Harborview Medical Center in Seattle.

Gary and Alea Culpepper
Donors, Husky Fans, Parents, Patients
University of Washington

The Culpepper Family

When you first meet Gary and Alea Culpepper you immediately discover that, though they are busy people with many interests, they have two passions that stand out above the rest - family and sports. Particularly Husky Sports. A lifelong resident of the Puget Sound area, Gary has a long relationship with the University of Washington having been a student, an avid Husky sports fan, a parent (three of their seven children have graduated from UW), a donor, and even a patient at the University of Washington Medical Center. Alea, a lifelong sports fan, is just as committed and they both attend as many UW games as they can with their seven children and their growing families - often even traveling to attend games out of state.

The Culpeppers first learned about the Bob and Sally Behnke Endowed Professorship for the Health of the Student Athlete when their daughter, Suzanne, played for the UW Women's soccer team. Along with her teammates, Suzanne was occasionally treated by John O'Kane, M.D., a Husky team physician, who is also a faculty member in the UW Department of Orthopaedics and Sports Medicine and the holder of the Behnke Professorship. Over the years, the Culpeppers learned first-hand the importance of having a great physician on faculty who can advocate for the lifelong health of the student athletes and they wanted to help ensure that this valuable resource would always be available for Husky athletes in the future. "Doc O'Kane was just as important as any coach or athlete on that team", said Gary. By becoming donors to the Behnke Endowed Professorship for the Health of the Student Athlete, a partnership between UW Medicine Department of Orthopaedics and Sports Medicine and the Department of Intercollegiate Athletics, they helped ensure that student athletes would always have the same great care that their daughter received.

Daniel Flugstad, M.D.
2009 Grateful Alumnus
University of Washington School of Medicine

Jonathan (son), Matt (son), Cheryl (wife), Daniel Flugstad, Erin (daughter-in-law), Nick (son).

Daniel Flugstad, M.D. '76, '80, '85 is a Husky through and through. A Seattle native, he completed his bachelor of science (chemistry), medical school, and orthopaedic residency at the University of Washington, only leaving Seattle for a one-year fellowship in Orthopaedic Oncology at Massachusetts General Hospital. First drawn to orthopaedics as an undergraduate student after witnessing the transformation in his mother-in-law's life after she had a total hip replacement, he says that the University of Washington Department of Orthopaedics and Sports Medicine was a great place to learn the art of orthopaedic surgery. "They were trailblazers – especially in trauma," he said. Today, Flugstad has a busy practice at the Polyclinic and Swedish Hospital, but continues to make time to volunteer as a teacher in the anatomy labs and serves as a mentor for the medical student interns who spend time at Swedish Hospital. In addition to this, he and his wife, Cheryl (who also graduated from the University of Washington with a degree in clinical nutrition in 1982) have given generously to the University of Washington Orthopaedics Resident Education Discretionary Fund for many years because it provides money for books, travel to conferences, journal clubs – things that make for a great education that the department wasn't able to provide when he was a resident. He also appreciates that none of the money is used for overhead expenses. As Flugstad says, "the University of Washington gave me a career I love and I want to give back".

Richard Kirby, M.D.
2009 Grateful Alumnus
University of Washington School of Medicine
Founder, Kirby Orthopaedic Resident Endowed Fund

Richard (Dick) Kirby, '77, first grew interested in the field of orthopaedics during his second year of medical school at the University of Washington after working with a volunteer faculty member in his musculoskeletal anatomy lab. When the time came to apply for residency programs, the orthopaedics residency at UW was the obvious choice. Today, Dr. Kirby has a successful practice, but spends his spare time helping to inspire the next generation of orthopaedic surgeons by volunteering as a faculty member in the musculoskeletal anatomy lab. In addition to volunteering his time to the medical school, Dr. Kirby and his wife, Betsy, give annually to support the residency program in the Department of Orthopedics. One of the things Kirby likes best about supporting the residency program is knowing that all funds go directly to support the residents and help the department provide the same high-quality educational experience that he had. This year, the Kirbys took advantage of a special, one-time matching program – the Campaign for Students – and created the Kirby Orthopedic Resident Endowed Fund, which will provide a permanent source of funds to support educational expenses for orthopaedic residents at UW. For the Kirbys, giving to support the residency program where Dr. Kirby trained is a priority -- " we got where we are because of the education I received at UW. "

Elizabeth Anne Ouellette, M.D.
2009 Distinguished Alumnus
University of Washington School of Medicine

Dr. Elizabeth Anne Ouellette obtained her medical degree at the University of Texas San Antonio in 1978. In 1983 Anne became the second woman to graduate from the Orthopaedic Residency at the University of Washington School of Medicine (the first being our faculty member and UW Medicine's Dean of Admissions Carol Teitz who graduated in 1980). Dr. Ouellette traveled to the University of Miami in 1984 for her Hand Fellowship. Afterwards she stayed at the University of Miami for over 20 years where she achieved the rank of Professor and served as the Chief of Hand Surgery and the Director of the Hand Fellowship program at the Jackson Memorial Hospital. Dr. Ouellette is now the director of the Miami International Hand Surgical Services (MIHSS).

Dr. Ouellette's research interests include biomechanics of wrist instability, repair of nerve injuries, skin coverage and psychological intervention for the upper extremity trauma patients. Some of her most recent articles discuss the effect of gender on hand arthritis, imaging of athletic hand and wrist injuries, and management of soft tissues in fracture treatment.

Anne is a leader in the world of orthopaedics, participating actively in the American Orthopaedic Association, The American Academy of Orthopaedic Surgeons, American Society for Surgery of the Hand and the Ruth Jackson Orthopaedic Society for which she served as president last year. In addition to her professional life, Anne is centered in her family – fully admired by her two sons and husband.

We are proud to honor Anne as our 2009 alumnus emeritus.

New Faculty

Steven Bain, Ph.D.

Jerry I. Huang, M.D.

Dr. Steve Bain received his undergraduate degree from Northern Arizona University and a Ph.D. in Veterinary Science from Washington State University in 1987. Following his Ph.D., Dr. Bain was a NASA Space Biology Fellow in the laboratory of Dr. Clint Rubin in the Department of Orthopaedics at the State University of New York in Stony Brook, where he investigated effects and interactions of metabolic variables such as hormonal status, aging, and calcium status on skeletal remodeling responses engendered by disuse.

Dr. Bain's interests in metabolic bone disease led him to join Zymogenetics as a Senior Scientist in 1990 where he assisted in establishing the osteoporosis research program. Success in this research program led to an expatriate assignment with the Danish parent company of Zymogenetics, Novo Nordisk. While in Denmark, Dr. Bain managed discovery research for Women's Health Care Research. In his role as project leader, Dr. Bain led an international research team that identified a new class of small molecule, tissue selective estrogens that specifically targeted bone and hypothalamus. Upon his return to the United States in 1996, Dr. Bain was a co-founder of SkeleTech, a contract laboratory specializing in musculoskeletal biology. SkeleTech was sold in 2005 to MDS Pharma Services, where Dr. Bain served as the Senior Director of In Vivo Pharmacology. Dr. Bain's career came full circle in 2008 when he rejoined the academic ranks as a member of the Research Faculty in the Department of Orthopaedics. His research interests include the effects of physical stimuli on fracture repair and tissue regeneration, mechanisms of chronic bone pain, and the neuronal control of bone homeostasis.

Dr. Jerry I. Huang completed medical school at the University of California, Los Angeles (UCLA) School of Medicine followed by orthopaedic residency training at Case Western Reserve University in Cleveland, Ohio. Dr. Huang obtained subspecialty training in Hand and Microsurgery at UCLA Medical Center. Following his hand fellowship, Dr. Huang went on to an AO Traveling Fellowship at Lindenhof Hospital in Bern, Switzerland with world renowned upper extremity surgeons Professor Ralf Hertel and Professor Diego Fernandez.

Dr. Huang is committed to excellence in the care of problems related to the hand, wrist, and elbow. He has special clinical interests in upper extremity trauma and post-traumatic reconstructions. His research interests include bone and cartilage tissue engineering as well as stem cell-based therapy. Dr. Huang has authored over 20 peer-reviewed articles and book chapters in both clinical and basic science research. His extensive research has been presented at over 40 prestigious national and international meetings. In addition, he has been recognized with numerous awards including the Barry Friedman Award, the Zimmer Resident Research Award, and selection to the American Academy of Orthopaedic Surgeons (AAOS) Clinician-Scientist Development Program. His research has received funding from the Plastic Surgery Education Foundation (PSEF), American Association of Hand Surgery (AAHS), and AO-North America.

Dr. Huang's interests include basketball, snowboarding, golf, and beach volleyball. In addition, he enjoys rollerblading, traveling, going to theater, occasional wine tasting, and swing dancing with his wife, Brandi.

Department of Orthopaedics and Sports Medicine Faculty

Frederick A. Matsen III, M.D.
Professor and Chair
University of Washington Medical Center
Shoulder and Elbow
matsen@u.washington.edu

Richard J. Bransford, M.D.
Assistant Professor
Harborview Medical Center
Spine
rbransfo@u.washington.edu

Christopher H. Allan, M.D.
Associate Professor
Harborview Medical Center
Hand and Wrist
callan@u.washington.edu

Peter R. Cavanagh, Ph.D.
Professor
University of Washington Medical Center
Research
cavanagh@u.washington.edu

Steven Bain, Ph.D.
Research Associate Professor
Harborview Medical Center
Research
sdbain@u.washington.edu

Howard A. Chansky, M.D.
Professor
VA Puget Sound Health Care System
Tumor Service
chansky@u.washington.edu

David P. Barei, M.D.
Associate Professor
Harborview Medical Center
Trauma
barei@u.washington.edu

Jens R. Chapman, M.D.
Professor
Harborview Medical Center
Spine
jenschap@u.washington.edu

Daphne M. Beingessner, M.D.
Assistant Professor
Harborview Medical Center
Trauma
daphneb@u.washington.edu

Ernest U. Conrad III, M.D.
Professor
Children's Hospital and Regional Medical Center
Tumor Service
chappie.conrad@seattlechildrens.org

Carlo Bellabarba, M.D.
Associate Professor
Harborview Medical Center
Spine and Trauma
cbella@u.washington.edu

Robert P. Dunbar, M.D.
Assistant Professor
Harborview Medical Center
Trauma
dunbar@u.washington.edu

Stephen K. Benirschke, M.D.
Professor
Harborview Medical Center
Foot and Ankle
beniskb@u.washington.edu

David R. Eyre, Ph.D.
Professor
University of Washington Medical Center
Research
deyre@u.washington.edu

Department of Orthopaedics and Sports Medicine Faculty

Russell J. Fernandes, Ph.D.
Research Associate Professor
University of Washington Medical Center
Research
rjf@u.washingxton.edu

Jerry I. Huang, M.D.
Assistant Professor
University of Washington Medical Center
Hand and Wrist
jihuang@u.washington.edu

Michael J. Goldberg, M.D.
Clinical Professor
Children's Hospital and Regional Medical Center
Pediatric Orthopaedics
michael.goldberg@seattlechildrens.org

Walter F. Krengel III, M.D.
Clinical Professor
Children's Hospital and Regional Medical Center
Spine
wally.krengel@seattlechildrens.org

John R. Green III, M.D.
Associate Professor
University of Washington Medical Center
Sports Medicine
jgreen3@u.washington.edu

James C. Krieg, M.D.
Associate Professor
Harborview Medical Center
Trauma
jckrieg@u.washington.edu

Ted S. Gross, Ph.D.
Professor
Harborview Medical Center
Research
tgross@u.washington.edu

Roger V. Larson, M.D.
Associate Professor
University of Washington Medical Center
Sports Medicine
drlarson@u.washington.edu

Douglas P. Hanel, M.D.
Professor
Harborview Medical Center
Hand and Wrist
dhanel@u.washington.edu

Michael J. Lee, M.D.
Assistant Professor
University of Washington Medical Center
Spine
mjl3000@u.washington.edu

Sigvard T. Hansen, Jr., M.D.
Professor
Harborview Medical Center
Foot and Ankle
hansetmd@u.washington.edu

Seth S. Leopold, M.D.
Professor
University of Washington Medical Center
Hip and Knee
leopold@u.washington.edu

M. Bradford Henley, M.D.
Professor
Harborview Medical Center
Trauma
bhenley@u.washington.edu

Paul A. Manner, M.D.
Assistant Professor
University of Washington Medical Center
Hip and Knee
pmanner@u.washington.edu

Department of Orthopaedics and Sports Medicine Faculty

Vincent S. Mosca, M.D.
Associate Professor
Children's Hospital and Regional Medical Center
Pediatric Orthopaedics
vincent.mosca@seattlechildrens.org

Douglas G. Smith, M.D.
Professor
Harborview Medical Center
Foot and Ankle
dgsmith@u.washington.edu

Sean E. Nork, M.D.
Associate Professor
Harborview Medical Center
Trauma
nork@u.washington.edu

Kit M. Song, M.D.
Associate Professor
Children's Hospital and Regional Medical Center
Pediatric Orthopaedics
Kit.Song@seattlechildrens.org

John W. O'Kane, M.D.
Associate Professor
University of Washington Medical Center
Sports Medicine
jokane@u.washington.edu

Sundar Srinivasan, Ph.D.
Research Associate Professor
Harborview Medical Center
Research
sundars@u.washington.edu

Milton L. Routt, Jr., M.D.
Professor
Harborview Medical Center
Trauma
mlroutt@u.washington.edu

Lisa A. Taitsman, M.D., M.P.H.
Associate Professor
Harborview Medical Center
Trauma
taitsman@u.washington.edu

Bruce J. Sangeorzan, M.D.
Professor
Harborview Medical Center
Foot and Ankle
bsangeor@u.washington.edu

Carol C. Teitz, M.D.
Professor
University of Washington Medical Center
Sports Medicine
teitz@u.washington.edu

Gregory A. Schmale, M.D.
Associate Professor
Children's Hospital and Regional Medical Center
Pediatric Orthopaedics
Gregory.Schmale@seattlechildrens.org

Allan F. Tencer, Ph.D.
Professor
Harborview Medical Center
Research
atencer@u.washington.edu

John A. Sidles, Ph.D.
Professor
University of Washington Medical Center
Research
sidles@u.washington.edu

Thomas E. Trumble, M.D.
Professor
University of Washington Medical Center
Hand and Wrist
trumble@u.washington.edu

Department of Orthopaedics and Sports Medicine Faculty

Theodore Wagner, M.D.
Clinical Professor
University of Washington Medical Center
Spine
wagner@u.washington.edu

Christopher J. Wahl, M.D.
Assistant Professor
University of Washington Medical Center
Sports Medicine
wahlc@u.washington.edu

Winston J. Warme, M.D.
Associate Professor
University of Washington Medical Center
Shoulder and Elbow
warmewj@u.washington.edu

Jason S. Weisstein, M.D., M.P.H.
Assistant Professor
University of Washington Medical Center
Tumor Service
weisstei@u.washington.edu

Klane K. White, M.D., M.Sc.
Assistant Professor
Children's Hospital and Regional Medical
Center
Pediatric Orthopaedics
klane.white@seattlechildrens.org

Jiann-Jiu Wu, Ph.D.
Research Associate Professor
University of Washington Medical Center
Research
wujj@u.washington.edu

Emeritus Faculty
Stanley J. Bigos, M.D.
  Professor Emeritus

Theodore K. Greenlee, Jr., M.D.
  Associate Professor Emeritus

Lynn T. Staheli, M.D.
  Professor Emeritus

Adjunct Faculty
Basia R. Belza, R.N., Ph.D.
  Professor, Physiological Nursing

Jack W. Berryman, Ph.D.
  Professor, Medical History & Ethics

Cora Breuner, M.D.
  Associate Professor, Family Medicine

Charles H. Chesnut, M.D.
  Professor, Nuclear Medicine

Randal P. Ching, Ph.D.
  Associate Professor, Mechanical Engineering

Jeffrey B. Friedrich, M.D.
  Assistant Professor, Surgery

Gregory C. Gardner, M.D.
  Professor, Rheumatology

Daniel O. Graney, Ph.D.
  Professor, Biological Structure

Susan M. Ott, M.D.
  Associate Professor, Division of
  Metabolism

Wendy Raskind, M.D., Ph.D.
  Professor, General Internal Medicine

Michael L. Richardson, M.D.
  Professor, Radiology

Miqin Zhang, Ph.D.
  Associate Professor, Materials Science and Engineering

Joint Faculty
Michael M. Avellino, M.D.
  Associate Professor, Neurological Surgery

Randy M. Chestnut, M.D.
  Professor, Neurological Surgery

Janet F. Eary, M.D.
  Professor, Radiology

John E. Olerud, M.D.
  Professor, Division of Dermatology

Nathan J. Smith, M.D.
  Professor Emeritus, Pediatrics

Michael D. Strong, Ph.D.
  Research Professor, Surgery

Nicholas B. Vedder, M.D.
  Professor, Plastic Surgery

Marcelo D. Vilela, M.D.
  Associate Professor, Neurological Surgery

Clinical Faculty
Sarah E. Jackins, R.P.T.
  Assistant Professor, Rehabilitation Medicine

Visiting Lecturers

Marc Swiontkowski, M.D.
2009 LeCocq Lecturer

This year at our annual LeCocq lecture on January 22nd and 23rd, we were honored to have Dr. Marc Swiontkowski as our 2009 LeCocq Lectuerer.

Dr. Swiontkowski is Board Certified by the American Board of Orthopaedic Surgery. He is the immediate past president of the American Orthopaedic Association. Dr. Swiontkowski attended California State University at Fullerton and obtained his BS in biology. He then went on to the University of Southern California School of Medicine where in 1979 he obtained his M.D. He completed his internship and residency training at the University of Washington. He trained in Davos, Switzerland completing a fellowship in Laboratory for Experimental Surgery. In 1984 he accepted a position as Orthopaedic Consultant at Kilimanjaro Christian Medical Center in Moshi, Tanzania; in 1985 he was accepted as an Assistant Professor at Vanderbilt University; in January, 1988 he was promoted to Associate Professor at Vanderbilt; in July of 1988 was appointed at the University of Washington as Associate Professor. In 1989 he was promoted to Professor of Orthopaedic Surgery and assumed the position of Chief of Orthopaedic Surgery, Harborview Medical Center in Seattle, Washington. From September 1997 through October 2008, he held the position of Professor and Chairman of the Department of Orthopaedic Surgery at the University of Minnesota. He currently is the CEO of TRIA Orthopaedic Center in Bloomington, MN, and he continues to practice at the University of Minnesota.

Dr. Swiontkowski has published articles in peer review Journals on numerous topics including fractures, Laser Doppler Flowmetry, intermedullary nailing, and has lectured extensively in this country as well as abroad. He is currently the Deputy Editor for the Journal of Bone and Joint Surgery. He has contributed to numerous textbooks, as well as being editor to several. He has been awarded several grants as the Principal Investigator in the study of trauma injuries.

Dr. Swiontkowski holds appointments to numerous Societies such as AAOS, American College of Surgeons, American Association for the Surgery of Trauma, AOA, ORS, Orthopaedic Trauma Association, Association Health Services Research, and Cochrane Collaboration.

Mininder S. Kocher, M.D., M.P.H.
2009 OREF Hark Lecturer, Resident Research Day

This spring we were honored to have Dr. Mininder Kocher as our OREF Hark Lecturer for Resident Research Day, June 26th.

Mininder S. Kocher, M.D., M.P.H., is the Associate Director of the Division of Sports Medicine at Children's Hospital Boston and is an Associate Professor of Orthopaedic Surgery at Harvard Medical School.

Dr. Kocher graduated Phi Beta Kappa from Dartmouth College. He graduated with honors from the Duke University School of Medicine. He completed orthopaedic training in the Harvard Combined Orthopaedic Residency Program at Massachusetts General Hospital, Brigham & Women's Hospital, Children's Hospital Boston, and Beth Israel Hospital. He completed a pediatric orthopaedic fellowship at Children's Hospital Boston, a sports medicine and arthroscopic surgery fellowship at the Steadman Hawkins Clinic (Vail, Colorado), and an Orthopaedic Research and Education Foundation (OREF) clinical research fellowship at the Harvard School of Public Health.

Clinically, Dr. Kocher's practice specializes in pediatric, adolescent, and adult sports medicine. He is a well-recognized international expert in pediatric sports medicine.

In terms of research, Dr. Kocher is a renowned orthopaedic health services researcher. Dr. Kocher has published over 100 peer-reviewed scientific articles, over 30 book chapters, and 3 textbooks. Dr. Kocher has presented over 160 papers at major national and international meetings and has been a visiting professor at numerous institutions.

Administratively, Dr. Kocher is the Associate Director of the Division of Sports Medicine at Children's Hospital Boston. He is very involved with numerous professional organizations. He is a consultant reviewer for numerous medical journals and is a grant reviewer for numerous organizations. He has been elected to the American Orthopaedic Association for academic orthopaedic leaders.

Michael J. Lee, M.D.

Assistant Professor
University of Washington Medical Center
Spine
www.orthop.washington.edu/faculty/lee

Randal P. Ching, Ph.D.

Variations in Surgical Treatment for Lumbar Stenosis and Biomechanical Implications

- Laminectomy is the conventional method for treating lumbar stenosis.
- Instability of the lumbar spine has been reported to occur as frequently 8-31% after laminectomy. Symptomatic instability may require additional surgery, including possibly fusion.
- Less extensive surgeries, like bilateral laminotomy can be done to treat stenosis. These less extensive surgeries may preserve the tissues that provide lumbar stability.
- We have tested motion patterns in human cadaveric lumbar spines after laminotomy and laminectomy.
- Our preliminary data suggest that bilateral laminotomy may lead to less instability.

Spinal stenosis is a common condition in the elderly and can also occur in younger individuals on a congenital basis. In spinal stenosis there is a narrowing of the spinal canal resulting in mechanical compression and irritation of the nerve tissue within the canal. Stenosis can occur from a combination of disc bulging, disc herniation, facet osteophytes, endplate osteophytes, ligamentum flavum hypertrophy, and epidural lipomatosis. The majority of patients with spinal stenosis can be treated without surgery. Patients with substantial and refractory symptoms may require surgical management.

Traditionally, laminectomy has been the most frequently used method for surgical decompression used in the treatment of stenosis. In a laminectomy the surgeon removes the lamina, spinous processes, interspinous ligament, and undercuts of the facet joints. This procedure is effective in treating neurological leg pain, but there are concerns regarding the possibility of instability after this procedure. As a result, less invasive techniques for

decompression have been introduced, such as laminotomy. In a laminotomy the surgeon partially moves the lamina and the facet while maintaining the central structures (spinous process, inter and supraspinous ligaments). The advantage of the laminotomy is that it requires less resection of bone and soft tissue and may result in a more stable spine after the decompression. However, the disadvantage is that laminotomy is technically more difficult and requires more surgical time than the laminectomy. In addition, concerns exist if the decompression achieved by laminotomy is comparable to that achieved by laminectomy.

Numerous biomechanical studies have demonstrated that with sequential resection of posterior spinal column elements, there is sequentially increasing instability. When performing a laminectomy, it has been recommended to retain at least 50% of the facet bilaterally and sufficient pars to prevent instability. Despite these measures, the incidence of post laminectomy instability has been reported to range from 8 to 31%.

To our knowledge, there has been no biomechanical study examining stability of the decompressed spine with the posterior ligamentous complex intact. All previous biomechanical studies examined stability after resection of these structures. We hypothesize that laminotomy, with its retention of these structures will allow for a more stable spine than a laminectomy.

Research

Our research focuses on the biomechanical stability after decompression of the lumbar spine. We used human cadaveric lumbar spines and tested their motion under normal physiologic forces. We record the motion of the entire spine and the motion at each level. Using reflective spheres attached at each level and 4 cameras, we can accurately track the motion of each segment. We then mount the spines into our spine simulator, which mimics forces seen under physiologic human conditions. We evaluate the spine motion in flexion and extension, side to side bending, and rotation. We evaluate the spine's
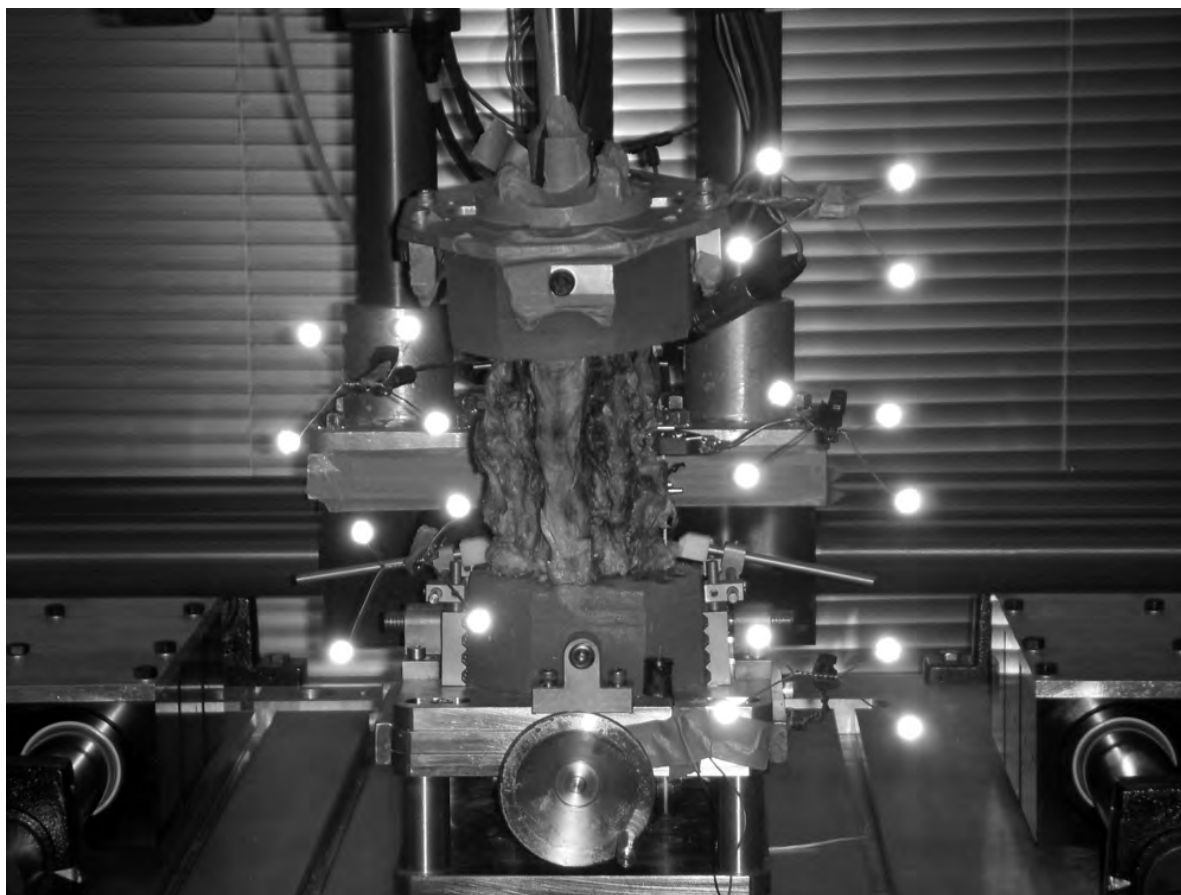
Figure 1: The intact spine loaded in the simulator using reflective spheres to record motion patterns.

motion and stiffness under three conditions for each specimen tested sequentially.

1) Trial 1:   Intact lumbar spine – no surgery (Figure 1).

2) Trial 2:   Lumbar spine after bilateral lumbar laminotomy at L2-3, L3-4 & L4-5. Laminotomy entails removal of ligamentum flavum, and partial facetectomy to visualize the medial aspect of the pedicle to ensure adequate lateral recess decompression. The spinous process, inter and supraspinatus ligaments were preserved (Figure 2).

3) Trial 3:   Lumbar spine after full laminectomies at L2-3, L3-4 & L4-5. This entails full removal of the lamina, supra and inter spinous ligaments, and spinous processes (Figure 3).

Lumbar spine kinematics (full spine and segmental) are measured using a Vicon motion tracking system (Vicon Motion Systems, Lake Forest, CA). The total range of motion (ROM) from L1 to L5 are assessed as well as the segmental range of motion between L1-2, L2-3, L3-4, and L4-5. Additionally, the overall and segmental stiffnesses are computed from the moment-angle plots.

The paired two-sample t test is used to evaluate differences in stiffness and range of motion after 1) bilateral laminotomy and 2) laminectomy. Statistical significance is defined as $p < 0.05$.

Results

In this study we found that there is a significant difference in the increase of motion and decrease of stiffness of the spine after laminectomy vs. laminotomy (Table 1). The laminectomy procedure resulted in almost twice

	% Change From Intact	
	Increase in Motion	Decrease in Stiffness
Laminotomy	17.49	11.80
Laminectomy	36.76	27.20
Significance	$p < 0.05$	$p < 0.05$

Table 1: Increased Motion and Decreased Stiffness for Laminotomy and Laminectomy.

Figure 2: An oblique view of the laminotomized spine with retention of central structures.

Figure 3: The laminectomized spine.

as much motion increase than the laminotomy procedure.

Discussion

We have learned from previous studies and experiences that the more of the lumbar spine we remove, the more unstable it becomes. Previous studies have suggested that at least 50% of the facets should be maintained and that the pars interarticularis should be preserved as well. Resection beyond these guidelines can result in an unstable spine. Newer studies have suggested that abnormal motion and subtle instability may result even despite following these guidelines. Our preliminary data suggest that laminotomy may result less instability than laminectomy.

In the surgical decision-making, numerous factors have to be taken into consideration. If the patient is elderly with multiple co-morbidities and cannot tolerate extended general anesthesia, the laminectomy procedure may be more appropriate as it is more easily done and with less operative time and less risk to the patient. If a patient's spine is stiff with severe arthritis and does not have much motion to begin with, the benefit of laminotomy may be lost on a spine that is already stiff and quite stable. If there is severe stenosis, a full laminectomy may be required to adequately treat the patient's neuro-compressive symptoms. Occasionally in spine surgery, a rent in the spinal sac may occur and cerebrospinal fluid may leak. To repair such a leak requires the adequate exposure. A full laminectomy may be required to adequately expose and repair such a leak.

Furthermore, it is recognized that spinal stenosis may recur after decompression by laminotomy or laminectomy. It is not clear how often or how soon stenosis recurs with each procedure. Future studies examining symptom relief, extent of decompression, resultant hyper-mobility and future predisposition to instability will help in determining the optimal procedure for the patient.

Acknowledgements

Recommended Reading

Fox MW, O.B., Onofrio BM, Hanssen AD., Clinical outcomes and radiological instability following decompressive lumbar laminectomy for degenerative spinal stenosis: a comparison of patients undergoing concomitant arthrodesis versus decompression alone. J Neurosurg, 1996. 85(5): p. 793-802.

Detwiler PW, S.C., Taylor SB, Crawford NR, Porter RW, Sonntag VK., Biomechanica;comparison of facet-sparing laminectomy and Christmas tree laminectomy. J Neurosurg, 2003. 99(2 (Suppl)): p. 214-220.

Abumi K, P.M., Kramer KM, Duranceau J, Oxland T, Crisco JJ., Biomechanical evaluation of lumbar spinal stability after graded facetectomies. Spine, 1990. 15(11): p. 1142-7.

Atlas, S.J., et al., The Maine Lumbar Spine Study, Part III. 1-year outcomes of surgical and nonsurgical management of lumbar spinal stenosis. Spine, 1996. 21(15): p. 1787-94; discussion 1794-5.

Richard J. Bransford, M.D.

Assistant Professor
Harborview Medical Center
Spine
www.orthop.washington.edu/faculty/bransford

Carlo Bellabarba, M.D., and Jens R. Chapman, M.D.

The Halo: Allowing the Severely Injured Neck to Regenerate Stability Without Surgery

- Cervical fractures and dislocations are common neck injuries.
- We have found that the majority of these injuries can be successfully managed without surgery.
- Halo vest immobilization is the most secure way to stabilize the cervical spine without surgery. In this method a graphite horseshoe-shaped 'halo' is placed around the head and connected to it by pins that engage the skull. This halo is then secured to a vest that fits on the patient's chest.
- 74% of halos placed can remain in place for the planned duration and 85% successfully manage the cervical injury without the need for surgery.
- The major complications associated with halo management are pin tract infections and pin tract loosening.

Halo vest immobilization (HVI) with pins in the skull attached to a chest brace is an effective means for stabilizing the injured cervical spine. However, studies citing high complication rates such as infection, instability, scarring, and unacceptable success rates have called into question its clinical usefulness. The success of HVI for specific fracture types has also been studied, with published success rates ranging from 10% to 40%. At the University of Washington/Harborview Medical Center, faculty spine surgeons conducted a prospective study leading to improved safety and effectiveness of the halo in treating neck injuries. Currently we use state-of-the-art materials and a care map to guide patient management after application of the halo.

Methods

We used HVI to treat 342 patients between 1998 and 2006, the largest series published to date. Our technique used a graphite horseshoe-shaped Halo-ring secured to the patient's skull with 4 Titanium pins applied in the typical locations (Figure 1). We followed these patients until their halo was removed, recording adverse events such as problems related to the pins, pulmonary problems and skin breakdown related to the vest, swallowing difficulties, deterioration of neurologic function, and complications. Pin tract infections were classified into 3 categories of severity (Table 1). We differentiated HVI failures into the two following categories: 1) Aborted HVI, other intervention undertaken; and 2) Premature HVI discontinuation, no further intervention necessary. Intended duration of HVI was plotted against weeks of HVI treatment in the form of a HVI treatment-survivorship analysis.

Our patients ranged in age from 2 to 94 years with an average age of 41.2 years. 311 of our patients with 445 cervical spine injuries were available for analysis. From this data set we also excluded 22 patients who died

for reasons that were not attributable to HVI. 289 patients with 418 injuries were therefore followed to completion of halo removal and healing of their injury.

Results

No patient had neurological deterioration while being treated with HVI.

There were 113 complications in 100 patients (35% of survivors). The most common complications were pin tract infection (13%, 39/311) and persistent instability (12%, 38/311). 38% (15) of infections could be managed with local care; 56% (22) required pin removal or exchange; and 5% (2) needed surgical debridement and antibiotics. Sixteen other patients (5%) had episodes of pin site loosening without infection.

Twenty-nine of 38 patients were diagnosed with fracture instability an average of 6.6 days (range 1 to 42 days) after halo application, and 9/38 were identified as having subluxation
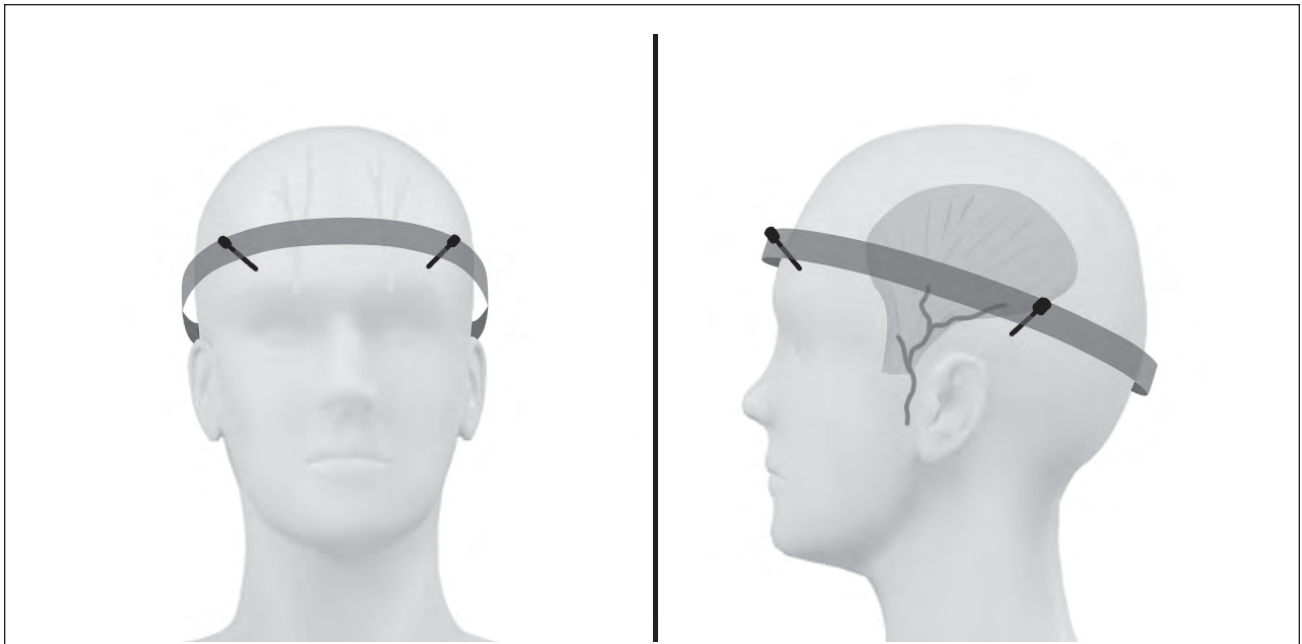
Figure 1: Recommended Halo pin placement. Temporal pins should avoid the frontal sinus and supraorbital nerve medially and the temporal artery and fossa laterally. The posterior pins should avoid the mastoids.

or non-union requiring surgery an average of 101 days (range 84-140 days) after halo application.

Of the 289 patients available for final follow-up, 207 (74%) completed the initially prescribed course of HVI (Figure 2: Survivorship Curve).

Overall 85% (208/247) of patients whose injuries were treated with HVI were successfully treated, without the need for unplanned operative management.

