History of Orthopedic Research at KU Medical Center

In slightly over 50 years, the orthopedic laboratory has grown from a single small room with approximately $10,000 in seed money, to include multiple labs with approximately 6,000 square feet of space, a multi-million dollar endowment and a grant-funded research program.

Almost from its inception, KU orthopedics engaged in clinical research and made important contributions to the medical literature based on patient studies and case reports.

In 1957, space and funds were made available for the James B. Weaver Orthopedic Laboratory with a single small room for laboratory investigations located next to the orthopedic clinic and directly across the corridor from the cast room. Within several months of the lab’s opening, hospital administrators awarded the department a three-room laboratory that was considered quite well equipped at the time. It included a room for chemical analyses, a larger general laboratory and an animal operating room with a small X-ray unit.

Over the years, the Weaver laboratory was the site of several projects that led to numerous literature publications on fat embolism, total joint bone cement interface analysis and the Isola spine implant studies among others.

In October 2000, Terence E. McIff, Ph.D., was recruited to direct and expand orthopedic research efforts. He inherited the Weaver laboratory and immediately set about planning and negotiating to obtain the old KUMC machine shop and develop it into the large and modern facility it is today.

The new 4,000 square foot Orthopedic Research Center includes space for specimen preparation and dissection, a machine shop, a wet lab, a biomechanical lab, a molecular lab, and computer lab space for computational biomechanical analysis. In addition to orthopedic residents and faculty, medical students, graduate students and biomechanical engineers use the center for educational purposes as well as research.

The Harrington Laboratory for Molecular Orthopedics, directed by Jinx Wang, MD, PhD, was established in early 2005. The laboratory is well equipped for research in morphology, biochemistry, cellular and molecular biology of bone and cartilage tissues. These facilities are dedicated to the study of bone and cartilage biology and diseases. Currently, research in this laboratory focuses on the following projects: (1) the role of bone-sialoprotein (BSP) in osteogenesis and bone regeneration, (2) the mechanism for tissue-specific molecular and cellular responses to bone morphogenetic protein (BMP) implants, and (3) novel molecular mechanisms and therapeutics for osteoarthritic joint degeneration.

Table of Contents

<table>
<thead>
<tr>
<th>History</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Resources</td>
<td>4</td>
</tr>
<tr>
<td>Academic Collaboration</td>
<td>5</td>
</tr>
<tr>
<td>Wang Investiture</td>
<td>6</td>
</tr>
<tr>
<td>Vitamin D Cancer Study</td>
<td>7</td>
</tr>
<tr>
<td>Faculty</td>
<td>8</td>
</tr>
<tr>
<td>Ongoing Studies</td>
<td>10</td>
</tr>
<tr>
<td>Grant-Funded Research</td>
<td>12</td>
</tr>
<tr>
<td>Resident Research</td>
<td>14</td>
</tr>
<tr>
<td>Student Research</td>
<td>20</td>
</tr>
<tr>
<td>Peer-reviewed Publications</td>
<td>22</td>
</tr>
</tbody>
</table>

An International Orthopedics Symbol with a Kansas Signature

The illustration of the "crooked tree tied to the straight stake" - with various modifications - has become the logo of the specialty of orthopedics around the world. Its origin can be traced to its first use in Nicolas Andry’s L’Orthopedie published in Paris in 1741. In the early 1960s Dr. Leonard Peltier, Kansas University’s Chairman and Program Director of Orthopedics and Beverly Brewster of the KU Department of Design and Illustration, modified the venerable image by using a staked sunflower with an accompanying medical Conestoga wagon and oxen skull to “brand” the KU Department of Orthopedics. It remains the department symbol to this day.
Internal Sources for Orthopedic Research and Education

The following are internal endowment and special research accounts set up to accept contributions from clinical earnings, voluntary internal contributions, and external donations. Much of the research and resident educational activities are funded through these accounts:

- Marc A. & Elinor J. Asher Orthopedic Research Endowment
- Orthopedic Surgery Education Endowment Fund
- Scoliosis Research Fund (KUOA)
- Mary Alice & Paul R. Harrington Distinguished Professorship of Molecular Orthopedics
- Reckling Orthopedic Education Endowment
- Marc A. & Elinor J. Asher Endowment for the Study of Spinal Deformities
- Orthopedic Spine Endowment
- James R. Neff/John and Harriett Wiebe Chair of Orthopedic Biomechanics

Federico & Betty Adler Residency Award Endowment

In 2007 Dr. Fred Adler established this award which recognizes the orthopedic resident who has performed the most original research or made the most original contribution.

*Past Recipients of This Award:*

<table>
<thead>
<tr>
<th>Year</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Joshua Nelson, MD</td>
</tr>
<tr>
<td>2008</td>
<td>Chad Waits, MD</td>
</tr>
<tr>
<td>2009</td>
<td>Hugh Brock, MD</td>
</tr>
<tr>
<td></td>
<td>Shane Schutt, MD</td>
</tr>
<tr>
<td>2010</td>
<td>David Anderson, MD</td>
</tr>
<tr>
<td>2011</td>
<td>Ryan Dunlay, MD</td>
</tr>
</tbody>
</table>

“I established this award to stimulate original research by a resident and try to stimulate the formation of clinician scientists, which are in short supply. I also wanted this award to honor the memory of my late wife, and finally to celebrate my 50 years at KU.”

--Federico Adler, M.D.
In orthopedic research the ability and willingness to work in interdisciplinary teams of researchers is essential to successful and innovative research. As the pace of our research programs continue to accelerate, the Department of Orthopedic Surgery also realizes the importance of collaborations with scientists in other departments, other schools, other campuses, and universities. Over the last few years we have successfully worked and collaborated with many external groups. These collaborations have been fruitful, yielding increased numbers of national presentations, publications, and grants. We are currently working with:

- Baylor Scoliosis Center (Dallas, TX)
- Canadian Institutes of Health Research (Ottawa, ON, Canada)
- Hospital for Special Surgery (New York, NY)
- Johns Hopkins University (Baltimore, MD)
- Massachusetts General Hospital (Boston, MA)
- McMaster University (Hamilton, ON, Canada)
- New York University Hospital for Joint Disorders (New York, NY)
- Oregon Health Sciences University (Portland, OR)
- Rocky Mountain Hospital for Children (Denver, CO)
- San Diego Center for Spinal Disorders (San Diego, CA)
- Vanderbilt Orthopaedic Institute (Nashville, TN)
- University of California San Francisco (San Francisco, CA)
- University of California Davis (Sacramento, CA)
- University of Iowa (Iowa City, IA)
- University of Kansas (Main Campus – Lawrence, KS)
- University of Minnesota (Minneapolis/St. Paul, MN)
- University of Virginia (Charlottesville, VA)
On November 21, 2011 an investiture ceremony was held for Dr. Jinx Wang as he was installed as the new Mary Alice and Paul R. Harrington, M.D., Distinguished Professor in Molecular Orthopedics. Since 2005 Dr. Wang, M.D., Ph.D. has been the director of the Orthopedic Research Center’s Harrington Laboratory for Molecular Orthopedics. Dr. Wang’s mission when he joined the faculty of the Orthopedic Surgery in 2005 was to establish and develop a new bone biology laboratory for both research and education.

For 2011, the KU Orthopedic Department was ranked 23rd in NIH grant funding among 140 orthopedic departments affiliated to university school of medicine according to the Blue Ridge Institute for Medical Research. In addition to the two ongoing grants, we are receiving two new grants, a Department of Defense and a new collaborative NIH R01, in 2012. Thus, it is expected that the ranking in federal research funding will be higher for 2012, but 2012 ranking information is not yet available.

He developed and leads a new biology laboratory named “The Harrington Laboratory for Molecular Orthopedics.” This laboratory is well organized and equipped with instruments not only for scientific research but also for education, such as micro-dissection and presentation of bone and cartilage cells, bone microstructure, function of various skeletal cells, and histopathology of skeletal tissues. This educational lab setting has provided a learning environment to greatly help medical students and orthopedic residents better understand the morphology and cellular/molecular biology of the skeletal system, which is an important part of their required examinations. For example, Step 1 of USMLE (for medical students) and Orthopedic In-Training Examination (OITE, for orthopedic residents) contain basic sciences of the skeletal system. He has been teaching medical, dental and graduate students, orthopedic residents, and postdoctoral research fellows since 1992 in the following areas: bone and cartilage biology, bone and cartilage regeneration, mechanisms for mineralization of bone and teeth, and specific skeletal diseases such as osteonecrosis and osteoarthritis.

He also serves as a mentor for other junior faculty members at KUMC by helping them with research design, data analysis, and preparation of grant proposals and manuscripts. At the national level, he serves on the New Investigator Mentoring Committee of the Orthopedic Research Society to assist junior faculty members and new scientists with grant writing.
KUMC study finds that vitamin D may help in treatment of pediatric bone cancer

A team of researchers at the University of Kansas Medical Center has shown that vitamin D turns malignant osteosarcoma cells into normal cells, making it potentially useful in the treatment of pediatric bone cancer. The finding appears in the Journal of Orthopedic Research.

Kim Templeton, MD, began thinking several years ago about vitamin D and the role it might play in the treatment of osteosarcoma. A professor in the Department of Orthopedic Surgery at the KU School of Medicine, Templeton had been invited to join a group of experts in New York City to talk about recommended levels of vitamin D intake. Research has linked vitamin D deficiency to cancer and other diseases. Given that vitamin D is also instrumental in bone health, Templeton, the first surgeon in the United States to use titanium alloy rods to save the limbs of patients who’ve lost bones to cancer, left the conference wanting to explore its effect on osteosarcoma cell lines.

Osteosarcoma is a malignant bone tumor that predominantly affects children and adolescents. The cancer tends to occur in larger bones when the bones are growing the fastest. Between 500 and 800 cases are diagnosed in the United States each year.

Typically, osteosarcoma patients receive 10 weeks of chemotherapy before the tumor is removed surgically. Templeton says the chemotherapy regimen is not all that different from the one administered to patients 20 years ago. The survival rate — 60 to 70 percent of patients live five years after being diagnosed — is largely unchanged as well. "It's a cancer where we really need to find a better way to treat it, to add something else into the chemotherapy regimen," she says.

Templeton kicked around ideas with colleagues Ossama Tawfik, MD, PhD, a professor in the Department of Pathology and Laboratory Medicine, and Stephen Smith, MD, professor of pediatric hematology and oncology. Tawfik says he was excited to explore the idea that vitamin D could be used as a weapon against osteosarcoma. Vitamin D, Tawfik says, takes care of the cell. "If it's not there, bad things are going to happen," he says.

They assembled an interdisciplinary team of physicians and scientists with expertise ranging from bone biology to biostatistics. In the first arm of the study, Tawfik went into the archives and retrieved samples of tissue from osteosarcoma patients who had been treated at KU Hospital. Placed under a microscope, the tissue samples indicated that bone tumors have the receptors necessary to bind with vitamin D.

In the second arm of the study, Rama Garimella, PhD, MS, MSc, a research assistant professor in the School of Health Professions’ Department of Dietetics and Nutrition, along with her graduate students Lindsey Thompson and Shanshan Wang, investigated the effects of vitamin D on human osteosarcoma cell lines at the cellular and molecular levels. "Vitamin D has been well studied in other different types of cancers, like prostate, breast and colon cancers," says Garimella, the senior and corresponding author of the study. "The role of vitamin D in osteosarcoma is not clearly defined."

