Jefferson®

ORTHOPAEDIC

OUTCOMES & RESEARCH

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

CONTENTS

A MESSAGE FROM THE CHAIR

Dear Colleagues,

It is an exciting time for researchers with Jefferson's Department of Orthopaedic Surgery as we continue to make advances in the care of patients with complex orthopaedic conditions. I am happy to share some of that work in this year's ***Orthopaedic Outcomes and Research Report***. We chose the theme "Bodies in Motion" to illustrate the report because it underscores our commitment to getting patients moving forward with their lives.

Jefferson's Department of Orthopaedic Surgery is fortunate to include specialists from the Rothman Institute at Jefferson and The Philadelphia Hand Center at Jefferson. It is the busiest orthopaedic surgery program in the Philadelphia region. Last year alone, through our collective experience, our staff performed more than 44,000 surgical procedures.

Every day our surgeons handle complex cases involving the spine, hand and wrist, joint revision, orthopaedic trauma and musculoskeletal oncology. From identifying methods to reduce complications from traumatic injuries to improving care for cancer patients undergoing orthopaedic surgery, Jefferson surgeons are setting new standards for orthopaedic care. Our patients also benefit from ready access to other specialists, including neurologists and oncologists, throughout the Jefferson system. Our staff's multidisciplinary approach to care means that bones aren't treated in isolation.

As an academic medical center we measure our progress on multiple fronts. Overarching everything we do is a focus on delivering the latest surgical techniques to minimize pain, accelerate recovery and optimize long-term function for patients. We recognize the important role that a patient's overall emotional and physical well-being plays in promoting positive outcomes. We are dedicated to patient and family comfort and open communication between patients and healthcare providers.

Our surgeons are widely published researchers who conduct clinical trials of orthopaedic techniques and treatments, in turn providing patients with access to new therapies that may not be available elsewhere. Our surgeons also collaborate with medical scientists in the laboratory, and their discoveries are pointing toward new approaches to reduce pain, minimize scarring and promote healing.

The pages ahead offer a look at some key research projects going on at Jefferson. We invite you to learn more about our services by visiting our website, Jefferson.edu/orthopedic. To refer a patient please call 1-800-JEFF-121 or have your patient call 1-800-JEFF-NOW.

I wish you all the best in 2016.

Alexander R. Vaccaro, MD, PhD, MBA

Richard H. Rothman Professor and Chair
Department of Orthopaedic Surgery
Thomas Jefferson University Hospitals
Sidney Kimmel Medical College at Thomas Jefferson University

Bodies in MOTION *an overview*

Jefferson's Department of Orthopaedic Surgery is committed to a singular goal: To get patients moving on with their lives. Every aspect of patient care – from initial evaluation and treatment planning to rehabilitation – is designed to speed recovery and return patients to their previous levels of function.

The department – which includes a proven team of specialists from the Rothman Institute at Jefferson and The Philadelphia Hand Center at Jefferson – is expert at handling complex cases involving joint revision, spine, hand and wrist, orthopaedic trauma and orthopaedic oncology. In 2015-16 *U.S.News & World Report* ranked Jefferson among the nation's best hospitals for orthopaedics – a confirmation of the outstanding outcomes experienced by patients.

Patient care is informed by the Department of Orthopaedic Surgery's robust research agenda, which includes clinical trials, evaluations of new surgical techniques and implant materials, and basic science projects that are furthering the understanding of the causes and prevention of orthopaedic conditions.

Surgeons and scientists in the department published nearly 200 papers in leading peer-reviewed journals last year and presented their research at major scientific meetings in the U.S. and abroad. One recurring theme is that certain patient populations – such as young, active patients, patients with a cancer history and elderly persons – present unique surgical challenges that need to be considered in surgical and postoperative planning. Many of the research findings have already been adopted into clinical practice at Jefferson, leading to refined surgical techniques and increased attention to minimizing complications such as infection and thromboembolism.

Research highlights include:

- **Complex spine.** A Jefferson study with more than four years of follow-up data found that patients over the age of 80 with lumbar stenosis and degenerative spondylolisthesis fared better with surgery than non-operative treatment. In fact, older patients who had surgery were no more likely than younger patients to experience complications.
- **Joint revision.** While much of the research on total knee arthroplasty has focused on optimizing outcomes for older patients, Jefferson researchers are focusing on risk factors for younger patients. They have found that younger patients present particular challenges for joint surgeons.
- **Hand and wrist.** Findings in the laboratory and clinic are pointing to new ways to improve patient outcomes. An ongoing series of lab experiments is exploring novel approaches to limit the formation of scar tissue and fibrosis in soft tissue and joints. Another study on the effect of smoking on bone healing found that the time to bony union following ulnar shortening osteotomy is almost double for smokers compared to non-smoking patients.
- **Orthopaedic oncology.** As the population of people living with cancer continues to grow, more cancer patients will need orthopaedic surgery to replace arthritic and aging joints. Researchers from Jefferson and the Sidney Kimmel Cancer Center quantified the risk of thromboembolism and other complications in cancer patients undergoing total joint arthroplasty.
- **Trauma.** A research team has demonstrated the importance of improving pressure measurement techniques to diagnose acute compartment syndrome, one of the most dreaded complications of orthopaedic injury. Researchers found that there is too much variability in pressure readings taken by clinicians.

These and other research projects from Jefferson's Department of Orthopaedic Surgery are detailed in the pages ahead. Read on to learn about the many ways that Jefferson is redefining care.

By the Numbers: September 2014 – August 2015
Source: Jefferson Internal Data

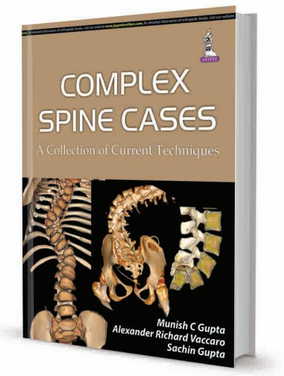
11,602	JOINT REPLACEMENT SURGERIES	14,697	HAND AND WRIST SURGERIES
4,546	SHOULDER AND ELBOW SURGERIES	2,835	FOOT AND ANKLE SURGERIES
3,058	SPINAL SURGERIES	503	ORTHOPAEDIC TRAUMA CASES
7,164	SPORTS MEDICINE CASES	422	MUSCULOSKELETAL ONCOLOGY CASES

complex **spine**

Jefferson spine surgeons are leaders in their field, helping to advance surgical and nonsurgical treatment of spinal injuries and disease. Their clinical expertise is matched by a rigorous research agenda.

Patients in an emergency situation experience the expertise that comes from Jefferson being both a designated Level 1 Regional Resource Trauma Center and a federally designated spinal cord injury center. Many patients are transferred to Jefferson for the expert management of their complex conditions by Jefferson's spine surgeons.

All patients with spinal disorders benefit from the spine team's commitment to translating research findings into better diagnostic, surgical and overall patient management techniques. One important area of research focuses on optimizing treatment modalities for patients in their 80s and beyond. Another key research project is exploring the molecular underpinning of disc degeneration.



SERVICES

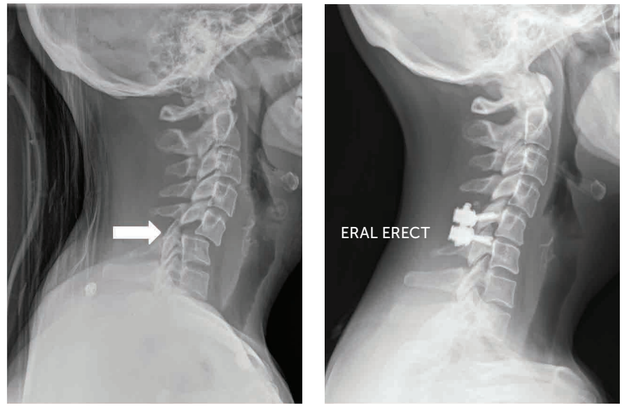
- Treatment for cervical, thoracic and lumbosacral spinal conditions
- Treatment for scoliosis/ spinal deformities, spondylolisthesis, spinal cord injury/ trauma, spinal infections and spinal tumors
- Minimally invasive techniques and image-guided technology
- Comprehensive treatment of disc disease, including disc replacement

Spine surgeons around the world are learning from Jefferson's team. Alexander R. Vaccaro, MD, PhD, co-director of Jefferson's Spinal Cord Injury Center, co-edited a newly published medical textbook called *Complex Spine Cases: A Collection of Current Techniques*.