Failure of treatment occurred within the first three weeks in 26 of the 39

(67%) patients who failed definitive HVI. For patients who completed the first three weeks without significant HVI related complications, the likelihood of HVI fulfilling the intended goal increased to 95 percent (208/219).
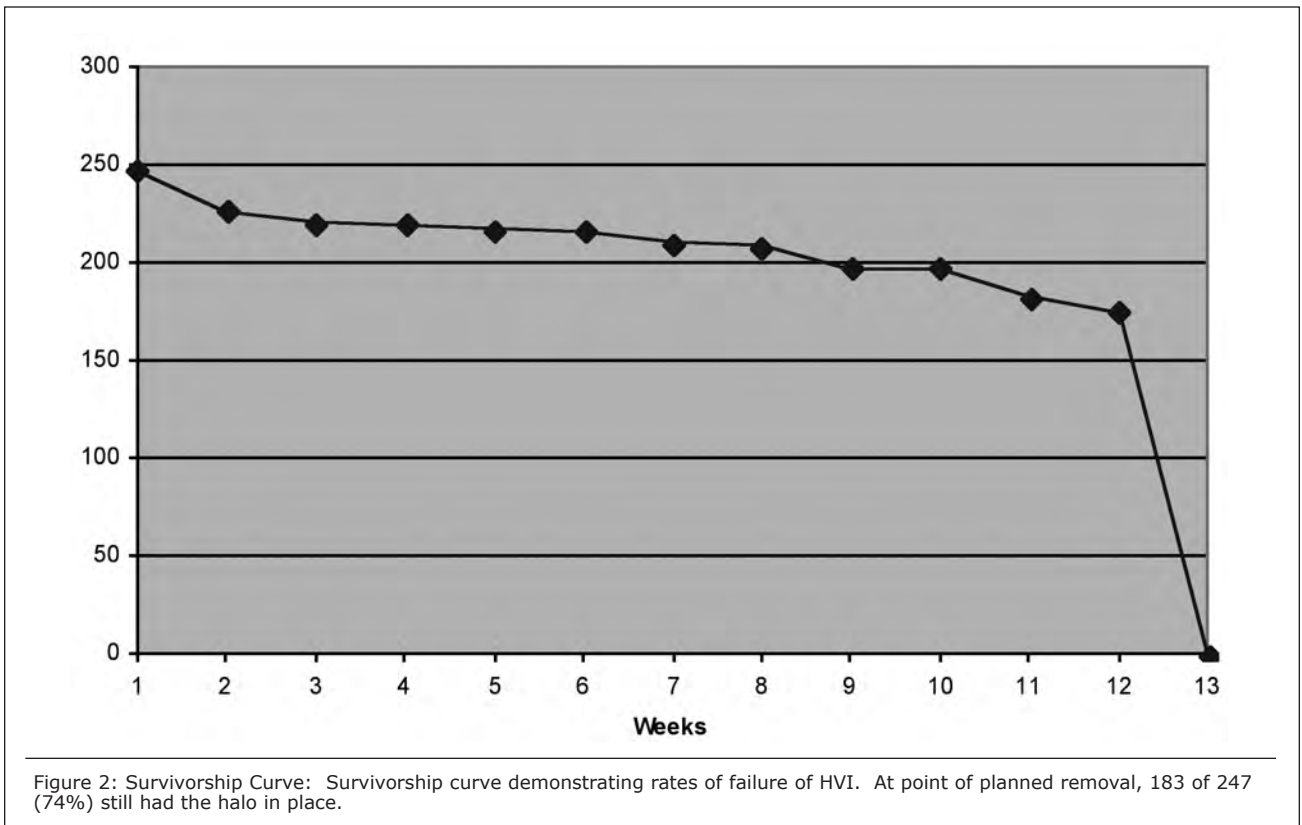
Figure 2: Survivorship Curve: Survivorship curve demonstrating rates of failure of HVI. At point of planned removal, 183 of 247 (74%) still had the halo in place.

Category	Definition	Prevalence (n / percentage)
Class I	Focal irritation or infection, no pin loosening, responsive to local measures, responds to local pin tract care, p.o. antibiotics, retightening of pin	15 (38.4%)
Class II	Pin loosening, productive purulent drainage; requires pin removal and local debridement	22 (56.4%)
Class III	Intracranial abscess, cranio facial abscess, surgical debridement / reconstruction, I.V. antibiotics	2 (5.1%)
	Sum total	39

Table 1: Classification and distribution of pin tract infections.

Discussion

We evaluated the survival of the halo-vest to full completion of the originally prescribed treatment plan, rather than only evaluating failure and complication rates. Using this approach we found that the intended duration of HVI was completed in 74% of patients who had the minimum required follow-up. When considering patients in whom HVI was discontinued earlier than intended but had served as the primary means of external fracture immobilization throughout the course of treatment, the desired clinical outcome of avoiding surgical intervention was achieved in 85% of patients.

Other than pin site infection, the primary complication among our cohort was instability which consisted of approximately one-third of all complications. In fact, failure to maintain acceptable stability of the spine was the leading cause of cessation of HVI. We found no adverse events in the 38 patients who required surgical treatment after HVI had been abandoned secondary to instability.

It is important to note that two-thirds of all failures occurred within the first three weeks of halo application, suggesting that this early phase is critical in determining the likelihood of success. In fact, the likelihood of successful fracture treatment without the need for surgical intervention increased from 85% to 95% in patients who had no adverse incident related to HVI within the first three weeks of treatment. Our finding that no patient suffered any permanent detrimental effects secondary to loss of alignment during HVI, combined with the observation that most HVI failures declare themselves within the first three weeks of treatment, render a HVI trial in well selected patients appealing as a means of avoiding fusion in situations where the need for operative intervention is uncertain.

Conclusion

The majority of patients were able to complete a full course of HVI without needing surgery. The primary reason for cross-over from HVI to surgical treatment was persistent fracture instability, which usually occurred within the first three weeks of treatment and was not associated with neurological worsening or long-term problems. Complications related to halo treatment are relatively common, but the majority of these can be effectively treated. While halo treatment can be challenging for patients and clinicians, it remains an effective treatment option in the management of cervical spine injuries and one that may be favorable to surgery in certain situations. Implementation of a systematic care program involving clinicians, orthotists and nursing staff along with patient and support education improves the quality of care and the outcome.

Our future research will seek to identify patient and injury characteristics that may be used to predict successful HVI treatment in an effort to enhance its effectiveness and to reduce unnecessary surgery.

Recommended Reading

Koch RA, Nickel V., The Halo Vest, An Evaluation of Motion and Forces Across the Neck. Spine, 1978. 3(2): p. 103-107.

Botte, MJ, Byrne, TP, Abrams RA, et al, Halo Skeletal Fixation: Techniques of Application and Prevention of Complications. J Am Acad Orthop Surg, 1996. 4(1): p. 44-53.

Askins V, Eismont FJ, Efficacy of five cervical orthoses in restricting cervical motion. A comparison study. Spine, 1997. 22(11): p. 1193-8.

Bucci M., Daucer RC, Maynard FA, et al., Management of post-traumatic cervical spine instability: operative fusion versus halo vest immobilization. Analysis of 49 cases. J Trauma, 1988. 28(7): p. 1001-6.

Bucholz, RD, Cheung KC, Halo vest versus spinal fusion for cervical injury: evidence from an outcome study. J Neurosurg, 1989. 70(6): p. 884-92.

Brook Martin, M.P.H.

Health Services Researcher
Harborview Medical Center
Research
WWW.ORTHOP.WASHINGTON.EDU

Reoperations Following Spine Surgery in Washington State

- We examined the cumulative incidence of second lumbar spine operation ("reoperation") following an initial lumbar operation for degenerative conditions using a hospital discharge registry.
- The 11-year cumulative incidence of reoperation following lumbar spine surgery was 19%.
- Patients with spondylolisthesis had a lower cumulative incidence of reoperation after fusion surgery than after decompression alone (17.1% vs. 28.0%; P= 0.002).
- For diagnoses other than spondylolisthesis, the cumulative incidence of reoperation was higher following fusion than following decompression alone (21.5% vs. 18.8%; p = 0.008).
- Among patients who underwent surgery for lumbar degenerative disease, more than twice as many had a fusion procedure in the 1997 to 2000 cohort (19.1%) compared with the 1990 to 1993 cohort (9.4%).
- The 4-year cumulative incidence of reoperation was higher in the 1997 to 2000 cohort compared with the 1990 to 1993 cohort (14.0% vs. 12.4%, p < 0.001).
- Among fusion patients, those in the 1997 to 2000 cohort were approximately 40% more likely to undergo a reoperation within the first year when compared with fusion patients the 1990 to 1993 cohort.
- A higher proportion of fusion procedures and the introduction of new spinal implants between 1993 and 1997 were not associated with reduced reoperation rates.

Lumbar decompression procedures such as laminectomy and discectomy are typically performed to relieve symptoms of leg pain, numbness, or weakness associated with compression of lumbar nerve roots. Lumbar spine surgery rates have increased over the past 2 decades. Rates of lumbar fusion surgery, in particular, increased 220% from 1990 to 2001, particularly accelerating after the 1996 Food and Drug Administration (FDA) approval of interbody fusion cage implants.

Reoperations following a decompression surgery are considered to be an indicator of a poor outcome of an initial surgery because they generally imply persistent symptoms, progression of disease, treatment complication, or failure of patients to comply with postoperative care. Preventing repeat spinal surgery therefore, is an important goal for surgeons and their patients. Previous research have provided some evidence of an association between poor outcomes and increased readmissions, and are commonly used for quality assurance purposes by the National Committee on Quality Assurance (1995), as part of the Health Plan and Employer Data and Information Set (HEDIS), for the VA's NISQIP program, and by the Leapfrog group.

Health service researchers affiliated with the UW Department of Orthopaedics and Sports Medicine performed a retrospective data analysis using the Washington State Comprehensive Hospital Abstract Reporting System (CHARS) to document the trends in reoperation rates from 1990 to 2001. The purpose of the CHARS system is to provide public health personnel, consumers, purchasers, payers, providers, and researchers with useful information by which to make informed decisions on health care. The CHARS system provides those concerned with the development of public policy with information necessary to analyze many significant health care issues. Specifically, the department uses

Figure 1: Cumulative incidence of reoperation following any lumbar procedure among 2 cohorts of patients (1990 -1993 and 1997-2000), adjusted for age, sex, comorbidity, and whether or not a patient is covered by workers' compensation.
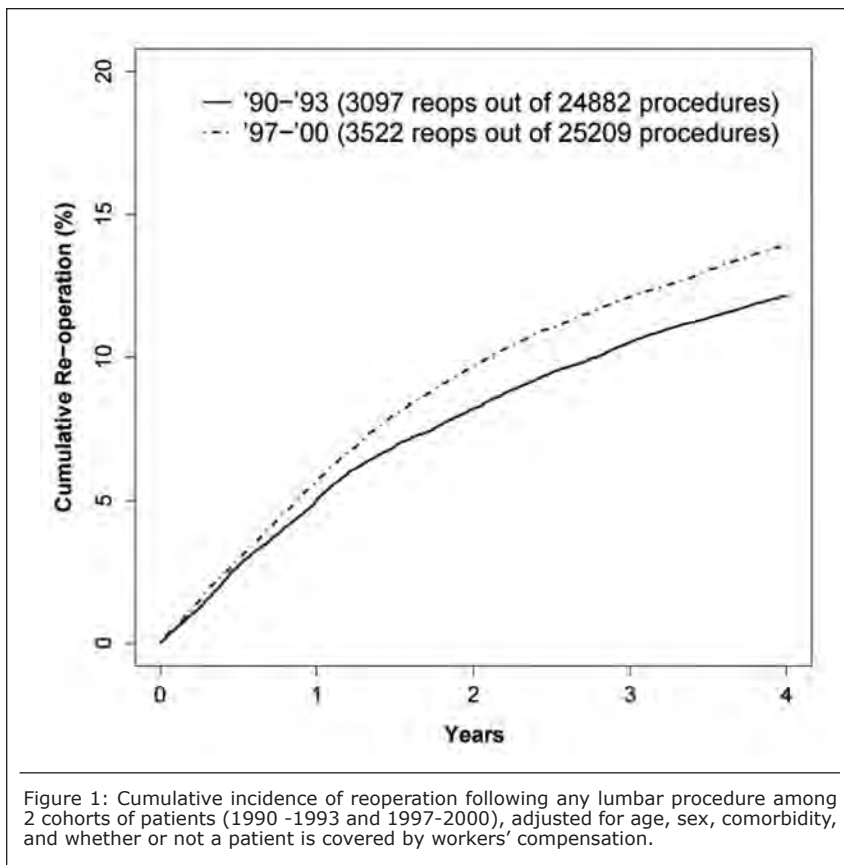
the CHARS data system to identify and analyze health trends related to patients' hospitalizations; establish statewide diagnosis related groups (DRG) weights; create hospital specific case mix indices; and identify and quantify issues related to health care access, quality, and cost containment.

Using a Cox-proportional Hazard regression model, we determined the cumulative incidence of reoperation following lumbar surgery and compared the frequency of reoperation following fusion surgery with that following decompression alone within four diagnoses (herniated disc, degenerative disc, spinal stenosis, and spondylolisthesis). Adults who underwent inpatient lumbar spine surgery for degenerative spine disorders in 1990-93 (n=24,882) were included in the study. We grouped patients as having either a spinal decompression surgery or spinal fusion surgery (with or without decompression). Our primary outcome measure was time until a second lumbar spine surgery (reoperation) of any type. Thus, reoperations did not necessarily occur at the same vertebral level as the initial surgery, but were always

lumbar procedures. We found that the cumulative incidence of reoperation at eleven years was 19.0%. For patients with spondylolisthesis, the cumulative incidence of reoperation was lower after fusion surgery than after decompression alone (17.1% versus 28%, p<0.001). However, for other diagnoses, the cumulative incidence of reoperation was significantly higher following fusion surgery than following decompression alone (21.5% vs. 18.8%, p=0.001). Following fusion surgery, 61.4% of reoperations were associated with a diagnosis code indicating device complication or pseudarthrosis.

In a separate analysis we also examined whether there was a trend in reoperation over time. For this study, we compared the 4-year cumulative incidence of a reoperation rate in two cohorts- a 1990-93 (n=24,882) cohort and a 1997-00 cohort (n=25,209). We used a Cox-proportional Hazard regression analysis, controlling for age, sex, insurance, and comorbidity to determine that the four-year cumulative incidence of reoperation was higher in the 1997-2000 cohort compared with the 1990-93 cohort (14.0% versus 12.4%, hazard ratio 1.16, p<0.001) despite increasing fusion surgery and

the availability of new implants.

Conclusions

Based on these findings we concluded that for spondylolisthesis, fusion surgery was associated with fewer reoperations than decompression alone. However, for other degenerative spine conditions, the cumulative incidence of reoperation is higher after a fusion procedure than after decompression alone. Furthermore, the study suggests that the introduction of new spinal implants, and increasing use of fusion surgery, did not reduce the incidence of reoperations during the 1990's.

Ongoing research will examine factors that influence the safety outcomes for spinal surgery. Specifically, we will examine the variation in the rates of reoperations as an indicator of surgical safety across providers, examining the association between procedure volume and reoperation rates, and providing a useful analysis of the influence that risk-adjustment measures of comorbidity have on spine surgery outcomes. Variation in rates of procedures is a commonly reported metric of professional uncertainty and has been reported across hospital referral regions for many procedures including those of spine surgery. However, variation of outcomes has not been substantially explored. High variation in reoperation rates may reflect uncertainty regarding patient selection, varying complication rates, progression of disease, or treatment failures. Examining the variation in reoperation rates following spine surgery may allow comparisons of safety outcomes across providers. This is an attractive target for reporting programs because large variation may reflect overuse of services, variation in the amount and quality of care, and variations in outcomes. Future research may also suggest a direction to improve indications for initial and repeat spine surgery; to involve patients in informed decision-making; and to determine the safest and most effective surgical techniques.

Figure 2: Diagnosis-specific cumulative incidence of reoperation following lumbar surgery. Age, sex, comorbidity, and workers' compensation status adjusted 10-year cumulative incidence of reoperation following lumbar spine surgery performed in the 1990-1993 cohort.
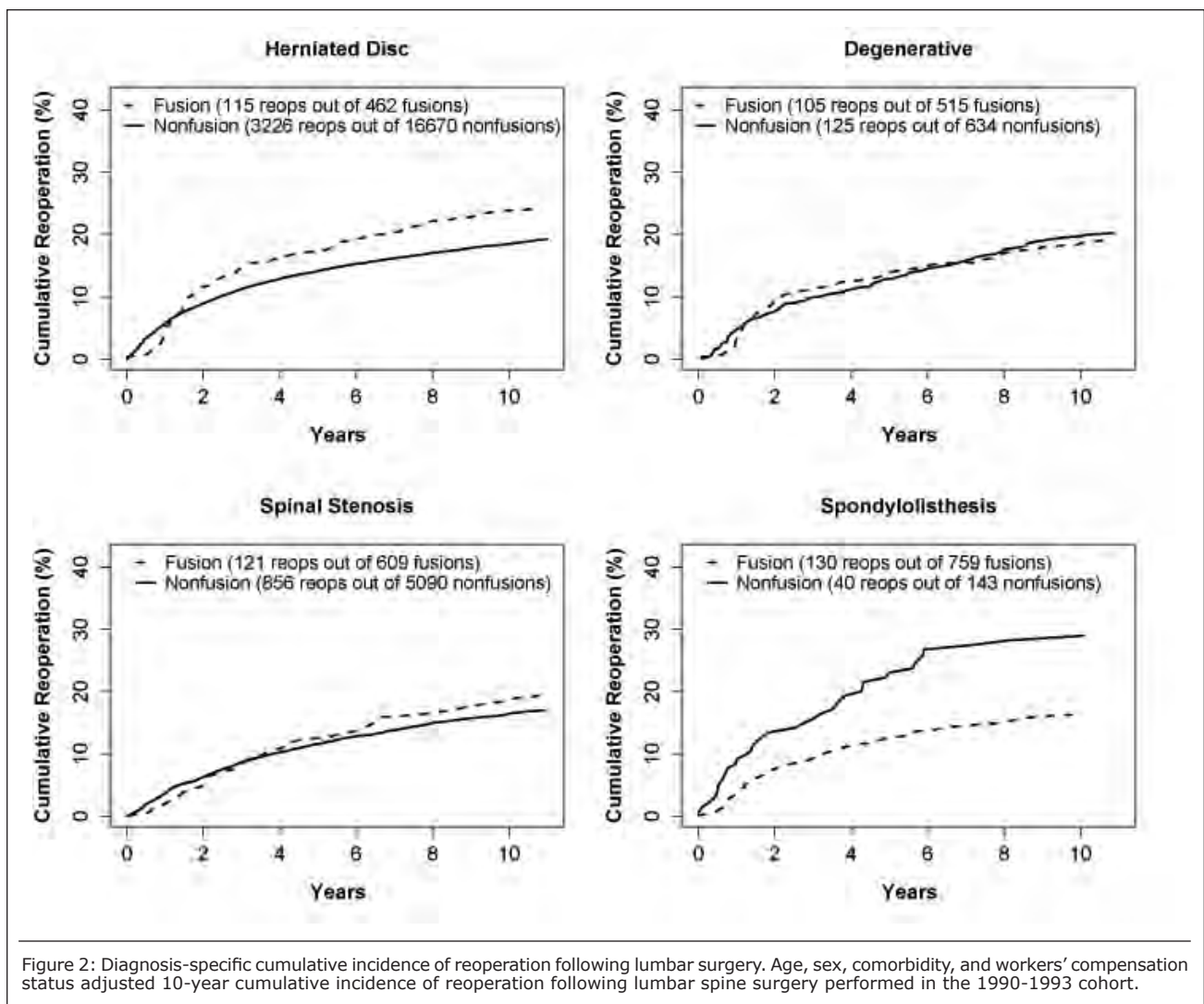
Recommended Reading

Martin BI, Mirza SK, Comstock BA, Gray DT, Kreuter W, Deyo RA. Are lumbar spine reoperation rates falling with greater use of fusion surgery and new surgical technology? Spine, 2007. 32(19):2119-26.

Martin BI, Mirza S., Comstock B., Gray DT, Kreuter W., Deyo, RA. Re-operations following Lumbar Spine Surgery and the Influence of Spinal Fusion Procedures. Spine, 2006. 32(3):382-7.

Juratli MS, Franklin GM, Mirza SK, Wickizer TM, Fulton-Kehoe D. Lumbar fusion outcomes in Washington State workers' compensation. Spine. 2006 Nov 1;31(23):2715-23

Hu RW, Jaglal S, Axcell T, Anderson G. A population-based study of reoperations after back surgery. Spine. 1997 Oct 1;22(19):2265-70;

Malter AD, McNeney B, Loeser JD, Deyo RA. 5-year reoperation rates after different types of lumbar spine surgery. Spine. 1998 Apr 1;23(7):814-20.

Minot J, Reducing Hospital Readmissions. AcademyHealth publication sponsored by the Commonwealth Fund. 2008.

Milton L. Routt, Jr., M.D.

Professor
Harborview Medical Center
Trauma
www.orthop.washington.edu/faculty/routt

Advanced Techniques of Minimally Invasive Pelvic Ring Fixation: Providing "Just Enough" Guidance to the Body's Regenerative Efforts

- The injured pelvis can regain the stability of its bony and ligamentous structures if they are held firmly in proper alignment during the healing process.
- Extensive, open surgical approaches have been associated with complications that interfere with healing.
- With minimally invasive yet stable methods for fracture fixation, the necessary restoration of anatomy can be achieved without the risks of open surgery.
- Accurate reduction and stable fixation of acetabular fractures avoids traction, allows early patient mobilization, and lowers the risk of post-traumatic hip arthritis.

High-energy traumatic events such as automobile crashes continue to cause significant pelvic ring injuries. Paramedical personnel and other primary responders to such accidents have refined their initial patient evaluation and resuscitation skills, which in turn have improved patient survivability. With increasing longevity and increasing activity, a growing number of older individuals are sustaining pelvic fractures. The management of pelvic instability in these patients can be complicated by poor bone quality and by concurrent health conditions affecting the heart, lungs, and urinary systems.

Due in large part to investigations at the University of Washington/ Harborview Medical Center, pelvic stabilization techniques have progressed far beyond prolonged bed-rest, body casting, and skeletal traction. The most recent advances are due to focused surgical experience and intra-operative fluoroscopic imaging techniques that enable fixation with minimal surgical exposure and dissection. For many surgeons, the pelvis is a difficult bone to understand because of its unique osseus morphology, anatomical variants, and topography. We have discovered several consistent pelvic osseus pathways that exist in most patients. These geometrically complex boney "tubes" are cancellous bone cylinders of different dimensions and orientations surrounded by cortical bone. These tubes accept and accommodate fixation devices that can be inserted using minimally invasive surgical techniques. Typically the fixation devices are large and long bone screws that span the fracture or ligamentous injury yet are contained safely and essentially completely within the bone tube. By stabilizing pelvic ring injuries, these percutaneously inserted implants decrease fracture related bleeding, provide patient comfort, prevent pelvic deformity, and allow mobilization while healing is taking place.

The pelvic osseus fixation pathways (OFP) are predictable and can be imaged in the operating room consistently. There are two consistent anterior pelvic OFP. One extends from the symphysis pubis to the supra-acetabular lateral iliac region and includes essentially the entire superior pubic ramus. The other anterior pelvic OFP includes the inferior pubic ramus extending from the symphysis pubis to the ischial tubersosity. In certain patients, both of these anterior pelvic OFP may span across the symphysis pubis. There are several mid-pelvic or iliac OFPs. One is deep and includes the anterior inferior iliac spine, pelvic brim, and posterior iliium. The second iliac OFP has two pathway options, extending from the iliac crest to either the supra-acetabular or quadrilateral surface areas. The third iliac OFP is superficial and extends along and within the iliac crest. The posterior pelvic OFP includes the lateral posterior ilium, sacroi-iliac joints, and upper two sacral vertebral segments. In some patients, the posterior pelvic OFP extends trans-iliac and trans-sacral spanning from one posterior illium, through the entire upper sacrum, and exiting the contralateral iliac cortical bone. Another pelvic OFP extends from the pelvic brim, remains intraosseus and posterior to the acetabulum, and
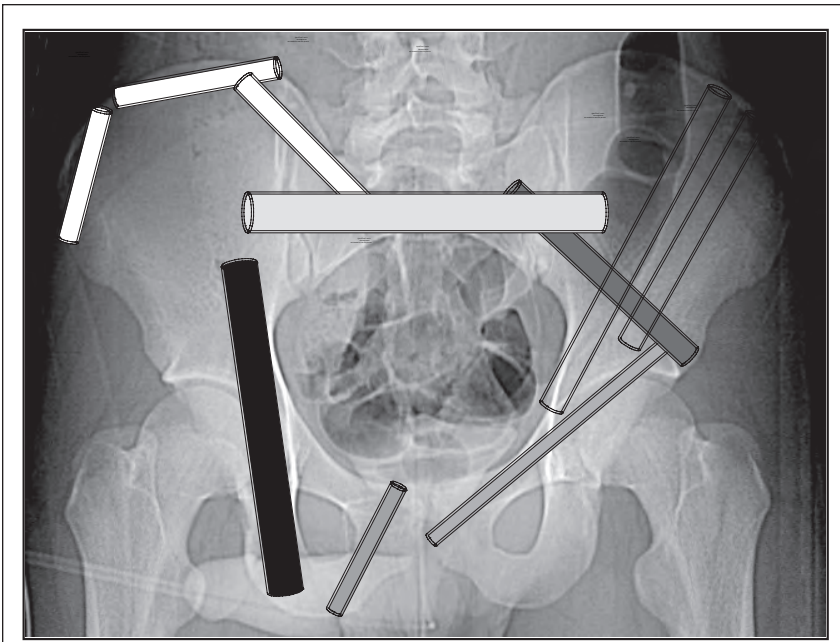
Figure 1: The common osseus fixation pathways (OFP) are represented as simple tubes superimposed on this anteroposterior pelvic radiograph. The white tubes represent the iliac crest areas. The black tube demonstrates the OFP posterior to the acetabulum from the ischium to the pelvic brim. The light grey OFP is the upper sacral area where iliosacral screws are applied. The dark grey tube represents the OFP extending from anterior inferior iliac spine to the posterior ilium. The empty tubes allow screw fixation from the iliac crest to either the supra-acetabular region or quadrilateral surface. The medium grey OFP extends from the pubic tubercle to the supra-acetabular area and is cranial and medial to the hip joint. The light medium grey OFP spans the inferior ramus from pubis to ischium. Both anterior pelvic OFPs can span the symphysis pubis if necessary for fixation.

be related to higher implant failure and fracture nonunion rates.

At Harborview Medical Center, we have used early manipulative reduction and minimally invasive or percutaneous fixation techniques for twenty years with overall excellent results. These procedures can be routinely performed as a portion of patients' resuscitation efforts if necessary. The early pelvic reduction and stability decreases related hemorrhage, which has a positive impact on patient survival. Similarly, early reduction and fixation provide comfort and allow the patient to be mobilized into a chair or onto crutches depending on the overall patient condition and injury details. Using the numerous pelvic OFP, stable fixation implants can be inserted safely and through small stab incisions. These small surgical wounds decrease bleeding, scarring, and infection rates significantly. Such procedures can be performed expeditiously benefiting the patient by saving anesthesia and surgery time. Health care dollars are saved as the patients are rehabilitated quickly and efficiently, and can be discharged to home sooner. These patients can return to work within several weeks if their job situations will allow them to. The accurate reduction and stable fixation promote normal healing and prevent disabling deformities. Avoiding pelvic deformity helps the patient avoid potential associated chronic pain and gait disturbances among others.

ends at the ischial tuberosity. Upper sacral morphology is quite variable, so preoperative planning and intra-operative imagings are vital to safe and successful implant insertions.

Reduction of the pelvic ring injury sites prior to fixation is similarly critical to safe implant application within these OFPs. Mis-alignment of these pelvic OFPs narrows the safe region for implant placement and therefore increases the injury risk for surrounding anatomical structures such as viscera, arteries, veins, and nerve roots. Poor reduction allows residual fracture instability and may

Figure 2: (A&B) A. The plain pelvic radiograph demonstrates an unstable and displaced pelvic ring disruption and extra-peritoneal bladder injury. The patient was injured in a high-speed car crash and also had a right sided femur fracture. The pelvic injuries include a symphysis pubis disruption, left mid-ramus fracture, left sacroiliac joint (SIJ) disruption, right incomplete SIJ injury, and right transverse acetabular fracture. B. After acute evaluation and resuscitation, her pelvic injuries were treated with manipulative reduction using an anterior pelvic compression device, followed by trans-iliac trans-sacral screw fixation. Antegrade bilateral superior pubic ramus screws were used to stabilize the acetabular and left ramus fractures, and the pelvic compressor was then exchanged for routine anterior pelvic external fixation. A total of six small stab wounds were used to apply the pelvic fixation. The pelvic procedures took less than 3 total hours to complete with negligible operative blood loss. Next her right femur fracture was treated with a medullary reamed locked nailing at the same anesthetic.
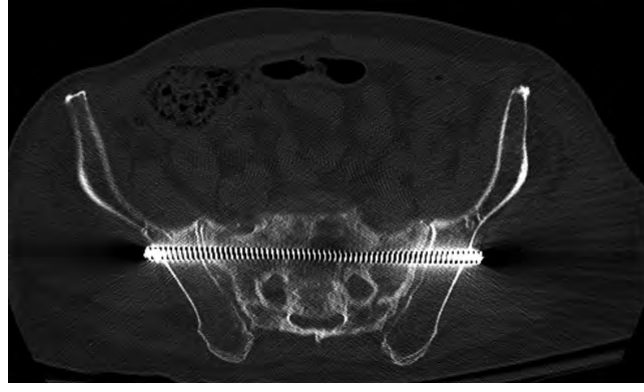
Figure 3: (A&B) A. This active 78 year old male developed severe lumbosacral pain weeks after external radiation treatment for his prostatic cancer. He was an avid tennis player but was unable to walk due to posterior pelvic and low back pain. Radiographic evaluation revealed a displaced U-shaped insufficiency fracture of the upper sacrum. He opted for percutaneous fixation of the fracture using bilateral transiliac-transsacral screws. B. The postoperative pelvic CT scan image demonstrates the fracture sites and screw locations. His pain resolved soon after surgery, and he returned to his prior activities 2 months later.

Minimally invasive pelvic surgery is obviously advantageous. While not every pelvic ring injury is amenable to it, the great majority of these injuries are. Its success depends on early intervention, complete preoperative planning, high quality fluoroscopic imaging, accurate overall pelvic reduction, thorough knowledge of the pelvic OFPs, and stable fixation.

Recommended Reading

Gardner MJ, Farrell ED, Nork SE, Segina DN, Chip Routt ML Jr. Percutaneous Placement of Iliosacral Screws Without Electrodiagnostic Monitoring. J Trauma. 2008 Sept.

Moed BR, Fissel BA, Jasey G. Percutaneous transiliac pelvic fracture fixation: cadaver feasibility study and preliminary clinical results. J Trauma. 2007 Feb; 62(2): 357-64.

Reilly MC, Bono CM, Litkouhi B, Sirkin M, Behrens FF. The effect of sacral fracture malreduction on the safe placement of iliosacral screws. J Orthop Trauma. 2006 Jan.

Starr AJ, Nakatani T, Reinert CM, Cederberg K. Superior pubic ramus fractures fixed with percutaneous screws: what predicts fixation failure? J Orthop Trauma. 2008 Feb; 22(2): 81-7.

Peter R. Cavanagh, Ph.D.

Professor
University of Washington Medical Center
Research
www.orthop.washington.edu/faculty/cavanagh

Kerim Genc, M.S., Andrea Hanson, Ph.D.,
Sara Novotny, M.S., Andrea Rice, M.S., and Rami Rizk

Bone Loss During Spaceflight – A Failure of Regeneration

- Bone loss during spaceflight has been a known health issue for more than 40 years.
- The mechanism appears to be enhanced resorption unbalanced by enhanced bone formation.
- Risk of fracture and renal stones have both been identified by NASA as potentially mission-limiting.
- Astronauts on long-duration missions typically lose 2% of hip bone mass per month.
- This loss is as much in a month as post-menopausal women lose in a year.
- International Space Station (ISS) crew members are returning with losses of up to 10% of proximal femoral in bone mineral density and 15% in predicted bone strength.
- The only countermeasure to bone loss that has been attempted to date is exercise.
- Our experiments on board the ISS have shown that exercise loads are less than those on Earth.
- 6-degree head-down bedrest is a ground-based analog of spaceflight.
- Our bedrest studies have shown that individualized exercise prescriptions can mitigate total hip bone loss in some people.
- A new resistance exercise device was recently delivered to the ISS.
- An experiment with oral bisphosphonates has been approved for flight.
- More information on bone loss in women astronauts is needed.
- Recovery from bone loss is lengthy and results in altered bone structure.

There are plans for humans to set foot on Mars sometime in the next 25 years. Before that can happen, researchers must solve a major problem that will put those space explorers at risk for fracture during and after their missions: the significant loss of bone from the skeleton that occurs during spaceflight. This phenomenon, which has been known for more than 40 years, appears to be caused by an uncoupling of the processes of bone formation and resorption - which are tightly linked in healthy people on Earth. This constant building and removal of bone replaces the entire skeleton in normal humans over a 10-year period, but work done by Smith and colleagues show that it appears the unloading which occurs in spaceflight results in an elevation of resorption while formation remains relatively unchanged.

The work done by Smith's group also showed that elevated excretion of calcium in the urine begins almost immediately once astronauts arrive in-orbit and appears to continue unabated during the entire flight. In addition to putting astronauts at risk for renal stones, this excretion of calcium leads to a loss in bone mineral density and an increased risk of fracture during and after long-duration missions.

Based on quantitative computer tomography (QCT) taken before and after 4-6 month missions to the International Space Station (ISS), Lang et al. demonstrated that a loss of cortical and, more notably, trabecular bone occurs in the proximal hip at rates between 1.2-2.7% per month. Such losses, extrapolated to the 2.5-year duration of Martian missions, would have severe consequences for skeletal integrity. Put in the context of bone health on Earth, these losses are approximately 10 times greater than those seen in a post-menopausal woman as reports by Mazzuoli et al.

Although bone mineral density (BMD) is typically used as a measure of change in bone health, this index is under significant assault because it is only one facet of the complex set of variables that contribute to bone strength - or resistance to

Figure 1: Astronaut running on a tethered treadmill on the ISS while wearing a set of instrumentation that we devised to measure joint motion, muscle activity, and ground reaction forces.

the lack of "Earth-like" loading during exercise.

To test this hypothesis, we are conducting an experiment that uses bed rest as a model of spaceflight. Healthy volunteers agree to remain in bed, tilted 6 degrees head-down, for 84 days without sitting up, stepping down, or otherwise allowing gravity to act along the long-axis of their legs. Half the subjects are randomized to a control condition in which they perform no load-bearing activity but some stretching exercise for the entire 12-week period. Five times per week, the other half of the subjects are taken in a horizontal position to a unique exercise facility called the Zero Gravity Locomotion Simulator (ZLS - Figure 3) that allows them to exercise as if they are in space. Just as occurs in space, we apply loads on the tether using a special harness that has been designed based on backpack technology to more comfortably distribute the greater loads that we are applying compared to the harnesses previously used in space. The control subjects are also suspended five times per week in the ZLS in the horizontal position but did not perform exercise. The BMD results from our study (Figure 4), which is currently at the half way point, are extremely promising. The bone mineral density data from QCT show a protective effect that represents the most successful mitigation of bone loss by exercise countermeasures compared to studies in the literature. The five exercise subjects completed to date show a mean gain in total hip volumetric bone mineral density (vBMD - measured using QCT) while all anatomical regions and compartments (cortical and trabecular) in the six control subjects show losses similar to those seen in spaceflight. Urine and serum bone marker results also support the efficacy of our countermeasure. Exercising subjects had higher levels of a bone formation marker and lower calcium and resorption marker levels when compared to controls. These findings suggest that the BMD changes that occurred as a result of our exercise intervention occurred partly through attenuation of the resorption typically seen in sedentary bedrest and partly due to increased formation.

A new exercise machine, called aRED (advanced Resistance Exercise Device), was delivered to the ISS in

fracture. This issue has recently been dramatically illustrated in relation to spaceflight by Keyak et al. who showed that the changes in BMD described above during missions to the ISS can result in reductions of up to 15% in the predicted strength of the proximal femur.

The only countermeasure to these skeletal changes that has so far been attempted is exercise. Current modes of exercises available on the ISS are resistance exercise, cycling, and tethered treadmill running. Such exercise requires that the subject be "tethered" to the exercise device (as shown in Figure 1) or they would

simply float away from the device after the first foot contact. The tether can be thought of as providing a "gravity replacement" and the tension in the tether will directly influence the load that is experienced on the feet. We have measured these loads during exercise on-orbit and have found that there is a 26% reduction compared with walking on Earth (0.89 BW vs. 1.2 BW) and a 45% reduction compared with running on Earth (1.3 BW vs. 2.36 BW). Mean on-orbit lower-extremity loads during cycling exercise were only 0.11 BW. We, therefore, believe that one of the reasons why exercise has been ineffective to date has been

Figure 2: Average peak ground reaction forces (in multiples of body weight) during bouts of exercise on Earth (1g) and on-orbit (0g). The walking and running data are mean values for a total of 16 trials on Earth and 16 trials and on-orbit in 4 crewmembers. Only one trial for cycling was available on-orbit. Peak forces during walking and running were on average 26 and 45% lower on-orbit than on Earth, respectively.

late 2008, and this machine allows considerably greater loads than were possible using previous on-orbit exercise devices. It will be interesting to see if use of this machine can have an impact on bone loss of future ISS occupants.

One important area in which more information is needed is the bone health of women during long-duration spaceflight. Currently, the menstrual periods of women astronauts are inhibited by hormonal therapy during spaceflights of up to 6-months duration and according to Mark et al., this is not a viable strategy for interplanetary missions lasting 2-3 years. Bedrest studies of young women volunteers conducted by Smith and hid group have suggested that they lose bone at a similar rate to young men, but since the average age of astronauts is currently about 43-years, we need more information about women in this age group.

Given the fact that millions of women around the world are taking anti-resorptive drugs, it is remarkable that these agents have not been used in space. There has been some concern about mid-life astronauts using drugs designed and tested for vertebral fracture prevention in post-menopausal women. The recent association of bisphosphonate use with osteonecrosis of the jaw by Silverman and Landesberg has also dampened enthusiasm among the Astronaut Corps for use of this class of drugs. However, a protocol using an oral bisphosphonate (alendronate) has been approved for flight, and the first astronaut subject is currently enrolled.

Lifetime bone health is a significant concern for returning long-duration astronauts. Studies by Sibonga, Lang and colleagues have shown that although 50% recovery of BMD appears to occur in the first 9 months after landing the bone structure is altered in a manner that suggests premature skeletal aging.

The integrity of the skeleton is critical to astronaut fitness for duty during interplanetary missions and much remains to be learned about strategies to prevent the current unacceptably high levels of bone loss. A combination of pre- and post-flight experiments and bedrest studies are beginning to provide leads that may solve this important problem well before astronauts take their first step onto the Martian surface.

Acknowledgments

Recommended Reading

Bouxsein ML. Technology insight: noninvasive assessment of bone strength in osteoporosis. Nat Clin Pract

Figure 3: The Zero Gravity Locomotion Simulator (ZLS) on which bedrest subjects are exercised to simulate exercise during spaceflight.