The results of pilot studies from Garimella’s lab suggest that vitamin D induces differentiation and apoptosis, or cell death, in human osteosarcoma cell lines. In other words, vitamin D promoted the growth of normal bone cells by expressing bone markers. "It remains to be tested whether vitamin D exerts a similar differentiation-inducing effect in vivo," Garimella says. Other co-authors of the study include Jakica Tancerubic, MD; David Pinson, DVM, PhD; H. Clarke Anderson, MD; and John Keighley, PhD.

The results suggest that vitamin D could become another tool in the treatment of osteosarcoma. Patients with low levels of vitamin D would potentially receive supplements during chemotherapy in an effort try to increase the number of osteosarcoma cells that turn into normal bone. "We're not saying that vitamin D is going to be the thing that cures osteosarcoma," Templeton says. "We wouldn't use it as a single agent, the only drug that you give, but rather would add it into current treatment regimens."

More tests are needed before doctors begin recommending vitamin D for their osteosarcoma patients. “All we know is what it does in a petri dish,” Templeton says. The next step is to introduce vitamin D to osteosarcoma cells in mice or dogs. (Bone tumors are fairly common in large breed dogs.) In any event, Templeton is encouraged by the discovery. The chemotherapy that is used now to treat osteosarcoma, she says, is effective but also poses significant side effects to the heart, kidneys or bone, depending on the regimen.

"The beauty of vitamin D is that at relatively normal doses it's not going to have a long-term side effect like that," she says. "When you're dealing with growing kids, that's something you really need to be concerned about. Yes, you want to try to eradicate their cancer, but you also, if they do survive, want to understand what those drugs and that treatment is doing 20 and 30 and 40 years after they've been treated."

Templeton also notes that vitamin D is inexpensive, an important consideration at a time of concern about health care spending.

By David Martin | December 22, 2011
Reprinted courtesy of the University of Kansas School of Medicine
Hand and Upper Extremity Service

E. Bruce Toby, M.D.
Hand and Upper Extremity Professor & Chairman
Peltier/Reckling Chair

Marc Asher, M.D.
Professor Emeritus

Spine Service

Doug Burton, M.D.
Marc and Elinor Asher Spine Professor
Chairman, Resident Research Committee

R. Sean Jackson, M.D.
Assistant Professor Orthopedic Surgery

Trauma Service

John Sojka, M.D.
Assistant Professor Orthopedic Surgery
Section Chief, Trauma Services

Archie Heddings, M.D.
Assistant Professor Orthopedic Surgery

Trauma Service

Mike Tilley, M.D.
Assistant Professor Orthopedic Surgery

Adult Reconstruction Service

Kelly Hendricks, M.D.
Assistant Professor Orthopedic Surgery
Foot and Ankle Service

Greg Horton, M.D.
Associate Professor Orthopedic Surgery

Musculoskeletal Oncology Service

Kimberly Templeton, M.D.
Professor Orthopedic Surgery
Residency Program Director
President, U.S. Bone & Joint Initiative

Sports Medicine Service

Vincent Key, M.D.
Assistant Professor Orthopedic Surgery

Steve Munns, M.D.
Associate Professor Orthopedic Surgery

Joshua Nelson, M.D.
Assistant Professor Orthopedic Surgery

Randy Goldstein, M.D.
Assistant Professor Orthopedic Surgery

Orthopedic Research

Terence McIff, Ph.D.
James R. Neff/John and Harriet Wiebe Chair of Orthopedic Biomechanics
Director of Orthopedic Biomechanical & Bioengineering Laboratories

Jinxi Wang, M.D., Ph.D.
Harrington Distinguished Professor
Director of Harrington Laboratory for Molecular Orthopedics
Randomized non-inferiority study comparing results of the PyroCarbon Radial Head Prosthesis to the Metal Radial Head Prosthesis
Sponsor - Integra (previously Ascension)
E. Bruce Toby, MD, Principal Investigator
John Sojka, MD, Co-Investigator
Michael Tilley, MD, Co-Investigator
Archie Heddings, MD, Co-Investigator
Radial Head Implants are used to treat arthritis of the elbow and radial head fractures, as well as to replace a prior radial head implant or removal of the radial head due to complications and symptoms such as pain or loss of function. Surgical treatment consists of removing the radial head and replacing it with a metal radial head and metal stem. PyroCarbon is a ceramic material that has shown to cause less tension and possibly less wear to the bone than a Metal Radial Head. The PyroCarbon Radial Head has not been approved by the US FDA and is considered investigational. Researchers are hoping to learn how well the PyroCarbon Radial Head device works in comparison to the Metal Radial Head for this type of surgery.

Multi-Center Prospective Cohort Study: Operative & Non-operative Treatment for Extra-articular Scapula Fractures
University of Minnesota and Vanderbilt Orthopaedic Institute
Archie Heddings, MD, Principal Investigator
John Sojka, MD, Co-Investigator
Michael Tilley, MD, Co-Investigator
Operative treatment of extra-articular scapula fractures is relatively new, as scapula fractures are relatively rare injuries and historically, have been treated non-operatively. Significant controversy exists concerning indications for surgical care of these injuries. However, high energy injuries are increasing in frequency due to a mechanized society and field resuscitation and a poor understanding of objective patient outcomes following these fractures has contributed to the current lack of consensus for treatment. The primary goal of this study is to compare patient-oriented outcomes following non-operative treatment for displaced extra-articular scapula fractures to those following operative treatment. Secondary aims include the comparison of objective functional outcomes and complication rates.

Trial to evaluate UltraSound in the Treatment of tibial fractures (TRUST)
Sponsor: Bioventus LLC (formerly Smith & Nephew, Inc.)
Funding - Canadian Institutes of Health Research (CIHR) and Smith & Nephew, Inc
Archie Heddings, MD, Principal Investigator
Co-Investigator: John Sojka, MD
Co-Investigator: Michael Tilley, MD
This is a prospective, blinded, randomized placebo-treatment controlled trial comparing the safety and effectiveness of the use of low intensity pulsed ultrasound in the treatment of tibial fractures treated with intramedullary nailing. Subjects are randomized to one of two study groups; one group has active devices, the other has inactive devices. Subjects will self-administer treatment with their study device (EXOGEN 4000+ ultrasound) for 20 minutes daily. Treatment will continue until a central adjudication committee has determined that the fracture demonstrates radiographic evidence of bridging all 4 cortices, or until the 52-week time point.
Multi-Center Prospective Evaluation of Operative versus Nonoperative Treatment for Adult Spinal Deformity: Differentiating Clinical and Radiographic Features and Evaluation of Treatment Outcomes
International Spine Study Group
Douglas Burton, MD, Principal Investigator

Compared to adolescent idiopathic scoliosis, operative treatment of adult scoliosis is associated with higher complication rates, prolonged recovery time, and greater economic cost. Postoperative outcomes are often compromised by complications and revision surgery. Consequently, physicians must carefully weigh the risk/benefit ratio when deciding upon operative or nonoperative treatment of adult scoliosis. There is little data currently available that considers age stratification of adult deformity patients treated operatively versus nonoperatively and followed over a period of time as regards clinical and radiographic outcomes. Psychological distress is known to have a negative impact on the outcomes of patients undergoing spine surgery. No data exists studying the adult spinal deformity patient population with regard to psychological distress and outcome after surgery. The potential implications of this study include identifying and appropriately treating patients with significant distress and ultimately adding a data point to the surgical decision making process.

Prospective Radiographic and Clinical Evaluation of Surgical Treatment for Cervical Deformity: A Multi-Center Study
International Spine Study Group
Douglas Burton, MD, Principal Investigator

This study aims to define the clinical and demographic features of the population affected by cervical deformities such as cervical kyphosis, cervical scoliosis, and basilar invagination. The study will assess for correlations between radiographic parameters and degree of pain/disability at baseline and assess and describe surgical strategies used to address the deformity and evaluate clinical outcome at 2 years following surgery.

Recidivism Rates after Smoking Cessation Prior to Spinal Fusion
Sponsor: Pfizer
Douglas Burton, MD, Principal Investigator

The primary purpose of this research study is to target the smoking recidivism rate through pharmacotherapy and relapse prevention behavioral counseling among patients that undergo spinal fusion surgery. To be eligible for elective spinal fusion by either investigator, patients that smoke are required to quit and verify their cessation with a negative cotinine blood test. The investigators are interested in the recidivism rates following spinal fusion surgery for patients that verifiably cease smoking prior to surgery and the possible effects on surgical outcomes.
**Bone Sialoprotein in Osteogenesis and Bone Regeneration**
7/1/2010—6/30/15, $1,550,000
Source of Support: NIH/RO1
**Jinxi Wang, M.D., Ph.D.,** Principal Investigator
The major goal of our studies is to explore the molecular and cellular mechanisms of tissue-specific BSP action in osteogenesis and its application to bone regeneration.

**Transcription Factor NFAT Deficiency and Osteoarthritis**
7/11/11—5/31/16, $1,690,000
Source of Support: NIH/NIAMS/RO1
**Jinxi Wang, M.D., Ph.D.,** Principal Investigator
The major goal of this project is to explore the biological mechanisms underlying the pathogenesis of Nfat1 deficiency-associated osteoarthritis.

**Integrative Collodial Gels for Cranial Defect Repair**
3/1/12—2/29/16, $1,390,000
Source of Support: NIH/NIDCR/RO1
**Cory Berkland, Ph.D.,** Principal Investigator
**Jinxi Wang, M.D., Ph.D.,** (PI on subcontract)
The long-term objective is to provide a new biodegradable material that can harden in a cranial defect and promote the repair of human cranial bone defects. The overall objective of this project is to refine the colloidal gel to minimize regeneration time and maximize final bone quality in a rat calvarial defect model.

**Deficiency of NFAT1 Transcription Factor and Post-Traumatic Osteoarthritis**
7/1/12—6/30/15, $1,132,000
Source of Support: Department of Defense
**Jinxi Wang, M.D., Ph.D.,** Principal Investigator
The major goal of this project is to explore the pathogenic mechanisms underlying NFAT1 deficiency-mediated progression of post-traumatic osteoarthritis.
MRI-Based Modeling to Evaluate Surgical Efficacy for Reduced OA Risk
7/1/09-1/29/14 • $992,085 ($278,466 subcontract)
Source of Support-NIH/RO1
Terence McIff, Ph.D., (PI on subcontract)
Kenneth Fischer, PhD., KU Principal Investigator
E. Bruce Toby, M.D., Co-Investigator
The goal of this research is to see if MRI based modeling can be used to reduce the risk of OA in a specific population having scaphoid-lunate dissociation in the wrist.

Gradient-based Strategy for Osteochondral Regeneration
4/1/10-3/31/15 • $1,457,633
Source of Support-NIH/NIAMS/ROI
Michael Detamore, Principal Investigator
Terence McIff, Ph.D., Co-Investigator
The goal of this research is to evaluate the effectiveness of scaffolds using a novel gradient based technology to fill osteochondral defects in the knee joint.