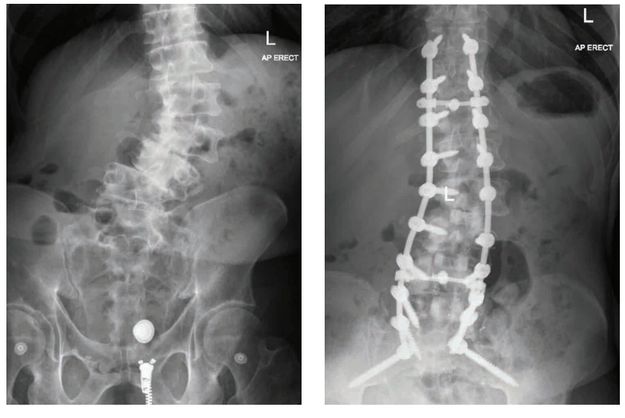
Here are some details on two of Jefferson's spine research projects.

Effectiveness of Surgery for Lumbar Stenosis and Degenerative Spondylolisthesis in the Octogenerian Population

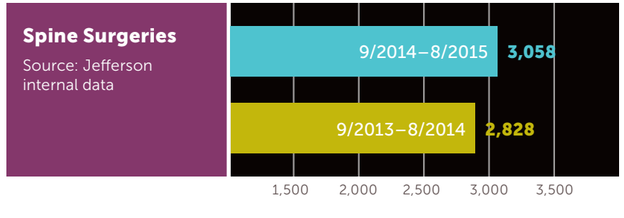
As the elderly population grows and healthcare resources are limited, it is important to identify interventions that are effective at improving the quality of life of elderly patients with spinal disorders. Lumbar stenosis and degenerative spondylolisthesis are common and debilitating conditions in older people. Although operative treatment of those conditions has been proven effective for patients in general, few studies have examined the effectiveness of surgery for patients age 80 and older.



Preoperative (left) and postoperative (right) x-rays of a 39-year-old woman who fell down the stairs at her home several weeks before she came to Rothman Institute and was thought to have whiplash. She had x-rays and was diagnosed with a dislocation of the C5 and C6 vertebrae. She underwent urgent surgery to realign and fuse the C5 and C6 vertebrae. She has returned to work and is symptom free.



Preoperative (left) and postoperative (right) x-rays of an otherwise healthy 74-year-old man with scoliosis, failed prior surgery and debilitating pain who underwent reconstructive surgery. By eight weeks after surgery, he had fully recovered and was pain-free. He has since resumed an active lifestyle and weaned himself off narcotics.



Jefferson surgeons are part of a study known as SPORT (The Spine Patient Outcomes Research Trial), which has analyzed up to 10 years of follow-up data on patients who received either surgical or nonsurgical treatment for lumbar stenosis with or without degenerative spondylolisthesis.

The group, led by Jeffrey A. Rihn, MD, analyzed the study data to compare long-term outcomes for 105 patients who were at least 80 years old at the time of treatment to 1,130 younger patients. The goal was to see whether older patients benefited from surgery as much as the younger population and whether operative treatment or nonoperative treatment was better in the long term for the elderly group. They compared baseline patient and clinical characteristics between the two age groups and also analyzed data obtained from patient-reported standardized questionnaires administered periodically up to four years after surgery.

At the time of enrolling in the study, the older group of patients presented with more complicated medical histories than younger patients. They had a higher prevalence of multiple levels of stenosis, severe stenosis and asymmetric motor weakness and were also more likely to have hypertension, heart disease, osteoporosis and joint problems. They were less likely than the younger patients to be overweight, smoke or have a history of depression. Of the 105 older patients, 58 (55.2%) underwent surgical treatment, while the rest were treated nonoperatively. Of the 1,130 younger patients, 749 (66.3%) had surgery.

An analysis of long-term data, published in *The Journal of Bone and Joint Surgery*, found:

- There were no differences in rates of intraoperative or postoperative complications, reoperation or postoperative mortality between the older and younger groups.
- Among the older group, those who had surgery showed significantly greater improvement over the four years in all primary and secondary outcome measures compared with older patients who were nonoperatively treated.
- The treatment benefits of surgery over nonsurgical treatment among patients 80 or older were similar to those in younger patients in nearly all primary and secondary measures. The exceptions were the scores for the SF-36 bodily pain domain (7.5 for the older group versus 14 for the younger group); and the percentage who self-rated their progress as a major improvement (23.5% of the older group versus 41.5% of the younger group).

"The substantial treatment effect that surgery has been shown to have in prior SPORT studies of patients with stenosis and degenerative spondylolisthesis appears to have been maintained in this octogenarian population," the study concluded.

The researchers said future research needs to consider cost issues.

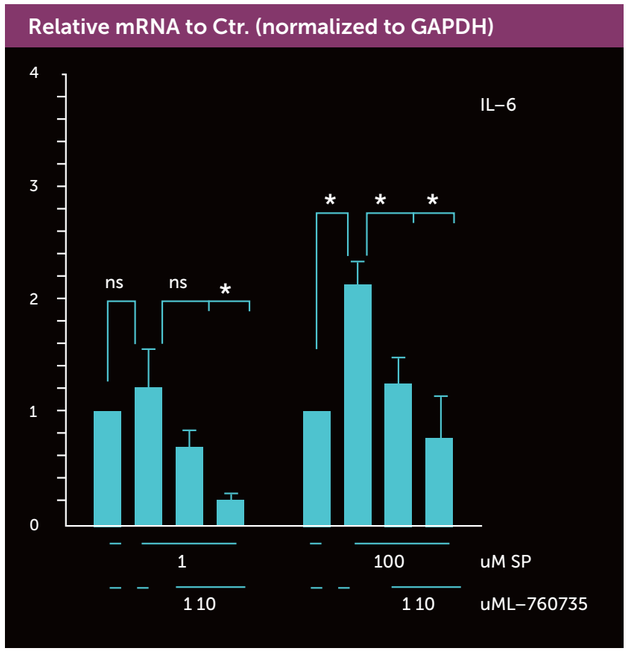
"Although the cost-effectiveness of surgery for stenosis and degenerative spondylolisthesis has been established for the general patient population, further studies specifically analyzing cost data and improvement on quality of life will be needed to determine whether such procedures are also truly cost-effective in this elderly and retired population."

The Role of Substance P in Symptomatic Disc Degeneration

Some patients with disc degeneration develop especially disabling pain and researchers want to understand why that is. Jefferson researchers are examining the role of a molecule called Substance P in degenerative disc disease.

In a series of laboratory experiments, a research team led by Christopher K. Kepler, MD, has shown that:

- Substance P, a known neurotransmitter, is made by degenerative disc cells.
- Exposure of normal disc cells to Substance P triggers degenerative changes, suggesting that the molecule is an important intermediary in painful disc degeneration.
- Substance P, which is important in pain transmission elsewhere in the body, may serve as a pathway for communication of disc-related pain to the brain.