Figure 4: Changes in vBMD in four regions of the hip (Neck = femoral neck, Troch = greater trochanter, Inter = intertrochanteric region T-Hip = total hip) as measured by QCT, after 12-weeks of bedrest. Control subjects (n=6), exercise subjects (n=5). Units are %change from pre-bedrest scan with bars indicating standard deviations. There was a slight mean gain in total hip vBMD in exercisers while controls lost approximately 5%. There were slight losses in the trochanter region of the exercise subjects.
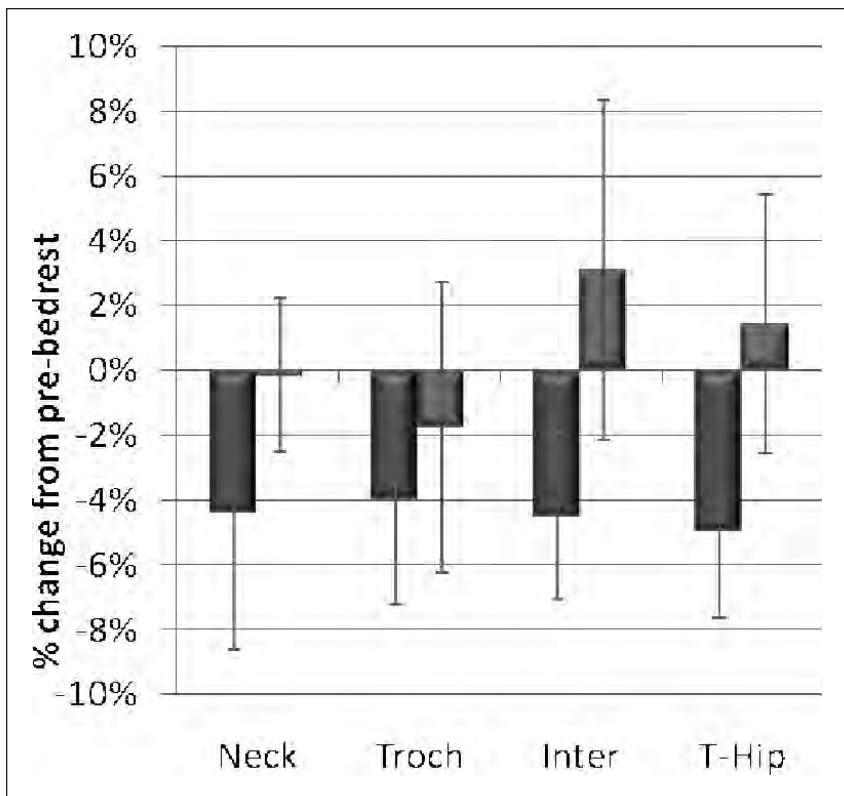
Rheumatol. 2008 Jun;4(6):310-8.

Cavanagh, P.R., Rice, A.J, Licata, A.A. 40 Years of Bone Loss in Space. Chapter 1 in Bone Loss during Spaceflight Cavanagh, PR. and Rice, AJ. (Eds). Cleveland Clinic Press, 2007.

Genc, K.O., Humphreys, B.T., and Cavanagh, P.R., Enhanced Daily Load Stimulus: A Method Accounting for Cyclical Loading and Standing on Osteogenesis. [Submitted to Aviat Space Environ Med].

Gopalakrishnan, R., Rice, A.J., Lee, S.M.C., Evans, H.J., Maender, C.C., Ilaslan, H., Genc, K.O. and Cavanagh, P.R. Changes in Muscle Volume, Strength and Endurance after Long-Duration Spaceflight. [To be submitted to Aviat Space Environ Med].

Keyak JH, Koyama AK, LeBlanc A, Lu Y, Lang TF. Reduction in proximal femoral strength due to long-duration spaceflight. Bone. 2009 Mar;44(3):449-53.

Keyak JH, Koyama AK, LeBlanc A, Lu Y, Lang TF. Reduction in proximal femoral strength due to long-duration spaceflight. Bone. 2009 Mar;44(3):449-53.

Lang T, LeBlanc A, Evans H, Lu Y, Genant H, Yu A. Cortical and trabecular bone mineral loss from the spine and hip in long-duration spaceflight.J Bone Miner Res. 2004 Jun;19(6):1006-12.

Lang TF, Leblanc AD, Evans HJ, Lu Y. Adaptation of the proximal femur to skeletal reloading after long-duration spaceflight. J Bone Miner Res. 2006 Aug;21(8):1224-30.Adaptation of the proximal femur to skeletal reloading after long-duration spaceflight. J Bone Miner Res. 2006 Aug;21(8):1224-30.

Mark, S. Sex-differences in bone health. Chapter 22 in Bone Loss during Spaceflight Cavanagh, PR. and Rice, AJ. (Eds). Cleveland Clinic Press, 2007.

Mazzuoli G, Acca M, Pisani D, Diacinti D, Scarda A, Scarnecchia L, Pacitti MT, D'Erasmo E, Minisola S, Bianchi G, Manfredi G. Annual skeletal balance and metabolic bone marker changes in healthy early postmenopausal women: results of a prospective study. Bone. 2000 Apr;26(4):381-6.

McGowan, J.A. The Basics of Bone in Health and Disease. Chapter 2 in Bone health and osteoporosis: a report of the Surgeon General. - Rockville, Md. : U.S. Dept. of Health and Human Services, Public Health Service, Office of the Surgeon General ; Washington, D.C.

Pietrzyk RA, Jones JA, Sams CF, Whitson PA. Renal stone formation among astronauts. Aviat Space Environ Med. 2007 Apr;78(4 Suppl):A9-13.

Sibonga JD, Evans HJ, Sung HG, Spector ER, Lang TF, Oganov VS, Bakulin AV, Shackelford LC, LeBlanc AD. Recovery of spaceflight-induced bone loss: bone mineral density after long-duration missions as fitted with an exponential function. Bone. 2007 Dec;41(6):973-8.

Silverman SL, Landesberg R. Osteonecrosis of the jaw and the role of bisphosphonates: a critical review. Am J Med. 2009 Feb;122(2 Suppl): S33-45. Review.

Smith SM, Nillen JL, Leblanc A, Lipton A, Demers LM, Lane HW, Leach CS. Collagen cross-link excretion during space flight and bed rest. J Clin Endocrinol Metab. 1998 Oct;83(10):3584-91.

Smith SM, Wastney ME, Morukov BV, Larina IM, Nyquist LE, Abrams SA, Taran EN, Shih CY, Nillen JL, Davis-Street JE, Rice BL, Lane HW. Calcium metabolism before, during, and after a 3-mo spaceflight: kinetic and biochemical changes. Am J Physiol. 1999 Jul;277(1 Pt 2):R1-10.

Smith SM, Zwart SR, Heer M, Lee SM, Baecker N, Meuche S, Macias BR, Shackelford LC, Schneider S, Hargens AR.WISE-2005: supine treadmill exercise within lower body negative pressure and flywheel resistive exercise as a countermeasure to bed rest-induced bone loss in women during 60-day simulated microgravity. Bone. 2008 Mar;42(3):572-81.

Sundar Srinivasan, Ph.D.

Research Associate Professor
Harborview Medical Center
Research
www.orthop.washington.edu/faculty/srinivasan

Brandon J. Ausk, M.S., Jitendra Prasad, Ph.D.
Thomas S. Richardson, Ph.D., and Ted S. Gross, Ph.D.

Every Second Counts - Discovering Mild Physical Activity to Build-Up Bone Mass - Putting Regeneration to Work

- Osteoporosis and resulting non-traumatic fractures are an inevitable consequence of aging and menopause.
- Anabolic options are required to build-up bone mass at adolescence such that non-traumatic fractures can be prevented later in life.
- Physical exercise offers promise as a therapy but requirements for high-impact, strenuous activity have prevented realization of this potential.
- We have therefore sought to design mild exercise based interventions by focusing upon observations that brief exercise (~ 2 – 3 mins) can elicit robust bone adaptation.
- Using this basis, we have developed a novel computational model that simulated activation of the Ca2+/NFAT pathway, a signaling mechanism critical in how bone cells and tissue perceive and respond to brief mechanical loading or physical exercise.
- Interestingly, optimization using this model suggested that loading bone once every 10 mins could result in substantially more bone formation than loading bone 1800 times over a 30 min 'exercise' bout.
- Remarkably, our preliminary experiments confirm predictions of this computational model, demonstrate the utility of our approach and suggest that mild activity can indeed be 'engineered' to be potently anabolic for the skeleton.
- Ultimately, a similar strategy could be used to design mild physical exercise to robustly build-up bone mass at adolescence as a bulwark against the inevitable ravages of age and menopause.

Osteoporosis and related non-traumatic fractures can be thought of as the inevitable consequence of aging superimposed upon a previously insufficient peak bone mass 'bank' balance. As such, the search is on for anabolic therapies that build up this bone 'bank' from adolescence through adulthood, thereby providing a bulwark against the inevitable declines in bone mass accrued over a lifetime. Physical exercise can be substantially osteogenic for bone and holds promise as a non-invasive means to enhance the bone mass at adolescence. However, the vigorous and high impact activities that have proven to be osteogenic are not trivial to safely implement in the young, growing skeleton. Our group at the OSL seeks to explore bone mechanotransduction function with a view to ultimately discovering physical exercise based strategies that are both mild to perform and substantially osteogenic for young and old alike.

Given this goal, we have focused upon studies that suggest that physical exercise need only be brief, in order to beneficially influence bone mass and structure. Remarkably, loading bone for as little as 5 seconds a day has been found to be sufficient to enhance bone mass and strength. Given this, bone cell activity induced during and by loading (i.e., within seconds to minutes) must clearly be critical in regulating downstream tissue adaptation. However, the activity and responses induced in bone cells in vivo within this acute time frame are highly inaccessible. Therefore, and using a novel technique suited for the exploration of complex systems, we developed a biophysical agent-based computational model (ABM) for how cell signaling initiated within seconds by mechanical stimuli could influence bone tissue adaptation weeks downstream.

Our ABM for cell signaling induced within seconds simulates activation of the Ca2+/NFAT pathway, a critical mechanism known to underlie
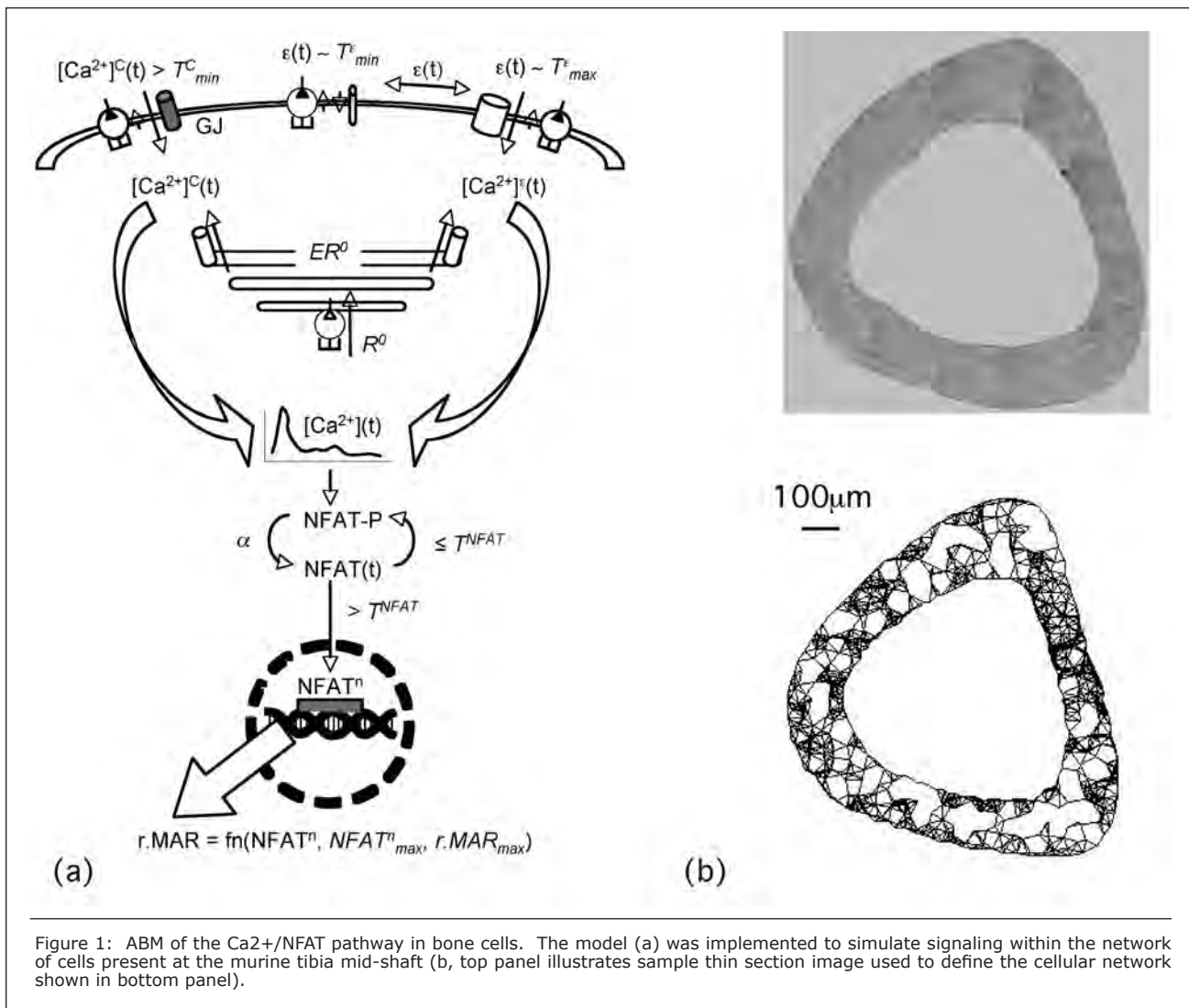
Figure 1: ABM of the Ca2+/NFAT pathway in bone cells. The model (a) was implemented to simulate signaling within the network of cells present at the murine tibia mid-shaft (b, top panel illustrates sample thin section image used to define the cellular network shown in bottom panel).

mechanotransduction (Figure 1 a). Briefly, our parametric model is based upon experimental reports and assumes that mechanical strain induced on a cell body causes Ca2+ oscillations within the cell cytoplasm due to the confluence of 1) Ca2+ influx into the cell cytoplasm through stretch activated ion channels, 2) Ca2+ efflux from the endoplasmic reticulum, and 3) influx of Ca2+ into the cell body from neighboring networked cells via gap junctional exchange of Ca2+ ions. Downstream of Ca2+ oscillations, our model simulates the dynamics of de-phosphorylation and nuclear transport of the cytoplasmic protein, NFAT. Finally, given the known biology, our model simulates accumulated NFAT protein binding with DNA and its control over mineral apposition by surface osteoblasts. We have implemented this biophysical model to simulate signaling interactions

within and between cells present at the mid-shaft cross-section of young adult female C57BL/6 mice (4 Mo; Figure 1 b).

As such, the model was designed to simulate loading induced activation of the Ca2+/NFAT pathway within and between bone cells at the murine tibia mid-shaft and the bone formation that ensues following repeated bouts of loading over a 3-wk period. To determine model parameters, we 'trained' the model using bone formation data derived from young adult animals exposed to 10 different mechanical loading waveforms. The loading waveforms involved subjecting mice to increasing strain magnitudes, loading repetitions and inserting 0 or 10 s unloaded 'rest' intervals between each loading event. We found that our model was sufficient to accurately simulate bone formation induced by a variety of loading protocols in young

adult animals (error < 15%, p =0.57; Figure 2). Given this, we sought to use this model in a predictive role and examined our ability to optimize mechanical stimuli in young adult animals.

We utilized our ABM to explore whether a 30 min 'exercise' protocol could be optimized for young adults such that bone tissue adaptation would be substantially enhanced while requiring minimal loading 'effort'. To perform the optimization, we first simulated bone adaptation induced by 'control' loading regimens (Figure 3). Bone formation rates induced by a baseline control involving 1800, 1-Hz load cycles provided 3 days/wk for 3-weeks was first simulated. Next, we used the model to simulate bone formation induced by a positive control regimen involving 164 c/d, with a 10-s rest between each cycle, for 3 days/wk for 3-wks. Finally, we used

Figure 2: ABM of the Ca2+/NFAT pathway accurately simulates relative periosteal bone formation rates (rp.BFR) induced by a variety of mechanical stimuli. For the in vivo experiments, animals were subject to loading 3 d/wk for 3-wk using protocols defined by induced strains, cycles/d, and rest between load cycles (e.g., 1250, 250, 10, would imply peak strains of 1250 me were induced for 250 cycles/d with a 10-s unloaded rest interval inserted between each load cycle.

our ABM to design a protocol that could induce bone formation greater than our baseline control, equivalent to our positive control, while requiring minimal loading effort. Our analysis suggested that loading bone 4 times a day, with a 10 min rest-interval between each loading event, would induce the required bone formation. To test these predicted outcomes, we implemented these regimens in young adult female C57BL/6J mice (4 Mo, n = 8) and determined bone formation rates in vivo via dynamic histomorphometry. While preliminary, our finding that loading bone every 10 mins during a 30 min 'exercise' period can substantially enhance bone formation was stunning, not just in validating the predictive ability of an in silica model, but in suggesting that a minimal loading effort can indeed be 'engineered' to be substantially anabolic for bone.

In conclusion, we have focused upon a pathway that is activated during brief mechanical stimuli as a means to both explore mechanotransduction and to design novel approaches to loading bone. Our in silica model has proven to be predictive, and more importantly, has identified that loading bone just 4 times during a 30 min exercise bout, can be substantially osteogenic. While we are seeking to confirm these findings, they indeed offer promise to both our approach of using in silica models to design in vivo experiments and our supposition for the existence of mild loading protocols that would be safe to implement yet substantially anabolic for the young adult skeleton. Ultimately, we expect to be able to use a similar approach in designing mild physical exercise regimens for trials in adolescent and school age populations with the goal of sufficiently building up their bone 'banks'.

Recommended Reading

Ausk, B.J., T.S. Gross, and S. Srinivasan, An agent based model for real-time signaling induced in osteocytic networks by mechanical stimuli. J Biomech, 2006. 39(14): p. 2638-46.

Berridge, M.J., M.D. Bootman, and P. Lipp, Calcium--a life and death signal. Nature, 1998. 395(6703): p. 645-8.

Dolmetsch, R.E., K. Xu, and R.S. Lewis, Calcium oscillations increase the efficiency and specificity of gene expression. Nature, 1998. 392(6679): p. 933-6.

Genetos, D.C., D.J. Geist, D. Liu, H.J. Donahue, and R.L. Duncan, Fluid shear-induced ATP secretion mediates prostaglandin release in MC3T3-E1 osteoblasts. J Bone Miner Res, 2005. 20(1): p. 41-9.

Umemura, Y., T. Ishiko, T. Yamauchi, M. Kurono, and S. Mashiko, Five jumps per day increase bone mass and breaking force in rats. J Bone Miner Res, 1997. 12(9): p. 1480-5.
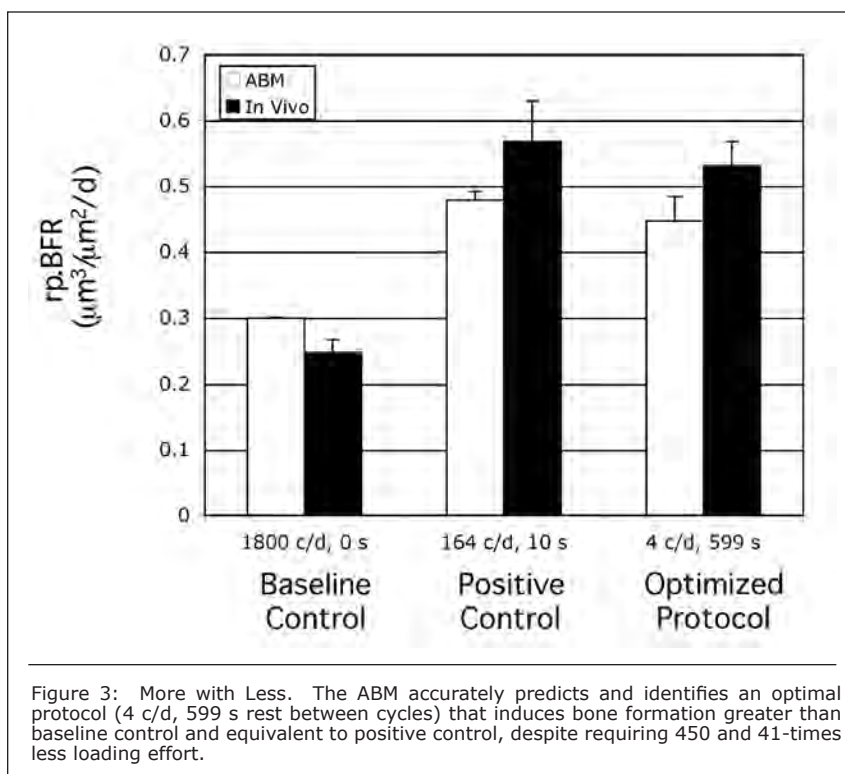
Figure 3: More with Less. The ABM accurately predicts and identifies an optimal protocol (4 c/d, 599 s rest between cycles) that induces bone formation greater than baseline control and equivalent to positive control, despite requiring 450 and 41-times less loading effort.

Jeremiah M. Clinton, M.D.

Affiliate Professor
University of Washington Medical Center
Shoulder and Elbow
www.orthop.washington.edu

Amy Franta, M.D., Nayak Polissar, Ph.D.,
Blazej Neradilek, M.S., Doug Mounce, M.S.,
Howard A. Fink, M.D., M.P.H.,
John T. Schousboe, M.D., M.S.,
and Frederick A. Matsen III, M.D.

Proximal Humerus Fractures and the Risk of Subsequent Hip Fracture: Timing is Everything

- In osteoporosis, the rate of bone regeneration fails to keep up with the rate of bone degeneration.
- Fragility factures in individuals with osteoporosis are debilitating, expensive and lethal.
- Having a fracture associated with osteoporosis significantly increases the risk of subsequent hip fracture.
- 25% of patients who have a hip fracture will die within the first year following the hip fracture.
- 70% of proximal humerus fractures occur in women.
- Having a proximal humerus fracture increases the risk of having a hip fracture 6-fold within the first year following the humerus fracture.
- Interventions and medical treatments can substantially decrease the risk of subsequent hip fractures as soon as 3-6 months after initiation of treatment.

Osteoporosis and associated fragility fractures are a major health concern and a source of significant morbidity and mortality around the world. For the year 2006, it was estimated that in the United States the economic burden associated with hip fractures alone might be in excess of $20 billion dollars. Given the enormous social and monetary costs of hip fractures, their prevention is a pressing concern. It is well established that patients having had a single fragility fracture are at significantly increased risk of having a second fracture in the future. A history of proximal humerus fractures (Figure 1) also appears to be a risk factor for other incident fractures, including those at the hip. These data suggest that a fracture of the proximal humerus may be predictive of increased risk for a subsequent hip fracture, however the methodology of previous studies did not control for many important variables. Interestingly, the mechanism of proximal humerus fractures is similar to that of hip fractures in that patients are unable to break their forward or oblique fall and therefore land directly onto their shoulder or hip. Given the similar mechanism of fracture, it is intuitive that the timing of a hip fracture would be relatively close to the timing of a proximal humerus fracture in contrast to other osteoporotic fractures.

We hypothesized that patients who sustain a proximal humerus fracture will be at higher risk for a subsequent hip fracture and that the hip fractures would tend to occur within the five years after the fracture of the proximal humerus.

Methods

The Study of Osteoporotic Fractures is a prospective multicenter cohort study of 9,704 women age 65 years and older who were enrolled from September 1986 to October 1988 in four separate geographic areas of the United States. Women were recruited if they were over the age of sixty-five, community dwelling, ambulatory, and had no history of bilateral hip replacements. The women were followed prospectively for up to 10 years at regular intervals. The participants attended seven examinations at approximately two-year intervals and were contacted by phone or postcard every four months to ascertain fracture history with over a 99% follow-up rate and 90% accuracy.

The original Study of Osteoporotic Fractures' cohort included 9,704 women, of whom 1,655 (17%) were excluded from our study due to missing data regarding prior fracture status or age, lack of complete follow-up, history of hip or humerus fracture prior to Exam 2, or missing bone mineral density data. A total of 8,049 (83%) women, therefore, were considered for our present study and their information was used in the univariate Cox regression

Figure 1: Low energy proximal humerus fracture a common "fragility fracture."

between incident humerus fracture and the risk of subsequent hip fracture. STATA (StataCorp LP, College Station, Texas) statistical software was used for all analysis. All models were adjusted for current age and total hip bone mineral density. Each observation in the Cox regression was left-censored at the age upon entering the study and either ended at the hip fracture or was right-censored at the end of the follow-up period.

In order to examine whether or not the risk of a subsequent hip fracture attributable to an incident humerus fracture changes over the time elapsed after the humerus fracture, two multivariate models were run categorizing time after humerus fracture as a time-varying variable. The three post-humerus fracture intervals were: a) <1 year, b) 1-5 years, and c) >5 years after the humerus fracture, with subjects not experiencing an incident humerus fracture utilized as the reference group for all analyses.

Results

Three hundred and twenty-one women sustained a proximal humerus fracture and forty-four sustained a subsequent hip fracture. The hazard ratio for hip fracture for subjects with a fracture of the proximal humerus relative to those without after multivariate analysis was 1.83 (95% C.I. 1.32 - 2.53). After multivariate adjustment, this risk appeared attenuated but was still significant (1.57; 95% C.I. 1.12-2.19). The risk of subsequent hip fracture after proximal humerus fracture was highest within 1 year of the proximal humerus fracture with a Hazard Ratio of 5.68 (95% C.I.3.70 - 8.73). This association was not significant after the first year, with a Hazard Ratio of 0.87 (95% C.I. 0.48 - 1.59) for the time period between 1-5 years post humerus fracture and 0.58 (95% C.I. 0.22 - 1.56) at >5 years.

Discussion

In this cohort of older, community dwelling women, incident proximal humerus fractures significantly

analyses. A total of 1,128 (12%) were excluded from the final multivariate analysis due to missing data for one or more covariates, leaving 6,921 (71%) women to be analyzed.

Cox proportional hazards models were used to quantify the association

Risk factor	N	HR (95% C.I.)	p
Total hip bone mineral density (per 1 SD decrease*)	8049	2.11 (1.94 – 2.29)	<0.001
Humerus fracture	8049	1.83 (1.32 – 2.53)	<0.001
Non-humerus, non-hip fracture	8049	1.43 (1.20 – 1.72)	<0.001
Height at 25 years (per 10 cm)	7904	1.41 (1.24 – 1.61)	<0.001
Depth perception (per 10 times SD of 4 Howard-Dohlman optical distance scores (cm))	7851	1.43 (1.13 – 1.82)	0.003
Weight gain since age 25 (per 10 kgs)	7823	0.94 (0.85 – 1.04)	0.2
Maternal history of hip fracture after 50 yrs	6153	1.33 (1.06 – 1.66)	0.013
Estrogen use	8048	1.09 (0.86 – 1.40)	0.5
Use of long acting benzodiazepines at baseline	8008	0.98 (0.75 – 1.23)	0.9
Self related health status (1-5)	8049	1.33 (1.20 – 1.46)	<0.001
Walking for exercise	8049	0.85 (0.73 – 0.99)	0.04
On feet less than 4 hours a day	8046	1.27 (1.04 – 1.55)	0.02
Use of arms to stand	8046	1.37 (1.12 – 1.67)	0.002
History of falls	8049	1.38 (1.18 – 1.61)	<0.001

Table 1: Effect of risk factors for hip fracture, adjusted for age and total hip bone mineral density. * 1 SD = 0.133 g/cm2 Total hip bone mineral density adjusted for age only.

Risk factor	HR (95% C.I.)	p-value
Total hip Bone mineral density (per 1 SD decrease)	2.08 (1.91 – 2.27)	<0.001
Self related health status (1-5)	1.24 (1.12 – 1.38)	<0.001
Height at 25 years (per 10 cm)	1.39 (1.22 – 1.59)	<0.001
History of falls	1.29 (1.10 – 1.52)	0.002
Depth perception	1.53 (1.19 – 1.97)	0.001
Non-humerus fracture	1.28 (1.06 – 1.55)	0.01
Humerus fracture	1.57 (1.12 – 2.19)	0.009

Table 2: Final multivariate Cox proportional hazards model for hip fracture, including humerus fracture as a risk factor. (N=6921 subjects).

increased risk of subsequent hip fracture. In particular, the risk of a subsequent hip fracture was six-times higher within the first year following the proximal humerus fracture, even when controlled for other important risk factors in a multivariate analysis. This association is not statistically significant at time intervals greater than one year after the incident humerus fracture. Although our study could have missed a modest persistent association between humerus fractures and incident hip fractures occurring after one-year of follow-up, the excess risk of hip fractures attributable to a prior humerus fracture clearly sharply waned after one-year of follow-up.

The results of the current study have significant implications in the clinical evaluation, treatment, and prevention of future fractures in patients sustaining a proximal humerus fracture. They demonstrate that the most concerning time frame for the risk of a subsequent hip fracture is

within a year of a proximal humerus fracture, and therefore intervention following a humerus fracture should be initiated without delay to reduce risk of subsequent fractures. Studies have suggested that oral bisphosphonates begin to reduce the risk of fractures within 3 to 6 months after being started. In addition to initiation of medical treatment for osteoporosis, steps should be taken in the prevention of falls in the at-risk population, as nearly 80% of proximal humerus fractures and 90% of hip fractures are related to falls from a standing height. A recent meta-analysis demonstrated the need for a multifaceted approach in the prevention of falls in hospitals and nursing homes and that no single intervention had a significant effect in a hospital setting. And although this study evaluated patients in a hospital or nursing home setting and not community ambulators as in our study, they too likely needed a multifaceted approach to the prevention of further

falls whether it be assistive devices at home, adjustment of medications, or the evaluation of environmental factors that lead to initial falls as well as the initiation of medical therapy for osteoporosis. A recent statement on the guidelines for the prevention of falls in the elderly was formulated by the American Geriatric Society, British Geriatric Society, and American Academy of Orthopaedic Surgeons and serves as a useful resource in the evaluation and prevention of falls in the geriatric population. It is also important to note that the risk of subsequent fracture is increased after proximal humerus fracture not only in women but also in men as noted by Ettinger et al.

In conclusion, the current study supports our hypothesis that proximal humerus fracture is an independent risk factor for subsequent hip fracture. Importantly, the time of greatest risk is the first year following proximal humerus fracture, and the risk of

Period	Hazard ratio, adjusted for age and Bone mineral density (95% C.I.)	Hazard ratio, adjusted for age, Bone mineral density and variables from the final multivariate model* (95% C.I.)
Before the humerus fracture	1.00	1.00
First year after the humerus fracture	6.16 (4.01 – 9.44)	5.68 (3.70 – 8.73)
1 - 5 years after the humerus fracture	1.16 (0.67 – 2.02)	0.87 (0.48 – 1.59)
> 5 years after the humerus fracture	0.64 (0.24 – 1.71)	0.58 (0.22 – 1.56)

Table 3: The risk of a hip fracture over time following a humerus fracture.

incident hip fracture attributable to prior humerus fractures wanes sharply after that. This small window of time provides an opportunity to implement medical and environmental interventions that may decrease the risk of subsequent hip fractures and their cost to the patient and to society.

Recommended Reading

Cummings SR, Rubin SM and Black D, The future of hip fractures in the United States. Numbers, costs, and potential effects of postmenopausal estrogens. Clin. Orthop. Rel. Res. 252 1990, pp. 163-166.

Ray NF, Chan JK, Thamer M, Melton LJ 3rd. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: report from the National Osteoporosis Foundation. J Bone Miner Res. 1997 Jan;12(1):24-35.

Klotzbuecher, CM. Ross PD, Landsman PB, Abbott TA 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res, 2000. 15(4): p. 721-39.

Wu F, Mason B, Horne A, Ames R, Clearwater J, Liu M, Evans MC, Gamble MD, Reid IR. Fractures between the ages of 20 and 50 years increase women's risk of subsequent fractures. Arch Intern Med, 2002. 162(1): p. 33-6.

Haentjens P, Autier P, Collins J, Velkeniers B, Vanderschueren D, Boonen S. Colles fracture, spine fracture, and subsequent risk of hip fracture in men and women. A meta-analysis. J Bone Joint Surg Am, 2003. 85-A(10): p. 1936-43.

Lauritzen, JB, Scharz P, McNair P, Lund B, Transbol I. Radial and humeral fractures as predictors of subsequent hip, radial or humeral fractures in women, and their seasonal variation. Osteoporos Int, 1993. 3(3): p. 133-7.

Robinson CM, Royds M, Abraham A, McQueen MM, Court-Brown CM, Christie J. Refractures in patients at least forty-five years old. a prospective analysis of twenty-two thousand and sixty patients. J Bone Joint Surg Am. 2002. 84-A(9): p. 1528-33.

Palvanen M, Kannus P, Parkkari J, Pitkajarvi T, Pasanen M, Vuori I, Jarvinen M. The injury mechanisms of osteoporotic upper extremity fractures among older adults: a controlled study of 287 consecutive patients and their 108 controls. Osteoporos Int. 2000;11(10):822-31.

Silverman SL, Watts NB, Delmas PD, Lange JL, Lindsay R. Effectiveness of bisphosphonates on nonvertebral and hip fractures in the first year of therapy: the risedronate and alendronate (REAL) cohort study. Osteoporos Int. 2007 Jan;18(1):25-34.

Lind T, Krøner K, Jensen J. The epidemiology of fractures of the proximal humerus. Arch Orthop Trauma Surg. 1989;108:285-287.

Oliver D, Connelly JB, Victor CR, Shaw FE, Whitehead A, Genc Y, Vanoli A, Martin FC, Gosney MA. Strategies to prevent falls and fractures in hospitals and care homes and effect of cognitive impairment: systematic review and meta-analyses. BMJ. 2007 Jan 13;334(7584):82.

Guideline for the prevention of falls in older persons. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. J Am Geriatr Soc. 2001 May;49(5):664-72.

Ettinger B, Ray GT, Pressman AR, Gluck O. Limb fractures in elderly men as indicators of subsequent fracture risk. Arch Intern Med. 2003 Dec 8-22;163(22):2741-7.

Christopher J. Wahl, M.D.

Assistant Professor
University of Washington Medical Center
Sports Medicine
www.orthop.washington.edu/faculty/wahl

Jason J. Wilcox, M.D., Michael Hwang, M.D.,
Patrick Cunningham, B.S.,
and Suzanne L. Slaney, P.A.-C, M.S., A.T.C.

Arthroscopic Reconstruction of Engaging Humeral Hill-Sachs Defects Using Cannulated Ostoeoconductive Grafts

- Shoulder instability and shoulder dislocations are among the most commonly occurring and disabling of sports injuries.
- In the majority of cases, traumatic dislocations result not only in a disruption of the stabilizing glenohumeral ligaments, but also an impression/compression defect on the humeral head (termed a *Hill-Sachs defect*).
- When large enough, these volumetric bony defects will cause re-dislocation of the shoulder even after anatomic repair of the ligaments; these are termed *engaging Hill-Sachs defects*.
- Because the region of the defect is hard to access with traditional surgical approaches, previous treatment strategies have centered on open non-anatomical surgical procedures (Latarjet, Eben-Hybinette, etc) that alter the normal shoulder anatomy to try and prevent re-dislocation - these non-anatomic procedures can be complicated by shoulder stiffness and pain.
- Working in the University of Washington Arthroscopy, Research and Training Laboratory (ART-lab), the authors were able to develop a minimally invasive, arthroscopic technique that restores the circumferential surface area of the humeral head by grafting the volumetric bone loss with synthetic bio-conductive plugs.
- We present the short-term clinical results of this novel technique, which appears to restore exceptional range of motion and a return to athletic participation with a minimally invasive, anatomic procedure.

It is generally accepted that most small Hill-Sachs defects and bony Bankart lesions will not significantly alter the results of Bankart reconstruction. However, it has been shown that larger bone defects may result in "engaging" Hill-Sachs defects, which have been associated with a poor result following arthroscopic reconstruction (Figure 1). Some surgeons will attempt to over tension the anterior glenohumeral ligaments to restrict motion to avoid engagement, bone loss can lead to significant motion deficits and such stiffness may predispose to degenerative arthropathy over the long term.

Numerous procedures have been designed to increase the surface area for bony constraint of the glenohumeral joint. These reconstructions are usually performed at the anterior glenoid and include the Eden-Hybinette, Bristow, and Latarjet procedures, among others. Miniaci, Gerber, Kropf and others have described open posterior and anterior approaches to reconstruct bony defects with allografts, and recently Chapovsky described the arthroscopic placement of osteochondral allograft plugs to reconstruct such a defect. Kazel described a percutaneous approach to perform retrograde disimpaction of these defects in a cadaveric model, while Re described a similar retrograde technique using a deltopectoral approach. A minimally invasive arthroscopic approach to repair large Hill-Sachs defects would be ideal, but the visualization and arthroscopic access to these defects can be difficult.

Biologic osteoconductive graft plugs (TruFit BGS Plug, Osteobiologics, Inc. Smith+Nephew, Andover, MA), have been approved and widely for the reconstruction of traumatic bone defects and to 'backfill' cartilage defects after osteoarticular transplant harvests in the knee.

We described a technique that allows excellent visualization and access to the large Hill-Sachs defect that allows placement of pre-cannulated biphasic

Patient	Age-Sex	Dominance /Inj Side	Revision?	Mechanism	Glenoid Loss	Humeral Arc Deficit (mm)	AP Glenoid Width (mm)	HAD/APGW
1	40-M	R/R	N	Diving	N	20.5	25.0	0.82
2	22-M	R/R	N	Football	Y	23.7	25.9	0.91
3	22-M	R/R	N	Wakeboard	N	19.3	27.1	0.71
4	21-M	L/L	N	Skateboard	N	15.0	21.8	0.69
5	17-F	R/R	Y	Basketball	Y	22.1	25.9	0.85
6	22-M	R/L	Y	Basketball	Y	18.1	20.0	0.91
7	38-M	R/R	Y	Waterskiing	Y	16.5	19.4	0.85
8	16-F	R/R	N	Motocross	N	15.6	21.3	0.73
9	25-M	R/R	N	Skydiving	N	14.7	23.2	0.63
10	39-M	R/R	N	MVC	N	18.3	24.1	0.76
Totals/Avg	26.2	89%	33%		40%	18.4	23.8	0.79

Table 1: Demographic and pre-operative imaging data on 10 patients who underwent arthroscopic placement of grafts. (HAD, Humeral Articular Arc Deficit-the largest arc of lost surface area ; APGW, Antero-Posterior Glenoid Width-the width of the glenoid socket; HAD/APGW, a circumference ratio-ratios higher than .85 are shoulders in which dislocation is extremely likely without repair of the bone defect).

bone graft substitute plugs into large defects via an all-arthroscopic technique (Figure 2A, 2B). We have performed this technique on ten patients thus far, three of whom presented with recurrent instability after previously failed open and arthroscopic Bankart repairs.

Patients and Methods

From April 2007 to January 2009 ten patients presented to our institution with primary or recurrent instability in the setting of large or massive volumetric bone loss of the postero-superior humeral head (Hill-Sachs lesion). Date on the initial traumatic dislocation, previous surgical procedures and recurrences, and demographic and injury data were available for all patients (Table 1).