Effectiveness of Negative Pressure in Promoting Tissue Ingrowth into Porous Metal Implants: An idea for Early Stabilization of Extremity War Injuries
7/1/10-12/31/11 • $100,000
Source of Support-US Department Of Defense PRORP Hypothesis Development Award
Terence McIff, Ph.D., Principal Investigator
Steven Bubb, M.D., Co-Investigator
The goal of this preliminary series of studies is to evaluate whether negative pressure therapy can be applied to porous scaffolds used to fill large osseous defects.
ORTHOPEDIC SURGERY RESIDENTS

Class of 2012

Ryan Dunlay, M.D.
Undergraduate:
University of Iowa
Iowa City, Iowa
Medical School:
University of Iowa
Roy J. and Lucille A. Carver School of Medicine
Iowa City, Iowa
Fellowship:
Sports Medicine
TRIA Orthopedic Center
Minneapolis, Minnesota

Todd Lansford, M.D.
Undergraduate:
Truman State University
Kirkville, Missouri.
Medical School:
University of Kansas
School of Medicine
Kansas City, Kansas
Fellowship:
Spine
University of California
San Francisco, California

Erik McGoldrick, M.D.
Undergraduate:
University of California - Davis
Davis, California
Medical School:
St. Louis University
School of Medicine
Saint Louis, Missouri
Fellowship:
Shoulder & Elbow
University of Washington
Seattle, Washington

John Paul Schroeppele, M.D.
Undergraduate:
University of Kansas
Lawrence, Kansas
Medical School:
University of Kansas
School of Medicine
Kansas City, Kansas
Fellowship:
Sports Medicine
TRIA Orthopedic Center
Minneapolis, Minnesota

Class of 2013

Tanay J. Amin, M.D.
Undergraduate:
University of Virginia
Charlottesville, VA
Medical School:
Baylor College of Medicine
Houston, TX

Johnathan C. Cotton, M.D.
Undergraduate:
Marquette University
Milwaukee, WI
Medical School:
University of Nebraska
College of Medicine
Omaha, NE

William C. Kramer, M.D.
Undergraduate:
University of Colorado
Boulder, CO
Medical School:
University of Colorado
School of Medicine
Denver, CO
ORTHOPEDIC SURGERY RESIDENTS

Class of 2014

Aaron T. Althaus, M.D.
Undergraduate: Marquette University
Medical School: University of Iowa
Roy J. and Lucille A Carver College of Medicine
Iowa City, IA

C. Daniel Benson, M.D.
Undergraduate: Georgetown College
Medical School: University of Louisville School of Medicine
Louisville, KY

Kenneth L. Caldwell, M.D.
Undergraduate: Texas Southern University
Medical School: University of Texas School of Medicine at Galveston
Galveston, TX

Kevin J. McCarthy, M.D.
Undergraduate: Emory University
Medical School: St. Louis School of Medicine
St. Louis, MO

Scott M. Mullen, M.D.
Undergraduate: University of Kansas
Medical School: University of Kansas School of Medicine
Kansas City, KS

Class of 2015

Paul C. Cowan, M.D.
Undergraduate: Kansas State University
Medical School: University of Kansas School of Medicine
Kansas City, KS

Adam M. Goodyear, M.D.
Undergraduate: University of Oklahoma
Medical School: Univ. of Texas School of Medicine at Houston
Houston, TX

Richard A. Seagrave III, M.D.
Undergraduate: Drury University
Medical School: St. Louis University School of Medicine
St. Louis, MO

David L. Whitney, M.D.
Undergraduate: University of Southern Indiana
Medical School: Indiana University School of Medicine
Indianapolis, IN

Class of 2016

Derek L. Breder, M.D.
Undergraduate: University of Iowa
Medical School: University of Iowa
Iowa City, IA

Joshua T. Bunch, M.D.
Undergraduate: University of Missouri-Columbia
Medical School: University of Missouri-Columbia School of Medicine
Columbia, MO

Grant M. Rowland, M.D.
Undergraduate: Texas A&M University
Medical School: University of Texas Medical Branch School of Medicine at Galveston
Galveston, TX

Clayton E. Strong, M.D.
Undergraduate: Butler University
Medical School: Indiana University School of Medicine
Indianapolis, IN
Adolescent Runners: The Effect of Training Shoes Upon Running Kinematics
Resident Investigator: Scott Mullen, MD
Faculty Mentor: E. Bruce Toby, MD
Largely padded running shoes may be deleterious to the young athlete because it alters their running style. The cushioning absorbs the shock and results in a heel strike running style. The barefoot running style allows the runner to strike the ground with the forefoot or full foot, which allows the muscles and ligaments to inherently cushion the impact. Using an optical scanner, we capture data, such as stride length, height of backswing and forward swing, and contact time, from adolescent runners while running at different speeds on a treadmill. The runners all perform barefoot, in racing flats, and heavy trainers. The primary goal of this study is to prove that running dynamics are altered by shoe wear.

Barefoot Running: The Effects of an 8-Week Barefoot Training Program
Resident Investigator: Scott Mullen, MD
Faculty Mentor: E. Bruce Toby, MD
Running in the heavily padded running shoe results in a heel strike technique, which is far different from running barefoot and naturally striking the ground first with the forefoot or the entire foot. This is a progressive 8 week training program where participants are randomized into group barefoot or group shoe. Each group will perform baseline functional tests, complete the 8 week program, and return for follow up functional tests. We will compare the results of both groups to determine the effects of a barefoot running regimen on the musculature of the lower extremities. We also hope to determine if a barefoot running program decreases running related injuries in the lower extremities of runners.

Clinical Outcomes of a Novel Intramedullary Fixation Technique for Treatment of Closed Calcaneus Fractures
Resident Investigator: Kevin McCarthy, MD
Faculty Mentor: Greg Horton, MD
While anatomic reduction of closed calcaneus fractures has been demonstrated to improve patient outcomes, this often comes at the cost of soft tissue complications due to hardware prominence from the traditional plate and screw fixation technique. In an effort to limit these complications without compromising the strength of the fixation construct, an intramedullary technique utilizing a headless compression screw was developed and biomechanically validated. Through a retrospective chart review, we are looking at the clinical outcomes, specifically; maintenance of reduction, return to work, infection, and need for hardware removal or revision. Our study demonstrates that this novel technique is associated with an acceptable rate of wound complications when compared to traditional plate fixation. Prospective data continues to be collected which may allow us to make stronger recommendations in the future.

Comparison of Pedicle Screw Cementing Methods
Resident Investigator: C. Daniel Benson, MD
Faculty Mentor: Terence McIff, Ph.D.
This study investigates three cement injecting methods used for pedicle screw fixation which includes open injection, pressurized injection, and injection through a fenestrated screw. The injections are performed on lumbar cadaver vertebrae which are then mechanically loaded with a toggle test. The displacement data from the toggle tests is used to compare and evaluate the three methods.
Cytotoxic and Anti-proliferative Effects of Vancomycin on Osteosarcoma Cell Lines  
Resident Investigator: Aaron Althaus, MD  
Additional Research Support: John Weitlich  
Faculty Mentor: Terence McIff, PhD  
Patients with local recurrence of osteosarcoma have a poorer overall prognosis than those without local recurrence. An option to decrease the risk of local recurrence among patients undergoing limb salvage surgery is the local delivery of cytotoxic agents. We asked whether vancomycin could act as a cytotoxic agent against osteosarcoma cells while sparing osteoblast cells and whether bone cement could provide and effective mode of delivering Vancomycin for this purpose. The effect of various concentrations of vancomycin on three human osteosarcoma cell lines (SaOS-2, MG63, KHOS) is now being studied.

The Role of NFAT1 in Articular Cartilage Healing  
Resident Investigator: Kenneth Caldwell, MD  
Faculty Mentor: Jinxi Wang, MD, PhD  
This study investigates the link between the biological processes of articular cartilage repair and OA by determining the effects of NFAT1 expression on the healing of articular cartilage defects. This study uses 3 mice types and two study arms to study histology and gene expression at set time intervals. Degeneration of cartilage repair tissue appears to largely entail a progression of involved chondrocytes through endochondral ossification. NFAT1 plays a major role in maintenance of the permanent cartilage phenotype. It is expected that NFAT1 deficiency will not affect the initial reparative response to the extent it will affect the overall quality of repair tissue, NFAT1 deficiency will lead to a predominance of mature/hypertrophic chondrocyte proliferation and possibly even repair tissue resembling frank bone within the chondral defect. Furthermore, the presence of NFAT1 overexpression may enhance the quality of repair tissue to better resemble articular cartilage.
Resident Research is a required part of the Resident Education Program as mandated by the Accreditation Council for Graduate Medical Education. In the orthopedic residency program at KUMC, each resident is required to complete a three month research rotation which is expected to yield one or two published orthopedic related research projects. One resident is always on research rotation at any given time. Research projects are selected in consultation with the Orthopedic Surgery Faculty. Monthly Resident Research Committee meetings are held to supervise, monitor, and direct resident research progress. Laboratory research facilities and personnel are made available to the residents as required to complete their research. Monetary support for resident research and orthopedic research infrastructure comes from a variety of sources including: the Marc A. and Elinor J. Asher Orthopedic Research Endowment, resident research grants from independent foundations, unrestricted grants from orthopedic device and orthopedic related companies, orthopedic clinical earnings, and local/federal grants.

**Amin, T.** Moodie, P, Hendricks, K, McIlff, T.  *Augmentation of Vancomycin Elution from High Dose Antibiotic Loaded Bone Cement.*  
Podium presentation at AAOS 2012 Annual Meeting, San Francisco, CA

**Amin, T.** Hendricks, K, McIlff, T.  *Increasing the Elution of Vancomycin from High Dose Antibiotic Loaded Bone Cement: A Novel Preparation Technique*  
Poster presentation at ORS, San Francisco, CA, February 4-7, 2012

Podium presentation at KUMC Resident Research Day, Kansas City, KS; May 15, 2010  
Podium presentation at Mid-Central States Orthopaedic Society, Branson, MO; June 3-6, 2010

Podium presentation at AAOS, San Francisco, CA, February 4-7, 2012

**Dunlay R,** Wang S, McIlff T, Garimella R, Templeton K.  *Vancomycin Inhibits Proliferation of Osteosarcoma Cells In vitro Growth of Osteosarcoma Cells*  
Poster presentation at ORS, San Francisco, CA, February 4-7, 2012

**Dunlay R,** Moodie P, Zhu H, Hendricks, K, McIlff, T.  *Mixing Technique Impacts Antibiotic Elution from Bone Cement and Its Elution Compromises Cement Strength*  
Poster presentation at ORS, San Francisco, CA, February 4-7, 2012

**Kramer W,** Wang J.  *NFAT1 and Posttraumatic Arthritis in Mice.*  
Podium presentation KUMC Resident and Fellow Research Day, Kansas City, KS; May 5, 2011  
Podium presentation at the Kansas Orthopaedic Society, Kansas City, KS; September 16, 2011

**Kramer W,** Lu Q, Wang J.  *Transcription Factor Nfat1 Deficiency: A Risk Factor for Progression of Posttraumatic Osteoarthritis in Mice.*  
Poster Presentation at ORS, San Francisco, CA, February 4-7, 2012

**Lansford T,** McIlff T, Burton D.  *The Effects of Cement Augmentation Technique and Volume on Pedicle Screw Fixation in Ostopenic Bone.*  
Podium presentation at KUMC Resident Research Day, Kansas City, KS; May 15, 2010  
Poster presentation at ORS, Long Beach, CA; January 13-16, 2011  
Podium presentation at AAOS, San Diego, CA; February 15-19, 2011
RESIDENT POSTER & PODIUM PRESENTATIONS

Podium presentation at AOFAS, San Diego, CA, June 20-23, 2012

Poster Presentation at ORS, Long Beach, CA; January 13-16, 2011

Podium presentation at KUMC Resident Research Day, Kansas City, KS; May 15, 2010

Schroppel J, Anderson D, Adler F, Moodie P, McIff TE. The Use of Naringin to Accelerate Healing of a Segmental Defect in the Rat Femur.
Poster Presentation at Mid-America Orthopaedic Association, Tucson, AZ; April 6-11, 2011