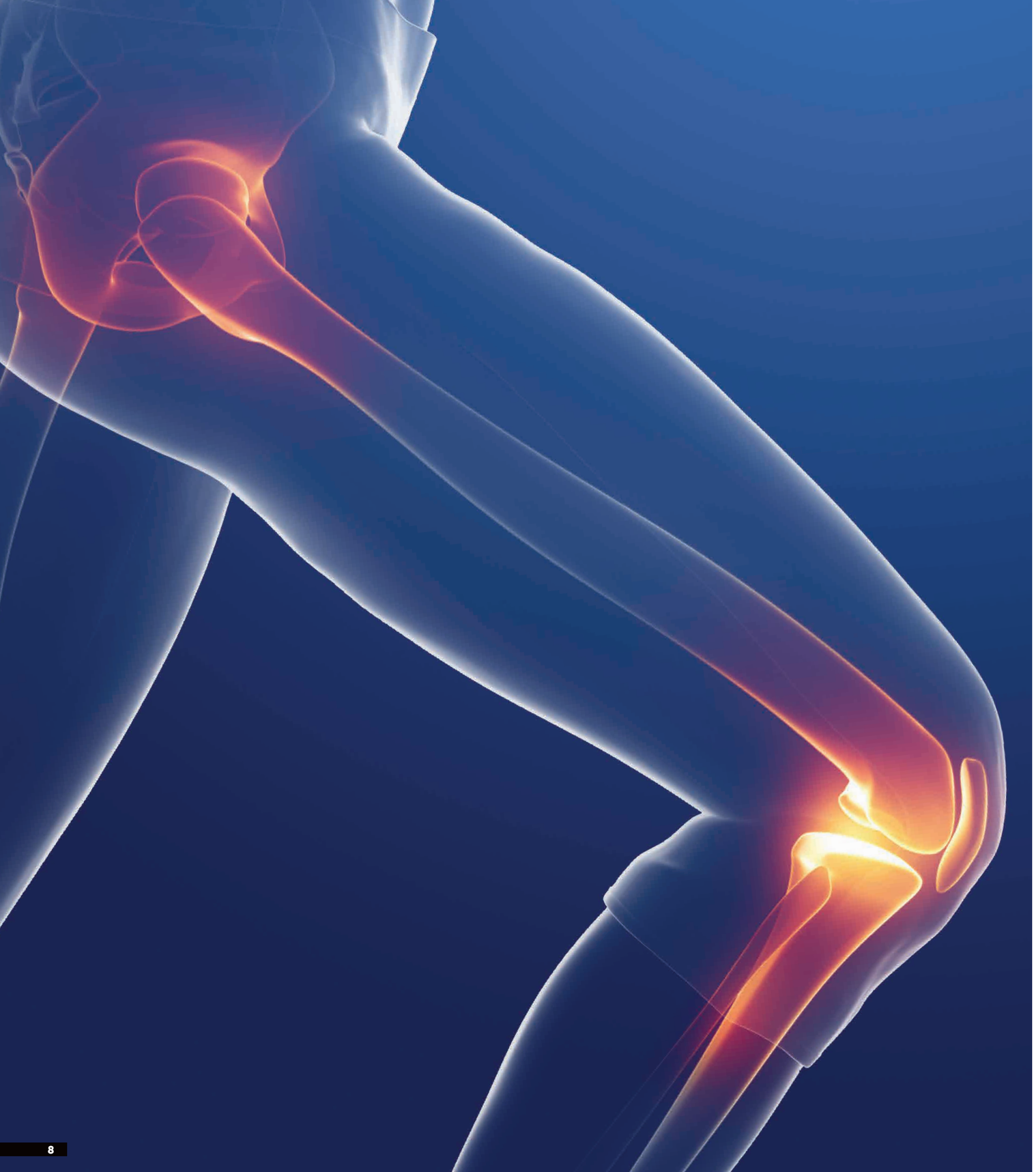


At both low (left grouping) and high (right grouping) concentrations of Substance P, increasing concentrations of the blocking agent (right two bars within each grouping) decreased IL-6 expression. IL-6 is an inflammatory molecule that has been shown to be present in the discs of patients with severe associated pain. The highest concentration of the Substance P blocking agent (far right bar in each grouping), dropped IL-6 levels to below levels seen in normal discs, suggesting a potential therapy to treat painful disc degeneration.

Source: Christopher K. Kepler, MD

- Treating disc cells with a molecule that blocks the effect of Substance P eliminated degenerative changes. It also eliminated the production of several cytokines associated with the inflammatory process that contributes to painful disc degeneration.

While the research, published in *Spine*, is still in the early stages, the goal is to develop a therapeutic strategy that would target Substance P to prevent or reverse painful disc degeneration. The therapy might eliminate the need for surgery for some patients.



joint revision

There are two trends occurring simultaneously in the field of total joint arthroplasty. The growing population of older people is leading to an increased demand for treatment for degenerative joint disease. At the same time, younger patients are seeking surgical intervention so that they can continue to participate in sports and other physical activities at a high level. More primary total joint arthroplasties, in turn, increase demand for revision surgeries.

SERVICES

- Anterior-approach total hip replacement
- Minimally invasive hip and knee replacement
- Custom knee replacement
- Adult joint reconstruction
- Hip resurfacing
- Partial knee replacement
- Treatment of hip and knee disorders in young adults
- Rapid-recovery surgery
- Computer-assisted surgery
- Pelvic reconstruction
- Pelvic osteotomy and hip-impingement surgery
- Joint preservation procedures

Jefferson's surgeons are continually refining surgical techniques and materials to improve outcomes for patients regardless of their age. One question being examined is whether younger patients present different surgical challenges than older patients.

Jefferson researchers are also interested in how health economic policies – in particular Medicare reimbursements – might unintentionally affect access to care for patients needing total joint arthroplasty.

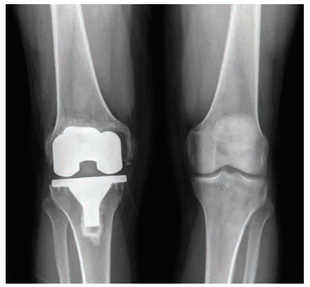
Here is a look at some of that research:

Revision Total Knee Arthroplasty in the Young Patient: Is There Trouble on the Horizon?

The volume of primary and revision total knee arthroplasty is expected to increase tremendously over the next two decades, with patients younger than 65 years of age accounting for most of the growth. Surgeons are especially likely to see more patients in their forties and fifties – a group that could face multiple revisions in their lifetime. Finding ways to make total knee arthroplasty, whether primary or revision, more durable is essential so that patients do not have to undergo multiple surgeries.

Orthopaedic surgeons who specialize in total knee arthroplasty need to better understand whether younger patients respond to total knee arthroplasty differently than older patients and whether the risk factors for failure of the procedure differ depending on what age range a patient falls into.

To help answer those questions, Jefferson researchers designed a retrospective study comparing 84 patients age 50 or younger to 84 patients age 60 to 70 who all underwent revision total knee arthroplasty between



- The average time from primary arthroplasty to first revision was 36 months for the younger patients, compared to 59 months for the older ones.
- The mean time from the first revision to re-revision was 27 months for the younger patients compared to 28 months for the older group.
- Of the 25 second revisions among the younger patients, 32% were due to infection. Of the 26 second revisions among the older patients, 50% were because of infection.
- Overall six-year survival rates for revisions were 71% for the younger group and 66.1% for the older patients.
- Younger patients were 10% more likely than older patients to need a re-revision.
- Eight knees in the younger group required three or more revisions – three due to aseptic failure and five because of infection. Six knees in the older group had three or more revisions – three for aseptic failure, three for infection.
- The greatest risk factors for failure of revision were infection and BMI greater than 40 kg/m2.

Finding ways to make total knee arthroplasty more durable is essential so that patients do not have to undergo multiple surgeries.

August 1999 and December 2009. The younger and older patients were matched for date of surgery, sex and body mass index (BMI).

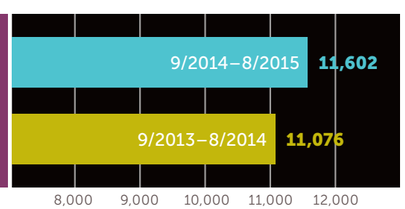
The researchers, led by Matthew S. Austin, MD, reviewed medical and surgical charts that included at least 24 months of follow-up to determine what factors influenced the need for revision and whether it was successful.

Their findings, published in *The Journal of Bone and Joint Surgery,* included:

- The most common reason for the first revision in younger patients was aseptic loosening (27.5%), while infection (30%) was the most common reason for the older patients.

Joint Replacement Surgeries

Source: Jefferson internal data



"We believe that this young population may have unique revision failure modes that surgeons must take into account when considering surgical risks and fixation methods," the authors concluded.

"The survivorship of knee revisions in younger patients is a cause of concern, and the higher rates of aseptic failure in these patients may be related to unique demands that they place on the reconstruction."

For instance, younger patients may be more active than older ones, putting greater stress on hardware.

The study also points to the need for finding additional ways to minimize the risk of infections.

"Infection as the reason for the initial revision surgery was a significant predictor of poor implant survival in both (younger and older) groups, supporting the fact that current methods to treat and eradicate periprosthetic joint infections are inadequate and contribute to substantial morbidity years after an infection diagnosis," the researchers said.

"Improvement in implant fixation and treatment of infections when these patients undergo revision total knee arthroplasty is needed," the researchers concluded.

Why Are Total Knee Arthroplasties Failing Today – Has Anything Changed after 10 Years?

Total knee arthroplasty is considered one of the most successful surgical interventions of the past two decades. There were 402,100 primary total knee arthroplasties performed in 2003 in the United States, and that number is expected to increase to more than three million by 2020. The dramatic increase in the number of primary and revision total knee arthroplasties is being driven by an aging population and a growing acceptance of the procedure by young, active patients.