Digital MR arthrograms were available for every patient. CT scans were performed in patients who presented to our institution without MRI in whom plain shoulder radiographs demonstrated Hill-Sachs
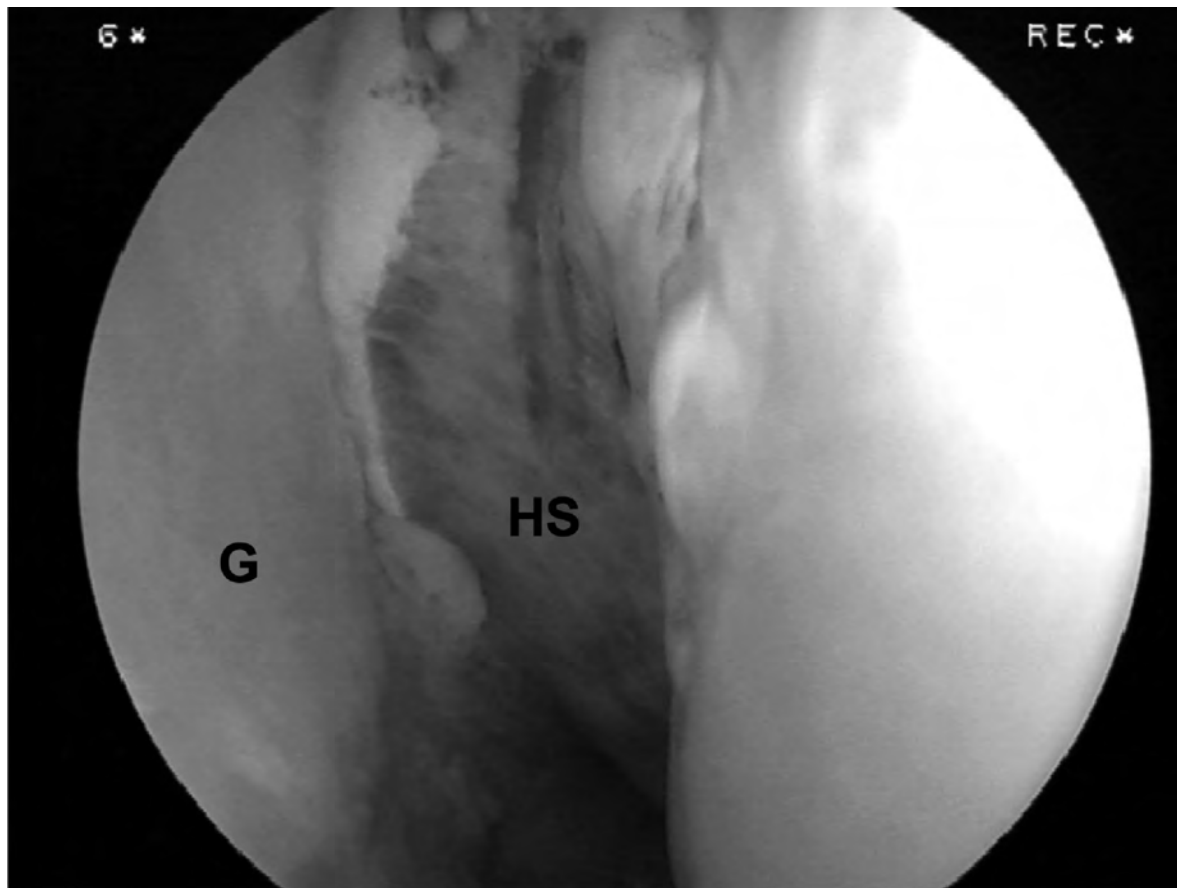

Figure 1: Arthroscopic view of an engaging Hill-Sachs defect from the posterior viewing portal. With external rotation, the Hill-Sachs defect is observed to engage the antero-inferior glenoid rim. (G) Glenoid. (HS) Hill-Sachs defect.
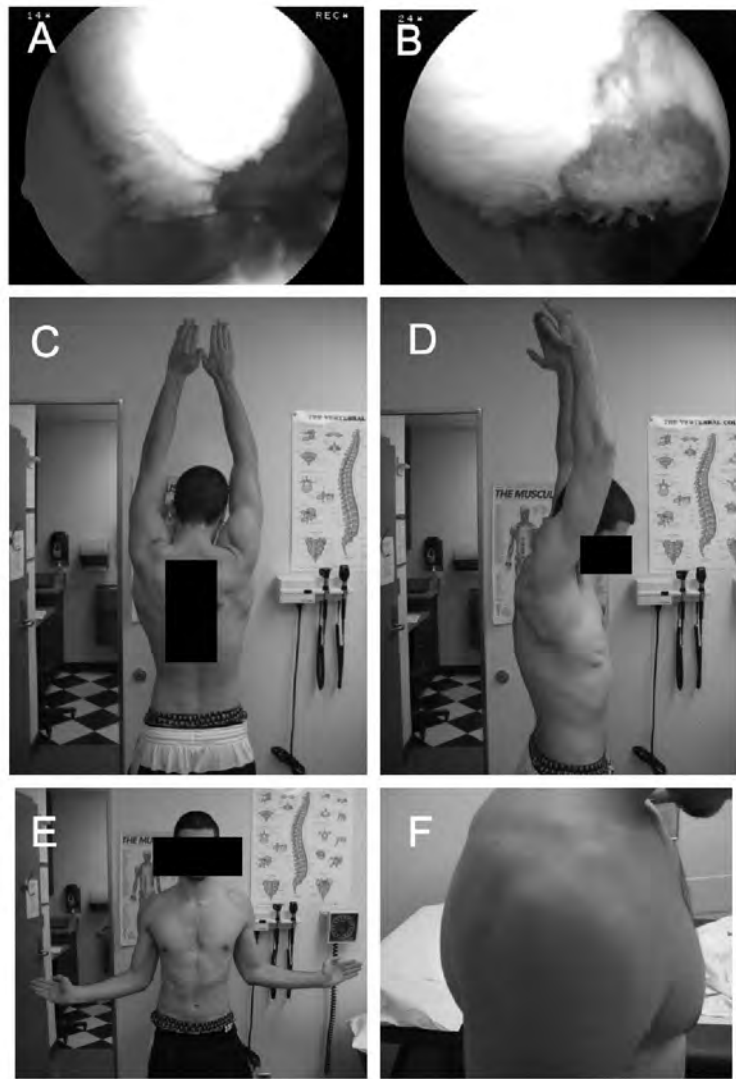
Figure 2: 17-year old male with recurrent right shoulder instability after a failed arthroscopic Bankart repair. A. View of the posterior humeral head from the Neviaser portal. A volumetric Hill-Sachs defect is apparent. B. View of the posterior humeral head after grafting with two cannulated synthetic grafts. C-E. Abduction, forward elevation, and external rotation evaluated 6-months following revision Bankart with arthroscopic placement of grafts. F. Shoulder incisions used for revision reconstruction.

or bony Bankart lesions. Using the electronic media, the size of the defects was measured. Previous cadaveric studies have defined criteria in which a defect is likely to lead to recurrent instability.

All patients underwent a diagnostic arthroscopy, arthroscopic grafting of the Hill-Sachs defect and arthroscopic ligament repair. Clinical results were graded based on range of motion, return to work, and return to athletics as 'excellent', 'good', 'fair', or 'poor'.

Results

The average age at the time of surgery was 26.2 years. The injury involved the dominant hand in 9 of 10 patients. Three of 10 patients (33%) presented after having failed one or more previous stabilization procedures.

On physical examination, clinical signs of instability were uniformly present with positive findings on apprehension, relocation, and surprise tests (all tests positive in all patients). Two patients had clinical evidence ligamentous laxity without multidirectional instability.

Deficits of the anterior glenoid rim were apparent on 4 of 10 patients (40%), three of whom were revision cases. All patients with anterior glenoid bone deficits had significantly reduced contact between the glenoid

and humeral surfaces.

The average length of follow-up after surgery in this group is 12.3 months (range, 4-24 mo.) All patients have regained a functional range of motion and 9 of 10 returned to their pre-operative sporting activities. Based on our clinical grading criteria, 8 patients have excellent results, 1 patient has a good result, and one patient re-dislocated while skydiving 6-months after the surgical procedure.

Discussion

Numerous clinical studies of failures after arthroscopic Bankart repair have implicated the presence of engaging bone defects as a potential contributing factor.

Many approaches to addressing engaging bony deficits have been described. The most commonly performed procedures include open, non-anatomic coracoid transfers (Bristow, Latarjet), glenoid autologous or allograft bone grafting procedures (Eden-Hybinette). These non-anatomic approaches do not directly address the Hill-Sachs defect, but rather increase the glenoid articulating surface area and/or potentially alter the normal mechanics of the subscapularis muscle to stabilize the shoulder. Although an arthroscopic Latarjet has been described, most surgeons perform an open approach, which is more invasive and has been associated with permanent weakness of the subscapularis, stiffness, or premature arthrosis.

In our initial treatment of 10 patients, 100% of persons who have been followed more than 6 months were able to return to athletic participation, including contact sports. Thus far, 90% of these patients have stable shoulders and a normal range of motion. It should be noted that the failure rates associated with arthroscopic ligament repair of shoulders without defects is approximately 85-92%.

Conclusion

We believe that an anatomic solution to the anatomic problem of shoulder instability may be the best alternative in terms of preserving a functional range of motion, preserving shoulder joint stability, and avoiding morbidity and the risks of shoulder arthritis. Further follow-up on this patient group will indicate whether

this minimally invasive procedure is superior to current open non-anatomic techniques. In the UW ART-lab, we continue to challenge the status quo in care of athletic injuries in an effort to find less-invasive techniques that will restore normal function with rapid rehabilitation.

Recommended Reading

Boileau P, Villalba M, Hery J, Balg F, Ahrens P, Neyton L. Risk factors for recurrence of shoulder inatability after arthroscopic Bankart repair. J Bone Joint Surg Am. 2006 2006;88:1755-1763.

Burkhart SS, De Beer JF. Traumatic glenohumeral bone defects and their relationship to failure of arthroscopic Bankart repairs: significance of the inverted-pear glenoid and the humeral engaging Hill-Sachs lesion. Arthroscopy. Oct 2000;16(7):677-694.

Itoi E, Lee SB, Berglund LJ, Berge LL, An KN. The effect of a glenoid defect on anteroinferior stability of the shoulder after Bankart repair: a cadaveric study. J Bone Joint Surg Am. Jan 2000;82(1):35-46.

Wahl CJ, Seifert EE, Ellis ED, Matt S, Matsen FAI. The latent failure: an analysis of capsulorraphy arthropathy in patients presenting after failed shoulder stabilizations. Paper presented at: Annual Meeting of the American Orthopaedic Society for Sports Medicine, 2006; Hershey, Pennsylvania.

Yamamoto N, Itoi E, Abe H, et al. Contact between the glenoid and the humeral head in abduction, external rotation, and horizontal extension: a new concept of glenoid track. J Shoulder Elbow Surg. Sep-Oct 2007;16(5):649-656.

Winston J. Warme, M.D.

Associate Professor
University of Washington Medical Center
Shoulder and Elbow
www.orthop.washington.edu/faculty/warme

Peter T. Scheffel, M.D., Jeremiah M. Clinton, M.D.,
Joseph R. Lynch, M.D.,
and Frederick A. Matsen III, M.D.

Glenohumeral Chondrolysis After Shoulder Arthroscopy

- Chondrolysis of the shoulder, (rapid dissolution of the articular cartilage), is being diagnosed with increased frequency since the advent of shoulder arthroscopy.
- No definitive etiology has been identified, although strong associations have been made with the use of thermal devices and with the administration of intra-articular anesthetics.
- Management of glenohumeral chondrolysis is problematic as many of the patients are very young for treatment with conventional total shoulder arthroplasty.
- We have analyzed the existing literature along with a series of new cases in search of factors that may contribute to the development of chondrolysis.

Chondrolysis is a reported complication of shoulder arthroscopy. Up through 2008, a total of 51 patients, (55 shoulders), had been reported. Given the thousands of shoulder arthroscopies that are conducted on an annual basis, this number seems minute. It is likely that there are more cases that have escaped detection or were not reported. As such the incidence is not known.

To date, the development of chondrolysis has been associated with the use of Gentian violet dye to detect cuff tears, thermal treatment within the joint and intra-articular anesthetics. Other possible associations include bioabsorbable implants and absorbable suture as well as possibly infection, osteoarthritis and trauma.

No prospective analysis or randomized clinical trial has been done in humans, so the study of anecdotal cases along with bench and animal research efforts is the best information available. To study the problem, we obtained sixty-one patient records (67 shoulders) from other institutions of patients who developed post-arthroscopic glenohumeral chondrolysis, (PAGCL), and reviewed them in a systematic fashion along with the existing cases in the literature noted above. This allowed us to study all the available cases and more than double the information previously available. Ultimately we had data on 113 patients (122 shoulders) (Table 1).

A total of 122 shoulders in 113 patients with post-surgical glenohumeral chondrolysis were analyzed. The average patient age was 33 and 31 at the time of surgery for the case series and literature review respectfully (Range 14-64). The most common indications for surgery were instability and SLAP lesions. Pain pumps were utilized in 93 shoulders, 67 in case series and 26 in the literature review. Lidocaine (2%) was used in 14 patients in the case series, and bupivacaine (0.25-0.5%) in 31 patients in the case series and 17 patients in the literature review, with and without epinephrine. Radiofrequency capsulorrhaphy was performed in 24 shoulders with all patients in the case series having the addition of a pain pump.

Chondrolysis manifested clinically as progressive, severe and refractory pain and loss of motion. Radiographic documentation of chondrolysis was established at an average of 506 days (Range 42-1823) after the arthroscopic procedure, (Figure 1A & B). X-ray and MRI changes were consistent: joint space narrowing (97 patients), subchondral cysts of the glenoid (45 patients) and humeral head (45 patients), and minimal or no osteophytosis (10 patients and 23 patients).

Conclusion

Glenohumeral chondrolysis can be associated with the combination of arthroscopic surgery and post-arthroscopy infusion of local anesthetic. In contrast to previous reports, the arthroscopic operations associated with chondrolysis in this series were not limited to stabilization procedures and the infused anesthetic was not limited to bupivacaine.

It is of note that the 67 patients presented here were located based on their presentation of chondrolysis following the use of pain pumps. This did not allow for meaningful statistical

	Case Series	Literature Review
Number of shoulders	67	55
Number of patients	62	51
Number of males*	37	12
Number of females*	25	18
Mean Age in Years (SD, range)	33 (11, 15-57)	31 (14, 14-64)
Arthroscopic surgery	67	51
Open surgery	3 (arthroscopic converted to open)	4
Instability procedures	47	51
Bankart repairs for instability	17	23
Capsular plication for instability	30	28
SLAP repairs	27	6
Rotator cuff repairs	9	4 (open)
Rotator cuff debridements	2	4
Capsular releases	1	3
Cases using suture anchors	42	24
Cases using radiofrequency	28	24
RF Capsulorrhaphies	6	18
RF Only for releases or debridements	11	6
RF used in subacromial space only	11	0
Cases involving Thermal capsulorrhaphy and Pain Pumps	6	18
Cases involving radiofrequency and Pain Pumps	28	24
Laser Capsulorrhaphies	0	3
Cases using intraarticular dye	0	4
Cases with intraarticular pain pump	67	26
Cases with bupivacaine in infusate (concentration range)	31 (0.25-0.5%)	17 (0.25-0.5%)
Cases with lidocaine in infusate (concentration range)	14 (2%)	0
Cases with epinephrine in infusate (concentration range)	37 (1:100K-1:200K)	13 (unknown)
Flow rate range in cases where it was specified	2-5 ml/hr	4-4.16 ml/hr

Table 1: Summary of clinical findings. Data represent the number of shoulders with the finding. * 21 patients in the literature review did not have gender identified.

analysis or comparison to previously reported studies. Additionally, we are unable to ascertain the population at risk and therefore were unable to calculate the true incidence and prevalence of chondrolysis in this population. In spite of these limitations, this study demonstrated that chondrolysis can occur in patients in a broad age range, with many routine arthroscopic procedures, using bupivacaine or lidocaine with and without epinephrine. Moreover, there is often a substantial delay between the arthroscopic procedure and the diagnosis of chondrolysis.

The pathology of chondrolysis is characteristic and remarkable in terms of the involvement of essentially all of the joint's articular cartilage, (Figure 2A & B). Once the process begins, there is no evidence that it can be arrested. Arthroscopic surgeons may wish to consider avoiding factors associated

Figure 1A & B: Characteristic radiograph of pre-operative normal apparent joint space, (a) and 18 months after arthroscopic surgery with a post-operative intra-articular pain pump (b).

with chondrolysis, such as the post-operative infusion of local anesthetics and thermal energy, if these factors are not essential to the success of the procedure.

Future Developments in Optimizing Patient Care

In that we are seeing an increasing number of individuals with post-arthroscopic chondrolysis, we are striving to optimize the treatment of each of them. Some patients with early chondrolysis may be effectively managed with an arthroscopic approach of debridement and capsular release. More advanced cases may require a humeral hemiarthroplasty with non-prosthetic glenoid arthroplasty (the

"Ream and Run" procedure) (www.orthop.washington.edu/reamandrun).

Recommended Reading

Chu CR, Izzo NJ, Papas NE, Fu FH. In vitro exposure to 0.5% bupivacaine is cytotoxic to bovine articular chondrocytes. Arthroscopy. 2006;22(7):693-699.

Dragoo JL, Korotkova T, Kanwar R, Wood B. The effect of local anesthetics administered via pain pump on chondrocyte viability. Am J Sports Med. 2008;36(8):1484-1488.

Gomoll AH, Kang RW, Williams JM, Bach BR, Cole BJ. Chondrolysis after continuous intra-articular bupivicaine

infusion: an experimental model investigating chondrotoxicity in the rabbit shoulder. J Arthroscopic Rel Surg. 2006;22:813-819.

Karpie JC, Chu CR. Lidocaine exhibits dose- and time-dependent cytotoxic effects on bovine articular chondrocytes in vitro. Am J Sports Med. 2007;35(10):1621-1627.

Levy JC, Virani NA, Frankle MA, Cuff D, Pupello DR, Hamelin JA. Young patients with shoulder chondrolysis following arthroscopic shoulder surgery treated with total should arthroplasty. J Shoulder Elbow Surg. 2008;17(3):380-388.
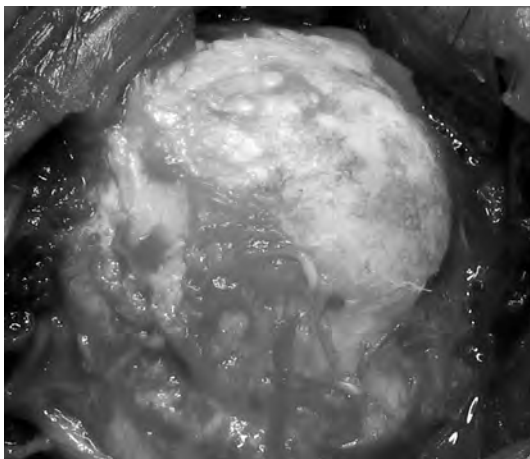

Figure 2A & B: Routine findings at arthroplasty surgery with complete loss of the (a) humeral head and (b) glenoid articular cartilage without proliferative osteophytes. Bone cysts were commonly seen.

Frederick A. Matsen III, M.D.

Professor and Chairman
University of Washington Medical Center
Shoulder and Elbow
www.orthop.washington.edu/faculty/matsen

Matthew Saltzman, M.D., Deana Mercer, M.D.,
Alexander L. Bertelsen, P.A.-C,
and Winston J. Warme, M.D.

Characteristics of 1030 Patients Having Primary Shoulder Arthroplasty, Contrasting Those Under and Over 50 Years of Age

- Shoulder arthritis is a disabling condition in which the normally smooth cartilage surfaces of the ball and socket of the shoulder are lost because of injury, degeneration, inflammation, or surgical misadventure.
- Modern shoulder replacement surgery was introduced by Dr. Charles S. Neer II in the 1950s and has been performed by the Shoulder and Elbow Team at the University of Washington since 1975.
- Shoulder joint replacement surgery is most commonly used in individuals over the age of 50 years to treat primary glenohumeral arthritis. The outcomes in this patient group are generally excellent.
- The reported outcomes of shoulder arthroplasty in individuals under 50 years of age have been reported to be worse than those in individuals over 50 years of age.
- We found that patients under 50 years of age presenting for shoulder arthroplasty are more likely to have complex pathologies and less likely to have primary shoulder arthritis than their older counterparts.

Shoulder arthroplasty is most commonly used in individuals over the age of 50 years to treat primary glenohumeral arthritis. The outcomes are generally good from the perspective of the patient and the surgeon. Shoulder arthroplasty is also frequently used to manage destruction of the glenohumeral joint from a variety of causes in younger individuals. The reported outcomes of shoulder arthroplasty in younger individuals are inferior to those for their older counterparts. Sperling et al reviewed seventy-eight Neer hemiarthroplasties and thirty-six Neer total shoulder arthroplasties performed in patients aged 50 years or younger. The results using the Neer rating system were not good. Among the hemiarthroplasties, there were 6 excellent, 19 satisfactory, and 37 unsatisfactory results. Among total shoulder arthroplasties, there were 6 excellent, 9 satisfactory, and 14 unsatisfactory results. As a result the

authors concluded, "Great care must be exercised, and alternative methods of treatment considered, before either hemiarthroplasty or total shoulder arthroplasty is offered to patients aged 50 years or younger."

In that surgeons will continue to be consulted by patients under 50 with glenohumeral arthritis, it is important to identify factors that may contribute to these suboptimal outcomes. These factors could include the possibilities that, in comparison to their older counterparts, the younger patients had (1) relatively greater impairment of their shoulder function before their surgery, (2) a different gender mix leading to different perceptions of outcome, (3) different diagnoses, including more complex pathology, (4) increased demands and activity that increase the risk of loosening and wear, (5) increased expectations, making them at greater risk for dissatisfaction, and (6) increased longevity enabling

more problems to appear over time. Identification of such factors would enable the surgeon to have a more informed preoperative discussion with the young patient considering arthroplasty. In this study, we were able to explore the first three of these factors. One thousand and thirty patients with glenohumeral arthritis having a shoulder arthroplasty at the University of Washington comprised this case series. For each decade of age the prevalence of twelve different diagnoses, the gender distribution, and the self-assessed shoulder comfort and function were characterized prior to primary shoulder arthroplasty.

Results

Sixteen percent of the patients were under 50 and 84% over 50 years of age (Table 1).

Hypothesis 1: the gender distribution for patients less than fifty years of age had a higher percent of

	females < 50	males <50	females > 50	males > 50	Total
Capsulorrhapy Arthropathy	19	39	8	40	106
Degenerative Joint Disease	5	31	168	399	603
Post traumatic arthritis	9	16	29	18	72
Avascular Necrosis	7	11	13	4	35
Rheumatoid arthritis	13	5	43	8	69
Other Inflammatory Arthritis	8	2	13	6	29
Cuff Tear Arthropathy	0	1	52	44	97
Post Infection Arthritis	1	1	2	3	7
Glenoid Dysplasia	0	1	2	3	6
Instability Arthritis	2	0	2	0	4
Charcot Arthropathy	1	0	0	0	1
Giant Cell Tumor	0	0	0	1	1
Total	65	107	332	526	1030

Table 1: Age and Gender Distribution for the Seven Most Common Diagnoses.

Decade	Female	Male	p value
3	2.0 +/- 3.1	3.9 +/- 2.2	2.87E-01
4	2.3 +/- 1.9	3.4 +/- 2.5	1.25E-01
5	2.1 +/- 2.3	4.3 +/- 2.7	4.13E-06
6	2.7 +/- 2.5	4.1 +/- 2.8	5.12E-04
7	1.9 +/- 2.0	3.9 +/- 2.8	1.54E-12
8	2.1 +/- 2.2	3.7 +/- 2.8	3.17E-07
9	1.7 +/- 2.1	3.1 +/- 2.5	1.17E-02
10	0.8 +/- 0.5		

Table 2: Total SST Score by Decade and Gender.

Diagnoses for Patients under 50 yrs

- CA 35%
- AVN 11%
- PTA 15%
- Other Infl 6%
- RA 11%
- DJD 22%
- CTA 1%

Diagnoses for Patients over 50 years

- CA 6%
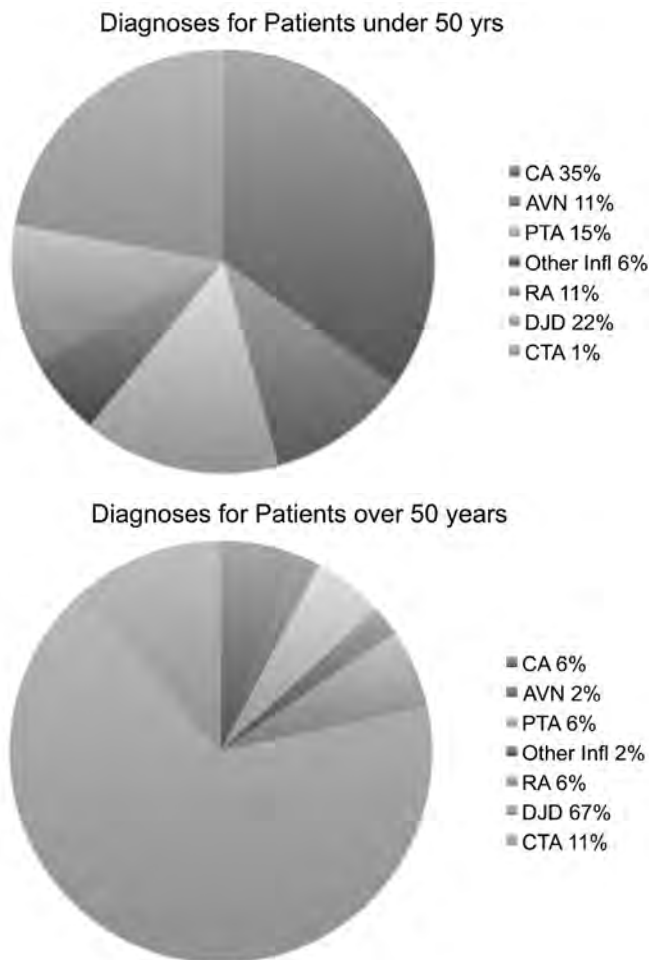- AVN 2%
- PTA 6%
- Other Infl 2%
- RA 6%
- DJD 67%
- CTA 11%

Figure 1 (top) and Figure 2 (bottom): Diagnoses for patients under and over 50 years. CA = capsulorrhaphy arthritis, AVN = avascular necrosis, PTA = post-traumatic arthritis, Other Infl = Other Inflammatory arthritis, RA = rheumatoid arthritis, DJD = degenerative joint disease, CTA = cuff tear arthropathy.

females. Thirty-six percent of the patients under 50 were female and 39% of the patients over the age of 50 were female. The hypothesis was rejected.

Hypothesis 2: the pre-arthroplasty self-assessed comfort and function was worse for the patients under fifty years of age. The average Shoulder Test scores were not lower for the younger patients: 3.37 +/- 2.66 for the patients under 50 and 3.15 +/- 2.71 for the patients over 50 years of age (Table 2). The hypothesis was rejected.

Hypothesis 3: the distribution of diagnoses is different for patients under fifty years of age, with a higher prevalence of diagnoses more complex than straightforward primary degenerative joint disease. The distribution of patients among these diagnoses was different for patients under 50 from that for patients over 50, with the former having a 78% prevalence of diagnoses other than primary degenerative joint disease in comparison to 33% for the latter. (Figures 1 and 2). The chi square test revealed a p value of < .00000001 for this difference. The hypothesis was accepted.

Clinical Relevance

In discussing shoulder arthroplasty with younger patients, surgeons should explain that more complex pathology, such as capsulorrhaphy arthropathy (Figure 3), rheumatoid arthritis, and post traumatic arthritis, may complicate the surgical procedure and compromise the effectiveness of the procedure in comparison to the situation with primary degenerative joint disease which is more commonly seen in older individuals.

Recommended Reading

Barrett WP, Franklin JL, Jackins SE, Wyss CR, Matsen FA, 3rd: Total shoulder arthroplasty. J Bone Joint Surg Am 1987:69:865-872.

Boorman RS, Kopjar B, Fehringer E, Churchill RS, Smith K, Matsen FA, 3rd: The effect of total shoulder arthroplasty on self-assessed health status is comparable to that of total hip arthroplasty and coronary artery bypass grafting. J Shoulder Elbow Surg 2003:12:158-163.
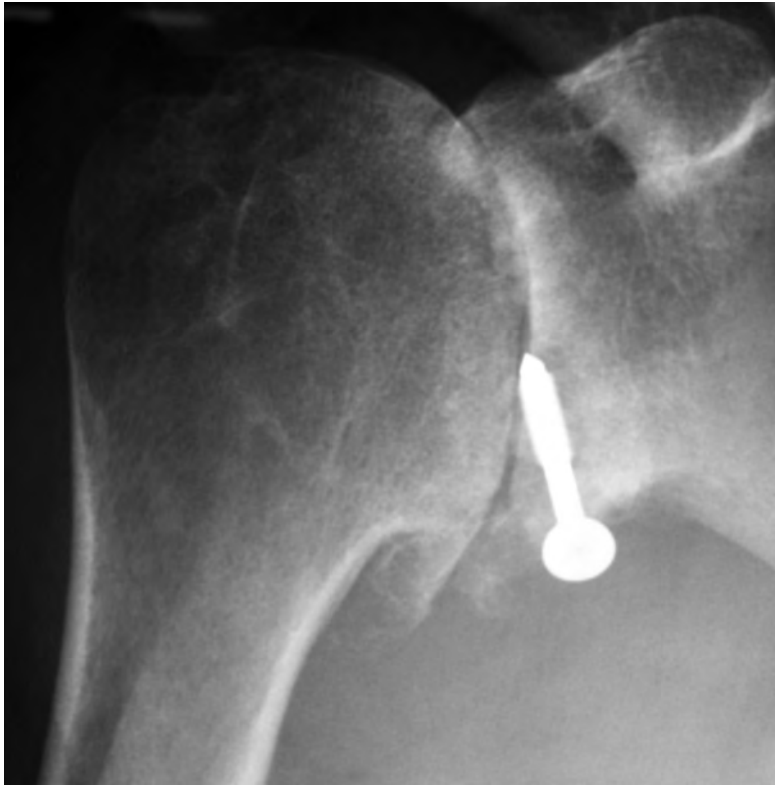
Figure 3: An example of capsulorrhaphy arthropathy.

Cofield RH: Total shoulder arthroplasty with the Neer prosthesis. J Bone Joint Surg Am 1984:66:899-906.

Fehringer EV, Kopjar B, Boorman RS, Churchill RS, Smith KL, Matsen FA, 3rd: Characterizing the functional improvement after total shoulder arthroplasty for osteoarthritis. J Bone Joint Surg Am 2002:84-A:1349-1353.

Matsen FA, 3rd: Early effectiveness of shoulder arthroplasty for patients who have primary glenohumeral degenerative joint disease. J Bone Joint Surg Am 1996:78:260-264.

Matsen FA, 3rd, Antoniou J, Rozencwaig R, Campbell B, Smith KL: Correlates with comfort and function after total shoulder arthroplasty for degenerative joint disease. J Shoulder Elbow Surg 2000:9:465-469.

Neer CS, 2nd, Watson KC, Stanton FJ: Recent experience in total shoulder replacement. J Bone Joint Surg Am 1982:64:319-337.

Parsons IMt, Buoncristiani AM, Donion S, Campbell B, Smith KL, Matsen FA, 3rd: The effect of total shoulder arthroplasty on self-assessed deficits in shoulder function in patients with capsulorrhaphy arthropathy. J Shoulder Elbow Surg 2007:16:S19-26.

Wirth MA, Lim MS, Southworth C, Loredo R, Kaar TK, Rockwood CA, Jr.: Compaction bone-grafting in prosthetic shoulder arthroplasty. J Bone Joint Surg Am 2007:89:49-57.

Wirth MA, Tapscott RS, Southworth C, Rockwood CA, Jr.: Treatment of glenohumeral arthritis with a hemiarthroplasty: a minimum five-year follow-up outcome study. J Bone Joint Surg Am 2006:88:964-973.

Sperling JW, Cofield RH, Rowland CM: Neer hemiarthroplasty and Neer total shoulder arthroplasty in patients fifty years old or less. Long-term results. J Bone Joint Surg Am 1998:80:464-473.

Peter R. Cavanagh, Ph.D.

Professor
University of Washington Medical Center
Research
www.orthop.washington.edu/faculty/cavanagh

Andy Dong-Gil Lee, Ph.D., John R. Green III, M.D.,
Roger V. Larson, M.D., Paul A. Manner, M.D.,
John W. O'Kane, M.D., Gregory A. Schmale, M.D.,
Carol C. Teitz, M.D., and Christopher J. Wahl, M.D.

Understanding Knee Injuries in Women Athletes: Can Robotics Help?

- Knee injuries in women collegiate athletes have been consistently reported to be at least twice greater than those of men in comparable sports.
- Many of these injuries occur in situations where there is no contact with an opposing player.
- Among the most frequent injury is damage to the anterior cruciate ligament (ACL).
- A broad range of modifiable and non-modifiable factors have been implicated in the disparity in ACL injuries.
- Anatomical factors such as notch width, tibial plateau slope and size, as well as functional factors such as excessive or mistimed internal rotation and adduction have been proposed as among the potential causative factors although much uncertainty remains.
- Computer modeling can be used to simulate the effects of different structures and movements on the length of the ACL.
- Direct measurement of ligament length is possible during mechanical testing in anatomical specimens.
- Traditional mechanical testing loads a ligament along a single axis sometimes including torsion.
- Linear robots, such as those used on automobile production lines, and the more unusual parallel robots, allow accurate positioning and carefully controlled loads to be generated.
- In an orthopaedic context, robotic methods allow the accurate simulations of multi-axis functional joint movements thereby loading a ligament such as the ACL in a more realistic manner.
- New approaches to surgical reconstruction of the ACL can also be simulated using robots.
- A Musculoskeletal Robotics Laboratory is under construction at the University of Washington Medical Center.
- The UW Orthopaedics Knee Biomechanics group is a multi-disciplinary team of faculty members that is using robotics and simulation to provide insight into knee injuries and their surgical reconstruction in women.

The higher burden of knee injuries in women collegiate athletes compared to their male counterparts has been demonstrated by injury surveys conducted by the National Collegiate Athletic Association (NCAA) over the last 15 years. The comparison is possible in sports where rules and equipment are similar such as volleyball, soccer, and basketball but not where these factors vary between sexes in sports such as lacrosse (where there is no contact and different protective equipment for women). Between 1989 and 2004, the relative injury rates for women compared to men, adjusted for exposure, remained fairly steady at approximately 2.6 times greater in collegiate soccer and 3.5 times greater in collegiate basketball. Injury analysis has indicated that many of these injuries occur in situations where there is no direct contact with an opposing player. Amongst the most common knee injuries to women athletes in these sports are injuries to the anterior cruciate ligament.
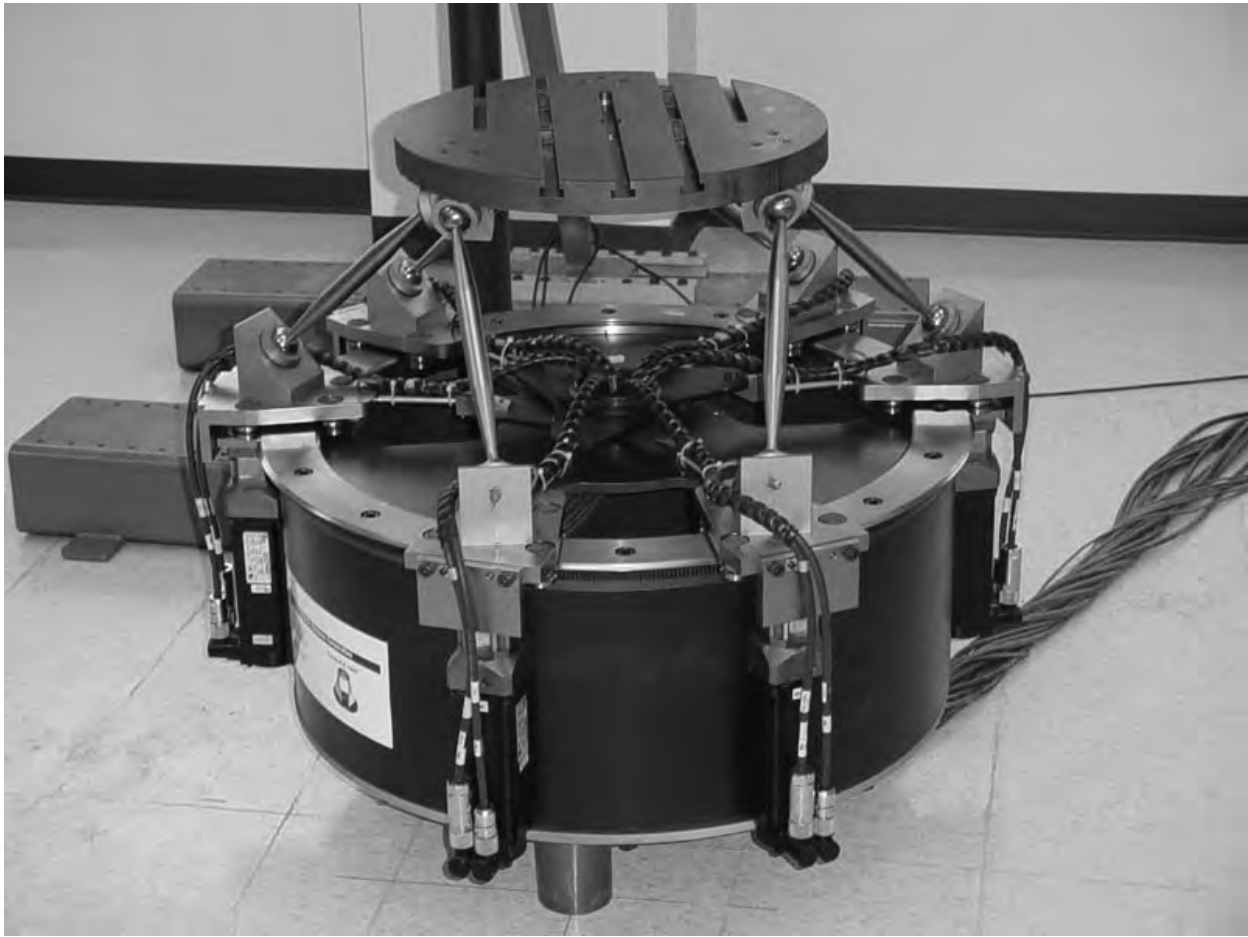
Figure 1: The R2000 Rotopod that is the basis for the Musculokeletal Robotics Laboratory in the Orthopaedics and Sports Medicine at the University of Washington.