Podium presentation at ORS, New Orleans, LA; March 9-13, 2010

Adler F, McIff T, Poisner A, Herndon B, Lankachandra K, Schutt S, Molteni A. Captopril and Losartan mitigate the time dependent histopathology associated with Triolein induced fat embolism.
Poster presentation at ORS, New Orleans, LA; March 9-13, 2010

Adler F, McIff T, Poisner A, Herndon B, Lankachandra K, Schutt S, Molteni A. Ace inhibitor and Angiotensin receptor blocker protect against effects of pulmonary fat embolism.
Poster presentation at AAOS, New Orleans, LA; March 9-13, 2010

Podium presentation at ASBMR, Toronto, Canada; Oct. 15-19, 2010

Podium presentation at ORS, New Orleans, LA; March 6-9, 2010

Podium presentation at KUMC Resident Research Day, Kansas City, KS; May 15, 2010
Podium presentation at Mid-Central States Orthopaedic Society, Branson, MO; June 3-6, 2010.
Podium presentation at Mid-America Orthopaedic Association, Tuscon, AZ; April 6-10, 2011
Poster presentation at ORS, Long Beach, CA; January 13-16, 2011
STUDENT RESEARCHERS

Graduate Research Assistants

Jessica Witherspoon, DPT
BS, Delaware State University
MS, Univ. of North Carolina—Greensboro
Exercise Physiology
DPT,
KU School of Health Professions
Ph.D. Candidate,
KU School of Health Professions
Physical Therapy

Aly Boyer, BS
BS, University of Memphis,
Bioengineering and Math

Jeff Lamping, MS
BS, Olivet Nazarene University,
Mechanical Engineering,
MS, University of Kansas,
Bioengineering
University of Kansas School of Medicine
Year I Medical Student

Aaron Heller, BA
T32 Clinical Research Scholar
BA, Indiana University -Purdue University, Biology
Kansas City University of Medicine and Biosciences,
Year III Osteopathic Medical Student

Second Year KUMC Medical Student Research Assistants

Daniel Rhoades, BA
University of Kansas
Human Biology

Kevin Colbert, BS
University of Kansas
Bioengineering

John Weitlich, BA
Benedictine University
Biology

Dan Sisk, BA
University of Kansas
Human Biology
Intrawound Vancomycin Powder Decreases Acute, Deep *Staphylococcus aureus* Infection Rates in Posterior Instrumented Spinal Arthrodeses

Aaron Heller, BA, T32 Clinical Research Scholar
Terence E. McIf, PhD, Co-Investigator

Surgical site infection is a serious complication for patients undergoing instrumented spinal surgery. *Staphylococcus aureus* is the most common causative agent associated with post-op wound infections. Recent studies have reported a decreased infection rate with intrawound vancomycin use in spine surgeries. We sought to determine if intrawound vancomycin would decrease the rates of acute, deep *S. aureus* infections in our posterior instrumented spinal arthrodesis patients. Intrawound vancomycin has decreased the rate of acute, deep *S. aureus* infections in our posterior instrumented spinal fusion patient population from 1.61% to 0. Our vancomycin group was significantly older and underwent a significantly greater number of surgeries with pelvic fixations, though had fewer infections. This work is adding to the growing body of evidence in support of this effective adjuvant to standard antimicrobial prophylaxis.

Effects of Negative Pressure to Promote Tissue Growth into Porous Metal Implants

Primary Researcher: Jeff Lamping, MS

This two-part study investigates the application of negative pressure wound therapy (NPWT) and its effect on tissue growth in a goat model. The first part of the study investigates the effect of NPWT on the soft tissue growth into a subdermal porous metal implant. The second part of the study focuses on the effect of NPWT on bone growth into a porous metal implant used to repair a segmental bone defect. The goal of this pilot study aims to show the effectiveness of NPWT applied to the treatment of segmental bone defects and to serve as a basis for further research on this topic.

Collagen Composition and Neural Properties of the Glenoid Capsule and Labrum may Contribute to Glenohumeral Joint Laxity.

Primary Researcher: Jessica Witherspoon, DPT
Additional Research Support: Dan Sisk, BA

This study investigates correlations between collagen composition (type 1 to type 3 collagen ratio), innervation density, and joint laxity in the human shoulder. Mechanical testing of cadaveric shoulders will be used to measure joint laxity. Capsular and labral samples harvested from the glenohumeral joint will be analyzed to measure collagen type ratio, mechanoreceptor distribution as well as innervation density. The goal of this study is to provide clinicians with a greater understanding of how the collagen composition and neural properties may contribute to increased joint laxity, and ultimately recurrent instability.

The Effect of Nebulized Captopril on Fat Induced Lung Pathology

Primary Researcher: Aaron Heller, BA
Additional Research Support: Daniel Rhoades, BA

Fat embolism research has a long history at the Kansas University Medical Center and within the Department of Orthopedic Surgery. Fat emboli occur in 90% of patients with long bone fractures, and up to 20% of them will develop respiratory distress associated with these emboli. Our lab has previously characterized the pulmonary damage caused by fat emboli and demonstrated that injections of the ace inhibitor captopril or the angiotensin receptor blocker losartan attenuates this pathology. Currently, over concerns of administering an anti-hypertensive systemically to an already hypotensive trauma patient, we are testing the efficacy of delivering captopril locally to the lungs by nebulization.

Transcutaneous Osseointegration for Weight Bearing Prostheses

Primary Researchers: Aly Boyer, BA; Kevin Colbert, BS

This study investigates the application of a porcine model to address wound healing and infection concerns at the implant/skin interface. A gait study will enable a better understanding of loading associated with lower limb prostheses. An associated soft tissue finite element model focuses on the biomechanics involved with the prosthetic limb. The goal of this pilot study aims to show the effectiveness of transcutaneous osseointegrated prostheses and to serve as a basis for further research on this topic.

**STUDY DESIGN:** Case report.

**OBJECTIVE:** Two cases are presented in which the use of recombinant bone morphogenetic protein-2 (rh-BMP-2) in a posterior cervical decompression and instrumented arthrodesis may have contributed to seroma formation and cord compression.

**SUMMARY OF BACKGROUND DATA:** The use of rh-BMP-2 has been proven effective in promoting bone formation in anterior lumbar spine arthrodesis. Whether rh-BMP-2 is safe and/or effective in the cervical spine has not been determined. Adverse effects when it is used for anterior cervical fusion procedures have been reported but its role in posterior cervical decompression and instrumented fusions has yet to be determined.

**METHODS:** We report on two cases. The first is a 68-year-old man presenting with a substantial decline in his neurologic status approximately 2 weeks after surgery. The second is a 44-year-old man presenting with a substantial decline in his neurologic status approximately 5 days after surgery. Both complications occurred after a posterior cervical laminectomy and instrumented arthrodesis when rh-BMP-2 was used as a bone graft substitute.

**RESULTS:** Both patients were found to have a moderate-to-large seroma causing severe compression on the spinal cord and were urgently taken to an operating room for evacuation of the seromas. Both showed improvement of their neurologic status immediately after surgery. As rh-BMP-2 is known to occasionally cause seroma formation it is postulated that it may have been the cause of the seromas.

**CONCLUSION:** Caution should be exercised with rh-BMP-2 use in posterior cervical applications when a laminectomy has been performed. The safe and effective dose and technique for application have yet to be determined. Seroma formation is possible, which can cause acute stenosis with cord compression and neurologic compromise.


**BACKGROUND:** During the past 25 years, spinal instrumentation systems and surgical techniques used to treat idiopathic scoliosis have evolved, achieving fewer patient restrictions during arthrodesis healing, shorter constructs, and better correction. The purposes of this retrospective comparative study were to determine the survivorship of the implant/fusion without reoperation and the risk factors influencing such survival.

**METHODS:** From 1989 through 2002, 208 consecutive patients (index patient included, age 10-20 years) underwent primary posterior instrumentation and arthrodesis with the same multiple anchor implant system by one surgeon, a co-designer of the system. Two hundred seven were followed for more than 2 years; reoperation status was available for them at an average follow-up of 8.3 years. Twenty-one independent demographic, deformity, instrumentation, and process variables possibly influencing the need for reoperation were studied by comparing the reoperated group with the un-reoperated group.
RESULTS: Nineteen patients (9.2%) had reoperation; 16 (7.7%) were for indications related to posterior spine instrumentation. Survival of the implant/fusion without reoperation for spine instrumentation-related indications was 96% (95% confidence interval [CI], 93.2-98.7%) at 5 years, 91.6% (95% CI, 86.9-96.3%) at 10 years, 87.1% (95% CI, 79.5-94.6%) at 15 years, and 73.7% (95% CI, 48.6-98.6%) at 16 years, when the number at risk was nine. Reoperation need was significantly influenced by two implant variables: transverse connector design (p=0.0012) and the lower instrumented vertebra anchors used (p=0.0004). At 9 years, the longest interval allowing comparison, survival of the implant/fusion without reoperation for these two variables was 100% (six subjects at risk) compared to 82% (95% CI, 74.2-90.3%) with 59 patients still at risk for reoperation for those who did not have them, p=0.0014.

CONCLUSIONS: The most stable lower instrumented vertebra anchor configuration, bilateral pedicle screws, and the stronger transverse connector design, closed drop entry, provided the best survival of the implant/fusion without reoperation with this system and the techniques used at 9-year follow-up. We hope that this post-market study using survivorship techniques will be a guide for studies of other spinal implants.


STUDY DESIGN: Retrospective study of a prospectively assembled cohort.

OBJECTIVE: To characterize the survival from subsequent spine surgery and the life survival of patients treated surgically for severe spinal deformity due to neuropathic diseases.

SUMMARY OF BACKGROUND DATA: Survivorship analysis is widely used to study the natural history of disease processes and of treatments provided, but has very seldom been used to study patients’ course after surgery for spinal deformity associated with neuropathic diseases.

METHODS: Patients with neuropathic spinal deformity treated with primary posterior instrumentation and arthrodesis from 1989 through 2002 were identified and studied by review of charts and radiographs, and by mail survey. Subsequent spine surgery and death events, and the time interval from surgery were identified. Fifteen variables possibly influencing survivorship were studied.

RESULTS: There were no perioperative deaths, spinal cord injuries, or acute wound infections in the 117 eligible patients. Reoperation and life survival statuses were available for 110 patients (94%) at an average follow-up of 11.89 years (+/-5.3; range: 2-20.9 yr). Twelve patients (11%) had subsequent spine surgery. Survival from subsequent spine surgery was 91% at 5 years, 90% at 10 and 15 years, and 72% at 20 years. Proximal fixation problems occurred in 4 patients. Twenty-two patients (20%) had died from 4 to 20 years postoperative. Life survival was 98% at 5 years, 89% at 10 years, 81% at 15 years, and 56% at 20 years. The only variable associated with life survival was the occurrence of one or more perioperative complications, P = 0.0032. The younger half of the series at operation (<13.75 yr) was significantly more likely to have one or more perioperative complications, P = 0.0068. Spinal deformity type and magnitude were similar for the younger and older halves of the patients. Life survival of the patients with cerebral-palsy and not-cerebral-palsy upper motor neuron disease was not different. One-hundred-two of 105 were at least satisfied or would have the surgery again for the same condition.

CONCLUSION: Survival from subsequent spine operation was similar to adolescent idiopathic scoliosis series studied in the same manner. Life survival decline began at 4 years postoperative and was significantly associated with the occurrence of one or more perioperative complications. Even after successful spine deformity surgery, this population’s health status is often precarious.