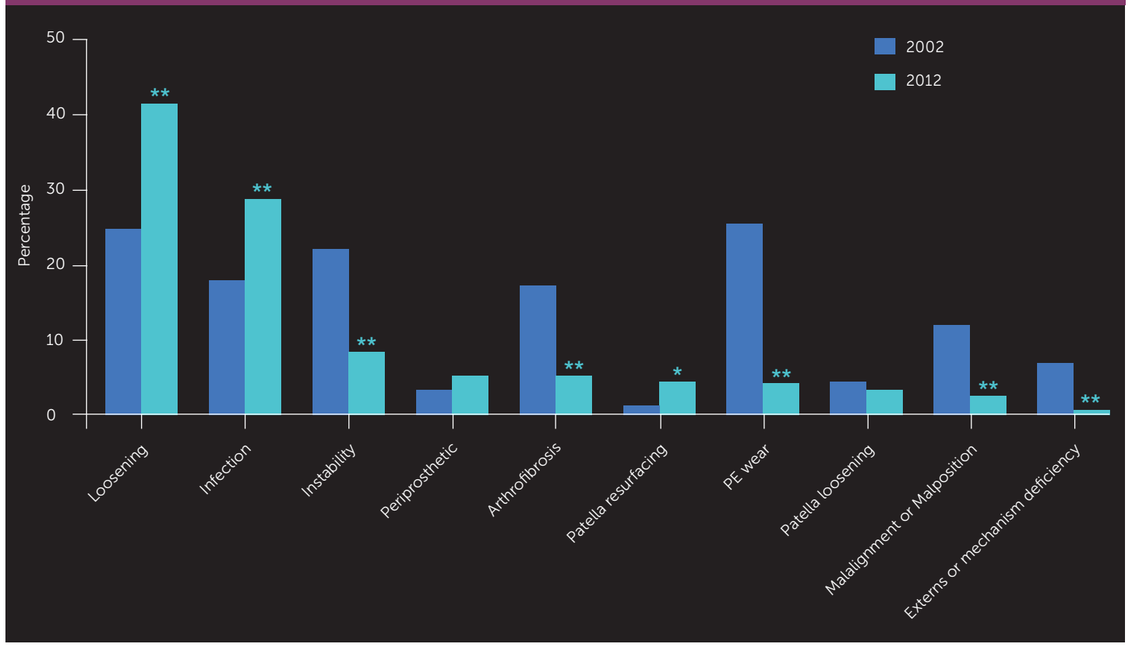
Jefferson researchers published a study in 2002 that looked at the factors involved in total knee arthroplasty failure among patients who underwent revisions at the hospital between 1997 and 2000. Because surgical techniques and instrumentation, prosthetic design, perioperative care and surgical experience have evolved since then, a research team decided to do a follow-up study 10 years later to determine if factors influencing the success and failure of the procedure had changed.

For the latest study, led by Peter F. Sharkey, MD, researchers conducted a retrospective review of 781 revision total knee arthroplasties performed at the institution between July 2003 and July 2012. Of those, 41% were referred from outside institutions. The cases were classified as early or late revision, with two years being the dividing mark. Causes of total knee arthroplasty failure were identified and the trends were then compared to the data collected 10 years earlier.

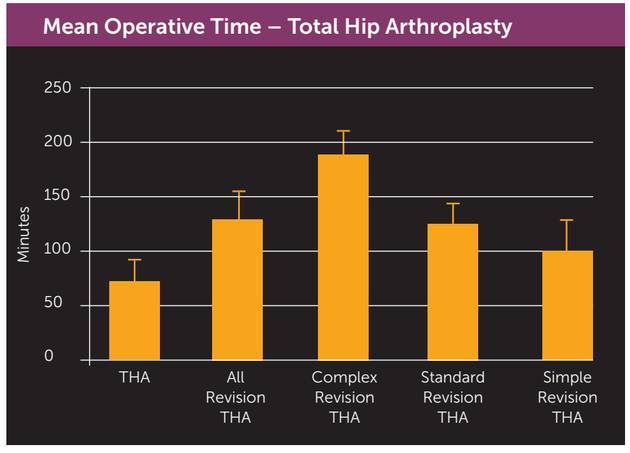
The study, published in *The Journal of Arthroplasty*, found that:

- The average time before revision was 0.84 years in the early failure group, and 6.9 years for the later group.

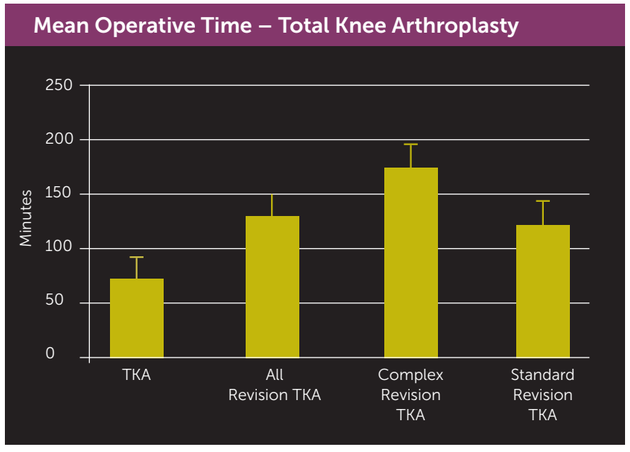
Overall Incidence of Failure



Comparison of overall incidence of failure between 2002 and 2012 stratified by mechanism. *P <0.05, **P<0.01.
Source: Peter F. Sharkey, MD



Mean operative times for primary and revision total hip arthroplasty.
Source: Gregory K. Deirmengian, MD



Mean operative times for primary and revision total knee arthroplasty.
Source: Gregory K. Deirmengian, MD

- 38% of the revision surgeries involved exchanging all total knee arthroplasty components. Two components were exchanged in 35% of cases.

- Aseptic loosening of the prosthetic was a factor in 39.9% of the revisions. Infection was a factor in 27.4% of the revisions. By comparison, 10 years earlier aseptic loosening was a factor in 51.3% of total knee arthroplasty cases and infection was a factor in 33.2% of cases.

- Unlike 10 years earlier, when polyethylene (PE) wear was the leading factor in the need for revision (56.2% of cases), it was involved in only 4.7% of the more recent cases.

- In addition, the incidence of instability, arthrofibrosis, malalignment and exterior mechanism deficiency also decreased since the time of the first study.

"According to our study," researchers said, "infection has become the most common mode of early failed total knee arthroplasty." It is the second most common cause of failure in the late revision group. Those findings are consistent with other studies.

They said that infection remains a big concern in all types of orthopaedic surgery despite the widespread use of perioperative prophylactic antibiotics and other anti-infection modalities.

"Ruling out infection should be prioritized in patients with primary total knee arthroplasty," the researchers said. They said another priority needs to be finding ways to achieve better long-term stability with primary total knee arthroplasty. Jefferson is taking steps to finding novel ways to diagnose infection and to improve long-term stability by performing primary total knee arthroplasty with different surgical techniques.

Medicare Fails to Compensate Additional Surgical Time and Effort Associated with Revision Arthroplasty

The increasing demand for total joint arthroplasty over the next couple of decades may outpace the availability of surgeons to perform the procedures.

By one estimate, by 2016 anywhere from approximately 1,900 to 4,200 orthopaedic surgeons may retire, creating more limited access for patients who need total hip or knee replacement. Some experts predict that Medicare reimbursement trends may drive some surgeons away from doing complex revision procedures in favor of primary procedures that can be done more quickly.

A Jefferson team headed by Gregory K. Deirmengian, MD, examined the issue of reimbursement for revision total joint arthroplasty compared to primary procedures by analyzing length of operative time and other factors. They hoped that the findings would lend some objective data to the ongoing debate over whether surgeons should be better compensated for their time by public and private insurers.

The study included 651 hip and knee arthroplasty procedures performed between January 2010 and December 2011 by one surgeon. The study group included 462 primary cases (216 hips, 246 knee) and 189 (113 hip, 76 knee) aseptic revision joint arthroplasty procedures.

Of the 113 hip revisions, 23 were classified as simple revisions, 62 as standard and 28 as complex. Of the 76 knee revisions, 66 were classified as standard and 10 as complex.

Operative time – from incision to closure – was determined for each case as was length of stay (LOS) and whether there was a need for a repeat procedure.

The findings, published in *The Journal of Arthroplasty,* included:

- In comparison to primary total knee arthroplasty, surgical time for revision total knee arthroplasty was 1.8 times greater. For complex cases, surgical time was 1.4 times greater. That difference translated into 70.5 minutes for primary total knee arthroplasty versus 128.5 minutes for total knee arthroplasty revisions and 174.5 minutes for complex revisions.