The average ACL length is approximately 27mm and 30mm long in men and women respectively with a minimum cross-sectional area of approximately 73mm^2 and 57mm^2 (about the area of a 3/16" circle) in men and women respectively. The ligament is narrower in the midsection than at the tibial and femoral attachments. Length measurements are complicated by the fact that the ACL may consist of at least three distinct bundles of fibers and, even within the bundles, there are differences between fibers in the change in length with joint motion. The primary quantity of interest in anatomical studies of the ACL is the "strain" of the ligament as a function of joint position. Strain is an engineering term denoting the relative elongation of a structure compared to its initial length. This allows the response of ligaments of different lengths to be compared on the same basis. Typically, the strain in the ACL can approach 25% (and in one report 50%) before failure

is noted in the laboratory.

A broad range of modifiable and non-modifiable factors have been implicated in the disparity in ACL injuries. Potential causative factors are also often grouped into the following categories: environmental, anatomical, biomechanical, hormonal, neuromuscular, and familial. It is likely that a complex combination of many or all of the above factors contributes to the disparity and thus a deeper understanding of any one area will provide insight into this multifaceted problem. While the popular literature often seems to treat anatomical sex differences (such as pelvic width, Q angle, tibial slope, and knee valgus) as known determinates of injury, a close examination of the refereed literature shows more uncertainty as to their role. These and other anatomical factors are amenable to a number of research approaches including imaging, modeling, and mechanical testing.

Direct measurement of ACL length

as a function of applied force is possible during mechanical testing in anatomical specimens. This has traditionally been done in a machine that applies a tensile load or a combination of tensile and torsional loads. More recently, linear robots - such as those often seen on automobile production lines - have been employed to move the joint through functionally realistic patterns of motion while simultaneously applying realistic loads in three dimensions. To simulate muscle forces, electro-mechanical actuators are attached to tendons in the specimens using freeze clamps and this allows the application of realistic muscle forces. This means that the ACL length can be directly measured using small sensors while the joint is loaded in an injury-relevant manner. In addition, new surgical reconstruction techniques can be performed and their integrity can be tested and compared with existing approaches.

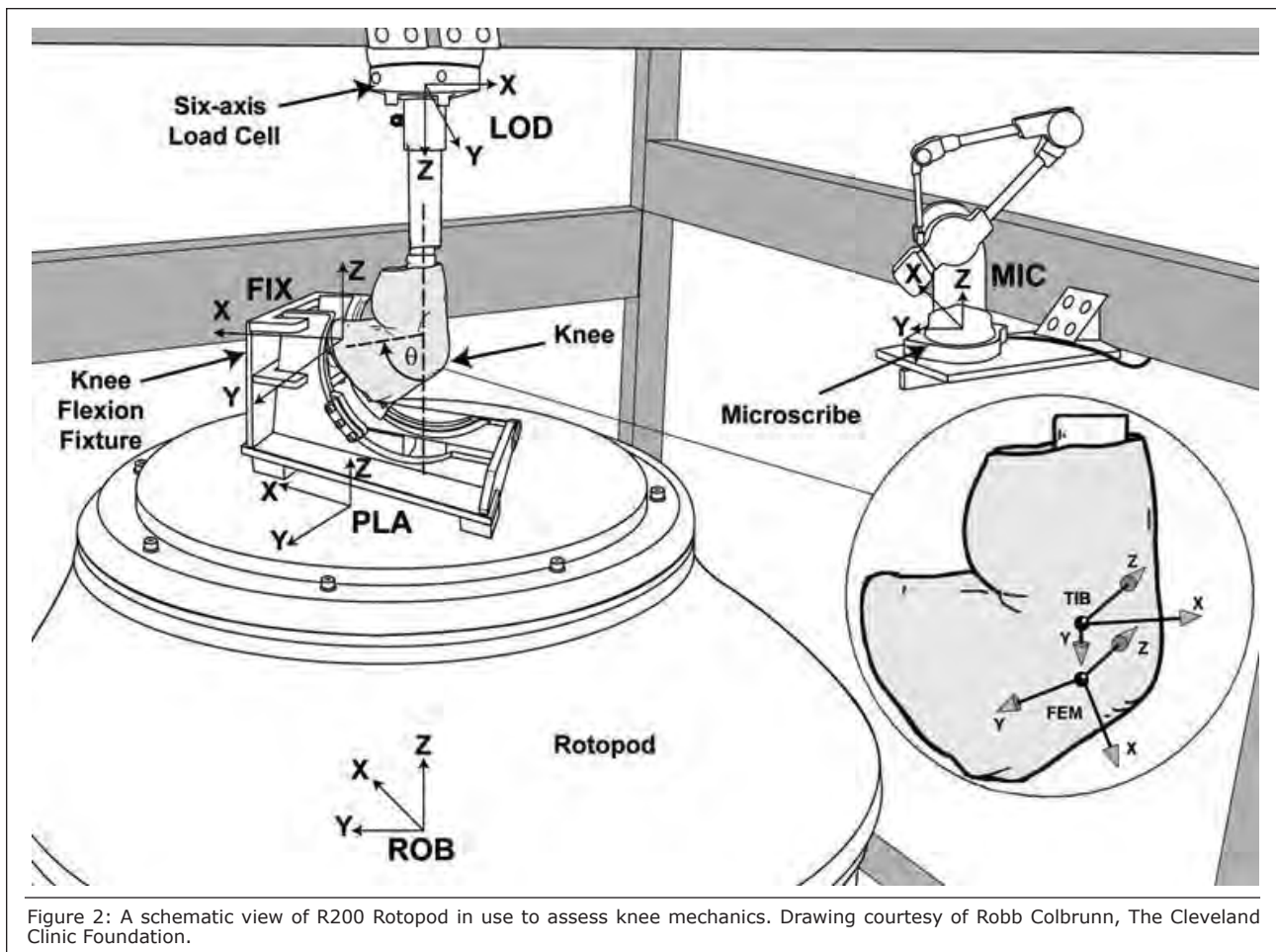A Musculoskeletal Robotics Laboratory is under construction at

Figure 2: A schematic view of R200 Rotopod in use to assess knee mechanics. Drawing courtesy of Robb Colbrunn, The Cleveland Clinic Foundation.

the University of Washington Medical Center and is scheduled for completion in Summer 2009. In this laboratory, we are installing an R2000 Rotopod parallel robot (see Figures 1 and 2) which allows much more accurate positioning of specimens than what can be achieved with conventional linear robots. The UW Department of Orthopaedics and Sports Medicine Knee Biomechanics group is a multi-disciplinary team of faculty members that is using robotics, 3-dimensional modeling, finite element analysis and simulation to provide insight into knee injuries in women and their surgical reconstruction. Our findings will be described in articles in future Research Reports.

Recommended Reading

Defranco MJ, Bach BR. A comprehensive review of partial anterior cruciate ligament tears. J Bone Joint Surg Am. 2009 Feb;91: 198-208.

Griffin,L.Y and the Hunt Valley Team. Understanding and Preventing Noncontact ACL Injuries Am J Sports Med. 2006; 34(9), 1512-1532.

Hashemi J, Chandrashekar N, Gill B, Beynnon BD, Slauterbeck JR, Schutt RC Jr, Mansouri H, Dabezies E. The geometry of the tibial plateau and its influence on the biomechanics of the tibiofemoral joint. J Bone Joint Surg Am. 2008 Dec;90(12):2724-34.

Hashemi J, Chandrashekar N, Mansouri H, Slauterbeck JR, Hardy DM. The human anterior cruciate ligament: sex differences in ultrastructure and correlation with biomechanical properties. J Orthop Res. 2008 Jul;26(7):945-50.

Mihata LC, Beutler AI, Boden BP. Comparing the incidence of anterior cruciate ligament injury in collegiate lacrosse, soccer, and basketball players: implications for anterior cruciate ligament mechanism and prevention. 2006. Jun;34(6):899-904

Quatman CE, Hewett TE. The anterior cruciate ligament injury controversy: is "valgus collapse" a sex-specific mechanism? Br J Sports Med. 2009 May;43(5):328-35.

Shultz SJ.J   ACL injury in the female athlete: a multifactorial problem that remains poorly understood. Athl Train. 2008 Sep-Oct;43(5):455.

Woo SL, Fisher MB.Evaluation of knee stability with use of a robotic system. J Bone Joint Surg Am. 2009 Feb;91 Suppl 1:78-84.

Van de Velde SK, Gill TJ, Li G. Evaluation of kinematics of anterior cruciate ligament-deficient knees with use of advanced imaging techniques, three-dimensional modeling techniques, and robotics. J Bone Joint Surg Am. 2009 Feb;91 Suppl 1:108-14.

Paul A. Manner, M.D.

Assistant Professor
University of Washington Medical Center
Hip and Knee
www.orthop.washington.edu/faculty/manner

Buddy D. Ratner, Ph.D.

A Cell-seeded Implant Scaffold for Articular Cartilage Resurfacing - Stimulating the Body's Regenerative Powers

- Osteoarthritis - the loss of the normal cartilage of a joint - is a painful, disabling disease affecting up to 40 million people in the US alone.
- When cartilage is lost, the current best treatment requires replacing the joint with artificial surfaces made of metal and plastic.
- We are investigating an approach to the regeneration of cartilage that would provide a biological treatment for osteoarthritis.
- We are exploring the concept that cartilage can be regenerated by embedding cartilage-generating cells in engineered structures that imitate the extracellular matrix of mature cartilage.
- We created a bilayer scaffold with two pore sizes: a bone side with pore sizes of about 35 micrometers and a cartilage side with pore sizes of about 80-100 micrometers.
- We tested this construct in a rabbit model of osteoarthritis.
- Preliminary results show excellent incorporation of the new construct.
- Bioengineered joint regeneration would represent a revolution in treatment of arthritis.

Background of clinical challenges in OA: Osteoarthritis (OA) is a painful, disabling disease of synovial joints characterized by the erosion of cartilage, osteophyte or bone spur formation, hardening of bone mass and bone cysts beneath the surface.

The magnitude of disability due to OA is high, both for individual patients as well as for society as a whole. In the US, an estimated 40 million suffer from OA. In 2003, arthritis and other rheumatic conditions cost the United States $127.8 billion ($80.8 billion in medical care expenditures and $47.0 billion in lost earnings). With overall aging of the population, the projected costs are expected to increase at a rate of 4-5% per year for the foreseeable future.

Current treatment modalities include medication and surgical intervention. Arthroscopic treatment is frequently employed; however, recent studies using sham procedures in matched patient groups have shown no benefit to many of these procedures. Other techniques, such as microfracture, autologous chondrocyte implantation, and mosaicplasty have shown disappointing results, with formation of fibrocartilage and scar, which are markedly inferior to true articular cartilage. The most common treatment disabling hip and knee arthritis at this time is total joint replacement, which is performed for at least 300,000 hip and 450,000 knee patients per year in the United States. Although highly successful in the vast majority of patients, this represents a substantial surgical intervention, with attendant risks. All of these metal and plastic implants are subject to loosening and wear, limiting their use and their life span.

The importance of bone-marrow cell components in repair of cartilage has been emphasized by various surgical techniques, such as microfracture and abrasion chondroplasty, which attempt to provide these cells to the area of cartilage loss. However, in the majority of cases utilizing these techniques, the repair tissue takes the form of fibrocartilage, which displays inferior mechanical properties and durability. A regenerative biological approach to resurfacing the arthritic joint holds promise as a living and durable solution for an arthritic joint.

Tissue engineering refers to the cross-disciplinary application of engineering and life sciences to study the function and structure of normal and abnormal tissues with the goal of developing functional tissue and cell substitutes. In the treatment of arthritis, the ideal tissue engineering approach would place cartilage-making cells from the stem cells in the patient's
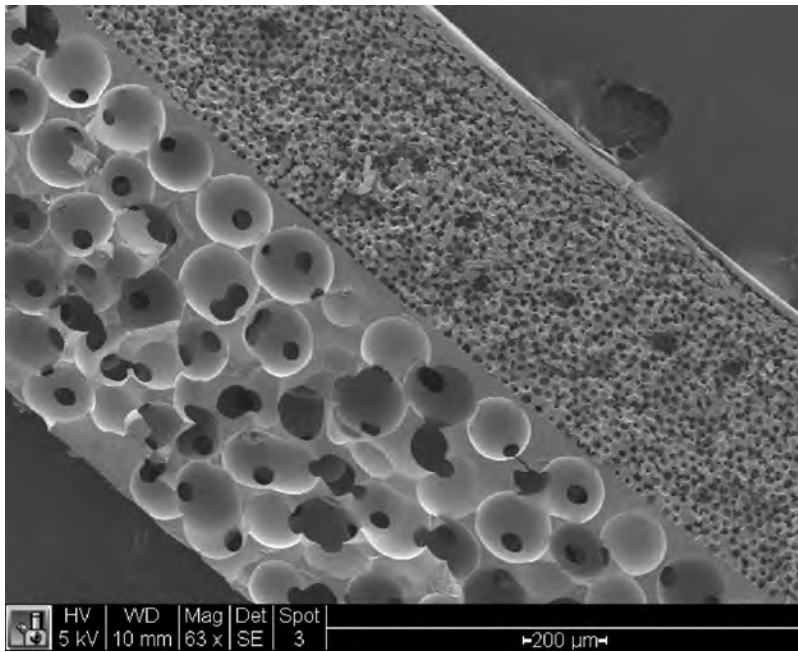
Figure 1: Bilayer polyHEMA sphere-templated scaffold. The upper layer consists of an average pore size of 35 microns; the lower layer, 80 microns. The upper layer is felt to be more advantageous for bone ingrowth, while the lower layer more closely approximates the pore size found in cartilage.

bone marrow in an appropriate matrix and allow them to produce articular cartilage.

Recent work by the University of Washington Engineered Biomaterials team has resulted in the synthesis of a novel biodegradable hydrogel, composed of a synthetic biodegradable polymer, poly(-caprolactone) (PCL) copolymerized with 2-hydroxyethyl methacrylate (HEMA). Structurally, the scaffold is porous, with a pore size which can be tightly controlled. This nanostructure scaffold represents a significant improvement in the formation of a synthetic extracellular matrix (Figure 1).

Current work is now directed at utilization of this tissue-engineered construct in vivo. Cartilage defects created in the rabbit knee form the initial model for placement of a tissue-engineered construct, comprised of rabbit mesenchymal stem cells cultured in a nanostructure scaffold. At 28 days and at 12 weeks, acellular nanostructure scaffolds placed in these defects remain in place, with no evidence of rejection or resorption by the host. Importantly, bone cells grow into the scaffold, fixing it to the underlying bony structure (Figure 2).

This is in contrast to defects where no scaffold has been placed, and only scar and fibrous tissue can form (Figure 3).

One of the challenges of tissue engineering is getting cells to enter the scaffold and survive. Here, rabbit stem cells have been grown for a week in culture conditions which encourage cartilage formation along the engineered scaffold. The cells have begun to enter the scaffold and make new cartilage (Figure 4).

Further studies will advance the use of the nanostructure scaffold/stem cell construct in the treatment of the osteoarthritic joint. The next studies will address implantation of cell-seeded constructs in the rabbit model, with subsequent use of a large-animal model such as a goat. In addition, the possible use of the scaffold for healing of bone defects will be explored.

Recommended Reading

Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. Clin Orthop Relat Res. 2004 Oct;(427 Suppl):S6-15.

Fukui N, Purple CR, Sandell . Cell biology and osteoarthritis: the chondrocyte's response to injury. Curr Rheumatol Rep. 2001 Dec;3(6):496-505.

Goldring SR, Goldring MB. The role of cytokines in cartilage matrix degeneration in osteoarthritis. Clin Orthop Relat Res. 2004 Oct;(427 Suppl):S27-36.

Borrelli J Jr., Ricci WM. Acute effects of cartilage impact. Clin Orthop Relat Res.
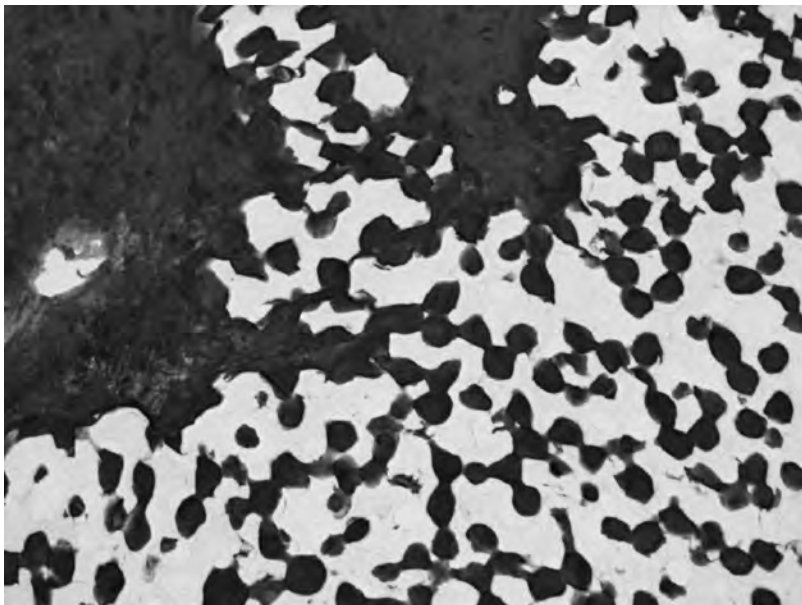
Figure 2: By 4 weeks, bone cells have entered the scaffold and formed bone matrix; at 12 weeks (above) the matrix has calcified and begins to resemble normal bone.
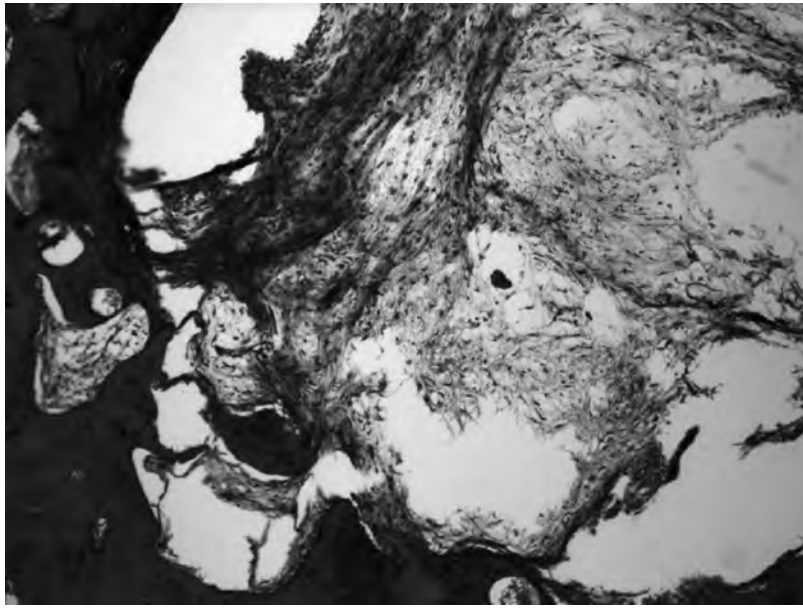
Figure 3: By contrast, in defects not filled with the scaffold, fibrous tissue and scar predominate. There is no evidence of bony ingrowth.

2004 Jun;(423): 33-9.

Brandt KD. 2002. Animal models of osteoarthritis. Biorheol 2002;39: (1-2)221-235.

Milentijevic D, Rubel IF, Liew AS, Helfet DL, Torzilli PA. 2005. An in vivo model for cartilage trauma: a preliminary study of the influence of impact stress magnitude on chondrocyte death and matrix damage. J Ortho Trauma 2005

Aug;19(7):466-473.

Newberry WN, Garcia JJ, Mackenzie CD, Decamp CE, Haut RC. Analysis of acute mechanical insult in an animal model of post-traumatic osteoarthritis. J Biomech Eng. 1998 Dec;120(6):704-9.

Majumdar MK, Banks V, Peluso DP, Morris EA. Isolation, characterization, and chondrogenic potential of human

bone marrow-derived multipotential stromal cells. J Cell Physiol. 2000 Oct;185(1):98-106.

Tuli R, Seghatoleslami MR, Tuli S, Wang ML, Hozack WJ, Manner PA, Danielson KG, Tuan RS. A simple, high-yield method for obtaining multipotential mesenchymal progenitor cells from trabecular bone. Mol Biotechnol. 2003 Jan;23(1):37-49.

Song L, Tuan RS FASEB J. 2004 Jun;18(9):980-2. Transdifferentiation potential of human mesenchymal stem cells derived from bone marrow.

Tuli R, Tuli S, Nandi S, Wang ML, Alexander PG, Haleem-Smith H, Hozack WJ, Manner PA, Danielson KG, Tuan RS. Characterization of multipotential mesenchymal progenitor cells derived from human trabecular bone. Stem Cells. 2003;21(6):681-93.

Tuli R, Nandi S, Li WJ, Tuli S, Huang X, Manner PA, Laquerriere P, Noth U, Hall DJ, Tuan RS. Human mesenchymal progenitor cell-based tissue engineering of a single-unit osteochondral construct. Tissue Eng. 2004 Jul-Aug;10(7-8):1169-79.

Song L, Baksh D, Tuan RS Cytotherapy. 2004;6(6):596-601. Mesenchymal stem cell-based cartilage tissue engineering: cells, scaffold and biology.

Li WJ, Mauck RL, Tuan RS. Electrospun Nanofibrous Scaffolds: Production, Characterization, and Applications for Tissue Engineering and Drug Delivery. Journal of Biomedical Nanotechnology 2005; 1: 259-275.

Yelin E, Cisternas M, Foreman A, Pasta D, Murphy L, Helmick C. National and state medical expenditures and lost earnings attributable to arthritis and other rheumatic conditions - United States, 2003. Morbidity and Mortality Weekly Report 2007;56(1):4-7.
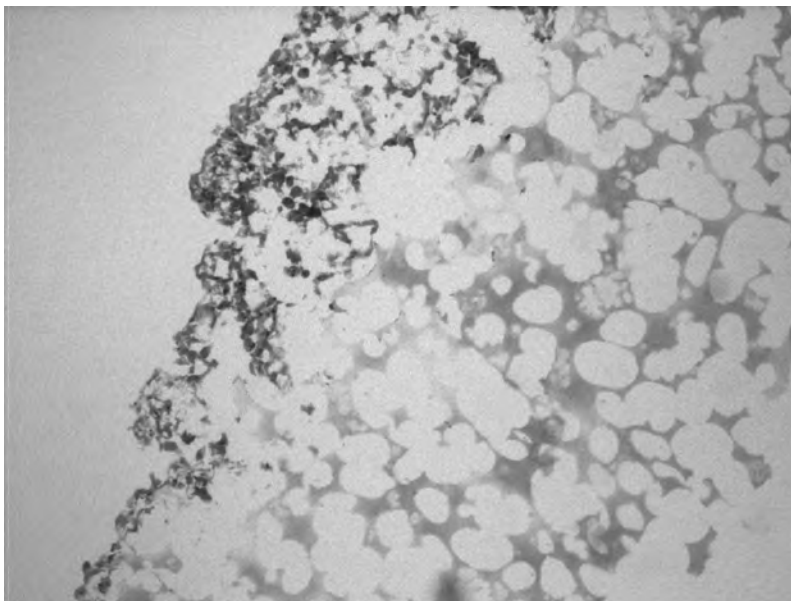
Figure 4: Stem cells, obtained by aspiration from the iliac crest of adult rabbits, have been cultured in medium promoting cartilage formation, and are shown adhering to and infiltrating the engineered scaffold.

Howard A. Chansky, M.D.

Professor
VA Puget Sound Health Care System
Tumor Service
www.orthop.washington.edu/faculty/chansky

Liu Yang, Ph.D., and Anna Zielinska-Kwiatkowska, M.S.

The Helix-Loop-Helix Protein Id2 Regulates Differentiation of Chondrocytes Clues to Cartilage Generation and Regeneration

- Healthy cartilage is critical for normal joint function.
- When injured or arthritic, cartilage does not heal or regenerate normal cartilage.
- Cartilage injuries are a common cause of severe disability.
- Understanding the molecular signals that regulate normal cartilage development may be a key to regenerating healthy cartilage after injury.
- We have identified a protein that appears to be critical for normal cartilage development in mice.

Bone heals and regenerates but cartilage does not. Only patients with cartilage injuries are more frustrated by this biological fact than are orthopaedic surgeons. While bone fractures can heal with minimal disability, the slightest injury to articular (joint) cartilage results in permanent injury that often leads to a self-perpetuating degenerative process resulting in the pain, stiffness and loss of function that are well-known consequences of osteoarthritis. Some progress has been made in stimulating cartilage injuries to heal but the results are at best unpredictable and imperfect. The tissue that typically repairs the cartilage defects lacks the perfect integration with surrounding healthy cartilage and is not nearly as robust and resistant to further damage as normal cartilage. Thus it is our belief that only further basic research to explain the process by which cartilage develops will lead to major improvements in treating cartilage injuries. In this paper we describe the small piece of this challenge that we are investigating within the Department of Orthopaedics and Sports Medicine.

Background

The process by which cartilage develops (chondrogenesis) can be mimicked in cell culture by treating mouse cartilage precursor cells (ATDC5 chondroprogenitor cells) with insulin. Following insulin stimulation, these cells condense to form nodules and synthesize cartilage-like extracellular matrix. Using these cells, we sought to identify new and potentially important factors that control chondrogenesis. To accomplish this we carried out a large-scale screening using the technique of retroviral insertion mutagenesis. Retroviruses insert (insertional mutagenesis) their DNA into the host DNA of the cells that they infect. This viral DNA is in general inserted into random locations of the host DNA and by screening infected ATDC5 cells to identify those in which chondrogenesis is disrupted, we can then back track and examine which host genes were interrupted by the insertion of viral DNA. A technique named inverse-polymerase chain reaction (inverse-PCR) is used to find the host (in our case the host cells are mouse cartilage precursor cells) sites (genes) in which the retroviral DNA integrated. Some of these genes will be critical to chondrogenesis when intact and thus interfere with chondrogenesis when disrupted by the retroviral DNA.

Results

Using these techniques we were able to identify a colony (clone) of ATDC5 (cartilage precursor) cells that were incapable of differentiating into cartilage cells when stimulated with insulin. Out of 10,000 colonies examined, the vast majority were normal clones such as E22-4 and F2-3 that could differentiate in response to insulin (Figure 1, left two panels). A few colonies such as E22-5 showed spontaneous differentiation in the absence of insulin (Figure 1, third panel). Several colonies, such as the one designated C15-6, did not stain with Alcian blue even when cultured in insulin for 21 days (Figure 1, right panel). Alcian blue binds to and stains cartilage; therefore a lack of blue staining indicates that in certain clones the retroviral insertion resulted in deregulation of genes that are important to chondrogenic differentiation of ATDC5 cells. These cells could no longer become cells that

Figure 1: Screening for mutant ATDC5 clones after retroviral insertion. ATDC5 cells were seeded into wells on a 24-well plate, cultured in medium with or without insulin for 21 days and then stained with 0.2% Alcian blue to detect components of cartilage. Individual retrovirus-infected ATDC5 clones were isolated. Normal clones E22-4 and F2-3 underwent normal chondrocytic differentiation in response to insulin. Mutant clone E22-5 underwent spontaneous differentiation even in the absence of insulin. We chose to study the mutant clone C15-6 that was unable to undergo normal differentiation even in the presence of insulin.

make cartilage. We chose to study this C15-6 clone to identify what gene was preventing the ATDC5 cells from undergoing their normal progression through chondrocytic development and synthesis of cartilage. Our assumption is that the product of such a gene would be important and necessary for normal cartilage development and perhaps cartilage repair.

Inverse-PCR analysis of this clone revealed that the retroviral DNA was inserted into the mouse Id2 gene and nowhere else. Id2 is a member of the Id (inhibitors of DNA binding) family of proteins that have a special section referred to as a helix-loop-helix (HLH) domain. Specifically, the DNA was inserted into what is called the promoter region of the Id2 gene. The promoter of a gene typically responds to signals in a cell by increasing the synthesis of the gene product (protein). Improper activation or inhibition of a gene could lead to disruption of cartilage production. In fact, we found that this retroviral insertion increased Id2 protein level to twice the level found in normal ATDC5 cells.

We performed a series of experiments to further characterize and check our assumption that overexpression of ID2 protein was

somehow preventing ATDC5 cells from differentiating and synthesizing type II collagen. We first wanted to analyze what would happen to our ATDC5 cells if we drove down the expression of ID2, in essence the opposite experiment of increasing its expression by insertional mutagenesis. To accomplish this we used the technique of RNA interference to prevent expression of ID2. This did indeed result in acceleration of differentiation of ATDC5 cells and expression of SOX9 and collagen type II, typical products of chondrocytes. In one other experiment we drove higher levels of ID2 expression by introducing Id2 nucleic acid into the ATDC5 cells using a viral vector. Again, even modest increases in Id2 expression in chondroprogenitor cells had a significant negative impact on differentiation and production of cartilage-like matrix. Thus these experiments supported our hypothesis that a certain amount of ID2 must be present for normal cartilage development, at least in this model system.

ATDC5 cells are one of the best model systems that we have to study cartilage development. However, even the best model system is only an approximation of the biology of a living organism. To further examine how Id2

is expressed in chondrocytes in vivo (in a "living" system), we carried out immunostaining of mouse embryos. Immunostaining with an antibody to Id2 enabled us to selectively locate cells that are producing this particular protein. In this case we found that in mouse embryos, Id2 is expressed in articular chondrocytes and proliferating chondrocytes but barely detectable in hypertrophic chondrocytes (Figure 2). In general, staining for Id2 decreases in cells further away from the joint, cells that are therefore more committed to terminal differentiation into non-articular cells. This result at first glance appears to contradict our earlier findings. However, immunostaining is not quantitative and what is stained here represents the normal baseline expression of Id2 in mouse embryo. Putting all of this data (and other experiments not discussed here) strongly suggests that for there to be normal development of chondrocytes and cartilage there must be a precisely regulated level of Id2 present in these precursors of articular chondrocytes.

Discussion

Our study, for the first time, demonstrates that over-expression of Id2 in ATDC5 cells inhibits insulin-
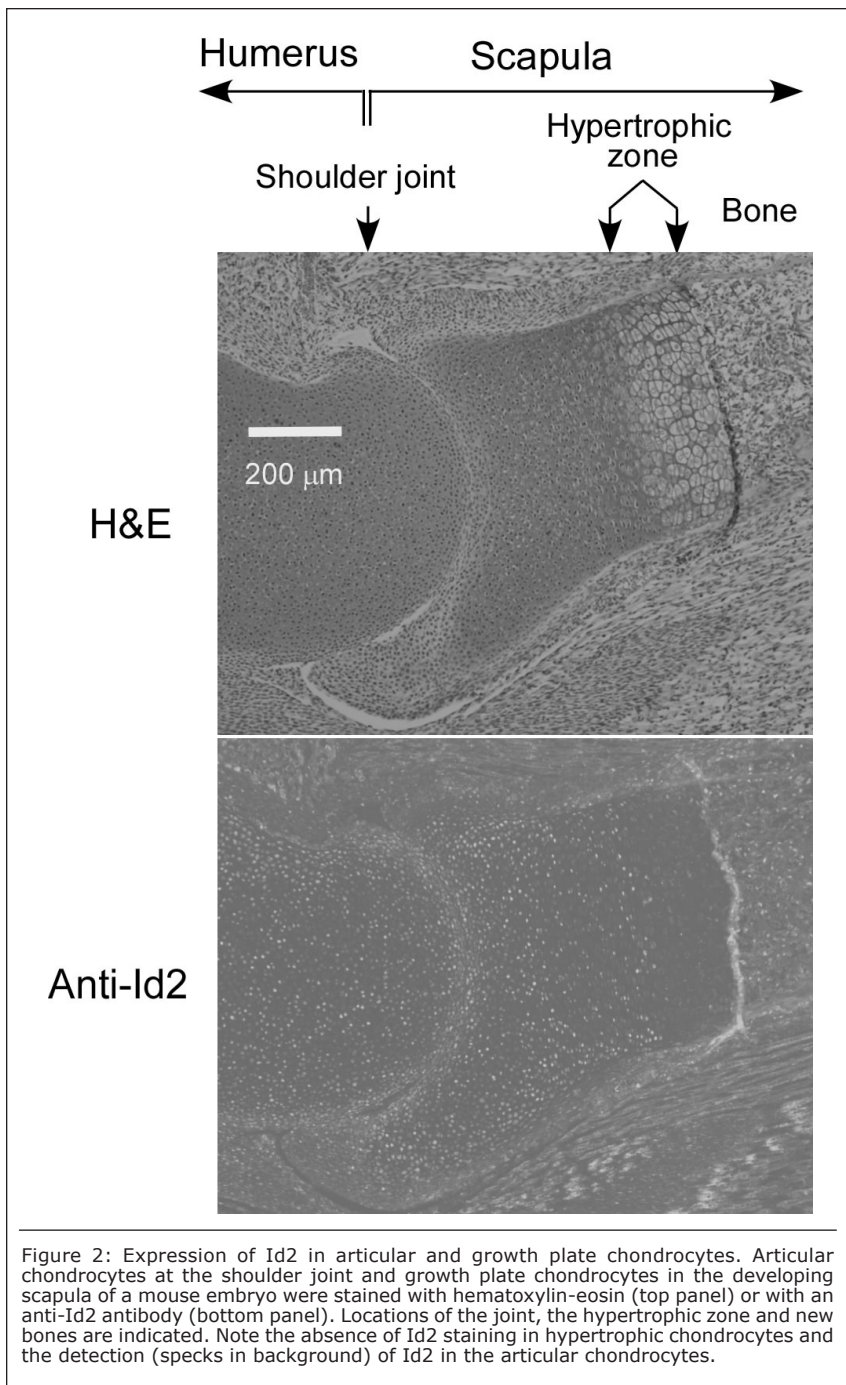
Figure 2: Expression of Id2 in articular and growth plate chondrocytes. Articular chondrocytes at the shoulder joint and growth plate chondrocytes in the developing scapula of a mouse embryo were stained with hematoxylin-eosin (top panel) or with an anti-Id2 antibody (bottom panel). Locations of the joint, the hypertrophic zone and new bones are indicated. Note the absence of Id2 staining in hypertrophic chondrocytes and the detection (specks in background) of Id2 in the articular chondrocytes.

induced chondrogenic differentiation and synthesis of collagen type II. Consistent with this finding, using RNA interference to shut down production of Id2 can accelerate the differentiation of ATDC5 cells and stimulate the synthesis of collagen type II, permitting them to escape the requirement of needing insulin. In mouse embryo, the level of Id2 protein is inversely correlated with the progression of terminal differentiation of growth plate chondrocytes but is also present in articular chondrocytes. These results suggest that a subtle change in Id2 expression during chondrogenesis may have a big impact on the balance between growth and differentiation of chondrogenic cells. We are conducting further experiments to more precisely define the mechanism by which Id2 controls development of chondrocytes and cartilage. Ultimately we hope to control levels of Id2 or the molecules it interacts with to encourage the regeneration of injured articular cartilage.

Recommended Reading

Kronenberg, H. M. (2003) Developmental regulation of the growth plate. Nature 423, 332-336.

Peng, Y., Kang, Q., Luo, Q., Jiang, W., Si, W., Liu, B. A., Luu, H. H., Park, J. K., Li, X., Luo, J., Montag, A. G., Haydon, R. C. and He, T. C. (2004) Inhibitor of DNA binding/differentiation helix-loop-helix proteins mediate bone morphogenetic protein-induced osteoblast differentiation of mesenchymal stem cells. J. Biol. Chem. 279, 32941-32949.

Yang, L., Clinton, J. M., Blackburn, M. L., Zhang, Q., Zou, J., Zielinska-Kwiatkowska, A., Tang, B. L. and Chansky, H. A. (2008) Rab23 regulates differentiation of ATDC5 chondroprogenitor cells. J. Biol. Chem. 283, 10649-10657.

Russell J. Fernandes, Ph.D.

Research Associate Professor
University of Washington Medical Center
Research
www.orthop.washington.edu/faculty/fernandes

William J. Landis, Ph.D., and David R. Eyre, Ph.D.

Matrix Assembly: Monitoring Collagen Heteropolymer Formation in Tissue-Engineered Cartilage

- In arthritis, a progressive breakdown of the collagen fibrillar network that frames cartilage leads to a loss of normal joint function since cartilage has a limited capacity to heal or regenerate.
- The current challenge in cartilage tissue-engineering is to direct chondrocytes and stem cells undergoing chondrogenesis to synthesize and deposit sufficient collagen in the extracellular matrix.
- Basic research on how the collagen fibril is assembled has led to an understanding that the type II/IX/XI collagen template is crucial for the growth and quality of the collagen fibril and consequently for an adequate amount of collagen in cartilage.
- Developing markers to monitor this assembly in normal cartilage and to assess correct assembly in tissue-engineered cartilage is a valuable and important goal.
- We seek to understand the changing quality of the cartilage collagen heteropolymer in disease or when produced as a healing or regenerative response.

Mature articular cartilage by dry weight is roughly two-thirds collagen. Chondrocytes synthesize and deposit three tissue-specific collagen molecules, types II, IX and XI in forming a cartilage matrix. Mutations in any one of the genes encoding the three primary collagen subunits can cause chondrodysplasia syndromes and/or premature osteoarthritis. The three collagens are co-polymerized and cross-linked by covalent bonds. Trivalent pyridinolines formed between the amino- (N) and carboxy- (C) telopeptides and helical sites in type II collagen molecules are the most prevalent cross-links. Pyridinoline and divalent cross-links also bond type IX collagen molecules to the N- and C- telopeptides of type II collagen. Type XI collagen is cross-linked exclusively by divalent ketoamine cross-links that include bonds to the C-telopeptide of type

II collagen as well as inter-type XI cross-links. The ability of cartilage to withstand mechanical stress depends on the quality of the cross-linked collagen framework.

A better understanding of chondrocyte biology has led to improved cell culture techniques and a new field of research, cartilage tissue engineering. Under suitable culture conditions chondrocytes can be induced to synthesize and form a matrix based on type II collagen and aggrecan. To what degree the fibrillar matrix is normal, in terms of the co-assembly of the minor collagens (types IX and XI), is not well characterized. We have focused our research efforts on developing a method of screening for normal collagen co-polymeric assembly to monitor the quality of the matrix deposited by chondrocytes in culture and in diseased cartilage.

This study investigated the ability of

articular chondrocytes, seeded within engineered scaffolds and implanted in immune compromised mice, to assemble collagen types II, IX and XI into the co-polymeric cross-linked network that typifies cartilage matrix *in vivo*.