BACKGROUND: We have occasionally observed clinically noticeable postoperative transverse plane pelvic rotation increase (TPPRI) in the direction of direct thoracolumbar/lumbar rotational corrective load applied during posterior instrumentation and arthrodesis for double (Lenke 3 and 6) adolescent idiopathic scoliosis (AIS) curves. Our purposes were to document this occurrence; identify its frequency, associated variables, and natural history; and determine its effect upon patient outcome.

METHODS: Transverse plane pelvic rotation (TPPR) can be quantified using the left/right hemipelvis width ratio as measured on standing posterior–anterior scoliosis radiographs. Descriptive statistics were done to determine means and standard deviations. Non-parametric statistical tests were used due to the small sample size and non-normally distributed data. Significance was set at P < 0.05.

RESULTS: Seventeen of 21 (81%) consecutive patients with double curves (7 with Lenke 3 curves and 10 with Lenke 6) instrumented with lumbar pedicle screw anchors to achieve direct rotation had a complete sequence of measurable radiographs. While 10 of these 17 had no postoperative TPPRI, 7 did all in the direction of the rotationally corrective thoracolumbar instrumentation load. Two preoperative variables were associated with postoperative TPPRI: more tilt of the vertebra below the lower instrumented vertebra (-23 degrees +/- 3.1 degrees vs. -29 degrees +/- 4.6 degrees, P = 0.014) and concurrent anterior thoracolumbar discectomy and arthrodesis (5 of 10 vs. 7 of 7, P = 0.044). Patients with a larger thoracolumbar/lumbar angle of trunk inclination or larger lower instrumented vertebra plus one to sacrum fractional/hemicurve were more likely to have received additional anterior thoracolumbar discectomy and arthrodesis (c = 0.90 and c = 0.833, respectively). Postoperative TPPRI resolved in 5 of the 7 by intermediate follow-up at 12 months. Patient outcome was not adversely affected by postoperative TPPRI, whether or not it persisted.

CONCLUSIONS: Our findings suggest that TPPRI is a decompensation caused by extension of the corrective thoracolumbar rotational load into the lumbosacral hemicurve below. As posterior instrumentation of adolescent idiopathic scoliosis becomes increasingly more effective in the transverse plane, postoperative TPPRI may become more widely noticed. This study provides some assurance that recompensation usually occurs, but that in either event TPPRI does not seem to affect clinical outcome.


We evaluated the ultimate compression strength (UCS), porosity, and fracture surface roughness of 2 commercially available single-antibiotic bone cements vacuum-mixed with additional amounts of vancomycin (2, 4, 6, and 8 g). At least 8 g could be added to Palacos R + 0.5 g gentamicin (UCS = 75.04 +/- 6.64 MPa) and no more than 6 g to Simplex P + 1 g tobramycin (UCS = 78.93 +/- 4.98 MPa) to maintain a UCS above the International Organization for Standardization minimum standard (70 MPa). Increasing vancomycin concentration correlated with a decrease in porosity, but showed a trend towards greater fracture surface roughness.


BACKGROUND: The use of thoracic pedicle screws in spinal deformity, trauma, and tumor reconstruction is becoming more common. Unsuccessful screw placement may require salvage
techniques utilizing transverse process hooks. The effect of different starting point placement techniques on the strength of the transverse process has not previously been reported. The purpose of this paper is to determine the biomechanical properties of the thoracic transverse process following various pedicle screw starting point placement techniques.

METHODS: Forty-seven fresh-frozen human cadaveric thoracic vertebrae from T2 to T9 were disarticulated and matched by bone mineral density (BMD) and transverse process (TP) cross-sectional area. Specimens were randomized to one of four groups: A, control, and three others based on thoracic pedicle screw placement technique; B, straightforward; C, funnel; and D, in-out-in. Initial cortical bone removal for pedicle screw placement was made using a burr at the location on the transverse process or transverse process-laminar junction as published in the original description of each technique. The transverse process was tested measuring load-to-failure simulating a hook in compression mode. Analysis of covariance and Pearson correlation coefficients were used to examine the data.

RESULTS: Technique was a significant predictor of load-to-failure (P = 0.0007). The least squares mean (LS mean) load-to-failure of group A (control) was 377 N, group B (straightforward) 355 N, group C (funnel) 229 N, and group D (in-out-in) 301 N. Significant differences were noted between groups A and C, A and B and C, and C and D. BMD (0.925 g/cm² [range, 0.624-1.301 g/cm²]) was also a significant predictor of load-to-failure, for all specimens grouped together (P < 0.0001) and for each technique (P < 0.05). Level and side tested were not found to significantly correlate with load-to-failure.

CONCLUSIONS: The residual coronal plane compressive strength of the thoracic transverse process is dependent upon the screw starting point placement technique. The funnel technique significantly weakens transverse processes as compared to the straightforward technique, which does not significantly weaken the transverse process. It is also dependent upon bone mineral density, and low failure loads even in some control specimens suggest limited usefulness of the transverse process for axial compression loading in the osteoporotic thoracic spine.


OBJECTIVES: To compare the short-term results of anterior pelvic external fixation (APEF) versus anterior pelvic internal fixation (APIF) applied subcutaneously in the context of surgical treatment of pelvic ring injuries.

DESIGN: A single center retrospective chart review.

SETTING: A level 1 trauma center.

METHODS: A consecutive series of 48 patients who underwent surgical stabilization of their anterior pelvic ring (24 utilizing APIF and 24 utilizing APEF) by 2 surgeons at a single hospital were studied. The choice to use either APEF or APIF was left up to each surgeon, the indications for use are the same. Data collected included surgical or postoperative complications including infection, implant failure, reoperation, documented surgical site pain persisting to clinical follow-up visits, and radiographic union. Measurements on inlet and outlet pelvic radiographs were made immediately postoperation and at all follow-up clinic visits to determine whether there were differences in maintaining pelvic fracture reduction. Statistical analysis was performed to evaluate significant differences between the 2 groups with regard to each of these variables.

RESULTS: The APIF group was found to have a significantly lower incidence of wound complication (P < 0.05) and a lower occurrence of associated morbidity events as compared with the APEF group. In addition, the APIF group was found to have a significantly lower rate of surgical site pain persisting through all clinical follow-up intervals (P = 0.05). There was no difference between the 2 groups in
terms of maintenance of pelvic reduction in the early postoperative phase or at final follow-up. No other significant differences were observed between the 2 groups.

CONCLUSIONS: The present study, which was based on our initial experience with the subcutaneous anterior pelvic fixator, demonstrated encouraging clinical outcomes in terms of a lower wound complication rate and associated morbidity, and surgical site symptoms, although maintaining equivalent reduction. These findings suggest that further analysis of this technique is warranted to determine if it can be definitively recommended for general use.

LEVEL OF EVIDENCE: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.


OBJECTIVES: This study was undertaken to determine if there is increased likelihood of popliteal artery injury as one places a fixed-angle lateral proximal tibia locking plate with posterior plate lift off and or anterior plate translation from the ideal position.

METHODS: A Synthes (Synthes USA, West Chester, PA) 3.5-mm and 4.5-mm lateral proximal tibia locking plate was placed consecutively on each of six specimens in the straight lateral (SL) position. Screw position with respect to the medial cortex was recorded as well as the distance of the posterior most screw tip to the popliteal artery. Next a 3-mm shim was placed under the posterior edge of the same plate to mimic posterior plate lift off (LO) followed by placement of a 6-mm shim. The same experiment was repeated with the plate translated 5 mm anteriorly (AT).

RESULTS: The popliteal artery was injured in zero of six specimens using the 3.5-mm plate. The popliteal artery was injured in six of six specimens using the 4.5-mm plate in the 5-mm AT 6-mm LO position, five of six with 5-mm AT and 3-mm LO, two of six with only 5-mm AT, four of six with SL and 6-mm LO, two of six with SL and 3-mm LO, and zero of six with SL.

CONCLUSION: The Synthes 4.5-mm plate can put the popliteal artery at risk with as little as 3-mm posterior liftoff in the intended straight lateral position or with 5-mm anterior plate translation with no posterior liftoff. Therefore, placement of the 4.5-mm plate in the proper position and confirmation of its position with a true lateral radiograph is paramount to avoid injury to the popliteal artery.


The objective of this study was to validate the MRI-based joint contact modeling methodology in the radiocarpal joints by comparison of model results with invasive specimen-specific radiocarpal contact measurements from four cadaver experiments. We used a single validation criterion for multiple outcomes to characterize the utility and overall validity of the modeling approach. For each experiment, a Pressurex film and a Tekscan sensor were sequentially placed into the radiocarpal joints during simulated grasp. Computer models were constructed based on MRI visualization of the cadaver specimens without load. Images were also acquired during the loaded configuration used with the direct experimental measurements. Geometric surface models of the radius, scaphoid and lunate (including cartilage) were constructed from the images acquired without the load. The carpal bone motions from the unloaded state to the loaded state were determined using a series of 3D image registrations. Cartilage thickness was assumed uniform at 1.0 mm with an effective compressive modulus of 4 MPa. Validation was based on experimental versus model contact area, contact force, average contact pressure and peak contact pressure for the radioscaphoid and radiolunate articulations.
Contact area was also measured directly from images acquired under load and compared to the experimental and model data. Qualitatively, there was good correspondence between the MRI-based model data and experimental data, with consistent relative size, shape and location of radioscaphoid and radiolunate contact regions. Quantitative data from the model generally compared well with the experimental data for all specimens. Contact area from the MRI-based model was very similar to the contact area measured directly from the images. For all outcome measures except average and peak pressures, at least two specimen models met the validation criteria with respect to experimental measurements for both articulations. Only the model for one specimen met the validation criterion for average and peak pressure of both articulations; however the experimental measures for peak pressure also exhibited high variability. MRI-based modeling can reliably be used for evaluating the contact area and contact force with similar confidence as in currently available experimental techniques. Average contact pressure, and peak contact pressure were more variable from all measurement techniques, and these measures from MRI-based modeling should be used with some caution.


Vitamin D, in addition to its effects on bone, is important in cell cycle regulation. Vitamin D receptor (VDR) has been identified in breast, prostate, and colon cancers, as well as in canine and human osteosarcoma (OS) cell lines; however, it has not been well investigated in human OS-archived specimens. We correlated VDR, retinoid X receptor (RXR), and MIB-1 (Ki-67) expression in 110 archived OS cases with several clinicopathologic parameters including patient’s age, sex, tumor location, tumor grade, and type and metastatic status. The expression of VDR and RXR was identified in human OS tissue obtained from primary and metastatic OS archival tissue. No statistically significant difference was found in VDR expression in relation with tumor grade, type, age, sex, or location. The expression of RXR was highest in higher-grade (P = .0006) and metastatic tumors but remained unchanged when correlated with tumor type, age, sex, or location. The expression of MIB-1 was statistically elevated in higher-grade tumors (P = .001), patients 25 years or younger (P = .04), tumors located in extremities (P = .005), and metastatic lesions, but was not impacted by tumor type or patient’s sex. Proliferative activity was significantly reduced after treatment, as the mean MIB-1 expression dropped from 11% in primary biopsy samples to 6% in resection specimens. There appears to be a relationship between proliferative tumor activity and tumor grade, location, and metastasis. Additional studies on the analysis of the effects of vitamin D and RXR on OS proliferation, apoptosis, and differentiation are critical to further evaluate their potential role in OS treatment.


BACKGROUND: We hypothesized that strict enforcement of ventilator-associated pneumonia (VAP) prevention (VAPP) strategies would decrease the incidence of VAP and improve patient outcomes.