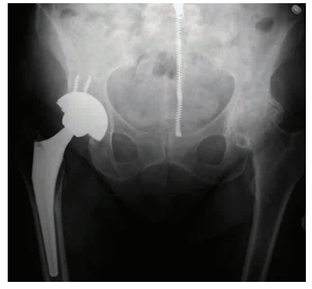
- The rate of 90-day repeat procedure was 8.5% greater for revision total knee arthroplasty compared to primary total knee arthroplasty.

- The average length of stay was 3.4 days for revision total knee arthroplasty compared to three days for primary total knee arthroplasty cases.

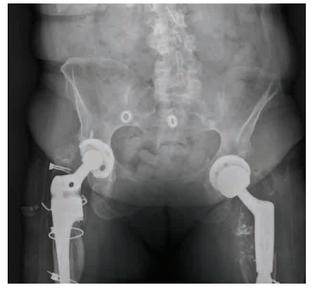
- In comparison to primary total hip arthroplasty, operative time for revision cases was 1.8 times greater. For complex cases, it was 2.6 times greater. Primary cases took 73 minutes on average compared to 135.4 minutes for revision cases. Complex revisions took 187.4 minutes on average.

- The rate of 90-day repeat procedure was 3.4% higher for revision total hip arthroplasty than for primary total hip arthroplasty.

- The average LOS for revision total hip arthroplasty was 3.7 days compared to 2.8 days for primary procedures.



Primary total hip and native hip osteoarthritis



Revision hip

The researchers noted that while there have been increases in Medicare reimbursement for total joint arthroplasty, they do not fully compensate for the differences in the operating time required for revision procedures. Longer hospital stays and more repeat procedures also translate into more time doing rounds and increases in other hospital-related costs.

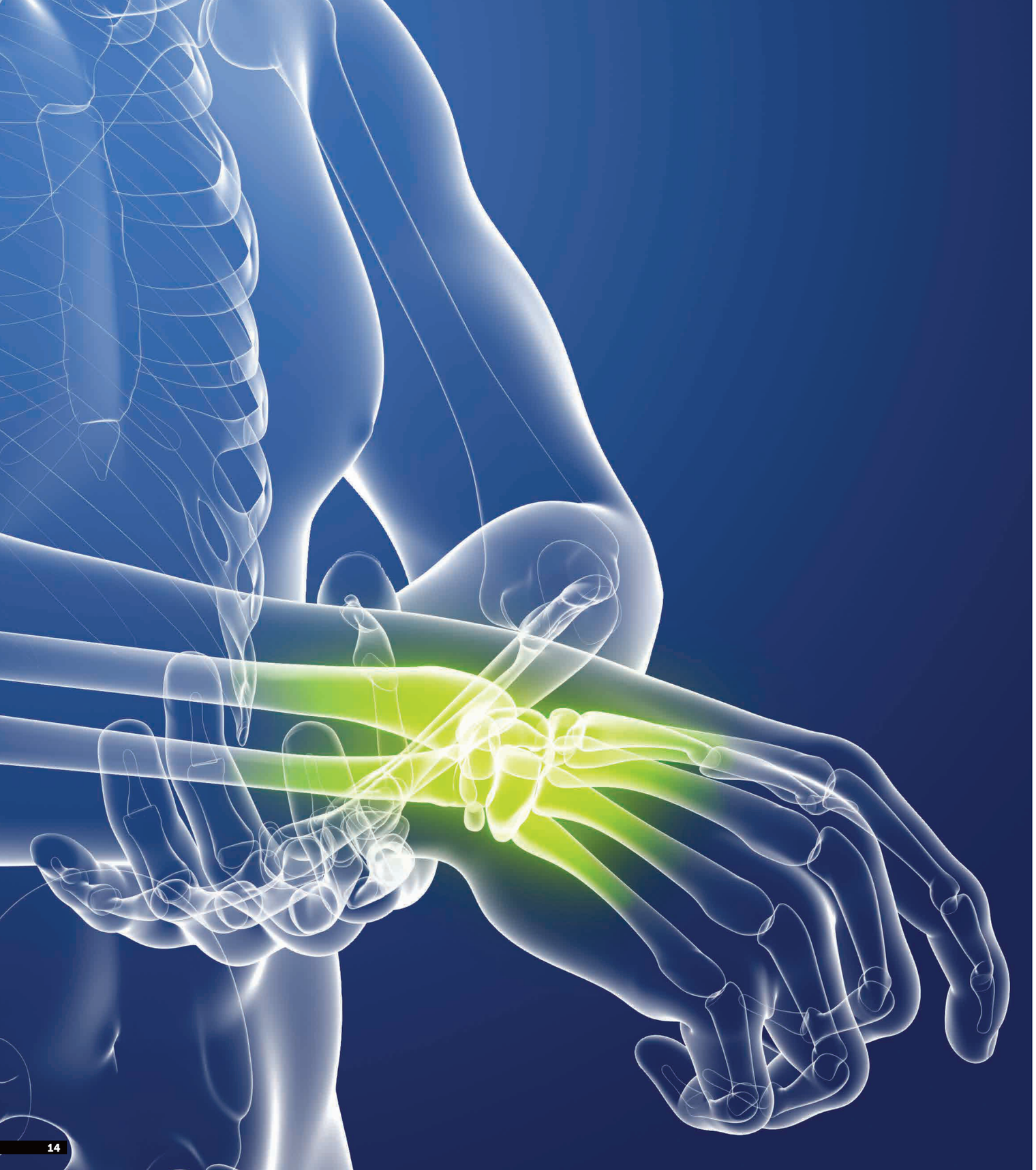
The study noted, for instance, that in 2011 Medicare reimbursed surgeons $1,697 for primary total knee arthroplasty versus $1,949 for a revision total knee arthroplasty. Reimbursement for primary total hip arthroplasty was $1,588 compared to $2,133 for revision total hip arthroplasty.

"This study demonstrates that the current system of Medicare reimbursement does not reimburse surgeons proportionally to the increased time and effort necessary for revision arthroplasty, and in particular complex revision cases," the researchers said.

They suggested that some surgeons may decide to fill their operating schedules with primary cases because they are quicker to do and relatively more financially attractive. However, since the demand for both primary and revision total joint arthroplasty is increasing because the population is aging, there will be fewer surgeons available to perform these cases.

"With the disparity between reimbursement and the time needed to perform revisions, our results raise concerns over patient access to surgeons able to undertake these surgeries in the future," the researchers concluded.

At Jefferson, many of the arthroplasty specialists are experts at performing revision arthroplasty, but patients must understand that these procedures are much more complex and technically demanding than regular procedures.



hand and **wrist**

Jefferson's Department of Orthopaedic Surgery benefits from the expertise of hand and wrist specialists from the Rothman Institute at Jefferson and The Philadelphia Hand Center at Jefferson. The surgeons are leaders in the treatment of simple and complex fractures, osteoarthritis, complex nerve conditions, sports injuries, carpal tunnel syndrome and other conditions. Successful treatment of injuries and disorders involving the hand, wrist or forearm requires an understanding of how ligaments, tendons, muscles, joints and bones work together to provide good function and flexibility. Key to optimizing recovery is putting in place a physical and occupational therapy plan specifically matched to a patient's needs.

The hand and wrist specialists also are widely published researchers who make significant contributions to their field. They evaluate new surgical techniques and materials and study how best to manage higher-risk patients. They conduct basic science research on the molecular mechanisms involved in scarring and healing and are exploring innovative ways to regenerate damaged connective tissue.

SERVICES

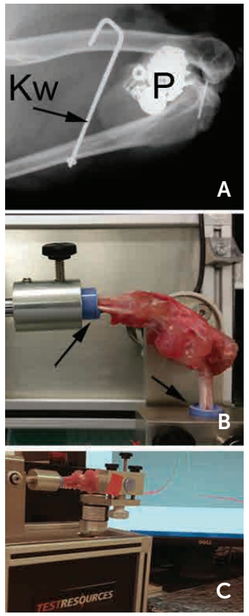
- Hand and wrist surgery
- Hand and wrist arthroscopy
- Upper-extremity surgery
- Microvascular surgery
- Hand arthritis surgery
- Brachial plexus reconstruction
- Treatment of ligament and tendon disorders of the hand and wrist
- Treatment of carpal and cubital tunnel syndromes
- Treatment of Dupuytren's disease
- Treatment of complex nerve conditions
- Treatment of hand and wrist sports injuries
- Joint reconstruction for thumb arthritis
- Minimally invasive nerve surgery
- Joint replacement for hand arthritis

Here is a summary of some of those research projects.