Tissue engineered constructs of the middle phalanges were prepared as described in Isogai et al 1999. Briefly, chondrocytes dissociated from shoulders and forelimbs of newborn calves were seeded into polyglycolic acid (PGA) polymer mesh 1x1 cm in size and 2mm in thickness. This mesh was sown onto the ends of a polycaprolactone (PCL)/poly-L-lactic acid (PLLA) scaffold shaped into the form of a human phalanx. Constructs were implanted into the dorsal subcutaneous space of 4-6 week old athymic nude mice. Implants were removed after 20 weeks and the collagenous meshwork formed in the
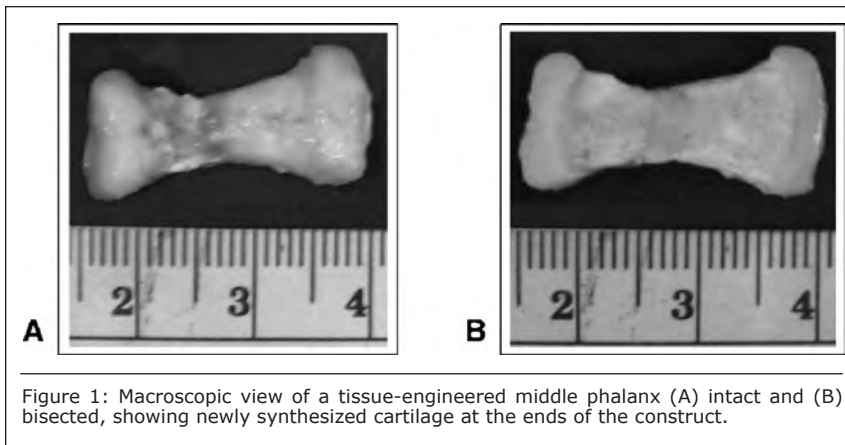
Figure 1: Macroscopic view of a tissue-engineered middle phalanx (A) intact and (B) bisected, showing newly synthesized cartilage at the ends of the construct.

tissue engineered cartilage examined biochemically.

The collagen network laid down by the bovine chondrocytes in the engineered cartilage was depolymerized and extracted using pepsin. The various collagen chains and chain fragments were resolved by Laemmli SDS-PAGE. The collagen chains were transferred onto PVDF and probed with monoclonal antibody (mAb) 10F2 which recognizes a cleavage-site (neoepitope) in a sequence in the C-telopeptide cross-linking domain of type II collagen. When necessary the blots were then probed with monoclonal antibody 1C10 that recognizes type II collagen chains. A colorimetric or luminescence detection system was used. A pepsin extract of bovine cartilage containing types II and XI collagen was used as a standard.

In-gel trypsin digests of $\alpha1(II)$ collagen chains from the tissue engineered cartilage were analyzed by mass spectrometry to confirm bovine-specific type II collagen protein.

Glossy, cartilaginous tissue at the ends of the engineered phalanx scaffolds 20 weeks after implantation in a nude mouse was observed (Figure 1). Histological analysis of this tissue showed intense Saffranin-O staining. A firm cartilage-like feel to the tissue was noted.

Analysis of pepsin extracted collagen by Western blots using mAb 1C10 (specific for type II collagen) showed the presence of $\alpha1(II)$ chains, (Figure 2A). SDS-PAGE followed by Coomassie blue staining confirmed that type II collagen was the major collagen solubilized by pepsin. Most importantly, mass spectrometry revealed type II

collagen peptides of bovine origin indicating that the seeded bovine chondrocytes remain differentiated and deposited an extensive extracellular matrix within the scaffold containing type II collagen.

Pepsin cleaves in the telopeptide domains of type II collagen and in the non-collagenous domains of the minor collagens, type XI and IX, leaving the triple helical domains intact. The short stubs of residual telopeptides remain cross-linked to the triple-helical sites to which they were attached in the matrix. Antibody 10F2 was used to detect such cross-linked $\alpha1(II)$ C-telopeptides.

In Figure 2B, mAb 10F2 reacted with the $\alpha1(II)$ chain indicating a cross-linked type II collagen network had formed within 20 weeks. The $\alpha1(XI)$ chain was also immunoreactive, showing that type XI collagen was co-polymerized and cross-linked to C-telopeptides of type II collagen. A pepsin extract of bovine cartilage revealed a similar pattern. The results indicate that a type II/XI collagen heteropolymeric network as present in normal cartilage had formed. The collagen content of tissue-engineered neocartilage approached values seen in bovine control articular cartilage (Table 1). The collagenous network in the tissue-engineered cartilage was stabilized by trivalent hydroxylysyl pyridinoline (HP) cross-links typical of normal articular cartilage (data not shown). The HP content of tissue-
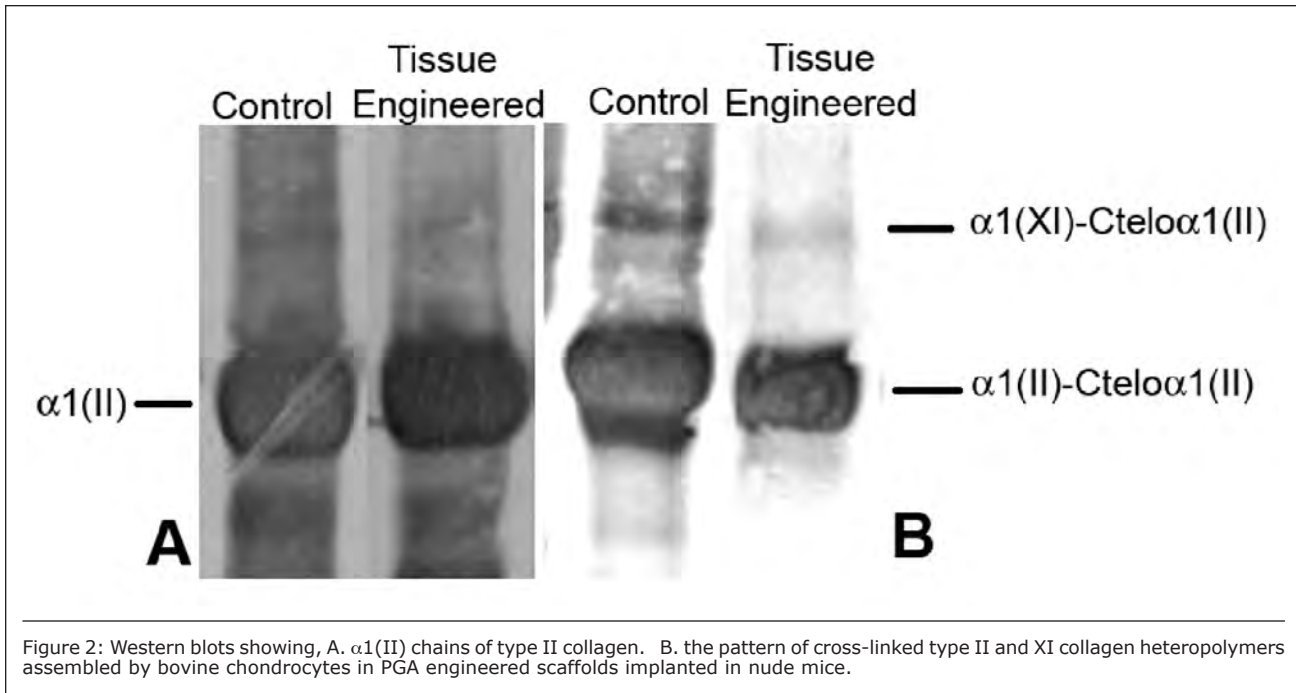

Figure 2: Western blots showing, A. $\alpha1(II)$ chains of type II collagen. B. the pattern of cross-linked type II and XI collagen heteropolymers assembled by bovine chondrocytes in PGA engineered scaffolds implanted in nude mice.

Sample	μg hydroxypro/mg dry wt	% collagen (dry wt)
Tissue-Eng cart.(P1)	63.15	47.36
Bovine articular cart.	69.91	52.43
Bovine tracheal cart.	37.63	28.22

Table 1: Collagen content of tissue-engineered neocartilage.

engineered cartilages approached values typical of normal articular cartilage.

The photographs illustrate the gross appearance of glistening, firm, cartilage-like tissue at the ends of one example of an engineered middle phalanx model retrieved 20 weeks after implantation in a nude mouse. Histological analysis of this and other such tissues showed intense Safranin-O staining and a developing growth plate.

An extensive collagenous matrix was synthesized by the seeded bovine chondrocytes. The collagen content of neocartilage approached values seen in normal bovine articular cartilage and was higher than the collagen content in normal bovine tracheal cartilage as expected.

Conclusions

Each minor collagen is essential for normal collagenous network organization (for example, fibril diameters modulated by type XI collagen), and fingerprinting inter-type cross-linking provides a screen for matrix assembly. As demonstrated here, this method has revealed the quality and biochemical nature of cartilage produced in a novel tissue-engineered model of the human middle phalanx.

In this context, bovine articular chondrocytes, seeded onto biodegradable scaffolds that are then implanted in nude mice, remain differentiated and they secrete collagen that forms a fibrillar matrix of the collagen II/IX/XI heteropolymer characteristic of normal hyaline cartilage *in vivo*. Type II collagen is still the major collagen synthesized. Cartilages engineered by this method show a high collagen content approaching that of normal cartilage. Trivalent hydroxylysyl-pyridinoline cross-links

typical of normal cartilage were also detected in the neocartilage. These results substantiate phalanx models with human cells for future tissue-engineering applications.

Knowledge gained from basic research concerning how the cartilage cells can reassemble or regenerate a functional extracellular matrix will lead to improved methods for treating arthritis, one of the greatest causes of disability in our population.

Support

Recommended Reading

Wu, J. J. & Eyre, D. R. (1984) Identification of hydroxypyridinium cross-linking sites in type II collagen of bovine articular cartilage, Biochemistry. 23, 1850-7.

Eyre, D. R., Apon, S., Wu, J. J., Ericsson, L. H. & Walsh, K. A. (1987) Collagen type IX: evidence for covalent linkages to type II collagen in cartilage, FEBS Lett. 220, 337-41.

Wu, J. J. & Eyre, D. R. (1995) Structural analysis of cross-linking domains in cartilage type XI collagen. Insights on polymeric assembly, J Biol Chem. 270, 18865-70.

Fernandes, R. J., Weis, M., Scott, M. A., Seegmiller, R. E. & Eyre, D. R. (2007) Collagen XI chain misassembly in cartilage of the chondrodysplasia (cho) mouse, Matrix Biol. 26, 597-603.

Isogai, N., Landis, W., Kim, T. H.,

Gerstenfeld, L. C., Upton, J. & Vacanti, J. P. (1999) Formation of phalanges and small joints by tissue-engineering, J Bone Joint Surg Am. 81, 306-16.

Fernandes, R. J., Schmid, T. M. & Eyre, D. R. (2003) Assembly of collagen types II, IX and XI into nascent hetero-fibrils by a rat chondrocyte cell line, Eur J Biochem. 270, 3243-50.

David R. Eyre, Ph.D.

Professor
University of Washington Medical Center
Research
www.orthop.washington.edu/faculty/eyre

Jiann-Jiu Wu, Ph.D.

Diversity in Skeletal Tissue Fibril Architecture: Role of an Ancestral Collagen Type V/XI Template

- Collagen type V/XI is a quantitatively minor but indispensable polymeric template for collagen fibril formation in vertebrate tissues.
- To understand better how different collagen V/XI isoforms may modulate fibril architecture, we compared biochemically the collagen components of developing and adult bovine articular cartilage and intervertebral disc.
- With maturation of articular cartilage, the $\alpha1(V)$ chain progressively replaced the $\alpha2(XI)$ chain. A prominence of $\alpha1(V)$ chains is therefore characteristic and a potential biomarker of mature mammalian articular cartilage.
- A unique molecular form of type V/XI collagen is revealed in the nucleus pulposus of the intervertebral disc.
- We propose an evolving role for collagen V/XI isoforms as an adaptable template of fibril macro-architecture and hence skeletal tissue diversity.

The collagen framework of hyaline cartilages is based on a covalently cross-linked heteropolymeric network of types II, IX and XI collagen. In that the bulk type II collagen is copolymerized on a template of type XI collagen. As illustrated in Figure 1, type XI collagen molecules are polymerized in the interior whereas type IX collagen molecules decorate and are covalently linked to surface type II molecules and to other type IX molecules. All three collagen subunits, II, IX, and XI, are heavily cross-linked in the same fibril through a lysyl oxidase-mediated mechanism.

In fetal cartilage, type XI collagen is a heterotrimer of three genetically distinct chains, $\alpha1(XI)$, $\alpha2(XI)$ and $\alpha3(XI)$ in a 1:1:1 ratio. The $\alpha3(XI)$ chain has the same primary sequence as $\alpha1(II)$ but the chains differ in their post-translational processing and cross-linking properties. However, from mature articular cartilage, the isolated type XI collagen fraction includes a significant proportion of the $\alpha1(V)$ chain, the chain ratios suggesting the existence of type V/type XI hybrid molecules in the tissue. Collagen type V/XI is a minor but essential polymeric template for collagen fibril formation in vertebrate tissues. The ratio of type XI collagen to type II collagen is about 1 to 10 in fetal bovine and human epiphyseal cartilage compared with 1 to 30 in adult articular cartilage. To understand better how different collagen V/XI isoforms may modulate fibril architecture, the collagen components of developing and adult bovine articular cartilage and intervertebral disc were compared. The results show changes with tissue developmental age and maturity in type V/XI α-chain isoform usage in articular cartilage and a unique profile of type V/XI molecular isoforms in the nucleus pulposus of the intervertebral disc.

Using an established two dimensional HPLC/SDS-PAGE method, we are able to resolve all five type V/XI gene products, $\alpha1(V)$, $\alpha2(V)$, $\alpha1(XI)$, $\alpha2(XI)$, and $\alpha3(XI)$ chains, from each other. The chain identities, assigned from their elution on reverse-phase HPLC and migration on SDS-PAGE, were established beyond doubt by in-gel trypsin digestion, and microbore liquid chromatography/mass spectrometry with data base matching and by amino-terminal protein sequence analysis. With maturation of articular cartilage, the $\alpha1(V)$ chain progressively replaced the $\alpha2(XI)$ chain. The proportion of $\alpha1(V)$ chains increased at the expense of $\alpha2(XI)$ chains. Type XI collagen is cross-linked by lysyl oxidase-mediated bonds. The pattern of type XI collagen cross-linking in fetal cartilage exhibits strict chain specificity. Each α chain is cross-linked through its triple-helix (approx. residue 930) to a specific N-telopeptide hydroxylysine aldehyde in a 4D-staggered adjacent type XI molecule (Figure 2). Structural analysis of cross-linked peptides showed that
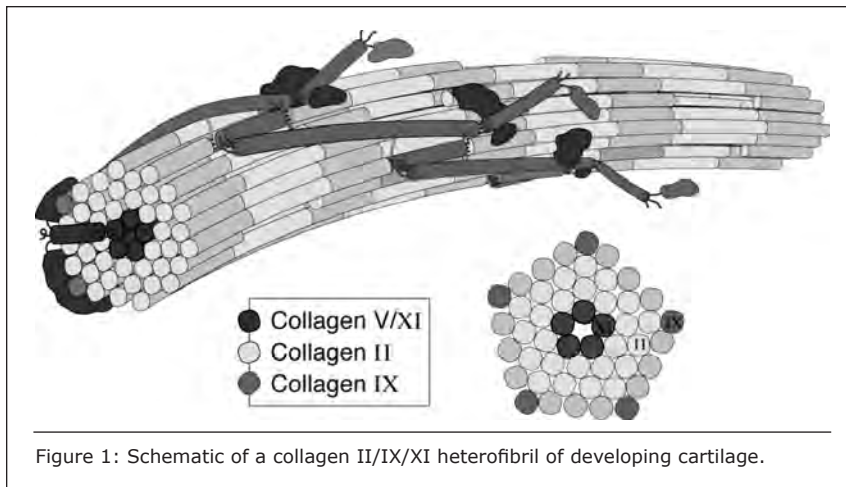
Figure 1: Schematic of a collagen II/IX/XI heterofibril of developing cartilage.

the α1(V) chain has the same cross-linking preferences as α2(XI), with the α1(V) N-telopeptide linked to an α1(XI) helix and the α1(V) helix linked to an α3(XI) N-telopeptide. Together with the observed decrease in α2(XI) in exchange for an increase in α1(V), we conclude that α1(V) replaces α2(XI) isomorphically in an increasing proportion and eventual majority of newly synthesized V/XI hybrid collagen molecules as articular cartilage matures. A mix of the molecular isoforms, α1(XI)α1(V)α3(XI) and α1(XI)α2(XI)α3(XI), best explained this finding. A prominence of α1(V) chains is therefore characteristic and a potential biomarker of mature mammalian articular cartilage. The findings imply that the expression of type XI collagen by chondrocytes is under a more complex regulation than

previously appreciated. In a related, but opposite phenomenon, the α1(XI) chain accumulates in the type V collagen component of bone with maturational age. It remains to be seen whether these changes reflect anatomically uniform metabolic changes throughout the tissues or, for example, surface-to-deep or pericellular, territorial and interterritorial micro-anatomical variations in articular cartilage. To speculate, α1(V)-containing type V/XI molecules may provide a polymeric filamentous template for the thicker collagen II fibrils (200-500 nm diameter) that accumulate in adult articular cartilage as opposed to the uniformly thin type II collagen fibrils (10-20nm) associated with the [α1(XI)α2(XI)α3(XI)] template of epiphyseal growth cartilages.

Nucleus pulposus, the central zone

of the intervertebral disc, is gel-like and has a similar collagen phenotype to that of hyaline cartilage in which the bulk collagen monomer is type II. Its type V/XI collagen isoforms, however are more complex than in hyaline cartilage. Five genetically distinct chains, α1(XI), α2(XI), α3(XI), α1(V), and α2(V), are present. Similar to the findings with articular cartilage, the N-telopeptide of α2(XI) was shown to be linked exclusively to α1(XI) in young nucleus pulposus. However, α1(XI) in the nucleus pulposus was shown to be linked to either α3(XI) or α2(V) but not to α1(XI), α2(XI) or α1(V). Based on the observed strict chain specificities in the cross-linking properties of the individual type V/XI chains found in articular cartilage, the results from disc tissue strongly suggest that in addition to forming heterotrimers with α2(XI) or α1(V) and α3(XI), α1(XI) chains can also form native heterotrimers that include α2(V) chains. The most likely molecular form of the latter is $[α1(XI)]_2α2(V)$, which is the same V/XI isoform found in bovine vitreous in association with collagens II and IX. In addition to $[α1(XI)α2(XI)α3(XI)]$ and $[α1(XI)]_2α2(V)$, it is possible that other heterotrimeric combinations are represented in the type V/XI collagen pool of the disc. Whether this reflects contributions by different cell types, for example the chondrocyte-like cells of mature disc and the notochordal cells that persist in young disc, is unknown. The presence of hybrid $[α1(XI)]_2α2(V)$ molecules in nucleus is similar to that of vitreous humor since nucleus pulposus and vitreous share a similar type II collagen phenotype, gel-like texture, low concentrations of very thin fibrils and lack of physical constraints between the fibrils when the tissue is removed from the eye or disc and swollen osmotically. The governing mechanism for these variants may largely be the interaction preferences of the different C-propeptide domains of the various procollagen chains and their relative expression levels into the endoplasmic reticulum.

The findings support and extend the concept that COL5 and COL11 gene products should be considered members of the same collagen subfamily. Developmental- and tissue-dependent usage of chains from gene products of clade A (α1(II)/α3(XI) and α2(V)) and clade B (α1(XI), α2(XI)

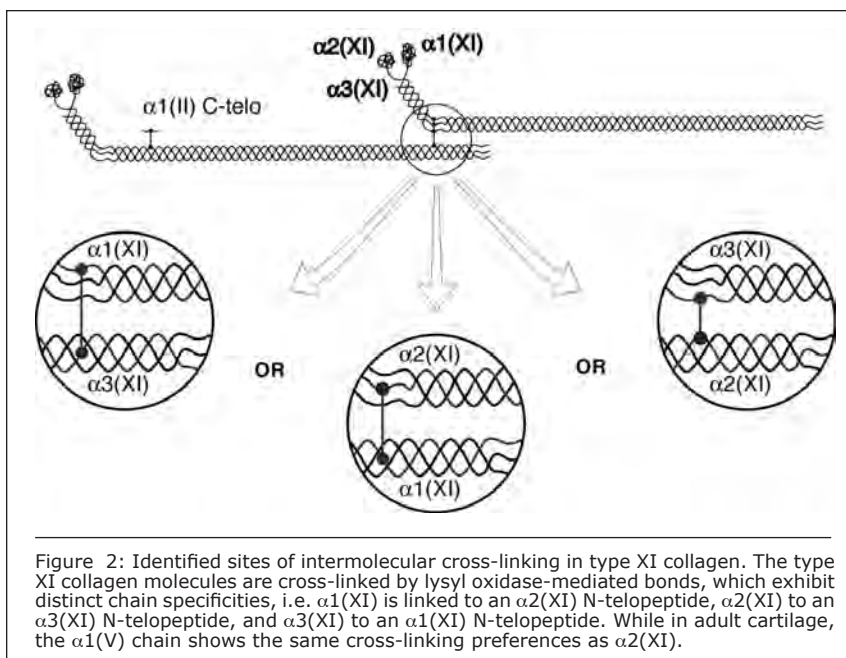Figure 2: Identified sites of intermolecular cross-linking in type XI collagen. The type XI collagen molecules are cross-linked by lysyl oxidase-mediated bonds, which exhibit distinct chain specificities, i.e. α1(XI) is linked to an α2(XI) N-telopeptide, α2(XI) to an α3(XI) N-telopeptide, and α3(XI) to an α1(XI) N-telopeptide. While in adult cartilage, the α1(V) chain shows the same cross-linking preferences as α2(XI).

and $\alpha1(V)$) has created a range of molecular isoforms. Such molecular variations are likely to be functionally associated with the diverse fibril organization patterns evident between tissues and during tissue development and maturation. We propose an evolving role for collagen V/XI isoforms as an adaptable template of fibril macro-architecture. This concept has important implications in understanding how the diverse connective tissues of the musculoskeleton have evolved their different properties.

Conclusion

The type V/XI collagen component of adult articular cartilage comprises four genetically distinct chains, $\alpha1(XI)$, $\alpha2(XI)$, $\alpha1(V)$, and $\alpha3(XI)$, assembled into at least two distinct heterotrimeric molecules, $[\alpha1(XI)\alpha2(XI)\alpha3(XI)]$ and $[\alpha1(XI)\alpha1(V)\alpha3(XI)]$. There is a shift in chain isotype usage as the hyaline cartilage precursor matures postnatally. With increasing tissue maturity, the type XI collagen fraction contains more $\alpha1(V)$ and less $\alpha2(XI)$ in proportion to $\alpha1(XI)$ and $\alpha3(XI)$. In contrast, type V/XI collagen from nucleus pulposus contains five genetically distinct chains, $\alpha1(XI)$, $\alpha2(XI)$, $\alpha3(XI)$, $\alpha1(V)$, and $\alpha2(V)$, which are distributed among several distinct heterotrimeric molecules. The findings support an evolving role for tissue-specific molecular variants of type V/XI collagen in regulating fibril form and function across vertebrate connective tissues.

Recommended Reading

Niyibizi C. and Eyre DR. (1989) Identification of the cartilage $\alpha1(XI)$ chain in type V collagen from bone. FEBS Lett. 242: 314-318.

Mayne R, Brewton RG, Mayne PM, and Baker JR. (1993) Isolation and characterization of the chains of type V/type XI collagen present in bovine vitreous. J. Biol. Chem. 268:9381-9386.

Wu JJ and Eyre DR. (1995) Structural analysis of cross-linking domains in cartilage type XI collagen: Insights on polymeric assembly. J. Biol. Chem. 270(32):18865-18870.

Wu JJ and Eyre DR. (2003) Intervertebral disc collagen: usage of the short form of the $\alpha1(IX)$ chain in bovine nucleus pulposus. J. Biol. Chem. 278: 27521-27525.

Huxley-Jones J, Robertson DL, and Boot-Handford RP. (2007) On the origins of the extracellular matrix in vertebrates. Matrix Biol. 26: 2-11.

Eyre DR, Weis MA and Wu JJ. (2008) Advances in collagen cross-link analysis. Methods 45: 65-74.

Wu JJ, Weis MA, Kim LS, Carter BG, and Eyre DR. (2009) Differences in chain usage and cross-linking specificities of cartilage type V/XI collagen isoforms with age and tissue. J. Biol. Chem. 284:5539-5545.

Seth S. Leopold, M.D.

Professor
University of Washington Medical Center
Hip and Knee
www.orthop.washington.edu/faculty/leopold

Christopher Wolf, M.D., Ning Yan Gu, M.S.,
Paul A. Manner, M.D., and Jason N. Doctor, Ph.D.

Physicians and Patients Value Quality Versus Length of Life Differently: A Time Trade-Off Model of Health Utilities Associated with Treating the Infected Total Hip Replacement

- When a patient and a surgeon are faced with an infected total hip implant, choices must be made among different treatment options.
- We explored the perspectives of the patient and the surgeon that may contribute to the decision-making process.
- Important differences were found between patients' and surgeons' perceptions of risk and reward concerning health states that may arise during the treatment of an infected total hip replacement (THR).
- In general, surgeons valued quality of life, and were willing to trade quantity (length) of life in order to decrease pain and improve function.
- In general, patients valued quantity (length) of life, and were willing to trade quality of life - even if the result was living in a state of poorer function or increased pain - in order to avoid risk of death associated with an intervention.
- It is important for surgeons to be mindful of this potential difference in perspective when counseling patients about surgical and non-operative alternatives.

Regardless of the orthopaedic intervention in question - whether a "traditional" approach to replace a worn joint surface, or a cutting-edge procedure that seeks to regenerate one - at some point a meeting of the minds between patient and physician must occur. The physician's job in this encounter is to share a menu of available treatment alternatives from which the patient can choose; often, the major treatment options are given as part of a risk-benefit analysis, which the patient can use to help guide the decision.

At the heart of any risk-benefit calculation is the concept of differential utility of the various health states that might occur after the intervention in question; "utility" is the benefit part of the risk-benefit analysis, and the health states are the possible outcomes. Consider surgery for the infected hip replacement as an example; patients will, subconsciously or explicitly, assign some value to the various possible health states that might occur after the operation, such as recurrent infection requiring more surgery, failed joint reconstruction and chronic pain, or success with eradication of the infection and relief of pain. Patients will process those possibilities by considering the likelihood of each, and arrive at a decision of whether or not the intervention seems worth the risk. However, if surgeons value those possible health states differently than patients do, and the difference is pervasive (across most or all of the possible health states) and significant (both statistically and clinically), then this difference can affect the how the patient-physician conversation about treatment options is delivered and perceived, and may call into question

whether true "informed consent" can even be achieved.

There is a literature suggesting that indeed there are differences between patients and physicians in terms of how utility is perceived; however, this topic has not been explored in the context of orthopaedic interventions.

The present study tested the hypothesis that there is no difference between patients naïve to the clinical problem (treatment of the infected THR, Figure 1) and surgeons in terms of how utility will be assigned to health states relevant to the management of the patient with the infected THR.

Methods

Two populations were surveyed in this IRB-approved study:

1. Patients naïve to the condition in question and without musculoskeletal pathology. A total of 50 patients,
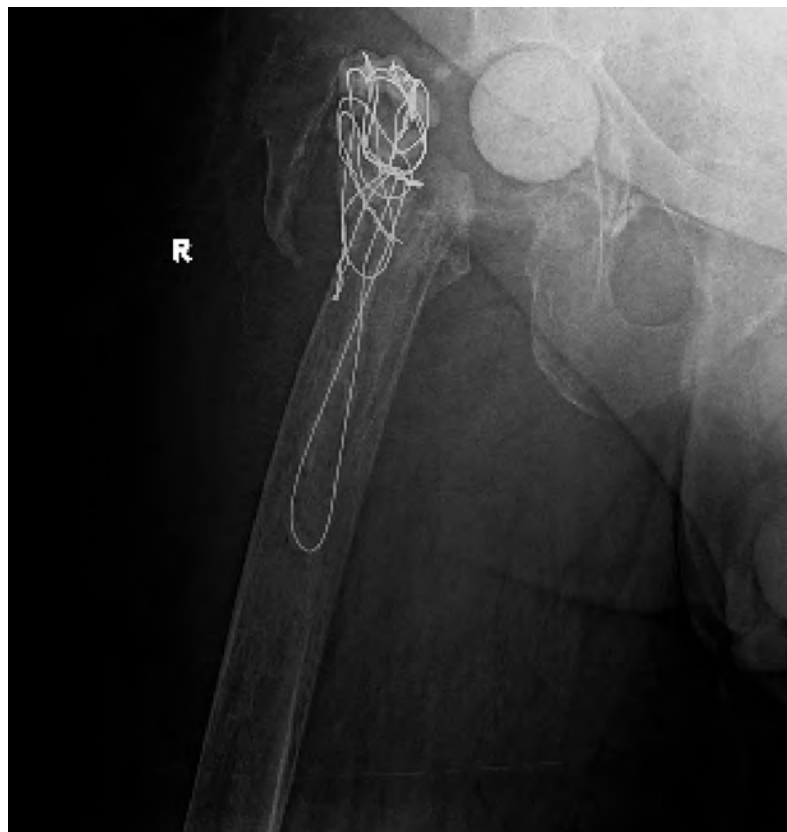
Figure 1: X-ray of a patient whose infected THR resulted in the need to remove the hip joint entirely; visible are antibiotic beads on metallic wires, and a large antibiotic spacer in the hip socket. Note that the result of this infection is severe loss of bone and joint deformity.

constant severe pain) to full health with shortened life, and between pairs of temporary health states (Figure 2). A mathematical model using the Time Trade-Off Technique3 converted these preferences to quality-adjusted life-year (QALY) utility values; in this model, death is assigned a value of 0, and perfect health without any disability is assigned a value of 1. There were 10 questions in the survey (Figure 3).

Results

There was generally good agreement between surgeons and patients; however, patients consistently (in 9 out of the 10 health states surveyed, with 5 of the 9 differences reaching statistical significance of $p<0.05$) reported higher utility values for the impaired health states than did surgeons (Figure 4). The most pronounced difference was found for the most disabling condition, "chronic severe pain." This finding indicates that on average, for nearly every kind of impairment that can occur in the course of treating the infected THR, patients were less willing than surgeons to relinquish years of life to improve quality of life, even when the impairment is as severe as constant severe pain.

Discussion, Ongoing Work, and Conclusions

These findings are consistent with other, non-orthopaedic research that suggests that patient and provider utility values commonly differ, and that severe health states can result in the largest discrepancies.

The results of this study form the basis of an expected-value decision analysis comparing two common treatments for the infected THR: single-stage direct-exchange arthroplasty and two-stage revision. This decision analysis is now in progress. Decision analysis is a very powerful mathematical approach that allows a data-driven, evidence-based approach to choosing a therapeutic course of action that considers the probability of the various possible health states that may result from treatment (ranging from success to severe complication of any type) and the utility of each health state that might occur. This approach, which was originally used to model and guide business decision-making, is becoming increasingly popular in clinical medicine

aged 20-80, participated. Patients without the conditions in question were used so as to avoid the chance that utility values would be skewed in an uncontrolled way by recent and diverse experiences.

2. High-volume THR surgeons. A total of 20 surgeons who do ≥50 THRs/ year were solicited, and 16 responded by completing the survey.

Preference measures were elicited using time trade-offs that compared various states of impaired health (from successful revision arthroplasty, which is a good outcome but does not represent perfect health, to

Imagine your friend/patient is expected to live for 15 years with the quality of life that is described below:

Constant Severe Pain
  - No ability to avoid severe pain regardless of position/activity
  - 7.5 - 10 Hip Pain on a 0 - 10 scale, indefinitely

Suppose a treatment could restore this person to full health, but would shorten their life. At most, how much time would you advise giving up out of 15 years?

I would advise my friend/patient to give up at most _____ years to avoid the above health state and return to full health.

YEARS: 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

Figure 2: A sample question from the survey, which demonstrates how a time trade-off is portrayed to survey participants.

Chronic Health States

1. Successful Revision Hip Arthroplasty
2. Re-Infection Treated with Long Term Antibiotics
3. Infected THA Treated with Resection
4. Infected THA Treated with Staged Revision
5. Long-Term Medical Complication
6. Constant Severe Pain

Temporary Health States

7. Interval between Stages Surgeries
8. Mechanical Complication Treated Non-Operatively
9. Mechanical Complication Treated Operatively
10. Short-Term Major Medical Complication

Figure 3: The 10 health states used in the time trade-off model of the infected THR; each of these was incorporated into a question analogous to that shown in Figure 2.

and surgery.

However, these results also stand alone as a cautionary reminder that patients may tend to make decisions that place greater emphasis on longevity, while surgeons favor trade-offs that will take risk to improve quality of life. This difference between patients and providers appears pervasive, and for that reason, surgeons need to bear this difference in mind when counseling patients about a procedure that seeks to improve quality of life but in which there is a risk of death.

Surgeons must not assume that patients will risk exchanging years of life to try to improve life's quality.

Support

This work was generously funded through the University of Washington Friends of Orthopaedic Research and Education, as part of the "Club Met" project, which is a multi-disciplinary partnership between the University of Washington Department of Orthopaedics and Sports Medicine and the Department of Medical Education

and Biomedical Informatics.

Recommended Reading

Drummond MF, Sculpher MJ, Torrance GW, et al. Methods for the Economic Evaluation of Health Care Programmes (3rd ed.). New York: Oxford University Press, 2005.

Fayers PM, Machin D. Quality of Life: The Assessment, Analysis and Interpretation of Patient-Reported Outcomes (2nd ed.). Hoboken, NJ: John Wiley & Sons Ltd, 2007.

Torrance GW, Thomas W, Sackett D. A utility maximization model for evaluation of health care programs. Health Serv Res 1972;7:118-33.

Zethraeus N, Johannesson M. A comparison of patient and social tariff values derived from the time trade-off method. Health Econ 1999;8:541-5.
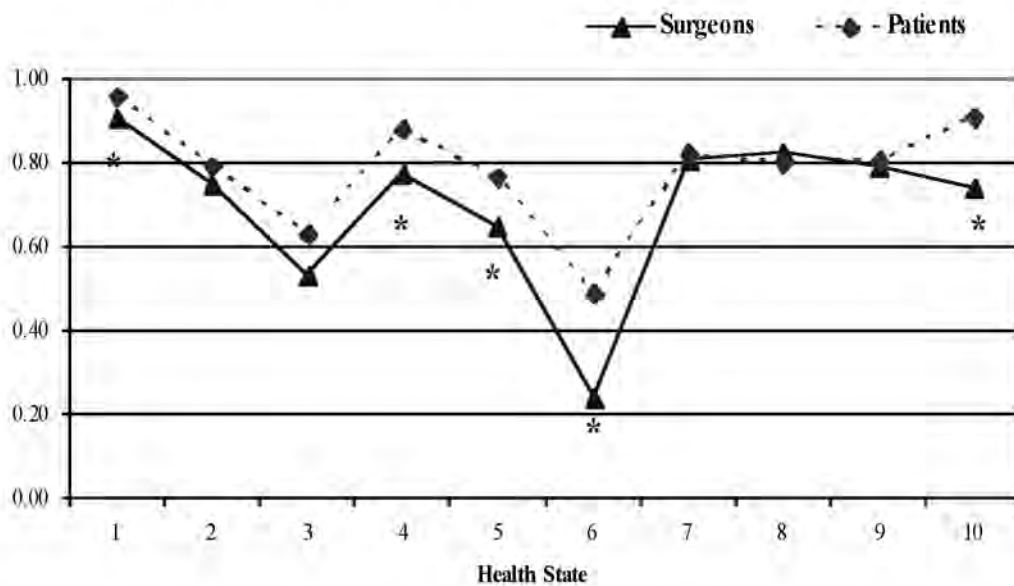
Figure 4: Comparison of mean patient and surgeon scores; statistical significance at the $p<0.05$ level is denoted by a star.

Bruce J. Sangeorzan, M.D.

Professor
Harborview Medical Center
Foot and Ankle
www.orthop.washington.edu/faculty/sangeorzan

William R. Ledoux, Ph.D., Jacynda Wheeler, B.A.,
Hannah Sutton, B.A., and Ava D. Segal, M.S.

Comparison of Function After Ankle Fusion and Ankle Replacement

- Ankle arthritis differs from that of the hip and knee in that it is most commonly caused by traumatic injury (rather than degeneration or inflammation) and predominantly affects younger males.
- Ankle fusion is a well-established treatment that can improve pain but does so at a loss of motion of the ankle. It doesn't work well when there is also arthritis in the nearby joints, because it puts extra load on these joints.
- Altered gait after ankle fusion can lead to arthritis in the surrounding small joints over time.
- The role of ankle replacement, while common in Europe, is limited in the US because of uncertainty of its effectiveness relative to ankle fusion.
- UW Medicine faculty surgeons have been treating patients with ankle replacement surgery since 1995. Initially, total ankle joint replacement was used primarily in patients who were not good candidates for fusion.
- To enable a comparison of outcomes from ankle replacement and ankle fusion we initiated a study in 2006 that compares activity and patient satisfaction after these two procedures.

Until recently, treatment options for advanced ankle arthritis have been limited to bracing, pharmacologic intervention and arthrodesis (also known as fusion). With improvements in the quality of ankle replacement implants, there has been significant interest in ankle replacement surgery and in determining in what circumstances ankle replacement may be more effective than ankle fusion for treatment of end stage ankle arthritis.

The accepted way to determine the better of two therapies is to study them blindly in a prospective fashion using the same criteria for both groups. Difficulties in studying the differences in surgical treatment outcome for ankle arthritis are numerous. Patients are reluctant to be randomized; surgeons often have ethical reservations about randomization; surgical expertise varies; different levels of function and etiology are not well defined. In 2006 we began collecting pilot data that would enable us to begin a prospective clinical trial.

Methods

We studied patients with end stage ankle arthritis who exhausted non-surgical care and were scheduled for treatment by ankle fusion or ankle replacement. Patients were included if they were between 18 and 85 years old, able to communicate, were ambulatory and had no other lower limb musculoskeletal condition that would affect gait. Part one of the pilot was to determine baseline function and factors that impact function as baseline. Since functional levels were highly variable, we felt that a small study would be unreliable without data to assess factors influencing activity levels. Two measures of baseline activity were collected: step monitors and gait analysis. We examined subjects who were scheduled to have ankle surgery. Subjects wore the StepWatch 3 Activity Monitors for 12.6 ± 2 days (collected in one-minute intervals) on their ankle (StepWatch values were multiplied by two to obtain total steps/day for both limbs as measured by pedometers). Subjects then completed five barefoot walking trials at a controlled speed (1.0 m/s). Gait biomechanics were collected using a 12-camera Vicon system and two Bertec force plates. Sagittal plane ankle range of motion (ROM), peak plantar flexor (PF) moment, and peak power absorption (ABS) and generation (GEN) were extracted. Percent difference (%DIFF) between

Figure 1: Ankle with arthritis.

the affected and unaffected limbs was calculated for each biomechanical measure to quantify limb symmetry. Subjects were separated into two groups based on average steps/day: LOW (<8000) and HIGH (>8000). Objective measures were then compared by patient age, height and weight.