METHODS: This retrospective study examined 696 consecutive ventilated patients in a Level One trauma center. Three study groups were compared: Pre-VAPP, VAPP implementation, and VAPP enforcement. Ventilator days were compared with occurrences of VAP, defined by the U.S. Centers for Disease Control and Prevention National Nosocomial Infection Surveillance criteria. Patients with and without VAP were compared to evaluate the effect of VAP on patient outcome. Fisher exact, Kruskal-Wallis, and chi-square analyses were used, and p < 0.05 was considered significant.
RESULTS: During the pre-VAPP protocol period, 5.2 cases of VAP occurred per 1,000 days of ventilator support. The number of cases of VAP decreased to 2.4/1,000 days (p = 0.172) and 1.2/1,000 days (p = 0.085) in the implementation and enforcement periods, respectively. However, when including all trauma patients, regardless of head Abbreviated Injury Score (AIS) score, the difference in the rate of VAP was statistically significant in the enforcement period, but not in the implementation period, compared with the pre-VAPP period (p = 0.014 and 0.062, respectively). A significant decrease was seen in the mortality rate (p = 0.024), total hospital days (p = 0.007), intensive care unit days (p = 0.002), ventilator days (p = 0.002), and hospital charges (p = 0.03) in patients without VAP compared with patients having VAP.

CONCLUSIONS: There was a statistically significant decrease in the occurrence of VAP with strict enforcement of a VAPP protocol, regardless of head AIS score. Although the difference in patients with a head AIS score <3 was not statistically significant, it was clinically meaningful, decreasing the already-low rate of VAP by half. Strict enforcement of VAPP protocols may be cost efficient for hospitals and prevent decreased reimbursement under the Medicare pay-for-performance strategies.


INTRODUCTION: Despite the widespread use of bisphosphonates, its effects on normal bone microarchitecture of the proximal femur are still poorly studied. The purpose of this study was to determine the effects of long-term high-dose treatment of alendronate on microstructure and bone mineral density of cancellous, cortical compact and subchondral compact bone of the femoral head and neck region in normal adult male rabbits.

MATERIALS AND METHODS: Thirty-two adult, male rabbits were randomized into and were treated with either alendronate or placebo for 6 and 12 months. Micro-QCT measurements were taken in the (1) trabecular region, (2) cortical region of the femoral neck and (3) the subchondral region of the femoral head.

RESULTS: In the trabecular region of the femoral head, alendronate treatment significantly increased vBMD at 6 and 12 months (+21.0%, p < 0.05 and +26.8%, p < 0.05, respectively) and BVF (29.6%, p < 0.05 and 35.6%, p < 0.05, respectively) with significantly altered bone microarchitecture when compared with their placebo group; 6- and 12-month alendronate treatment significantly increased the vBMD and thickness and decreased the porosity of the subchondral bone in the femoral head.

CONCLUSION: High-dose alendronate treatment led to significant and differential changes in bone microarchitecture in trabecular, cortical and subchondral bone of the proximal femur of adult male rabbits.


INTRODUCTION. Three-column vertebral resections are frequently applied to correct sagittal malalignment; their effects on distant unfused levels need to be understood.

METHODS. 134 consecutive adult PSO patients were included (29 thoracic, 105 lumbar). Radiographic analysis included pre- and postoperative regional curvatures and pelvic parameters, with paired independent t-tests to evaluate changes.

RESULTS. A thoracic osteotomy with limited fusion leads to a correction of the kyphosis and to a spontaneous decrease of the unfused lumbar lordosis (-8 degrees). When the fusion was extended, the lumbar lordosis increased (+8 degrees). A lumbar osteotomy with limited fusion leads to a
correction of the lumbar lordosis and to a spontaneous increase of the unfused thoracic kyphosis (+13 degrees). When the fusion was extended, the thoracic kyphosis increased by 6 degrees. Conclusion. Data from this study suggest that lumbar and thoracic resection leads to reciprocal changes in unfused segments and requires consideration beyond focal corrections.


Osteoarthritis (OA) is characterized by joint pain and stiffness with radiographic evidence of joint space narrowing, osteophytes, and subchondral bone sclerosis. Posttraumatic OA (PTOA) arises from joint trauma, which accounts for a fraction of all patients with OA. Articular cartilage breakdown can occur soon or for years after a joint injury. Even with the current care of joint injuries, such as anatomic reduction and rigid fixation of intra-articular fractures and reconstruction of ruptured ligaments with successful restoration of joint biomechanics, the risk of PTOA after joint injuries ranges from 20% to more than 50%. The time course for the progression of PTOA is highly variable and risk of PTOA increases with patient age at the time of joint injury, suggesting that biologic factors may be involved in the progression of PTOA. Therapeutic options are limited due largely to the lack of information on the mechanisms underlying the progression of PTOA. This review summarizes the current studies on the pathogenetic mechanisms of PTOA, with a main focus on the metabolic changes in articular cartilage in the acute posttraumatic phase and the early chronic phase, a clinically asymptomatic period. Recent studies have revealed that mechanical damage to the articular tissues may lead to changes in gene expression and cartilage metabolism, which could trigger a cascade of events leading to degradation of articular cartilage and pathologic changes in other joint tissues. Understanding the mecha-nobiologic, molecular and cellular changes that lead to continued cartilage degradation in the relatively early phases after joint injury may open up new opportunities for early clinical intervention.


**PURPOSE:** Three column thoracic osteotomy (TCTO) is effective to correct rigid thoracic deformities, however, reasons for residual postoperative spinal deformity are poorly defined. Our objective was to evaluate risk factors for poor spino-pelvic alignment (SPA) following TCTO for adult spinal deformity (ASD).

**METHODS:** Multicenter, retrospective radiographic analysis of ASD patients treated with TCTO. Radiographic measures included: correction at the osteotomy site, thoracic kyphosis (TK), lumbar lordosis (LL), sagittal vertical axis (SVA), pelvic tilt (PT), and pelvic incidence (PI). Final SVA and PT were assessed to determine if ideal SPA (SVA < 4 cm, PT < 25 degrees) was achieved. Differences between the ideal (IDEAL) and failed (FAIL) SPA groups were evaluated.

**RESULTS:** A total of 41 consecutive ASD patients treated with TCTO were evaluated. TCTO significantly decreased TK, maximum coronal Cobb angle, SVA and PT (P < 0.05). Ideal SPA was achieved in 32 (78%) and failed in 9 (22%) patients. The IDEAL and FAIL groups had similar total fusion levels and similar focal, SVA and PT correction (P > 0.05). FAIL group had larger pre- and post-operative SVA, PT and PI and a smaller LL than IDEAL (P < 0.05).
CONCLUSIONS: Poor SPA occurred in 22% of TCTO patients despite similar operative procedures and deformity correction as patients in the IDEAL group. Greater pre-operative PT and SVA predicted failed post-operative SPA. Alternative or additional correction procedures should be considered when planning TCTO for patients with large sagittal global malalignment, otherwise patients are at risk for suboptimal correction and poor outcomes.


STUDY DESIGN: Cross-sectional mail questionnaire. OBJECTIVE: Examination of the underlying construct validity of the Scoliosis Research Society-22r (SRS-22r) Health-Related Quality of Life (HRQoL) Questionnaire using factor analysis.

SUMMARY OF BACKGROUND DATA: The original SRS-24 HRQoL questionnaire has undergone a series of modifications in an effort to further improve its psychometric properties and validate its use in patients from 10 years of age until well into adulthood. The SRS-22r questionnaire is the result of this effort. To date, the underlying construct validity of the original English version has not been analyzed by factor analysis.

METHODS: A questionnaire including all questions on the SRS-24, -23, -22, and -22r questionnaires (49 total questions) was mailed to a consecutive series of 235 patients who had received primary posterior or anterior instrumentation and arthrodesis. Domain structure of the SRS-22r questions was analyzed using iterated principal factor analysis with orthogonal rotation.

RESULTS: One hundred twenty-one (51%) of the patients, age 23.34 +/- 4.52 years (range, 14.16-34.57 years), returned the questionnaire at 8.63 +/- 4.00 years (range, 2.32-15.94 years) following surgery. Factor analysis using all 22 questions resulted in 3 factors with many shared items because of significant collinearity of the satisfaction/dissatisfaction with management questions with the others. After 18 iterations, factor analysis using the 20 non-management questions revealed 4 factors that explained 98% of the variance. These factors parallel the assigned domains of the SRS-22r questionnaire. Three questions (2 self-image and 1 function) were identified that had high loading in 2 factors. However, internal consistency was best when 2 of the questions (1 self-image and 1 function) were retained in their assigned SRS-22r domains and the third decreased self-image internal consistency by only 0.01%. The internal consistencies (Cronbach alpha) of the assigned SRS-22r nonmanagement domains were excellent or very good: function 0.83, pain 0.87, self-image 0.80, and mental health 0.90. For the management domain it was good: 0.73.

CONCLUSION: Factor analysis of the SRS-22r HRQoL confirms placement of the 20 non-management domain questions in the assigned 4 domains, all with excellent or very good internal consistency.


STUDY DESIGN: Cross-sectional mail questionnaire.

OBJECTIVE: Assess the feasibility of translating total and domain scores from Scoliosis Research Society (SRS)-24, SRS-23, and SRS-22 to SRS-22r.

SUMMARY OF BACKGROUND DATA: Three successive editions of the original SRS-24 health-related quality-of-life questionnaire have resulted from efforts to improve its psychometric properties and validate its use in patients down to 10 years of age. This resulted in the need to establish, if possible, conversion equations to the last and most thoroughly validated version, SRS-22r.
METHODS: A consolidated questionnaire of 49 questions that incorporated the various questions in the four questionnaires was mailed to a consecutive series of 235 patients who had received primary posterior or anterior instrumentation and arthrodensis to treat adolescent idiopathic scoliosis. Regression modeling was used to establish conversion equations from the SRS-24, SRS-23, and SRS-22 to the SRS-22r.

RESULTS: One hundred twenty-one of the 235 patients (51%), aged 23.3 +/- 4.52 years (range 14.2-34.6 years), returned the questionnaire at 8.6 +/- 4.00 years (range 2.3-15.9 years) following surgery. Estimation of SRS-22r questionnaire and nonmanagement domains total scores and mean scores from SRS-22 and SRS-23 scores is excellent (R2 scores of 0.97-0.99) and good for SRS-24 scores (R2 scores of 0.80-0.82, improving to 0.86 and 0.87 after minimal domain reconfiguration). Estimation of SRS-22r individual domain total scores and mean scores from SRS-22 and SRS-23 is good to excellent (R2 scores of 0.81-0.99). Minimal domain reconfiguration improves conversion from SRS-24 pain from R2 = 0.71 to 0.76, which are both fair; SRS-24 function from R2 = 0.69 and 0.74 to 0.83, from poor and fair to good; and SRS-24 satisfaction/dissatisfaction with management from R2 = 0.64 to 0.80, from poor to good. Conversion of SRS-24 self-image is poor (R2 = 0.60) despite the correlation being statistically significant.

CONCLUSION: With one exception, SRS-24, SRS-23, and SRS-22 questionnaire, nonmanagement domains, and individual domain total scores and mean scores can be translated to SRS-22r scores with fair to excellent accuracy, which is further improved in some instances by minimal domain reconfigurations. The sole exception is SRS-24 self-image, which translates poorly.


BACKGROUND: Fat embolization (FE) is an often overlooked and poorly understood complication of skeletal trauma and some orthopedic procedures. Fat embolism can lead to major pulmonary damage associated with fat embolism syndrome (FES).