Auxiliary Proteins That Facilitate Formation of Collagen-Rich Deposits in the Posterior Knee Capsule in a Rabbit-Based Joint Contracture Model

Post-traumatic joint contracture and stiffness is a debilitating consequence of trauma or surgical procedures involving the hand. This limitation in motion can lead to significant functional disability with enormous societal costs. Jefferson surgeons, in close collaboration with Andrzej Fertala, PhD, are testing new approaches to understand and eventually limit the formation of scar tissue and fibrosis in soft tissue and joints of the hand.

Excessive collagen formation is widely considered a central factor in the development



A rabbit-based model of joint contracture. (A) An x-ray image of the operated knee. A k-wire (Kw) and a pump (P) delivering PBS are depicted. (B and C) Views of a system employed to measure the flexion contractures of analyzed knees. In B, arrows indicate femur and tibia whose ends are potted into tubes with the use of a PMMA. (D and E) Representative data from measurements of the flexion contractures of the healthy (D) and the contracted (E) knees at 0.2Nm torque. Ascending and descending parts of the depicted graphs represent extension and flexion behavior of the analyzed knees.

of joint contractures. In a series of laboratory experiments, funded by a multi-year research grant from the U.S. Department of Defense and reported in the *Journal of Orthopaedic Research*, the researchers used a rabbit injury model to study the key enzymes and chaperone proteins critical in collagen metabolism.

Biochemical and histological assays in the lining of injured joints indicated that there were changes in the expression patterns of two key proteins involved in processing growing collagen chains – Heat Shock Protein 47 and the α-subunit of prolyl 4-hydroxylase. Findings suggest that the abnormal organization of collagen, rather than excessive formation of fibril-stabilizing cross-links, may be a key reason for observed changes in injured joints.

"By following the fundamental steps in the path of fibrillar collagens, our study sheds new light on the fundamental mechanisms that control excessive production of fibrotic deposits," the researchers wrote. "These results extend our knowledge on the pathomechanisms of post-traumatic joint contracture, thereby contributing to developing new concepts for potential therapy approaches."

The Jefferson research team is in the process of evaluating data in a similar line of experiments using a monoclonal antibody that inhibits collagen I to collagen I interaction, thereby reducing the amount of collagen deposits and scar tissue formation.

Factors Influencing Recovery from Carpal Tunnel Surgery for Workers' Compensation Patients

Carpal tunnel syndrome is the most common compression neuropathy. According to the U.S. Bureau of Labor Statistics, the condition accounted for the third highest number of median days away from work in 2013, behind fractures and multiple injuries with fractures.

Workers' compensation (WC) patients who undergo carpal tunnel release (CTR) have been found to have poorer subjective results and delayed return to work (RTW) in many studies. Surgical outcomes in WC patients are multi-factorial, and may be dependent on economic, psychosocial, work-related and legal factors that are difficult to parse out.

To better understand the issue, Jefferson researchers, led by Eon K. Shin, MD, conducted a retrospective review of all WC patients who underwent CTR surgery from January 2010 to December 2014 by one of three fellowship-trained hand surgeons. One-hundred and fifty-two wrists in 108 patients (64 unilateral, 44 bilateral) were included in the analysis. Average age at the time of surgery was 49.5 years.

Demographic, social, medical and disease-specific data were obtained from departmental records. The primary outcome was time from surgery until full-duty RTW, measured in weeks as documented by the treating surgeon.

Other variables considered included the patient's psychiatric diagnosis, history of diabetes, history of fibromyalgia or chronic pain, narcotic use, work status at time of surgery, job type, marital status, body mass index (BMI) and preoperative motor nerve conduction velocity (NCV).

The study, which has been submitted to the journal *HAND* and accepted for presentation at the American Association for Hand Surgery (AAHS) and the American Academy of Orthopaedic Surgeons (AAOS), found that:

- 89% of all patients returned back to full duty.
- Average RTW in all of the WC cases was 12.5 weeks. That is much longer than a typical RTW of three weeks for non-WC patients.
- There was no significant difference in RTW between unilateral and bilateral surgery.
- Predictors of delayed RTW were depression with or without anxiety, fibromyalgia or chronic pain, history of opioid use and pre-operative work status (full-duty versus not full-duty).
- Pre-operative NCV, gender, job type, higher BMI, diabetes and marital status were not predictive of RTW.

"Knowledge of these factors can help surgeons, patients and employers forecast which WC patients will have a protracted post-operative recovery, so that appropriate therapies and accommodations can be made," the researchers said.

The study did not consider whether there was legal action around the patient's medical case.

"Litigation status, work environment and financial gain likely play a role in surgical outcome in the workers' compensation population," they noted, adding that other research has shown that "legal representation doubles the likelihood of a poor outcome."

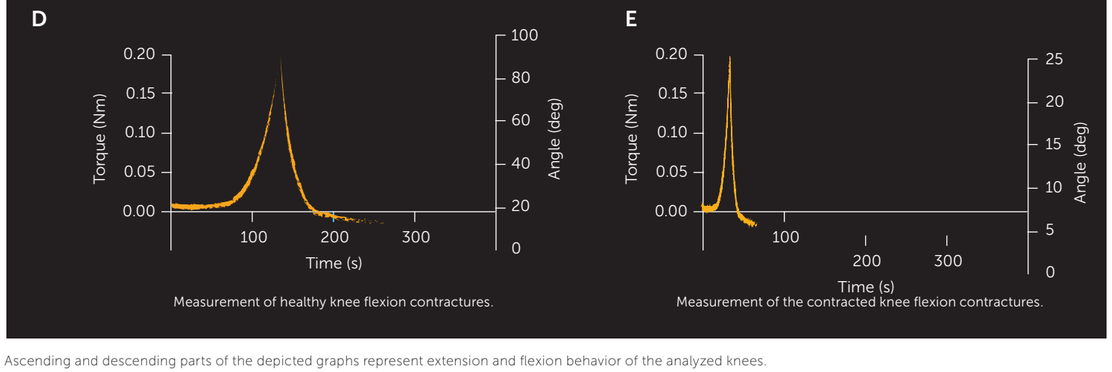
The researchers said it was particularly noteworthy that those patients who had already been on a reduced work schedule prior to surgery took longer to return to work.

"This suggests that work restrictions prior to a carpal tunnel release may forecast a longer post-operative recovery, due to an unwillingness of the patient to return back to work or the increased rehabilitation needed to regain function from a prolonged absence of work," they said. "Keeping patients working full-duty until the time of surgery may also be prudent to reduce time away from work post-operatively."

Comparison of Crossed Screw Versus Plate Fixation for Radial Neck Fractures

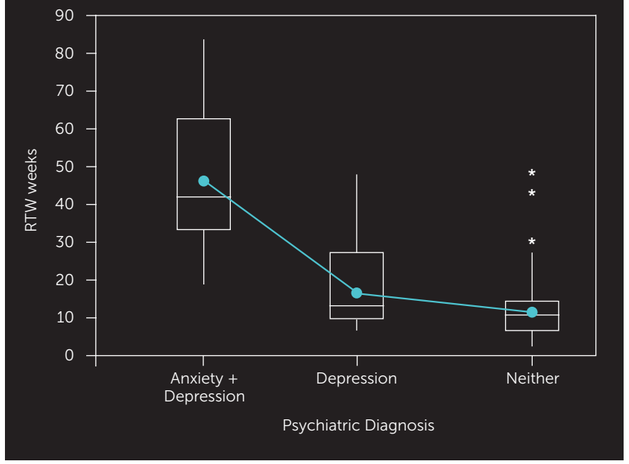
Fixation of radial neck fractures can be achieved with a plate and screw construct or, in absence of comminution, with two obliquely oriented screws. Jefferson researchers, headed by Christopher Jones, MD, conducted a comparison study of the two fixation strategies using a cadaver model. They analyzed

Data from Rabbit-Based Model of Joint Contracture



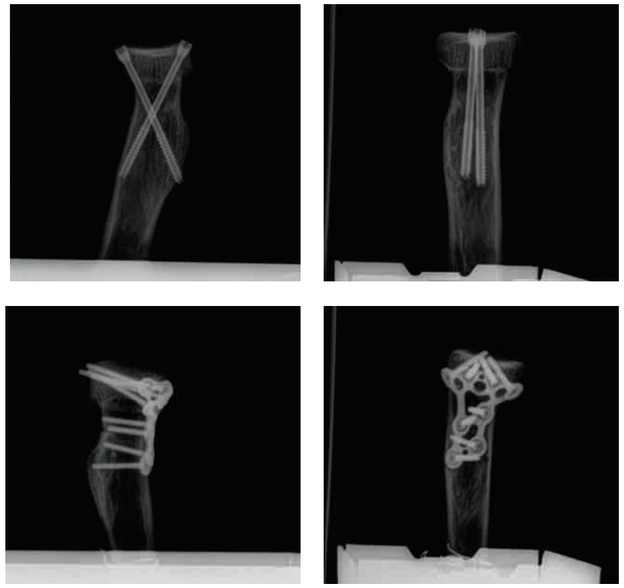
Ascending and descending parts of the depicted graphs represent extension and flexion behavior of the analyzed knees.
Source: Andrzej Fertala, PhD

Return to Work Following Carpal Tunnel Release



Return to Work Duration after Carpal Tunnel Release Based on Concomitant Psychiatric Disorder(s) Results demonstrate that in a population composed exclusively of workers' compensation patients, those with psychiatric disorders were at significantly higher risk for a longer post-operative recovery period before returning to work. In particular, patients with both anxiety and depression took more than four times as long to return to work, than those with no psychiatric disorders.