In step two of the trial subjects were tested by the same objective measures of activity, step counts and gait analysis. In addition to the mechanical measures, two outcome instruments were used; the Musculoskeletal Functional Assessment (MFA) and the SF-36. The SF-36 is the most widely used tool for assessment of health status. The MFA is a functional outcome measure created and validated in a group with musculoskeletal injury. These measures were repeated at 6 months, 12 months after surgery and will be repeated annually.

The relationship between step count group and outcome was tested with 1-way ANOVA (demographics = dependent variable) and repeated measures 1-way ANOVA (%DIFF = dependent variable) with step count group as the independent factor.

Results

There was a significant difference in the mean steps/day (± one standard deviation) between the LOW and HIGH groups (5890 ± 753 and 10,808 ± 2696, respectively, p = 0.0024). The LOW step group demonstrated significantly larger limb asymmetries in three of four biomechanical variables and higher weight compared to the HIGH step group (Table 1). This result suggests that 1) increased weight is associated with reduced activity and 2) lower activity level as measured by step count is predictive of increased biomechanical asymmetries and increased weight for an ESAA population. These baseline measurements can then be used to assess post-surgical outcomes and treatment efficacy.

Twenty-six patients completed the first year of the study, thirteen in each group. Pain improved in both groups from an average of 8 on a 10-point scale to 2 on the same scale at 12 months. Neither the arthroplasty group nor the arthrodesis group had significant changes in the number of steps at 6 months or 12 months. The SF-36 is a measure of general health. At 12 months the average score on the SF 36 changed from 77 to 84 in the arthrodesis group and from 72 to 71, these changes are not significant. The MFA is a measure of health status with an accent on musculoskeletal function. Both treatment groups improved when measured by the MFA. The arthrodesis group improved 15 points (on 50 scale) while the arthroplasty group improved 11 points. There was no statistical difference between the two groups.

Conclusion

Patients with ankle arthritis have different levels of function. High weight is associated with low levels of activity, low power outputs and decreased ankle motion. Ankle arthritis can be improved by surgical treatment with ankle arthrodesis or ankle arthroplasty. At one year after treatment both groups improved in comfort and function as measured by the MFA. At one year with only 13 patients in each group there is insufficient evidence to show greater improvement in either group. The study will continue to enroll patients. It is likely that differences sufficient to guide care will not be available for more than five years. Ideally enough data will be collected to learn when each treatment is indicated.

Acknowledgement

Recommended Reading

Segal AD, Rohr ES, Sutton H, Ledoux WR, Wheeler J, Sangeorzan BJ. Low function in patients with end-stage ankle arthritis is associated with reduced power generation, ankle range of motion, and higher weight. American Orthopaedic Foot and Ankle Society, Denver, Colorado, June 25-28, 2008.

MT Pyevich, M.D., CL Saltzman, M.D., JJ. Callaghan, Fg. Alvine, M.D. Total Ankle Arthroplasty: a Unique Design. Two to Twelve-Year Follow-up. J Bone Joint Surg 80:1410-20 (1998).

A A. Spirt, MD, PhD, M Assal, MD and ST. Hansen, Jr., MD Complications and Failure After Total Ankle Arthroplasty. The Journal of Bone and Joint Surgery

Figure 2: Ankle arthroplasty.
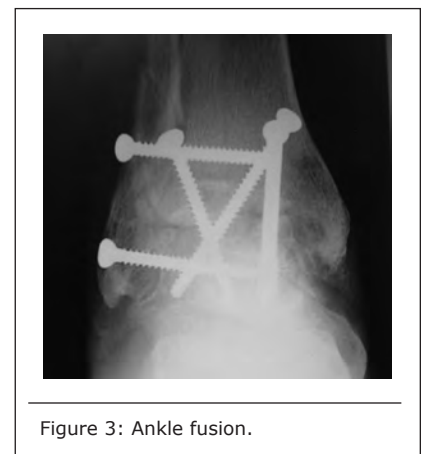
Figure 3: Ankle fusion.

	LOW step count (n=6)	HIGH step count (n =7)	p-value
Demographics			
Age (yrs)	51.0 ± 15.5	58.0 ± 10.8	0.4
Height (m)	1.72 ± 0.09	1.66 ± 0.12	0.4
Weight (kg)	104.4 ± 18.9	79.3 ± 16.3	0.03*
Gait Measures (%)			
Ankle angle ROM	34.8 ± 16.4	15.5 ± 15.2	0.029*
Peak PF moment	17.1 ± 14.0	7.9 ± 6.7	0.15
Peak power ABS	28.6 ± 20.1	2.1 ± 34.0	0.031*
Peak power GEN	49.8 ± 9.5	26.3 ± 12.7	0.0003*

Table 1: Subject demographics and gait measures (%DIFF) by step count group (mean ± one standard deviation). Statistical significance (*) set at $p < 0.05$. The low step activity group was significantly heavier than the high activity group.

(American) 86:1172-1178 (2004).

Greisberg, Justin MD*; Assal, Mathiea MD†; Flueckiger, Gerhard MD‡; Hansen, Sigvard T Jr MD Takedown of Ankle Fusion and Conversion to Total Ankle Replacement. Clinical Orthopaedics and Related Research:Volume 424July 2004pp 80-88.

JM Mazur, E Schwartz and SR Simon Ankle arthrodesis. Long-term follow-up with gait analysis The Journal of Bone and Joint Surgery, Vol 61, Issue 7 964-975, 1979.

Peter R. Cavanagh, Ph.D.

Professor
University of Washington Medical Center
Research
www.orthop.washington.edu/faculty/cavanagh

Ahmet Erdemir, Ph.D., Marc Petre, Ph.D.,
Sachin Budhabhatti, Ph.D.,
and Snehal Chockandre, B.S.

Finite Element Models of Footwear for People with Diabetes

- Injury to the feet of people with diabetes and neuropathy results from unperceived elevated mechanical stress.
- Once foot injuries, such as ulcers, are healed, appropriate therapeutic footwear is critical to prevent ulcer recurrence.
- Footwear design is still largely a trial-and-error process.
- In order to determine general footwear design principles, modeling offers tremendous potential since it allows exploration of a large range of conditions.
- The Finite Element Method (FEM) is a technique to model objects that can have complex shape and/or deformation characteristics by filling in the geometry with small, numerically manageable, simply shaped elements.
- Linear models are often adequate for bone but non-linear models are required to adequately describe the large deformation of soft tissues and most synthetic polymers used in footwear.
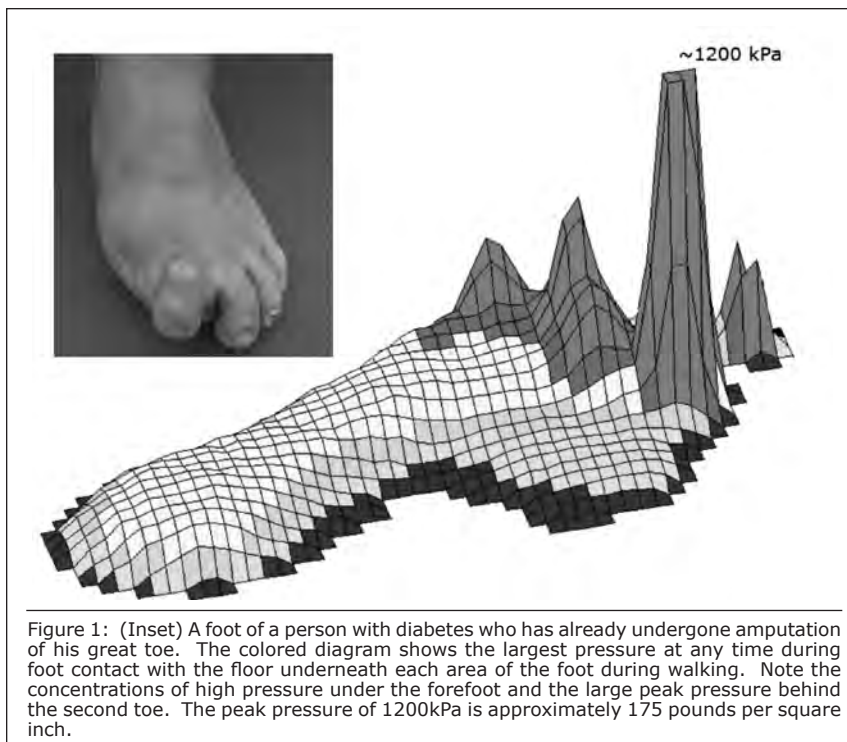- Nonlinear analysis also allows the simulation of complex interactions between two surfaces, which can be modeled using "contact" interfaces to represent friction, and mechanical interaction between foot and footwear.
- Relatively simple 2-dimensional models can provide useful insight. For example, the advantage of molded insoles in pressure reduction at the heel can be demonstrated.
- More complex 3-dimensional models are being developed to account for the varying geometries of individual feet and for footwear options aimed at pressure relief by redistributing the plantar loads.
- The measurement of pressure between the foot and the shoe can be helpful in individual cases to see if design objectives have been achieved.
- To facilitate building patient-specific models, rapid methods of mesh generation need to be developed, and for patient-specific simulations, advanced computational techniques need to be employed.

Diabetes is the leading cause of non-traumatic lower-extremity amputation. The pathway to amputation often starts with a wound on the plantar surface of the foot that is unperceived because of loss of peripheral sensation secondary to diabetic symmetrical distal polyneuropathy. An ulcer is particularly likely if, in addition to loss of sensation, the individual has foot deformity which leads to a concentration of pressure under localized areas (see Figure 1).

A break in the skin which penetrates to the deep fascia is called an ulcer. Such ulcers can become infected and, in the presence of vascular disease and/or continued weight-bearing, can be difficult to heal. However, a foot ulcer in a well-perfused limb can be healed relatively quickly (in 6-10 weeks) with appropriate treatment that include off-loading of the damaged tissue. This highlights the role of mechanical stress in the causation and healing of plantar foot ulcers. Ulcer recurrence

after healing is extremely common with some authorities reporting up to 100% recurrence in 4 years.

The design and prescription of footwear for neuropathic diabetic patients who are at-risk for foot injury offers the potential to prevent ulceration and re-ulceration of the foot. Footwear must be designed to reduce the high peaks of pressure seen in Figure 1 without adding additional stress to other vulnerable regions of the foot. But the design of footwear is

Figure 1: (Inset) A foot of a person with diabetes who has already undergone amputation of his great toe. The colored diagram shows the largest pressure at any time during foot contact with the floor underneath each area of the foot during walking. Note the concentrations of high pressure under the forefoot and the large peak pressure behind the second toe. The peak pressure of 1200kPa is approximately 175 pounds per square inch.
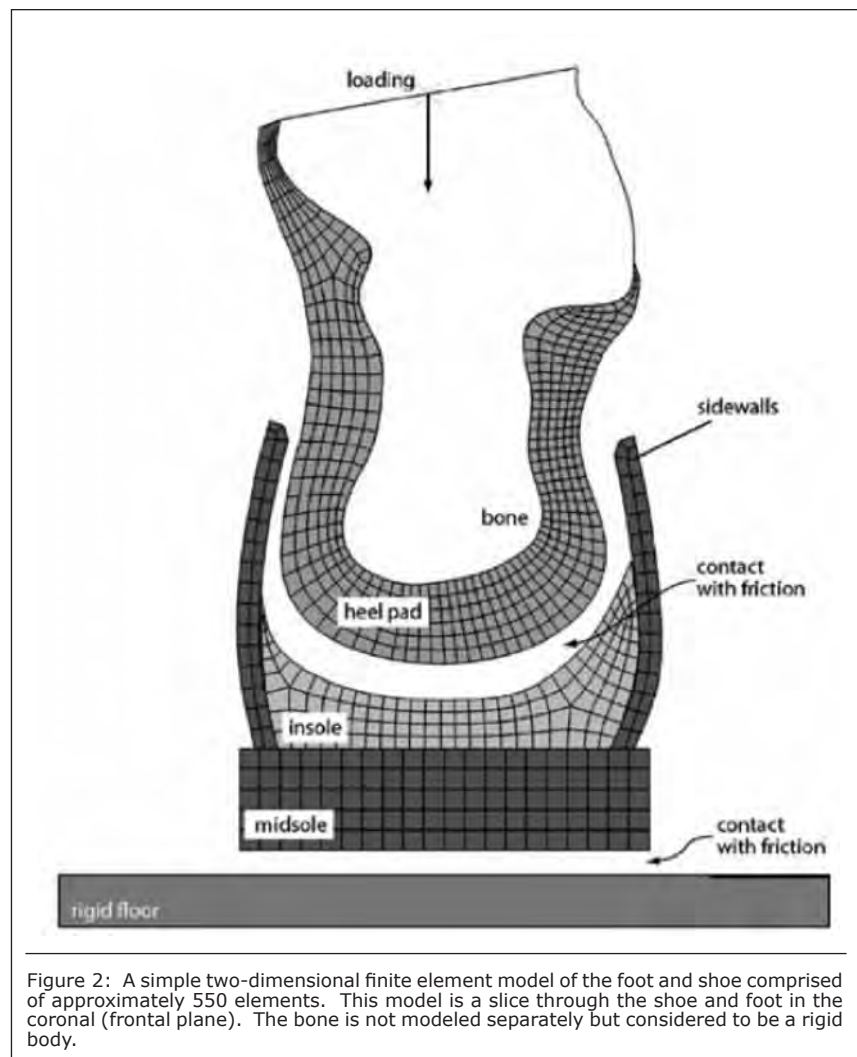
undergo large deformations, they exhibit nearly incompressible nonlinear deformation characteristics, and for footwear simulations, they interact with complex engineered materials, e.g. elastomeric foams. Since friction inside the shoe likely causes injury and is instrumental for the transfer of loads between the foot and its environment, tissue contacts with the ground or with footwear need to be modeled as frictional interfaces. Adding these characteristics to a model increases complexity and therefore solution time. Solution times for large models of the foot can be up to several days even on a very fast, multi-processor computer.

However, even simple two-dimensional models with only a few hundred elements can provide insightful results. Figure 2 shows an example of such a model of the rearfoot inside a shoe. This single slice model taken in the coronal (frontal) plane was solved

largely a trial-and-error process with little theoretical background and almost no measurement beside foot size and shape at the time of prescription.

Over a number of years our research team has worked to fill this void by building engineering models of feet and footwear using a technique called the finite element method. In this approach, large irregular complex structures (such as the foot) can be modeled as an assembly of many small regular elements, such as triangles or rectangles in two-dimensional models or tiny pyramidal or brick-shaped blocks, called tetrahedrons and hexahedrons respectively, in three-dimensional models. Each small element is ascribed a material property (which is different for the various structures such as bone, soft tissue, and footwear materials) and boundary conditions (such as external forces and contact with adjacent structures). Typical foot models can contain over 50,000 elements. Using a powerful computer, the stress and strain in each element can be calculated and the interactions between elements can be simulated.

Finite element models have been widely used in orthopaedics to model stresses in bone. Modeling of the foot is somewhat more complex than modeling a bone such as the femur because the soft tissues of the foot

Figure 2: A simple two-dimensional finite element model of the foot and shoe comprised of approximately 550 elements. This model is a slice through the shoe and foot in the coronal (frontal plane). The bone is not modeled separately but considered to be a rigid body.
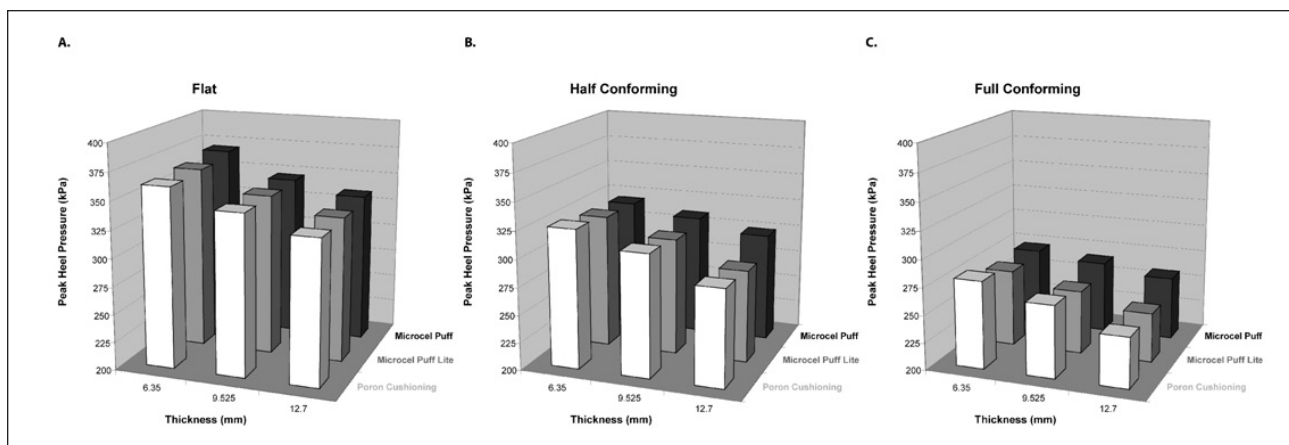
Figure 3: Predicted peak pressures (vertical axis) at maximal loading of the heel during walking while using a variety of insole designs. By providing conforming designs and increasing the thickness of the insoles (horizontal axis), pressures were reduced substantially; insole material properties (front to back axis), on the other hand, did not have a noticeable influence on pressure reduction. All three sets of results are drawn to the same scale.

using what is known as a plane strain formulation, in which out-of plane strains (perpendicular to the page in Figure 1) are assumed to be zero. This model was comprised of approximately 550 elements. The bones of the foot and ankle are not modeled separately but considered to be a single rigid body. One of the great advantages of finite element modeling is that the geometry of the model and its material properties can be changed at will to run "virtual experiments" that would not be feasible to conduct on human subjects.

For example, in the current model the conformity of the insole (flat, half-conforming, completely conforming), and its thickness and stiffness (from 6 - 12mm and from soft to hard, respectively) were varied to explore the influence of these factors on the predicted pressure between the foot and the shoe. Figure 3, which shows the results from 27 different simulations, illustrates the dominant effect of insole conformity and the secondary effect of thickness in reducing heel pressure. In comparison to these effects, the use

of different insole materials did not markedly affect heel pressure. Such insight is extremely useful to the shoe designer and represents a building block in the provision of evidence-based rules for therapeutic shoe design. Decreased computational cost of these simpler models also allows full design optimization studies, where an insole property (such as deformation characteristics) can be calculated to minimize peak contact pressure. Such analysis can stimulate novel insole material design and manufacturing practices.

A more complex three-dimensional model is shown in Figure 4. This forefoot model contains about 40,000 elements and was based on MRI studies of the foot of an individual for whom pressure data during walking (such as that shown in Figure 1) were available. The model was used to investigate the effects of metatarsal pads on relief of pressure at the metatarsal heads. This is a common intervention and the simulation results showed that its effectiveness is highly sensitive to small changes in placement. Model predictions can be validated by actual measurements of the pressure inside the shoes containing the same interventions that have been examined in the model.

We are also building models of the entire foot containing more than 80,000 elements but such models force us to confront a major limitation of this approach: the models take quite long to build and to perfect for robust foot and footwear simulations; the time involved can approach several months of a full-time engineer for a single foot.

★ - Metatarso-Phalangeal joint
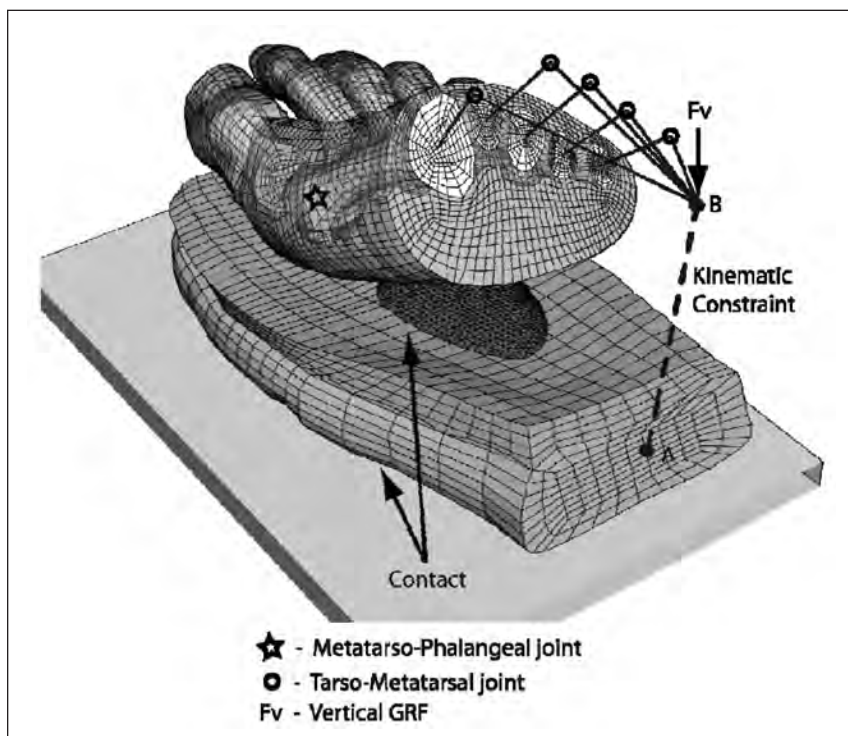O - Tarso-Metatarsal joint
Fv - Vertical GRF

Figure 4: A three-dimensional model of the forefoot interacting with footwear containing about 40,000 elements. This model was used to investigate the effects of metatarsal pads on relief of pressure at the metatarsal heads.

Therefore, fully individualized patient-specific solutions are not realistic. One way to overcome this limitation is to "morph" standard meshes into the shape of another patient's foot. We have made some promising steps in this direction and believe that patient-specific models may be within reach in the near future.

In summary, modeling has the potential to provide guidance for the practitioner in the complex task of preventing foot ulcers and their recurrence in people with diabetic neuropathy. Models of typical feet and frequently used interventions will provide general principles of footwear design while morphing "stock" models to resemble specific feet may allow more evidence-based management of complex individual patients.

Disclosure

The author has an equity interest in DIApedia LLC, a company that is the recipient of NIH grants to develop footwear solutions for diabetic patients. He is also an inventor on US patents 6,610,897, 6,720,470, and 7,206,718, which elucidate a load relieving dressing and a method of insole manufacture for offloading.

Recommended Reading

Budhabhatti SP, Erdemir A, Petre M, Sferra J, Donley B, Cavanagh PR. Finite element modeling of the first ray of the foot: a tool for the design of interventions. J Biomech Eng. 2007 Oct;129(5):750-6.

Bus SA, Valk GD, van Deursen RW, Armstrong DG, Caravaggi C, Hlavácek P, Bakker K, Cavanagh PR. The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review.Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S162-80. Review.

Cavanagh PR, Lipsky BA, Bradbury AW, Botek G. Treatment for diabetic foot ulcers. Lancet. 2005 Nov 12;366(9498):1725-35.

Goske S, Erdemir A, Petre M, Budhabhatti S, Cavanagh PR. Reduction of plantar heel pressures: Insole design using finite element analysis. J Biomech. 2006;39(13):2363-70.

Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. Diabetes Care. 1990 May;13(5):513-21.

Pound N, Chipchase S, Treece K, Game F, Jeffcoate W. Ulcer-free survival following management of foot ulcers in diabetes. Diabet Med. 2005 Oct;22(10):1306-9.

Lewis G. Zirkle, M.D.

Founder and President
Surgical Implant Generation Network
Northwest Orthopaedic and Sports Medicine
www.sign-post.org

Allan F. Tencer, Ph.D.

Professor
Harborview Medical Center
Research
www.orthop.washington.edu/faculty/tencer

Surgical Implant Generation Network (SIGN)
"Working Worldwide to Bridge the Gaps in Fracture Care"
How a Small, Nongovernmental Organization Without Foundation Grants or Government Funding Can Make a Big Difference

- The poor are in danger from disasters, conflicts, and road traffic accidents, 89% of which occur in developing countries. 50 million people are injured in traffic accidents each year.
- Accident victims without surgical care spend months in crowded wards while their families who depend on them anxiously wait.
- SIGN designs, manufactures, and ships fracture implants and trains surgeons in developing countries to use them effectively and to track their results.
- Extending the regenerative power of modern fracture care enables patients in these countries to get out of bed, walk, heal, and work.

The origins of SIGN go back to 1968 when Lewis G. Zirkle, Jr., M.D., served as an army orthopaedic surgeon in Vietnam. During his tour of duty, he spent much of his spare time treating Vietnamese civilians, as civilian medicine had all but ceased to exist during the war. Over the next three decades, Dr. Zirkle made numerous trips to Vietnam and other developing nations to assist local health care providers in devising more effective and successful surgical techniques for treating fractures. In the 1980s, he invested a great deal of time and effort in training surgeons in Indonesia, and establishing four teaching centers. Through his efforts, the number of trained orthopaedic surgeons in that country grew from one to more than 50.

Some years later, on his return to Indonesia, he found surgeons with great skills who were eager to learn and apply new techniques. However, they could not carry out modern fracture care because the necessary implants

Figure 1: Dr. Lewis G. Zirkle Jr., left, with an Afghanistan surgeon and the first patient to receive the SIGN Hip Construct.

Figure 2: It is common to have two operations going on at the same time in operating rooms in the developing world.

Figure 3: Residents in Afghanistan learning the SIGN technique for hip fixation. Dr. Zirkle is on the far right.

to fix fractures were not available. Patients lay in traction as long as three years before their fractured femur healed because intramedullary nails and interlocking screws were not available to them.

In response, Dr. Zirkle created SIGN to implement a comprehensive fracture care system that combined the provision of implants with training in their use. In important contrast to the systems in widespread use in the U.S. the SIGN implants were designed for use in hospitals where real time imaging and power equipment are not available. Dr. Zirkle along with Randy Huebner and others developed the SIGN nail, a target arm for the proximal interlocking screw and a slot finder for the distal interlocking screw – a technique that did not require fluoroscopy.

The craft of surgery must be learned differently when real time imaging and electricity are not available in operating rooms. Dr. Zirkle teaches surgeons to develop their tactile senses instead. This involves focusing on the far end of the instrument, for example when using a hand reamer the surgeon imagines being at the end of the reamer to judge whether it is in the canal of the bone by feeling the circumferential pressure on the reamer. Similarly, drilling, insertion of the SIGN nail and finding the interlock all involve the tactile senses rather than depending on an image on a fluoroscopy screen.

Now SIGN has more than 156 programs in 52 countries throughout the developing world. More than 3000 SIGN surgeons use the SIGN system to repair fractures from road traffic accidents. Since 1999 more than 45,000 patients have been treated with the SIGN system. Evaluation of these results is critical to the SIGN program so that we can learn from our experience as designers, teachers and surgeons.

Each SIGN program has an individual database, which surgeons can consult to recall solutions to similar problems that they might encounter in an upcoming operation. A central SIGN database allows us to collate results of different aspects of a procedure to find conclusions, for example how can a straight nail be best used in a curved femur and what is the best bony entrance point for the nail. We are particularly interested in discovering factors associated with complications, such as infections and non-unions. Many of the best ideas come from surgeons in developing countries who have a very large experience with these implants.

With the intramedullary nail and interlocking screw project well underway, SIGN is taking on a new challenge. In Afghanistan, fractured hips are treated with traction for three weeks and then a body cast. Dr. Zirkle traveled there in January 2008 and later in November, both times of the year when the temperature is below freezing. Can you imagine being placed

in a body cast and sent to a cold home where electricity is present only four hours per day? The SIGN team has worked to develop a hip fixation device that can be implanted without use of fluoroscopy. Our goal is to design an implant that would treat stable and unstable fractures. We have been joined by Dave Shearer, a graduate of MIT with a degree in mechanical engineering and a recent graduate of the University of Washington medical school, by Justin Roth, an engineer who is now in medical school in Los Angeles, and by Amy Johnson, an engineer at Pacific Research Laboratories. Along with Paul LaBarre they obtained a grant from The Program for Appropriate Technology in Health (PATH) to test the SIGN Hip Construct (SHC). Fortunately, one of the renowned experts in biomechanical engineering at the University of Washington, Dr. Allan Tencer, Ph.D., agreed to work with us. We met one morning in his lab and the project was underway. Dr. Zirkle implanted the first SHC in Afghanistan in November 2008 and two days later he helped the patient get back on his feet. The story continues…

   If you would like to keep current on our attempts to extend modern fracture care to the peoples of the world, please visit http://www.sign-post.org/.

Graduating Residents

Jason King, M.D.

Following residency, Jason will complete a sports medicine fellowship at Kerlan-Jobe Orthopaedic Clinic in Los Angeles. He will return to Seattle and begin private practice at Orthopedic Physician Associates. Jason likes to spend time with his wife, Jennie, and their two sons, Addison and Griffin, playing soccer, going to the beach and playing in the park.

Raj Maheshwari, M.D.

Following residency, Raj will pursue a one-year fellowship in hand and upper extremity surgery at Stanford University. She plans to practice orthopaedics on the west coast, and hopes to spend her free time traveling, reading, cooking, running, and enjoying the company of friends and family.

Annie Links, M.D.

This August, Annie Links will begin her upper extremity fellowship at Harvard's Brigham and Women's Hospital in Boston. Annie and her husband Kyle and baby boy plan to return to the Pacific Northwest after her fellowship.

Soren Olson, M.D.

After graduation Soren will spend a year as a sports medicine fellow in Taos, New Mexico, and the following year he is planning to return to Seattle as a Trauma fellow at Harborview. His eventual plans including pursuing an academic position but he has no definitive destination at this time.

Graduating Residents

Karen Perser, M.D.

After residency, Karen will complete a year of Sports Medicine Fellowship at the State University of New York at Buffalo. Afterwards she will return to the Pacific Northwest or Mountain West region and practice general orthopaedics. In her free time she enjoys traveling, camping, skiing, playing flag football, hiking and mountain biking.

Addison Stone, M.D.

Addison Stone will begin his Spine Fellowship at the SpineCare Medical Group in San Francisco, CA. He enjoys skiing, biking, camping, and woodworking. After fellowship he plans to start his career in private practice on the west coast.

Scott Ruhlman, M.D.

Scott is looking forward to an upcoming hand and upper extremity fellowship in Boston, MA at the Brigham and Womens Hand and Upper Extremity Fellowship. Scott is happily married to Mary Ruhlman and enjoys their son, Sam Ruhlman. After fellowship, Scott plans on working in private practice in the Seattle area, where both he and his wife were raised.

Jason Wilcox, M.D.

Jason will complete a fellowship in Sports Medicine at the University of Utah in Salt Lake City. Following the year in Salt Lake City, he will return to the Seattle area to begin practice.

Incoming Residents

Kyle Chun

Kyle Chun was born and raised in Wahiawa, Hawaii. He attended medical school at the University of Hawaii. Within orthopaedics, his interests include trauma outcomes, physiology, cartilage biology, and sports medicine. Outside of orthopaedics, he enjoys spending time with his wife and family, hunting the outer islands, fishing on his family's boat, and playing music.

Andrew Ghatan

Andrew is from San Marino, California. He attended medical school at the University of Southern California. In orthopaedics he is most interested in tumors and trauma. Away from work he spends his spare time hiking, fishing, camping, playing tennis, eating good food and spending time with family and friends.

Liz Dailey

Liz is from Moline, Illinois. She attended medical school at the University of Illinois at Chicago. Liz spends her time away from orthopaedics hiking, ultimate frisbee, cooking, baking, skiing, and snowboarding.

Brian Gilmer

Brian was born and raised in Sugar Land, Texas. For medical school, he attended the University of Texas at Galveston. He is most interested in shoulder and elbow, tomors, and trauma in orthopaedics. In his free time he likes being outdoors, fishing & hunting, playing ultimate frisbee, and writing & reading.

Incoming Residents

Jennifer Hagen

Jennifer Hagen is from Las Vegas, Nevada. She attended Case Western Reserve University for medical school. In her free time, she likes to travel, read, and hike.

David Patterson

David is from Sacramento, California and went to medical school at the University of Southern California. He is most interested in regenerative medicine, stem cells, and molecular biology of orthopaedics. For recreation, he enjoys food, wine, fresh air, the tv show The Office, and following sports of the Pac-10.

Mark Miller

Mark Miller is from Prosser, Washington. He attended Harvard Medical School. His orthopaedic interests include pediatrics and tissue engineering. In his spare time, he enjoys golf, tennis, and running.

Emily Squyer

Emily is from Nemo, South Dakota. She attended Penn State College of Medicine. Her areas of clinical and research interest include trauma and international health care. She enjoys running, cross-country & downhill skiing, and belting broadway showtunes in the car/shower.

ACEs

Foot/Ankle

Jeffrey A. Henning, M.D.

Alan J. Laing, MBBCh

Eric J. Novak, M.D.

Spine

Mark A. Freeborn, M.D.

Christopher R. Howe, M.D.

Trauma

Afshin Calafi, M.D.

Medardo R. Maroto, M.D.

Saam Morshed, M.D.

Chinedu Chuka Nwosa, M.D.

Frederick P. Oldenburg, M.D.

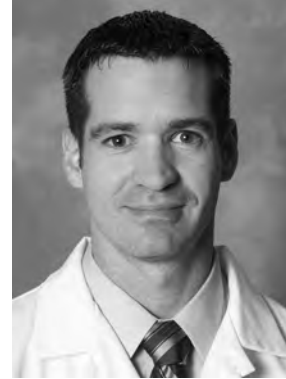Robert J. Orec, MB ChB

ACEs

SHOULDER/ELBOW

ONCOLOGY

Deana M. Mercer, M.D.

Matthew D. Saltzman, M.D.

Thomas J. Scharschmidt, M.D.

Fellows

HAND

Kane L. Anderson, M.D.

John P. Howlett, M.D.

Michael Mulligan, M.D.

Harris S. Rose, M.D.

Research Grants

National Institutes of Health (NIH)

Aging-Related Degradation in Bone
Mechanotransduction
Sundar Srinivasan, Ph.D.
Ted S. Gross, Ph.D.

Changes in the Characteristics of Plantar Soft Tissue
with Diabetes
Bruce J. Sangeorzan, M.D.

Collagens of Cartilage and the Intervertebral Disc
David R. Eyre, Ph.D.

Collagen Cross-Linking in Skeletal Aging and Diseases
David R. Eyre, Ph.D.

Collagen Type II/IX/XI Heteropolymer Assembly
Russell J. Fernandes, Ph.D.

Design Criteria for Therapeutic Footwear in Diabetes
Peter R. Cavanagh, Ph.D., D.Sc.

Disuse Induced Osteocyte Hypoxia
Ted S. Gross, Ph.D.
Steven D. Bain, Ph.D.
Sundar Srinivasan, Ph.D.

Predicting Bone Formation Induced by Mechanical
Loading Using Agent Based Models
Sundar Srinivasan, Ph.D.

Skeletal Dysplasias
David R. Eyre, Ph.D.
Russell J. Fernandes, Ph.D.

National Aeronautics and Space Administration

A Novel Bedrest Analog of Lunar Exploration
Peter R. Cavanagh, Ph.D. D.Sc

A Quantitative Test of On-Orbit Exercise
Countermeasures for Bone Demineralization Using a
Bedrest Analog
Peter R. Cavanagh, Ph.D. D.Sc

National Space Biomedical Research Institute

Monitoring Bone Health by Daily Load Stimulus
Measurement During Lunar Missions
Peter R. Cavanagh, Ph.D. D.Sc

An Integrated Musculoskeletal Countermeasure
Battery for Long-Duration Lunar Mission
Peter R. Cavanagh, Ph.D. D.Sc

A Quantitative Test of On-Orbit Exercise
Countermeasures for Bone Demineralization Using a
Bedrest Analog
Peter R. Cavanagh, Ph.D. D.Sc

Extent, Causes, and Counter measures of Impaired
Fracture Healing in Hypogravity
Peter R. Cavanagh, Ph.D. D.Sc

Veterans Affairs Rehabilitation Research and Development Service

Ewing's Sarcoma Fusion Proteins and mRNA Splicing
Factors
Howard A. Chansky, M.D.

Reducing Internal Stresses in Deformed Diabetic Feet
Bruce J. Sangeorzan, M.D.

Surgically Reestablishing Foot Shape in Severely
Deformed Flatfeet
Bruce J. Sangeorzan, M.D.

Treatment Outcomes for Ankle Arthritis
Bruce J. Sangeorzan, M.D.

VA Center of Excellence in Amputation Prevention and
Prosthetic Engineering
Bruce J. Sangeorzan, M.D.

VA Merit Review Functional Analysis of EWS/FLI-1
Howard A. Chansky, M.D.

A.O. North America

An Observational Study Assessment of Surgical
Techniques for Treating Cervical Spondylotic
Myelopathy (CSM)
Jens R. Chapman, M.D.

An Observational Study Comparing Surgical to
Conservative Management in the Treatment of Type II
Odontoid Fractures Among the Elderly
Jens R. Chapman, M.D.

AO North America Orthopaedic Trauma Fellowship
Bruce J. Sangeorzan, M.D.

AO Spine North America Fellowship
Carlos Bellabarba, M.D.

Anatomical and Radiographic Description of the
Starting Point for Antegrade Intramedullary Humeral
Nailing
James C. Krieg, M.D.

Research Grants

Reliability of a Percutaneous Approach to Hip Capsulotomy
Lisa A. Taitsman, M.D.
Aric A. Christal, M.D.

Bayer AG

A Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel Design, 2-Arm Study to Investigate the Effect of Aprotinin On Transfusion Requirements in Patients Undergoing Elective Spinal Fusion Surgery
Jens R. Chapman, M.D.

BioAxone Therapeutique, Inc.

Cethrin Trial
Jens R. Chapman, M.D.

Boston Medical Center

Intramedullary Nails versus Plate Fixation Re-Evaluation Study in Proximal Tibia Fractures: A Multi-Center Randomized Trail Comparing Nails and Platel Fixation
Robert P. Dunbar, M.D.

Christopher Reeve Paralysis Foundation

Using Muscle Stimulation to Mitigate Bone Loss due to Muscle Paralysis
Ted S. Gross, Ph.D.

Depuy Spine, Inc.

Kyphosis Correction From Combined Smith Peterson Osteotomy and an Interbody Strut
Michael J. Lee, M.D.

Clinical Spine Fellowship Grant
Theodore A. Wagner, M.D.