METHODS: A model of FE in un-anesthetized rats, using intravenous injection of the neutral fat triolein, was used to study the potential therapeutic effect on lung histopathology of altering the production of, or response to, endogenous angiotensin (Ang) II. Either captopril, an Ang I converting enzyme inhibitor, or losartan, an Ang II type 1 receptor blocker, was injected 1 hour after FE by triolein injection. After euthanasia at 48 hours, histopathologic evaluation was used to compare the drug-treated animals with control animals that received only triolein.

RESULTS: Histology of the lungs of rats treated only with triolein revealed severe, diffuse pathology. Alveolar septa showed severe, diffuse inflammation. Bronchial lumina showed severe mucosal epithelial loss. The media of the pulmonary small arteries and arterioles was thicker, and the lumen patency was reduced 60% to 70%. Trichrome staining confirmed the abundant presence of collagen in the media and adventitia, as well as collagen infiltrating the bronchial musculature. Both captopril and losartan treatments reduced the inflammatory, vasoconstrictor, and profibrotic effects present at 48 hours (p<0.001). With treatment, the vascular lumen remained patent, and the fat droplets were reduced in size and number. There was a reduction in the number of infiltrating leukocytes, macrophages, myofibroblasts, and eosinophils, along with a significant decrease in hemorrhage and collagen deposition (p<0.001). Pathologic changes in bronchial epithelium were also diminished.

CONCLUSIONS: The results suggest that the use of drugs that act on the renin-Ang system might provide an effective and targeted therapy for fat embolism syndrome.

OBJECTIVES: To determine what anatomic structures are at risk after the application of a subcutaneous anterior pelvic internal fixator (APIF), from an incision over the anterior iliac crest to an incision centered over the pubic symphysis (Pfannenstiel).

METHODS: A laboratory investigation was performed using 5 fresh, frozen, nonpreserved cadaveric specimens (3 male specimens, 2 female specimens). Dissections were carried out to identify the relationships and proximity between the fixator screw constructs and various anatomic structures, including the (1) lateral femoral cutaneous nerve (LFCN), (2) ilioinguinal nerve (IIN), (3) iliohypogastric nerve (IHN), (4) femoral nerve, (5) femoral artery, (6) femoral vein, (7) genitofemoral nerve; and (8) spermatic cord or round ligament. The mean and range of distance from each of these structures to the implant were measured with calipers.

RESULTS: Despite variations in pelvic anatomy and width of pelvic brims, precontoured fixators (3.5 locking reconstruction plates) did not violate any pelvic neurovascular structures using this recommended application of an APIF. The spermatic cord was easily avoided as they were directly visualized using our application technique (mean, 0.4 cm, range, 0-2 cm). Abdominal musculature protected the IHN and IIN for most of their course, with the precontoured plates remaining inferior to their course and resting superficial to their branches (IHN mean, 1.5 cm, range, 1.2-1.8 cm and IIN mean, 2.1 cm, range, 0.9-4 cm). The LFCN traveled safely posterior to the inguinal ligament, thus being bridged by the internal spanning fixation without visualized disruption, impingement, or violation (mean, 1.5 cm, range, 0.6-4 cm). Finally, the femoral nerve, artery, and vein collectively demonstrated safe distance from the risk of compression (mean, 2.2 cm, range, 0.8-3.7 cm).

CONCLUSIONS: The anatomic structures hypothesized to be potentially endangered because of the lack of direct visualization during APIF placement, include the LFCN, IIN, IHN, femoral nerve, femoral artery, and femoral vein. Based upon our anatomic study, APIF, which may be used for treatment augmentation of anterior pelvic ring disruptions, does not place these structures at significant risk. In addition, the reproductive structures (round ligament and spermatic cord) are in direct visualization and can easily be avoided during implant placement.

Most contemporary biomaterial designs for osteochondral regeneration utilize monolithic, biphasic, or even multiphasic constructs. We have introduced a microsphere-based approach to create a continuous gradient in both material composition and encapsulated growth factors. The gradients were fabricated by filling a cylindrical mold with opposing gradients of two different types of poly(D,L-lactic-co-glycolic acid) microspheres. The chondrogenic microspheres were loaded with transforming growth factor-beta1, whereas the osteogenic microspheres contained bone morphogenetic protein-2 with or without nanophase hydroxyapatite. The gradient scaffolds (material gradient only, signal gradient only, or material/signal gradient combination) or blank control scaffolds were implanted in 3.5 mm-diameter defects in rabbit knees for 6 or 12 weeks. This is the first in vivo evaluation of these novel gradient scaffolds in the knee. The gross morphology, MRI, and histology indicated that the greatest extent of regeneration was achieved when both signal and material gradients were included together. This combination resulted in complete bone ingrowth, with an overlying cartilage layer with high glycosaminoglycan content, appropriate thickness, and integration with the surrounding cartilage and underlying bone. The results suggest that osteochondral regeneration may benefit from biomaterials that integrate a continuous gradient in both material composition and encapsulated growth factors.


**BACKGROUND:** Internal fixation of the os calcis is often complicated by prolonged soft tissue management and posterior facet disruption. An ideal calcaneal construct would include minimal hardware prominence, sturdy posterior facet fixation and nominal soft tissue disruption. The purpose of this study was to develop such a construct and provide a biomechanical analysis comparing our technique to a standard internal fixation technique.

**METHODS AND MATERIALS:** Twenty fresh-frozen cadaver calcanei were used to create a reproducible Sanders type-IIB calcaneal fracture pattern. One calcaneus of each pair was randomly selected to be fixed using our compressive headless screw technique. The contralateral matched calcaneus was fixed with a nonlocking calcaneal plate in a traditional fashion. Each calcaneus was cyclically loaded at a frequency of 1 Hz for 4000 cycles using an increasing force from 250 N to 1000 N. An Optotak motion capturing system was used to detect relative motion of the three fracture fragments at eight different points along the fracture lines. Horizontal separation and vertical displacement at the fracture lines was recorded, as well as relative rotation at the primary fracture line.
RESULTS: When the data were averaged, there was more horizontal displacement at the primary fracture line of the plate and screw construct compared to the headless screw construct. The headless screw construct also had less vertical displacement at the primary fracture line at every load. On average those fractures fixed with the headless screw technique had less rotation than those fixed with the side plate technique.

CONCLUSION: A new headless screw technique for calcaneus fracture fixation was shown to provide stability as good as, or better than, a standard side plating technique under the axial loading conditions of our model. Although further testing is needed, the stability of the proposed technique is similar to that typically provided by intramedullary fixation.

CLINICAL RELEVANCE: This fixation technique provides a biomechanically stable construct with the potential for a minimally invasive approach and improved post-operative soft tissue healing.


BACKGROUND: Fat embolism (FE) after trauma and some orthopedic procedures is known to cause acute lung injury, including acute respiratory distress syndrome. However, its potential long-term effects on the lung are unknown. A previous study using a rat model of FE found significant histopathologic changes in the lungs after intravenous injection of triolein for up to 11 days. This study detailed the persistence of the lung damage and investigated the input of the renin-angiotensin system in its pathology.

METHODS: Unanesthetized rats were injected via the tail vein with 0.2 mL saline or triolein. After euthanasia, at 3 weeks or 6 weeks, lung sections were stained to highlight cellular structure, presence of collagen and fat, or immunolabeled for smooth muscle actin or angiotensin peptides.

RESULTS: At 3 weeks or 6 weeks after triolein injection, there was no dilatation of the heart or inferior vena cava, no congestion of the liver or spleen, no adventitial edema, nor was fluid present in alveoli or pleural cavity as reported in animals at earlier time points. Persisting pathology included reduced lumen patency, thickening of the media of small arteries and arterioles, and vascular and septal inflammation. Although the fat content of the lung decreased from week 3 to week 6, there was a progressive increase in collagen, smooth muscle actin, and angiotensin peptides.

CONCLUSIONS: This model extends the effect of FE on pulmonary pathology to 6 weeks, revealing persistent vasculitis, septal inflammation, and progressive fibrotic changes which are associated with increased presence of angiotensin peptides.


The development of disease-modifying pharmacologic therapy for osteoarthritis (OA) currently faces major obstacles largely because the regulatory mechanisms for the function of adult articular chondrocytes remain unclear. We previously demonstrated that lack of Nfat1, one of the nuclear factor of activated T cells (NFAT) transcription factors, causes OA-like changes in adult mice. This study aimed to identify whether Nfat1 specifically regulates adult articular chondrocyte function and its age-dependent regulatory mechanism using both Nfat1-deficient and wild-type mice. Deletion of Nfat1 did not induce OA-like articular chondrocyte dysfunction (e.g., overexpression of proinflammatory cytokines and matrix-degrading proteinases) until the adult stage. RNAi-mediated Nfat1 knockdown caused dysfunction of wild-type adult articular chondrocytes. Nfat1 expression in wild-type articular
upregulated Nfat1 expression concomitant with increased H3K4me2 at the Nfat1 promoter. Knockdown of Jmjc-containing histone demethylase-2a (Jhdm2a) in 6-month articular chondrocytes downregulated Nfat1 expression concomitant with increased H3K9me2 at the Nfat1 promoter. These results suggest that Nfat1 is an essential transcriptional regulator of chondrocyte homeostasis in adult articular cartilage. Age-dependent Nfat1 expression in articular chondrocytes is regulated by dynamic histone methylation, one of the epigenetic mechanisms that regulate gene transcription.


**INTRODUCTION:** Procurvatum or anterior bow deformity is a potential complication after treatment of femur fractures with flexible titanium nails (FTNs). This article reports on a clinical evaluation of angulation after treating pediatric femur fractures with FTNs. The article also reports on a complementary investigation of potential causes of these deformities using a biomechanical model.

**METHODS:** All pediatric femoral shaft fractures treated with FTNs over a 4-year period were reviewed. Fracture location, pattern, angulation, and nail shoe tip orientation were recorded from postoperative radiographs. Malunion was defined as greater than 10 degrees of angulation on the AP radiograph or greater than 15 degrees on the lateral view. As an adjunct to the clinical study, a synthetic femur model was created using midtransverse fractures. These femurs were nailed using 2 FTNs inserted so as to create constructs having the following combinations of nail shoe tip orientation: both anterior (AA), both posterior (PP), both neutral (NN), or 1 anterior and 1 posterior (AP). The resulting angular deformities noticeable upon gross inspection were then measured.

**RESULTS:** Of the 70 fractures reviewed, malunion occurred in 16 fractures, of which 11 had increased anterior bow. A majority of malunions was observed in older children with middle third of the femur fractures. They were significantly more prevalent in transverse fractures compared with all other fracture patterns. Clinically, increased anterior bowing did not occur if 1 of the nails was positioned to resist procurvatum, as seen in the lateral radiograph. Depending on nail tip orientation, the biomechanical femur fracture model showed significant differences in mean deformations after nail placement: AA had 12.6 degrees of posterior bow compared with 14.8, 3.7, and 0.3 degrees of anterior bow for PP, NN, and AP, respectively.

**CONCLUSION:** Anterior bowing greater than 15 degrees is the most common malunion noted in this series of femur fractures that were nailed using FTN’s. We conclude that final nail shoe tip orientation influences the likelihood of anterior bow deformity. The likelihood of large anterior bowing may be reduced if at least 1 of the nails is inserted with the tip pointing in an anterior direction. **LEVEL OF EVIDENCE/CLINICAL RELEVANCE:** Level III.


**PURPOSE:** Major peri-operative complications for adult spinal deformity (ASD) surgery remain common. However, risk factors have not been clearly defined. Our objective was to identify patient and surgical parameters that correlate with the development of major peri-operative complications with ASD surgery.