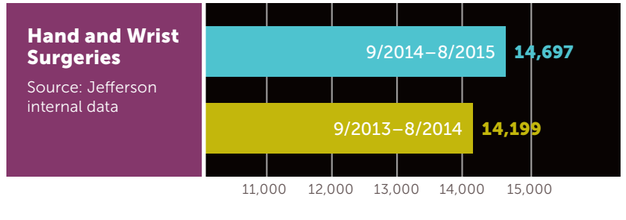
Source: Sidney M. Jacoby, MD



Radiographs of mounted cadaveric proximal radii. The fractured specimens were mechanically tested after repair with headless compression screws (top panels) or a mini plate and screws (bottom panels).

biomechanical properties, including load to failure, to determine if one approach was better than the other.

Ten matched-pair radii were removed from cadaver specimens. A transverse osteotomy was created at the neck of each radius. Right-sided radii were fixed with two oblique headless compression screws. The left-sided radii were fixed with a radial neck plate. The distal aspect of each radius was ported in urethane-casting resin. The radial head was loaded in shear in four different planes (medial to lateral, lateral to medial, posterior to anterior, and anterior to posterior) using an Instron machine. Stiffness and load to failure were recorded.



The findings, published in *Clinical Biomechanics*, included:

- The stiffness of both constructs was similar in all planes except for loading from medial to lateral. In that scenario, the screw construct was 1.8 times stiffer.
- Average ultimate failure occurred at 229 N for all the screws and 206 N for the plate. The difference was not statistically significant.
- Mode of failure differed for the two constructs. The plate failed in bending, while the screws failed in pullout and fracture.

"Both fixation strategies provide similar strength and stiffness for the fixation of transverse non-comminuted radial neck fractures," the researchers concluded. But they said certain circumstances may make a given approach more desirable.

"While plate and screw constructs are more appropriate for axially unstable or comminuted fractures, two oblique screws might be preferred for simple transverse neck fractures since this strategy requires less exposure and results in less hardware prominence."

Variables Prognostic for Delayed Union and Nonunion Following Ulnar Shortening Fixed with a Dedicated Osteotomy Plate

The adverse effects of smoking on bone healing have been well documented, though much of the research has been focused on elective spinal or ankle fusion, or long-bone fractures treated with or without fixation. Research on the effect of smoking on bony union in ulnar shortening osteotomy (USO) is more limited and a prior study conducted at Jefferson predated newer surgical techniques and dedicated osteotomy plating systems that eliminate the need for freehand cuts.

Jefferson researchers led by Sidney M. Jacoby, MD, investigated whether smoking remains a detrimental factor in healing with the newer surgical techniques and implants. They conducted a retrospective review of all patients who underwent USO using the TriMed single osteotomy dynamic compression plating system from January 2010 to December 2014 by one of two fellowship-trained hand surgeons. Demographic data and medical and social histories (including smoking history) were reviewed.

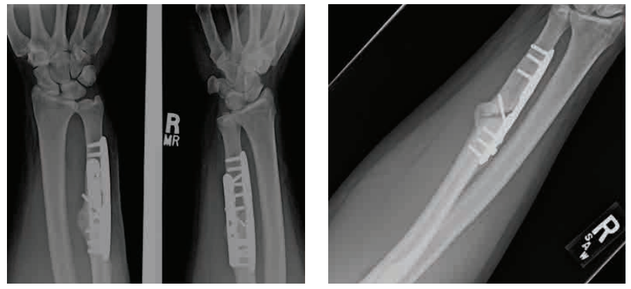
The study, accepted for publication in the *Journal of Hand Surgery* and for presentation at the American Association for Hand Surgery (AAHS), included 72 USOs performed in 69 patients, 17 in smokers and 55 in non-smokers. (Former smokers were classified as non-smokers.)

The primary outcome measure was time to bony union. Secondary outcomes included rate of revision for nonunion and other complications requiring additional surgery.

The results include:

- The average time to union was 4.0 months for the entire cohort.
- Time to union for smokers was 6.3 months versus 3.3 months for non-smokers.
- Delayed union, defined as ≥ 6 months to union, occurred in seven smokers (41%) and one non-smoker (2%).
- Four nonunions occurred overall, three of which were in smokers. All non unions required revision plating with placement of cancellous bone graft.
- Among smokers, the number of cigarettes smoked per day did not correlate with time to bony union.
- Time to union in diabetics was 5.1 months versus 3.9 months in non-diabetics, but this difference was not statistically significant.
- Rate of nonunion or delayed union in diabetics (38%) versus non-diabetics (14%) approached statistical significance.
- Patient age, gender, hand-dominance, BMI and the length of shortening of the ulna did not affect time to bony union, or incidence of delayed or nonunion.
- Symptomatic hardware necessitated plate removal in 13 cases (18%), with no significant difference between smokers and non-smokers.

"Our study provides sufficient evidence that even the latest implant technologies that offer precise osteotomy fixation cannot supersede the deleterious biological effects of smoking on bone healing following elective USO," the researchers concluded. "In particular, smokers remain at significantly higher risk for both delayed union and nonunion, the latter of which likely requires revision surgery. Diabetes may further increase the risk of delayed or nonunion, and surgeons should be extra vigilant in treating patients with both risk factors."



Hypertrophic nonunion in a smoker. Standard posteroanterior (PA) radiograph of the dominant right forearm of a 46-year-old male with a long history of smoking one pack per day. The patient underwent standard USO with the TriMed compression osteotomy system, but continued to have pain at the osteotomy site at six months post-operatively.Radiographs revealed hypertrophic nonunion of the osteotomy site, with some cortical reaction at the proximal margin of the plate, suggesting possible hardware loosening.

The researchers noted that knowledge of a patient's smoking status is unlikely to change initial management in most emergency situations.