Integra Lifesciences Corporation

Comparison of Bioabsorable Tubes for Repair of Nerve Injury
Thomas E. Trumble, M.D.

Defense Advanced Research Projects Agency

Phase II: Digit Regeneration in Mammals
Christopher H. Allan, M.D.

MDS Pharma Services, Inc.

Construction of an Controlled Femur Fracture Device
Steven D. Bain, Ph.D.

MPI Research, Inc.

Construction of an Controlled Femur Fracture Device
Steven D. Bain, Ph.D.

National Science Foundation

University of Washington Engineered Biomaterials
Paul A. Manner, M.D.

Orthopaedic Research and Education Foundation (OREF)

Clinical Efficacy and Cost Implications of Acute BMP-2
David P. Barei, M.D.

Perioperative Economic Analysis of Minimally Invasive Versus Traditional Total Knee Arthroplasty.
Seth S. Leopold, M.D.

Orthopaedic Trauma Association

The Effect of Obesity on Outcomes Among Trauma Patients with Lower Extremity Orthopaedic Injuries
Sean E. Nork, M.D.
Rajshri Maheshwari, M.D.

The Role of Muscle Function in Fracture Healing
Sean E. Nork, M.D.
Scott D. Ruhlman, M.D.
Ted S. Gross, Ph.D.

Ostex International, Inc.

Molecular Markers of Connective Tissue Degradation
David R. Eyre, Ph.D.

Research Grants

Paradigm Spine LLC

A Muti-Center, Prospective, Randomized, Clinical Trial Comparing Stabilization with Coflex vs. Pedicle Screw Fixation and Fusion after Decompression for at Least Moderate Lumbar Spinal Stenosis
Jens R. Chapman, M.D.

Smith & Nephew, Inc.

University of Washington Arthroscopy, Research and Training (ART) Lab
Christopher J. Wahl, M.D.

Synthes

PRODISC-C Versus Anterior Cervical Discectomy and Fusion (ACDF)
Jens R. Chapman, M.D.
Steven D. Bain, Ph.D.
Ted S. Gross, Ph.D.

Spine End-Results Research Fund
Frederick A. Matsen III, M.D.

The Role of Muscle Function in Fracture Healing: Development of a Translational Model
Sean E. Nork, M.D.
Steven D. Bain, Ph.D.
Ted S. Gross, Ph.D.

The Boeing Company

Randomized Clinical Trial of Open versus Endoscopic Carpal Tunnel Release and Hand Therapy Comparing Patient Satisfaction. Functional Outcome and Cost Effectiveness
Thomas E. Trumble, M.D.

US Army Research Office

UW Team-Advance on Single Nuclear Detection and Atomic-Scale Imaging
John A. Sidles, Ph.D.

US Department of Education

Advancing Orthotic and Prosthetic Care Through Research, Standards of Practice and Outreach
Douglas G. Smith, M.D.

Department Publications 2008-2009

1. Aminian A, Howe CR, Sangeorzan BJ, Benirschke SK, Nork SE, Barei DP. Ipsilateral talar and calcaneal fractures: a retrospective review of complications and sequelae. Injury 2009;40(2):139-45.

2. Baldridge D, Schwarze U, Morello R, Lennington J, Bertin TK, Pace JM, Pepin MG, Weis MA, Eyre DR, Walsh J, Lambert D, Green A, Robinson H, Michelson M, Houge G, Lindman C, Martin J, Ward J, Lemyre E, Mitchell JJ, Krakow D, Rimoin DL, Cohn DH, Byers PH, Lee B. CRTAP and LEPRE1 mutations in recessive osteogenesis imperfecta. Hum. Mutat. 2008; 29(12):1435-1442.

3. Barei DP, Nork SE. Fractures of the tibial plafond. Foot Ankle Clin 2008;13(4):571-91.

4. Barei DP, O'Mara TJ, Taitsman LA, Dunbar RP, Nork SE. Frequency and fracture morphology of the posteromedial fragment in bicondylar tibial plateau fracture patterns. J Orthop Trauma 2008;22(3):176-82.

5. Barei DP, Taitsman LA, Beingessner DM, Dunbar RP, Nork SE. Open Diaphyseal Long Bone Fractures: A Reduction Method Using Devitalized or Extruded Osseous Fragments. Current Orthopedic Practice. 19(1):574-8, 2008.

6. Bigliani LU, Cofield RH, Flatow EL, Fukuda HA, Hawkins RJ, Matsen FA, Morrison DS, Rockwood CA Jr, Warren RF. Charles Neer: on the giant of the shoulder. J Shoulder Elbow Surg 2009;18(3):333-8.

7. Birmingham P, Helm JM, Manner PA, Tuan RS. Simulated joint infection assessment by rapid detection of live bacteria with real-time reverse transcription polymerase chain reaction. J Bone Joint Surg Am 2008;90(3):602-608.

8. Bransford R, Falicov A, Nguyen Q, Chapman J. "The C1 Lateral Mass Sagittal Split Fracture: An Unstable Jefferson Fracture Variant" Journal of Neurosurgery: Spine, May 2009, 10(5): 466-473.

9. Bransford RJ, Chansky HA. "Trochanteric Cable Migration Through The Perineum – A Case Report" European Journal of Orthopaedic Surgery and Traumatology. January 2009; 19(1):39-41.

10. Brennan ML, Taitsman LA, Barei DP, Puttler E, Nork SE. Shortening osteotomy and compression plating for atrophic humeral nonunions: surgical technique. J Orthop Trauma 2008;22(9):643-7.

11. Bus SA, Valk GD, van Deursen RW, Armstrong DG, Caravaggi C, Hlavácek P, Bakker K, Cavanagh PR. The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S162-80. Review.

12. Bus SA, Valk GD, van Deursen RW, Armstrong DG, Caravaggi C, Hlavácek P, Bakker K, Cavanagh PR. Specific guidelines on footwear and offloading. Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S192-3.

13. Bushnell BD, May R, Campion ER, Schmale GA, Henderson RC. Hemiepiphyseodesis for late-onset tibia vara. J Pediatr Orthop 2009;29(3):285-9.

14. Chapman JR, Agel J, Jurkovich GJ, Bellabarba C. Thoracolumbar flexion-distraction injuries: associated morbidity and neurological outcomes. Spine 2008;33(6):648-57.

15. Chebli C, Huber P, Watling J, Bertelsen A, Bicknell RT, Matsen FA. Factors affecting fixation of the glenoid component of a reverse total shoulder prothesis. J Shoulder Elbow Surg 2008;17(2):323-7.

16. Clinton J, Franta A, Polissar NL, Neradilek B, Mounce D, Fink HA, Schousboe JT, Matsen FA. Proximal humeral fracture as a risk factor for subsequent hip fractures. J Bone Joint Surg Am 2009;91(3):503-11.

17. Conrad E, Burford N, McDonald R, Ferguson MJ. Coordination of arsine ligands as a general synthetic approach to rare examples of arsenic-antimony and arsenic-bismuth bonds. J Am Chem Soc 2009;131(14):5066-5067.

18. Dahl MC, Ananthakrishnan D, Nicandri G, Chapman JR, Ching RP. Helmet and Shoulder Pad Removal in Football Players with Unstable Cervical Spine Injuries. Journal of Applied Biomechanics. 2009, 25, 119-132

19. Daines SB, Rohr ES, Pace AP, Fassbind MJ, Sangeorzan BJ, Ledoux WR. Cadaveric simulation of a pes cavus foot. Foot Ankle Int 2009;30(1):44-50.

20. Dunbar RP, Barei DP, Kubiak EN, Nork SE, Henley MB. Early limited internal fixation of diaphyseal extensions in select pilon fractures: upgrading AO/OTA type C fractures to AO/OTA type B. J Orthop Trauma 2008;22(6):426-9.

21. Dunbar RP, Gardner MJ, Cunningham B, Routt ML. Sciatic nerve entrapment in associated both-column acetabular fractures: a report of 2 cases and review of the literature. J Orthop Trauma 2009;23(1):80-3.

22.   Eyre DR, Weis MA. The Helix-II epitope: a cautionary tale from a cartilage biomarker based on an invalid collagen sequence. Osteoarthritis Cartilage 2009;17(4):423-6.

23.   Eyre DR, Weis MA, Wu JJ. Advances in collagen cross-link analysis. Methods 2008;45(1):65-74.

24.   Fehlings MG, Theodore N, Harrop J, Maurais G, Kuntz 4th C, Shaffrey CI, Kwon BK, Chapman JR, Yee A, Tighe A, Hurtt MR, Flint SM, Haynes BA, McKerracher L: A phase I/IIa clinical trial of recombinant Rho protein antagonist in spinal cord injury. Submitted to Nature: Medicine March 2009.

25.   Gardner MJ, Farrell ED, Nork SE, Segina DN, Routt ML. Percutaneous placement of iliosacral screws without electrodiagnostic monitoring. J Trauma 2009; 66: 1411-15.

26.   Gardner MJ, Mehta S, Barei DP, Nork SE. Treatment protocol for open AO/OTA type C3 pilon fractures with segmental bone loss. J Orthop Trauma 2008;22(7):451-7.

27.   Gardner MJ, Nork SE, Barei DP, Kramer PA, Sangeorzan BJ, Benirschke SK. Secondary soft tissue compromise in tongue-type calcaneus fractures. J Orthop Trauma 2008;22(7):439-45.

28.   Gardner MJ, Nork SE, Huber P, Krieg JC. Stiffness modulation of locking plate constructs using near cortical slotted holes: a preliminary study. J Orthop Trauma 2009;23(4):281-7.

29.   Giunta C, Elçioglu N, Albrecht B, Eich G, Chambaz C, Janecke AR, Yeowell H, Weis MA, Eyre D, Kraenzlin M, Steinmann B. Spondylocheiro dysplastic form of the Ehlers-Danlos syndrome – An autosomal-recessive entity caused by mutations in the zinc transporter gene SLC39A13. Am. J. Hum. Genet. 2008; 82(6), 1290-1305.

30.   Goldberg M. Acts of Loving Kindness. J Child Orthop 2008;2: 247-249.

31.   Gu NY, Wolf C, Leopold S, Manner PA, Doctor JN. A Comparison of Physician and Patient Time Trade-Offs for Postoperative Hip Outcomes. Value Health 2008.

32.   Han M, Yang X, Lee J, Allan CH, Muneoka K. Development and regeneration of the neonatal digit tip in mice. Dev Biol 2008;315(1):125-35.

33.   Howard JL, Agel J, Barei DP, Benirschke SK, Nork SE. A prospective study evaluating incision placement and wound healing for tibial plafond fractures. J Orthop Trauma 2008;22(5):299-305.

34.   Howe C, Huber P, Wolf FM, Matsen FA. Differential suture loading in an experimental rotator cuff repair. Am J Sports Med 2009;37(2):324-9.

35.   Howlett JP, Mosca VS, Bjornson K. The association between idiopathic clubfoot and increased internal hip rotation. Clin Orthop Relat Res 2009;467(5):1231-7.

36.   Hu HM, Zielinska-Kwiatkowska A, Munro K, et al. EWS/FLI1 suppresses retinoblastoma protein function and senescence in Ewing's sarcoma cells. J Orthop Res 2008;26(6):886-93.

37.   Hwang MD, Pettrone S, Trumble TE. Work of flexion related to different suture materials after flexor digitorum profundus and flexor digitorum superficialis tendon repair in zone II: a biomechanical study. J Hand Surg [Am] 2009;34(4):700-4.

38.   Jeffcoate WJ, Lipsky BA, Berendt AR, Cavanagh PR, Bus SA, Peters EJ, van Houtum WH, Valk GD, Bakker K; International Working Group on the Diabetic Foot. Unresolved issues in the management of ulcers of the foot in diabetes. Diabet Med. 2008 Dec;25(12):1380-9.

39.   Jense RJ, Howe CR, Bransford RJ, Wagner TA, Dunbar PJ. University of Washington orthopedic resident experience and interest in developing an international humanitarian rotation. Am J Orthop 2009;38(1):E18-20.

40.   Klineberg E, McHenry T, Bellabarba C, Wagner T, Chapman JR: Sacral insufficiency fractures caudal to instrumented posterior lumbosacral arthrodesis. Spine. 2008 Jul 15;33(16):1806-11.

41.   Krieg JC, Mirza A. Case report: Patella baja after retrograde femoral nail insertion. Clin Orthop Relat Res 2009;467(2):566-71.

42.   Kubiak EN, Camuso MR, Barei DP, Nork SE. Operative treatment of ipsilateral noncontiguous unicondylar tibial plateau and shaft fractures: combining plates and nails. J Orthop Trauma 2008;22(8):560-5.

43.   Lee M, Chebli C, Mounce D, Bertelsen A, Richardson M, Matsen FA. Intramedullary reaming for press-fit fixation of a humeral component removes cortical bone asymmetrically. J Shoulder Elbow Surg 2008;17(1):150-155.

44.   Leopold SS. Minimally invasive total knee arthroplasty for osteoarthritis. N Engl J Med 2009;360(17):1749-1758.

45.   Links AC, Graunke KS, Wahl C, Green JR, 3rd, Matsen FA. Pronation can increase the pressure on the posterior interosseous nerve under the arcade of Frohse: a possible mechanism of palsy after two-incision repair

for distal biceps rupture--clinical experience and a cadaveric investigation. J Shoulder Elbow Surg 2009;18(1):64-68.

46.   Lisle JW, Eary JF, O'Sullivan J, Conrad EU. Risk assessment based on FDG-PET imaging in patients with synovial sarcoma. Clin Orthop Relat Res 2009;467(6):1605-11.

47.   Lowenberg DW, Nork SE, Abruzzo FM: Correlation of Shear to Compression for Progressive Fracture Obliquity. Clin Orthop Relat Res, 2008.

48.   Lynch JR, Clinton JM, Dewing CB, Warme WJ, Matsen FA. Treatment of osseous defects associated with anterior shoulder instability. J Shoulder Elbow Surg 2009;18(2):317-28.

49.   Lynch JR, Taitsman LA, Barei DP, Nork SE. Femoral nonunion: risk factors and treatment options. J Am Acad Orthop Surg 2008;16(2):88-97.

50.   Lynch JR, Waitayawinyu T, Hanel DP, Trumble TE. Medial collateral ligament injury in the overhand-throwing athlete. J Hand Surg [Am] 2008;33(3):430-7.

51.   MacLennan AJ, Nemechek NM, Waitayawinyu T, Trumble TE. Diagnosis and anatomic reconstruction of extensor carpi ulnaris subluxation. J Hand Surg [Am] 2008;33(1):59-64.

52.   Maheshwari R, Taitsman LA, Barei DP. Single-incision fasciotomy for compartmental syndrome of the leg in patients with diaphyseal tibial fractures. J Orthop Trauma 2008;22(10):723-30.

53.   Manner PA, Budashewitz E. Orthopaedic Liability: The Plaintiff's Perspective. An Interview with a Personal Injury Lawyer. AAOS Now. 2008 Mar 2(3): 6-8.

54.   Manner PA. TKA – Pearls and Pitfalls. AAOS Now. 2008 Jun; 2(6): 11-12.

55.   Martin BI, Deyo RA, Mirza SK, et al. Expenditures and health status among adults with back and neck problems. Jama 2008;299(6):656-64.

56.   Matsen FA. Clinical practice. Rotator-cuff failure. N Engl J Med 2008;358(20):2138-47.

57.   Matsen FA. Open rotator cuff repair without acromioplasty. J Bone Joint Surg Am 2009;91(2):487.

58.   Matsen FA. Fourier transform inequalities for phylogenetic trees. IEEE/ACM Trans Comput Biol Bioinform 2009;6(1):89-95.

59.   Matsen FA, Clinton J, Lynch J, Bertelsen A, Richardson ML. Glenoid component failure in total shoulder arthroplasty. J Bone Joint Surg Am 2008;90(4):885-96.

60.   Matsen FA, Boileau P, Walch G, Gerber C, Bicknell RT. The reverse total shoulder arthroplasty. Instr Course Lect 2008;57:167-74.

61.   McCarron J, Baumbusch C, Michelson JD, Manner PA. Economic evaluation of peri-operative admissions for direct lateral versus 2-incision minimally invasive total hip arthroplasty. Seminars in Arthroplasty 2008 Mar 19(1):45-49.

62.   Mehta S, Routt ML. Irreducible fracture-dislocations of the femoral head without posterior wall acetabular fractures. J Orthop Trauma 2008;22(10):686-92.

63.   Morgan TM, Pitts TE, Gross TS, Poliachik SL, Vessella RL, Corey E. RAD001 (Everolimus) inhibits growth of prostate cancer in the bone and the inhibitory effects are increased by combination with docetaxel and zoledronic acid. Prostate 2008;68(8):861-71.

64.   Mosca VS. Ragab AA, Stewart SL, Cooperman DR. Implications of Subtalar Joint Anatomic Variation in Calcaneal Lengthening Osteotomy. J Pediatr Orthop. 2003;23:79-83. J Pediatr Orthop 2009;29(3):315-6.

65.   Muneoka K, Allan CH, Yang X, Lee J, Han M. Mammalian regeneration and regenerative medicine. Birth Defects Res C Embryo Today 2008;84(4):265-80.

66.   Nork SE, Barei DP, Gardner MJ, Schildhauer TA, Mayo KA, Benirschke SK. Surgical exposure and fixation of displaced type IV, V, and VI glenoid fractures. J Orthop Trauma 2008;22(7):487-93.

67.   Owings TM, Woerner JL, Frampton JD, Cavanagh PR, Botek G. Custom therapeutic insoles based on both foot shape and plantar pressure measurement provide enhanced pressure relief. Diabetes Care. 2008 May;31(5):839-44. Epub 2008 Feb 5.

68.   Parada S, Beingessner DM, Barei DP. Technical Tip: Calcaneus Fracture Reduction Using A Novel Threaded Wire Technique. Foot Ankle Int. 2009. Accepted and in press.

69.   Petre M, Erdemir A, Cavanagh PR. An MRI-compatible foot-loading device for assessment of internal tissue deformation. J Biomech. 2008;41(2):470-4. Epub 2007 Oct 23.

70.   Poliachik SL, Threet D, Srinivasan S, Gross TS. 32 wk old C3H/HeJ mice actively respond to mechanical loading. Bone 2008;42(4):653-9.

71.   Rihn JA, Anderson DT, Sasso RC, Zdeblick TA, Lenke LG, Harris MB, Chapman JR, Vaccaro AR. Emergency evaluation, imaging, and classification of thoracolumbar injuries. Instr Course Lect 2009;58:619-28.

72.   Russell GV, Graves ML, Archdeacon MT, Barei DP, Brien GA, Jr., Porter SE. The clamshell osteotomy: a new technique to correct complex diaphyseal malunions. J Bone Joint Surg Am 2009;91(2):314-24.

73.   Saltzman M, Mercer D, Bertelsen A, Warme W, Matsen F. Postsurgical chondrolysis of the shoulder. Orthopedics 2009;32(3):215.

74.   Sasso RC, Vaccaro AR, Chapman JR, Best NM, Zdeblick TA, Harris MB. Sacral fractures. Instr Course Lect 2009;58:645-55.

75.   Schiff MA, Tencer AF, Mack CD. Risk factors for pelvic fractures in lateral impact motor vehicle crashes. Accid Anal Prev 2008;40(1):387-91.

76.   Seegmiller RE, Bomsta BD, Bridgewater LC, Niederhauser CM, Montano C, Sudweeks S, Eyre DR, Fernandes RJ. The heterozygous disproportionate micromelia (dmm) mouse: morphological changes in fetal cartilage precede postnatal dwarfism and compared with lethal homozygotes can explain the mild phenotype. J Histochem Cytochem 2008;56(11):1003-11.

77.   Song KM, Boatright KC, Drassler J, et al. The use of polymerase chain reaction for the detection and speciation of bacterial bone and joint infection in children. J Pediatr Orthop 2009;29(2):182-8.

78.   Standaert CJ, Manner PA, Herring SA. Expert opinion and controversies in musculoskeletal and sports medicine: femoroacetabular impingement. Arch Phys Med Rehabil 2008;89(5):890-3.

79.   Vileikyte L, Peyrot M, Gonzalez JS, Rubin RR, Garrow AP, Stickings D, Waterman C, Ulbrecht JS, Cavanagh PR, Boulton AJ. Predictors of depressive symptoms in persons with diabetic peripheral neuropathy: a longitudinal study. Diabetologia 2009.

80.   Vileikyte L, Rubin RR, Peyrot M, Gonzalez JS, Boulton AJ, Ulbrecht JS, Cavanagh PR. Diabetic feet. Br J Gen Pract 2009;59(561):290.

81.   Vilela MD, Gelfenbeyn M, Bellabarba C. U-shaped sacral fracture and lumbosacral dislocation as a result of a shotgun injury: case report. Neurosurgery 2009;64(1):E193-4.

82.   Waitayawinyu T, McCallister WV, Katolik LI, Schlenker JD, Trumble TE. Outcome after vascularized bone grafting of scaphoid nonunions with avascular necrosis. J Hand Surg [Am] 2009;34(3):387-94.

83.   Waitayawinyu T, Robertson C, Chin SH, Schlenker JD, Pettrone S, Trumble TE. The detailed anatomy of the 1,2 intercompartmental supraretinacular artery for vascularized bone grafting of scaphoid nonunions. J Hand Surg [Am] 2008;33(2):168-74.

84.   Wang X, Manner PA, Song YJ, Tuan RS (2009) Histone deacetylase inhibitors antagonize FGF2 and IL-beta effects on MMP expression in human articular chondrocytes. Growth Factors 2009 Jan 27: 40-49.

85.   Williams SL, Bachison C, Michelson JD, Manner PA. Component position in 2-incision minimally invasive total hip arthroplasty compared to standard total hip arthroplasty. J Arthroplasty 2008;23(2):197-202.

86.   Wong G, Howard K, Webster A, Chapman JR, Craig JC. The health and economic impact of cervical cancer screening and human papillomavirus vaccination in kidney transplant recipients. Transplantation 2009;87(7):1078-1091.

87.   Wu JJ, Weis MA, Kim LS, Carter BG, Eyre DR. Differences in chain usage and cross-linking specificities of cartilage type V/XI collagen isoforms with age and tissue. J Biol Chem 2009;284(9):5539-45.

88.   Yang L, Clinton JM, Blackburn ML, Zhang Q, Zou J, Zielinska-Kwiatkowska A, Tang BL, Chansky HA. Rab23 regulates differentiation of ATDC5 chondroprogenitor cells. J Biol Chem 2008;283(16):10649-57.

89.   Yang L, Ma X, Lyone A, Zou J, Blackburn ML, Pan J, Yang D, Matsushita H, Mei B, Zielinska-Kwiatkowska A, Chansky HA. Proper expression of helix-loop-helix protein Id2 is important to chondrogenic differentiation of ATDC5 cells. Biochem J 2009;419(3):635-43.

90.   Yaszay B, Kubiak E, Agel J, Hanel DP. ACGME core competencies: where are we? Orthopedics 2009;32(3):171.

91.   Zdeblick TA, Sasso RC, Vaccaro AR, Chapman JR, Harris MB. Surgical treatment of thoracolumbar fractures. Instr Course Lect 2009;58:639-44.

Alumni

Dear Residency Alumni and Orthopaedic Colleagues:
If you are an alumnus of the UW Residency or an Orthopaedic Surgeon colleague in Washington State, this message is for you. As you can see in this issue we are featuring two alumni: Dr. Dick Kirby and Dr. Dan Flugstad, each of whom has been a leader in their fiscal support of the residency. They are two of many. In fact, over 27 of our alumni gave $1000 or more in support of resident education at the University of Washington last year. It is also of note that 100% of the residents currently in the program have given to the Orthopaedics Resident Education Discretionary Fund. We hope that you will join Dick and Dan and the others in supporting our residents' ability to attend courses, their book and journal fund, and Resident Research Days. It is now more convenient than ever, just go to www.orthop.washington.edu/gift and click on "Orthopaedics Resident Education Discretionary Fund". This is a tax deductible donation.

We also hope that you can join us for the UW Ortho Grand Rounds, now at a new and more convenient time for you. Beginning July 1, 2009 (the first Wednesday of each month) at UWMC, Health Sciences Building, Room T435 at 6:15-7:15 a.m. Public parking is available in Lot E 11-12 by Husky Stadium. This information and directions will also be available on the Washington State Orthopaedic Association website www.wsoa.org.

Attendance at these grand rounds can earn CME credit for your maintenance of certification, as well as giving you a chance to see first hand the excellence of our residents. By any measure, these presentations are on par with the instructional course lectures you hear at the AAOS. The topics are listed below. Hope to see you there.

Also, I'd like to encourage everyone to participate in the WSOA - our state orthopaedic association has great new dynamic leadership and is committed to serving Orthopaedics - in all its dimensions - across our great state.

Lyle Sorensen
President, U.W. Orthopaedic Alumni

2009-10 Orthopaedic Grand Rounds
1st Wednesday of month
Time: 6:15-7:15 AM (followed by Residents' Meeting)
Location: UWMC, HSB, Room T435

July 1
Speaker: Douglas P. Hanel, MD
Professor and Director of Resident Education
Topic: Sexual Harrassment, Professionalism

August 5
Speaker: Peter Scheffel, MD (R4)
Topic: Sports Injuries to the Lower Extremity

October 7
Speaker: Cory Lamblin, MD (R4)
Topic: Posterolateral Corner Injuries of the Knee: Presentation, Evaluation, and Treatment.

November 4
Speaker: Edward Moon, MD (R4)
Topic: Hand and Finger Implants

December 2
Speaker: Derek Rains, MD (R4)
Topic: Complications of Hypotensive Anesthesia in Shoulder Surgery

January 6
Speaker: Vince Mosca, MD
Topic: Part 1: English grammar for American orthopedic residents.
Part 2: Clinic notes should do much more than just justify level of billing

February 3
Speaker: Aaron Chamberlain, MD (R4)
Topic: Hill-Sachs Lesions - Evaluation and Management

March 3
Speaker: Christian Sybrowsky, MD (R4)
Topic: Osteoporosis and the Orthopaedic Surgeon

May 5
Speaker: Brian Daines, MD (R4)
Topic: Non-unions

June 2
Speaker: Brett Wiater, MD (R4)
Topic: Dural Tears in Spinal Surgery

Alumni

1952
Park W. Gloyd, M.D. ★

1954
Trygve Forland, M.D. ★

1955
Robert W. Florence, M.D.

1956
J. Michael Egglin, M.D. ★
John E. Goeckler, M.D.
Robert L. Romano, M.D.

1957
John H. Aberle, M.D. ★
John R. Beebe, M.D.

1958
Harry H. Kretzler, Jr., M.D. ★
James R. Friend, M.D. ★
Kenneth L. Martin, M.D. ★
Samuel L. Clifford, M.D.

1959
James W. Tupper, M.D.

1960
Irving Tobin, M.D. ★
William V. Smith, M.D. ★

1961
Robert C. Colburn, M.D.

1962
Arthur Ratcliffe, M.D.
Marr P. Mullen, M.D. ★★★

1963
Alfred I. Blue, M.D.
Robert A. Kraft, M.D.

1964
David E. Karges, M.D. ★★★★★
Harold J. Forney, M.D. ★
Theodore K. Greenlee II, M.D.
★★★★★★
Thomas E. Soderberg, M.D.

1966
F. Richard Convery, M.D. ★
Joseph S. Mezistrano, M.D. ★
William A. Reilly, Jr., M.D.

1967
Ivar W. Birkeland, M.D.
J. Conrad Clifford, M.D. ★
Robert F. Smith, M.D. ★★★★★

1968
Lynn T. Staheli, M.D. ★
Stewart M. Scham, M.D. ★
William T. Thieme, M.D. ★★

1969
Edward E. Almquist, M.D. ★★★
Edward L. Lester, M.D.
Hugh E. Toomey, M.D. ★★★
Sigvard T. Hansen, Jr., M.D. ★★★★★

1970
John C. Brown, M.D. ★
John M. Coletti, Jr., M.D. ★
Malcolm B. Madenwald, M.D. ★
Michael T. Phillips, M.D. ★
Robert D Schrock, Jr., M.D.

1971
Bruce E. Bradley, Jr., M.D.
Franklin G. Alvine, M.D. ★★★★
Jerome H. Zechmann, M.D.
Louis A. Roser, M.D. ★
Nils Fauchald, Jr., M.D.

1972
David J. LaGasse, M.D.
David R. Nank, M.D. ★★
Donald D. Hubbard, M.D. ★
John A. Neufeld, M.D.
Thomas L. Gritzka, M.D. ★

1973
Frederick J. Davis, M.D. ★
Larry D. Hull, M.D. ★
Robert P. Watkins, Jr., M.D. ★
Theodore A. Wagner, M.D. ★★★★★

1974
Richard A. Dimond, M.D. ★★
Ronald B.H. Sandler, M.D. ★★★
Samuel R. Baker, M.D. ★★
Robert A. Winquist, M.D. ★★★★★★★

1975
Donald L. Plowman, M.D. ★★★
Frederick A. Matsen III, M.D.
★★★★★★★
Gunter Knittel, M.D.
Larry R. Pedegana, M.D. ★
Thomas M. Green, M.D. ★★★★★
William M. Backlund, M.D., P.S. ★

1976
Douglas K. Kehl, M.D.
Douglas T. Davidson III, M.D. ★
John F. Burns, M.D. ★
Peter Melcher, M.D.
Richard A. Zorn, M.D. ★

1977
Carl A. Andrews, M.D. ★
Geoffrey W. Sheridan, M.D. ★★
Larry D. Iversen, M.D. ★
Mark C. Olson, M.D. ★
Steven T. Bramwell, M.D.

1978
Arnold G. Peterson, M.D. ★★★★
Gary J. Clancey, M.D. ★★★★
John W. Brantigan, M.D.
Richard S. Westbrook, M.D. ★★
Robert J. Strukel, M.D.
William Oppenheim, M.D. ★★

1979
Allan W. Bach, M.D. ★★★★★
Gregory M. Engel, M.D. ★★
Jonathan L. Knight, M.D. ★★
Richard L. Semon, M.D. ★★★★

1980
Carol C. Teitz, M.D. ★★★
Douglas G. Norquist, M.D.
John M. Hendrickson, M.D. ★★
Michael A. Sousa, M.D. ★★★★
Stuart R. Hutchinson, M.D. ★

1981
Dennis J. Kvidera, M.D. ★
John M. Clark, Jr., M.D., Ph.D. ★★★
Martin S. Tullus, M.D. ★★★★★
Robert G. Veith, M.D. ★★★★★★

1982
John L. Thayer, M.D. ★
Richard M. Kirby, M.D. ★★★★★★
Steven S. Ratcliffe, M.D. ★★
William D. Burman, M.D.

1983
Elizabeth Anne Ouellette, M.D. ★★
Edward L. Farrar III, M.D. ★★★★★
Henry K. Yee, M.D.
Joseph D. Zuckerman, M.D. ★★★★
Keith A. Mayo, M.D. ★★★★
Robert M. Berry, M.D.

STARS INDICATE TOTAL DONATIONS IN SUPPORT OF THE RESIDENCY

★★★★★★★ = $20,000 and above
★★★★★★ = $15,000 - $19,999
★★★★★ = $10,000 - $14,999
★★★★ = $7,500 - $9,999
★★★ = $5,000 - $7,499
★★ = $2,500 - $4,999
★ = $1 - $2,499

1984
Jeffrey C. Parker, M.D. ★
Jeffrey W. Akeson, M.D. ★★★
Kevin P. Schoenfelder, M.D. ★
Marc F. Swiontkowski, M.D. ★★★★★★
Thomas J. Fischer, M.D. ★★★★

1985
Daniel L. Flugstad, M.D. ★★★★★
Jeffrey N. Hansen, M.D. ★★★
Paul J. Abbott, M.D. ★★★★
Richard J. Barry, M.D. ★
William P. Barrett, M.D. ★★★★★

1986
Carleton A. Keck, Jr., M.D. ★★★
Gary Bergman, M.D. ★★★★★
Lawrence E. Holland, M.D. ★
Michael E. Morris, M.D. ★★★★

1987
Craig T. Arntz, M.D. ★★★
Herbert R. Clark, M.D. ★★
Michael K. Gannon, M.D. ★
Steven L. Reed, M.D. ★

1988
Jonathan L. Franklin, M.D. ★★★★★
Michael A. Thorpe, M.D. ★★★★★★
Richard V. Williamson, M.D. ★

1989
James P. Crutcher, M.D. ★★★★★
Lawrence V. Page, D.O. ★★★
Martin G. Mankey, M.D. ★★★★★
Nancy J. Ensley, M.D.
Steve C. Thomas, M.D. ★★★★

1990
David M. Kieras, M.D. ★
J. Roberto R. Carreon, M.D.
Jay A. Winzenried, M.D. ★★
Ken Fujii, M.D. ★
Walter F. Krengel III, M.D. ★★★

1991
David H. Bishop, M.D. ★★
Kit M. Song, M.D.
Mark Remington, M.D. ★★★★
Mark E. Murphy, M.D., Ph.D. ★★
Tim P. Lovell, M.D. ★★

1992
Curt Rodin, M.D.
Don Striplin, M.D. ★★
Eli Powell, M.D. ★
Jeff Stickney, M.D. ★★
John D. West, M.D. ★★
Michael Sailer, M.D. ★★★

1993
J. Eric Vanderhooft, M.D. ★★★★★
Lyle S. Sorensen, M.D. ★★★★★★★
Philip J. Kregor, M.D. ★★
Susan R. Cero, M.D. ★★★★★

1994
Brodie Wood, M.D. ★★
Eric Bowton, M.D. ★★
Jim Vahey, M.D. ★
Sohail K. Mirza, M.D. ★
William Obremskey, M.D. ★★★

1995
Ron Kristensen, M.D. ★
Scott Hormel, M.D. ★★
Timothy Beals, M.D. ★★
Todd Clarke, M.D. ★★★
William J. Mills III, M.D. ★

1996
David Deneka, M.D. ★★
Peter Mitchell, M.D. ★★
Peter T. Simonian, M.D. ★★★★
Vernon Cooley, M.D. ★★
William Wagner, M.D. ★★★

1997
Daniel Stechschulte, Jr., M.D.
David Levinsohn, M.D. ★
L. Anthony Agtarap, M.D. ★
Mohammad Diab, M.D.
Randall W. Viola, M.D.

1998
Colin Poole, M.D. ★
David Belfie, M.D. ★
Don Ericksen, M.D. ★★★★
Jay Crary, M.D. ★★★
Oriente DiTano, M.D. ★

1999
Craig Boatright, M.D.
Jeffrey Garr, M.D.
John Michelotti, M.D. ★★
Julie A. Switzer, M.D.
Thomas D. Chi, M.D. ★

2000
Brett Quigley, M.D. ★
Cara Beth Lee, M.D.
Daniel Jones, M.D. ★
Joel Hoekema, M.D. ★★
Patrick McNair, M.D.

2001
Eric Novack, M.D.
Frederick Huang, M.D. ★★★
Matthew Camuso, M.D.
Michael Metcalf, M.D. ★★★
Richard Bransford, M.D. ★

2002
Timothy DuMontier, M.D.
Scott Hacker, M.D. ★
Timothy Rapp, M.D. ★
William Sims, M.D. ★
Carla Smith, M.D. ★

2003
Ben DuBois, M.D. ★
Andy Howlett, M.D.
Guy Schmidt, M.D. ★
Brian Shafer, M.D. ★
Emma Woodhouse, M.D. ★

2004
Jon Braman, M.D. ★
Alexis Falicov, M.D. ★
Mike McAdam, M.D. ★
Jason Thompson, M.D. ★
Thea Khan-Farooqi, M.D.

2005
Tony Buoncristiani, M.D. ★
Waqqar Khan-Farooqi, M.D.
Wren McCallister, M.D.
Tim O'Mara, M.D.
David Stevens, M.D. ★

2006
Heidi Shors, M.D. ★
Stacey Donion, M.D.
Eric Klineberg, M.D.
Bill Montgomery, M.D. ★
Mel Wahl, M.D.
Burt Yaszay, M.D.

2007
Jamie Antoine, M.D. ★
Jeremiah Clinton, M.D. ★
Mary Cunningham, M.D. ★
Evan Ellis, M.D. ★
Joseph Lynch, M.D. ★
Allison MacLennan, M.D. ★

2008
Drew Fehsenfeld, M.D. ★
Mark Freeborn, M.D. ★
Christopher Howe, M.D. ★
John Howlett, M.D. ★
Michael Lee, M.D. ★
Gregg Nicandri, M.D. ★

2009
Jason King, M.D. ★
Rajshri Maheshwari, M.D. ★
Soren Olson, M.D. ★
Karen Perser, M.D. ★
Scott Ruhlman, M.D. ★
Addison Stone, M.D. ★
Jason Wilcox, M.D. ★

Endowments

We express our appreciation to all who have contributed to the endowments of the Department of Orthopaedics and Sports Medicine. This assistance makes possible special research activities, educational programs, and other projects that we could not offer without this extra support from our alumni, faculty, and friends in the community. If you have any questions, please contact our Chair, Rick Matsen (matsen@u.washington.edu), or our Administrator, Ken Karbowski (kkarb@u.washington.edu).

Hansjoerg Wyss Endowed Chair - Jens R. Chapman, M.D.

Ernest M. Burgess Endowed Chair for Orthopaedics Investigation - David R. Eyre, Ph.D.

Sigvard T. Hansen Jr. Endowed Chair in Orthopaedic Traumatology - Ted S. Gross, Ph.D.

Jerome H. Debs Endowed Chair in Orthopaedic Traumatology - Stephen K. Benirschke, M.D.

Bob and Sally Behnke Endowed Chair for the Health of the Student Athlete - John W. O'Kane, M.D.

Endowed Chair for Women's Sports Medicine and Lifetime Fitness - Peter R. Cavanagh, Ph.D.

Surgical Dynamics Endowed Chair for Spine Research

Douglas T. Harryman II/DePuy Endowed Chair for Shoulder Research - Frederick A. Matsen III, M.D.

Synthes Spinal Surgery Outcomes Research Endowment

Zimmer Fracture Fixation Biology Endowed Professorship

Ostex Bone and Joint Research Endowment

Orthopaedic Traumatology Endowed Lectureship

John F. LeCocq Lectureship in Orthopaedic Surgery

Don and Carol James Research Fund in Sports Medicine and Fitness

Victor H. Frankel Award

Esther Whiting Award

Ed Laurnen Award

Spine Research Endowment

James G. Garrick Lectureship in Sports Medicine

Allan Treuer - Ted Wagner, M.D. Endowed Chair in Regenerative Spine Surgery

Kirby Orthopaedic Resident Endowed Fund

Huang-Biu Orthopaedic Resident Endowed Fund

Greenlee Orthopaedic Resident Endowed Fund

Josh and Max Myers Endowed Orthopaedic Fellowship Fund

Sarcoma Oncology Endowed Fund