**METHODS:** This is a multi-center, retrospective, consecutive, case-control series of surgically treated ASD patients. All patients undergoing surgical treatment for ASD at eight centers were retrospectively reviewed. Each center identified 10 patients with major peri-operative complications.
Randomization tables were used to select a comparably sized control group of patients operated during the same time period that they did not suffer major complications. The two groups were analyzed for differences in clinical and surgical factors. Analysis was restricted to non-instrumentation related complications.

RESULTS: At least one major complication occurred in 80 of 953 patients (8.4%), including 72 patients with non-instrumentation related complications. There were no significant differences between the complications and control groups based on the demographics, ASA grade, co-morbidities, body mass index, prior surgeries, pre-operative anemia, smoking, operative time or ICU stay (p > 0.05). Hospital stay was significantly longer for the complications group (14.4 vs. 7.9 days, p = 0.001). The complications group had higher percentages of staged procedures (46 vs. 37%, p = 0.011) and combined anterior-posterior approaches (56 vs. 32%, p = 0.011) compared with the control group.

CONCLUSION: The major peri-operative complication rate was 8.4% for 953 surgically treated ASD patients. Significantly higher rates of complications were associated with staged and combined anterior-posterior surgeries. None of the patient factors assessed were significantly associated with the occurrence of major peri-operative complications. Improved understanding of risk profiles and procedure-related parameters may be useful for patient counseling and efforts to reduce complication rates.


OBJECT: Pedicle subtraction osteotomy (PSO) is a surgical procedure that is frequently performed on patients with sagittal spinopelvic malalignment. Although it allows for substantial spinopelvic realignment, suboptimal realignment outcomes have been reported in up to 33% of patients. The authors’ objective in the present study was to identify differences in radiographic profiles and surgical procedures between patients achieving successful versus failed spinopelvic realignment following PSO.

METHODS: This study is a multicenter retrospective consecutive PSO case series. The authors evaluated 99 cases involving patients who underwent PSO for sagittal spinopelvic malalignment. Because precise cutoffs of acceptable residual postoperative sagittal vertical axis (SVA) values have not been well defined, comparisons were focused between patient groups with a postoperative SVA that could be clearly considered either a success or a failure. Only cases in which the patients had a postoperative SVA of less than 50 mm (successful PSO realignment) or more than 100 mm (failed PSO realignment) were included in the analysis. Radiographic measures and PSO parameters were compared between successful and failed PSO realignments.

RESULTS: Seventy-nine patients met the inclusion criteria. Successful realignment was achieved in 61 patients (77%), while realignment failed in 18 (23%). Patients with failed realignment had larger pre-operative SVA (mean 217.9 vs 106.7 mm, p < 0.01), larger pelvic tilt (mean 36.9 degrees vs 30.7 degrees, p < 0.01), larger pelvic incidence (mean 64.2 degrees vs 53.7 degrees, p < 0.01), and greater lumbar lordosis-pelvic incidence mismatch (-47.1 degrees vs -30.9 degrees, p < 0.01) compared with those in whom realignment was successful. Failed and successful realignments were similar regarding the vertebral level of the PSO, the median size of wedge resection 22.0 degrees (interquartile range 16.5 degrees -28.5 degrees), and the numerical changes in pre- and postoperative spinopelvic parameters (p > 0.05).

CONCLUSIONS: Patients with failed PSO realignments had significantly larger preoperative spinopelvic deformity than patients in whom realignment was successful. Despite their apparent need for greater correction, the patients in the failed realignment group only received the same amount of
correction as those in the successfully realigned patients. A single-level standard PSO may not achieve optimal outcome in patients with high preoperative spinopelvic sagittal malalignment. Patients with large spinopelvic deformities should receive larger osteotomies or additional corrective procedures beyond PSOs to avoid undercorrection.


**STRUCTURED ABSTRACT:**

**Study Design.** Retrospective, radiographic analysis of mathematical formulas used to predict sagittal vertical axis (SVA) following pedicle subtraction osteotomy (PSO). Objective. Evaluate the ability of different formulas to predict SVA following PSO. Summary of Background Data. Failure to achieve optimal spinal alignment (SA) following spinal fusion correlates with poor outcomes. Numerous mathematical models have been proposed to aid preoperative PSO planning and predict postoperative SA. Pelvic parameters have been shown to impact SA, however many preoperative planning models fail to evaluate these. Compensatory changes within unfused spinal segments have also been shown to impact SVA. Predictive formulas that do not evaluate pelvic parameters and unfused spinal segments may erroneously guide PSO surgery. A formula that integrates pelvic tilt (PT) and spinal compensatory changes to predict optimal SVA has been previously proposed. Methods. Comparative analysis of five mathematical models used to predict optimal postoperative SVA (<5cm) following PSO was evaluated using a multicenter PSO database. Results. Radiographs of 147 patients, mean age 52 yrs (SD, 15 yrs) that received 147 PSOs (42 thoracic, 105 lumbar) were evaluated. Mean preoperative and postoperative SVA was 108 mm (SD 95 mm) and 30 mm (SD 60 mm; p<0.001), respectively. Each mathematical formula provided unique prediction for postoperative SA (Pearson R-square < 0.15). Formulas that neglected pelvic alignment poorly predicted final SVA and poorly correlated with optimal SVA. Formulas that evaluated pelvic morphology (pelvic incidence; PI) had improved SVA prediction. The Lafage formulas, which incorporate PT and spinal compensatory changes, had the best SVA prediction (p<0.05) and best correlation with optimal SVA (R = 0.75). Conclusion. Preoperative planning for PSO is essential to optimize postoperative SA. Mathematical models that do not consider pelvic parameters and changes in unfused spinal segments poorly predict optimal postoperative alignment and may predispose to poor clinical outcomes. The Lafage formulas, which incorporated PT and spinal compensatory changes, best predicted optimal SVA.


Musculoskeletal diseases can be lifelong and affect and be affected by other health conditions. With their resulting pain and impact on loss of function and mobility, they can affect efforts to control hypertension, diabetes, obesity, and other conditions. They can impact the ability to maximize educational opportunities, earn a living, care for family, and participate in or contribute to other activities associated with a fulfilling life. Tremendous advances have been made in understanding the etiology and identifying treatment options for the vast majority of these conditions. However, understanding and defining the value of these various treatment options to patients, their families, and society are areas that have not been fully examined. Health care reform has drawn our attention to this gaping
hole in our knowledge and provides us with an opportunity to look for answers and contribute to the debate that is underway to ensure that resources are allocated to best meet patient needs. An interdisciplinary Summit (www.usbji.org/rd/?MSKSummit) organized by the US Bone and Joint Initiative and led by co-chairs Gunnar Andersson, MD, PhD, Steve Gnatz, MD, MHA, and David Pisetsky, MD, PhD, sought to define the value of musculoskeletal care. Although the value of such care would seem to be intuitive, describing and measuring that value is extremely complex. Foremost in the discussion was the recognition that any description of value should be framed in terms of outcomes prioritized by patients, rather than tolling costs of process measures. This Summit gathered representatives of more than 50 organizations and from government, payers, and industry and included 128 participants. The following Summary and Recommendations are a result of discussion during the Summit. These recommendations will now serve as a starting point for multidisciplinary action plans to improve the value of musculoskeletal conditions in the United States. These action plans will be intended to improve measurement of the treatment of musculoskeletal conditions, enhance public and professional education in this area, increase research, improve prevention and treatment measures, and to propose solutions for improving musculoskeletal health care and thus the quality of life for all Americans.


Osteosarcoma (OS) is a malignant bone tumor predominantly affecting children and adolescents. OS has a 60% survival rate with current treatments; hence, there is a need to identify novel adjuncts to chemotherapeutic regimens. In this pilot study, we investigated the dose-response to 1alpha,25-dihydroxyvitamin D(3) (1, alpha 25(OH)(2) D(3) ) and 25-hydroxyvitamin D(3) (25(OH)D(3) ) by human OS cell lines, SaOS-2, and 143B. We hypothesized that 1, alpha 25(OH)(2) D(3) and 25(OH)D(3) would stimulate differentiation and induce apoptosis in OS cells in a dose-dependent manner. Human OS cell lines, SaOS-2, and 143B, were treated with 1, alpha 25(OH)(2) D(3) or 25(OH)D(3) or an ethanol control, respectively, at concentrations ranging from 1 to 1,000 nM. Ki67 (a marker of cellular proliferation) immunocytochemistry revealed no significant changes in the expression of Ki67 or MIB-1 in 1alpha,25(OH)(2) D(3) or 25(OH)D(3) treated SaOS-2 or 143B cells. Both control and 1alpha,25(OH)(2) D(3) treated SaOS-2 and 143B cells expressed vitamin D receptor (VDR). Markers of osteoblastic differentiation in 143B cells and SaOS-2 cells were induced by both 25(OH)D(3) and 1alpha,25(OH)(2) D, and evident by increases in alkaline phosphatase (ALP) activity, osteocalcin (OCN) mRNA expression, and mineralization of extra-cellular matrix (ECM) by alizarin red staining. An increasing trend in apoptosis in response to 25(OH)D(3) in both SaOS-2 and 143B cells was detected by terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick end labeling (TUNEL) staining. With 1alpha,25 (OH)(2) D(3) treatment, apoptosis was evident at higher concentrations only. These preliminary findings suggest that OS cells express VDR and respond to 25(OH)D(3) and 1alpha,25(OH)(2) D(3) by undergoing differentiation and apoptosis. (c) 2011 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res.


Maximum anterior positioning of the tibia relative to the femur during posterior cruciate ligament (PCL) reconstruction is essential for achieving a tight graft and stable joint. A Schanz pin inserted in the proximal tibia is sometimes used to pull the proximal tibia forward during tensioning of the graft in PCL reconstruction. This study was designed to evaluate whether this technique provides more anterior translation than the traditional anterior drawer technique. Eight fresh-frozen cadaveric knees were tested using both methods in randomized order: pulling anteriorly on a 5-mm Schanz pin in the proximal tibia or a leather strap behind the calf designed to simulate a surgeon’s hand performing an anterior drawer maneuver. An anteriorly directed force was applied from 0 to 60 N, and the sagittal position of the tibia in relation to the femur was recorded using a mini C-arm. Tests were performed first on the intact knees, again after the PCL had been cut, and again following transection of the popliteal-fibular ligament. We found a statistically significant (p < 0.05) increase in tibial translation, ranging between 1 and 2 mm, when the tibia was pulled by the Schanz pin compared with the strap under every set of conditions. This greater anterior translation could improve the stability of the post-reconstructed knee.


Bone fillers have emerged as an alternative to the invasive surgery often required to repair skeletal defects. Achieving controlled release from these materials is desired for accelerating healing. Here, oppositely-charged Poly (D,L-lactic-co-glycolic acid) (PLGA) nanoparticles were used to create a cohesive colloidal gel as an injectable drug-loaded filler to promote healing in bone defects. The colloid self-assembled through electrostatic forces resulting in a stable 3-D network that may be extruded or molded to the desired shape. The colloidal gel demonstrated shear-thinning behavior due to the disruption of interparticle interactions as the applied shear force was increased. Once the external force was removed, the cohesive property of the colloidal gel was recovered. Similar reversibility and shear-thinning behavior were also observed in colloidal gels loaded with dexamethasone. Near zero-order dexamethasone release was observed over two months when the drug was encapsulated in PLGA nanoparticles and simply blending the drug with the colloidal gel showed similar kinetics for one month. Surgical placement was facilitated by the pseudoplastic material properties and in vivo observations demonstrated that the PLGA colloidal gels stimulated osteoconductive bone formation in rat cranial bone defects.