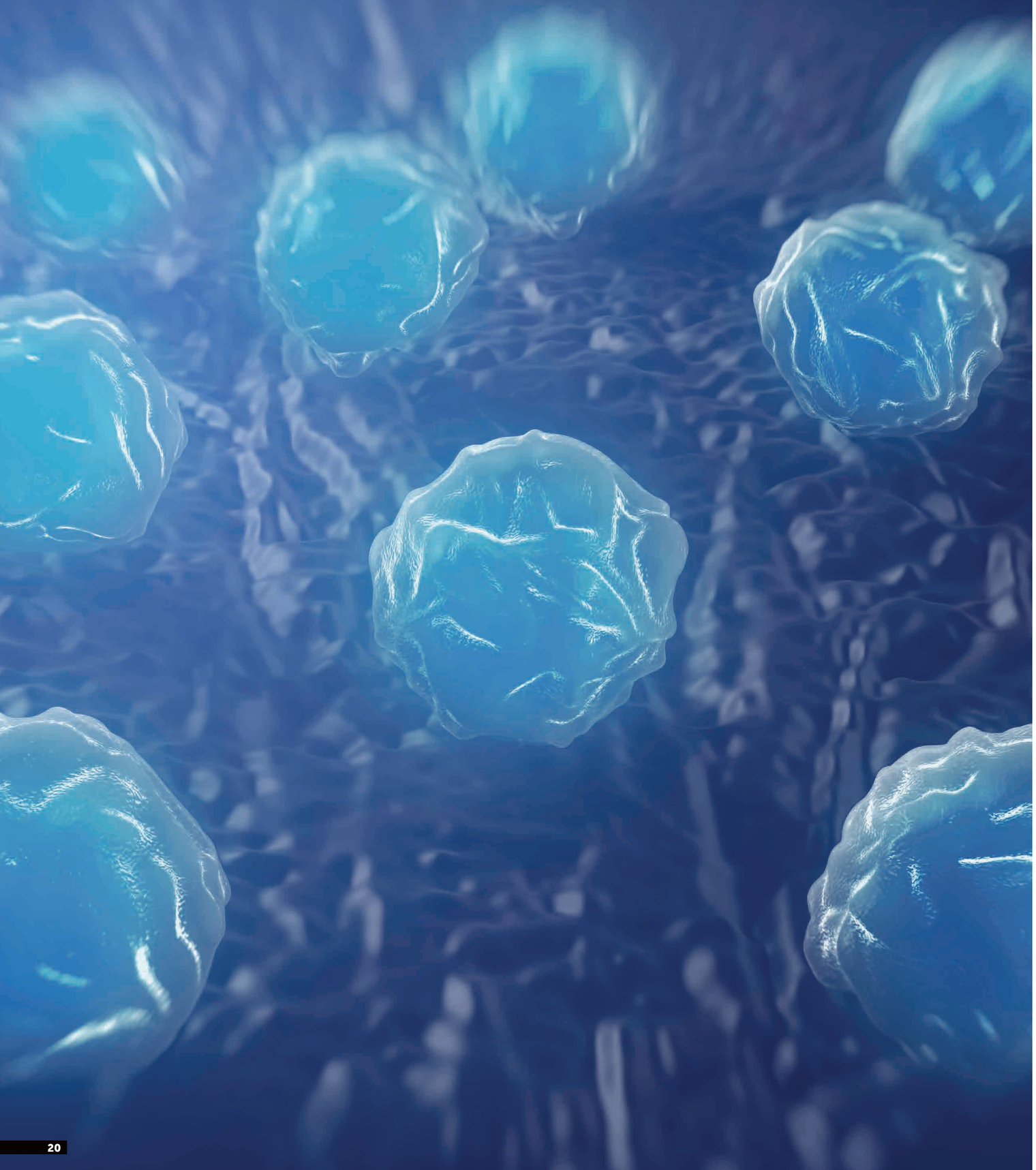
"However, in the elective or non-acute setting, the decision to operate on an active smoker is less clear-cut," they said, noting that some orthopaedic surgeons elect not to operate on active smokers.

"Unfortunately, basing this decision solely on patient history may be misleading, as responses to self-report questionnaires have been shown to be inaccurate for some populations of smokers, particularly if full disclosure were to preclude them from receiving surgery," the researchers said. If smoking is suspected, urine screening for cotinine, a major nicotine metabolite, may be useful, they said.

"A promising finding is that peri-operative smoking cessation has demonstrated improved bony union rates versus continued smoking in both animal and human studies."

The researchers made the following recommendations:

- Surgeons whose patients smoke should consider the potential complications of delayed healing when considering an elective osteotomy.
- When a patient's smoking history is in question, surgeons should consider urine testing.
- Patients who desire this operation should be counseled on methods for smoking cessation.



musculoskeletal **oncology**

The advantage of a multi-specialty orthopaedic program with immediate access to other areas of complementary expertise is especially apparent when it comes to bone and soft tissue cancer. Patients benefit from the care of specialists in the Department of Orthopedic surgery as well as those in Jefferson's Sarcoma and Bone Tumor Center which is part of our NCI-designated Sidney Kimmel Cancer Center.

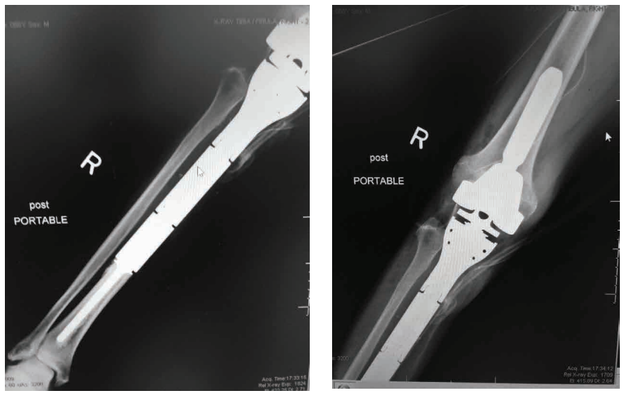
Tumors of the bone and soft tissue present an oncologic and orthopaedic challenge. Precise surgical attention is required to preserve limbs and function. Orthopaedic specialists trained in musculoskeletal oncology routinely handle complex cases at Jefferson's Sarcoma and Bone Tumor Center involving cancers such as Osteosarcoma, chondrosarcoma, Ewing sarcoma and all subtypes of soft tissue sarcoma.

SERVICES

- Management of extremity bone sarcoma
- Management of extremity soft tissue sarcoma
- Pelvis sarcoma resection, bone and soft tissue
- Computer-navigated bone tumor resection
- Treatment of benign bone tumors
- Treatment of benign soft tissue tumors
- Management of skeletal metastatic disease
- Management of spine lesions in conjunction with spine service
- Subspecialty imaging review
- Subspecialty pathology review
- Complex joint reconstruction
- Custom joint reconstruction
- Acetabular revision joint procedures

Jefferson has one of the few comprehensive sarcoma treatment centers in the country, an important distinction given that studies have shown that patients with sarcoma who are treated at sarcoma centers have better outcomes than those who are not. The Center's director, John A. Abraham, MD, is a leader in the use of surgical navigation to resect tumors in difficult locations such as the pelvis.

Jefferson also treats people with a history of cancer who want their orthopaedic needs tended to by surgeons with particular expertise in oncology. More patients than ever are living with a history of cancer, and they increasingly require common procedures such as total hip or knee arthroplasty. Researchers from Jefferson and the Sidney Kimmel Cancer Center are studying whether cancer patients are



Postoperative image following resection of the tibia and replacement with an oncology prosthesis.

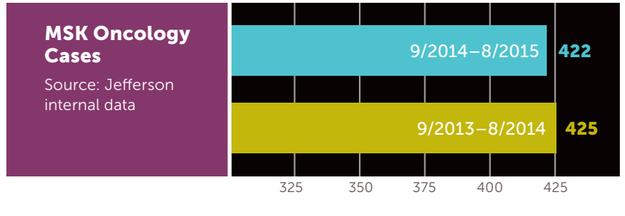
at heightened risk for complications from orthopaedic surgery and therefore may benefit from having even routine orthopaedic procedures performed by surgeons with added experience in cancer care.

The Jefferson Sarcoma and Bone Tumor Center has an extensive research agenda. It is conducting several clinical trials that could identify breakthrough medical treatments for sarcoma. Surgeons and scientists in the Department of Orthopaedic Surgery and the Sidney Kimmel Cancer Center collaborate to study the molecular basis of disease. One such study focuses on the biology of chordoma, with the goal of developing new treatment approaches.

Here is a look at some of their latest findings:

Thromboembolism after Intramedullary Nailing for Metastatic Bone Lesions

Impending and pathologic fractures of long bones in patients with metastatic skeletal disease are generally treated with intramedullary nailing. The combination of neoplastic disease, loss of mechanical stability, vessel damage and immobility put these patients at substantial risk for the development of venous thromboembolism (VTE), but the precise risk has not yet been defined through research.



Researchers from Jefferson and the Sidney Kimmel Cancer Center, led by John A. Abraham, MD, conducted a review of 336 cases of impending and pathological long-bone fractures due to metastatic disease that were stabilized with IM nails. The operations occurred between February 2011 and April 2013 at three NCI-designated cancer centers using the technique and protocols of the Orthopaedic Oncology section at Jefferson. The cases were reviewed for type of cancer, the use of anticoagulants, whether radiation therapy was done postoperatively and what complications, if any, occurred in the 90 days following surgery.

The findings, published in *Journal of Bone and Joint Surgery*, include:

- The overall rate of VTE was 7.1% (24 of 360 cases), significantly higher than the rate of 1% or less for routine lower extremity surgery.
- The rate of pulmonary embolism (PE) was 3.9% (13 cases).
- The rate of deep venous thrombosis (DVT) was 3.3% (11 cases).
- There was no significant relationship found between the type of anticoagulants used and VTE.
- There was a positive correlation between lung cancer histology and development of VTE or PE.
- The use of radiation therapy was also a risk factor for VTE.
- The rate of wound complications was not especially high, occurring in 3.3% of cases (11 of 336).

"There is a high rate of VTE in the skeletal metastatic disease population undergoing intramedullary nailing even while receiving postoperative thromboembolic prophylaxis," the researchers concluded. "Current anticoagulation protocols may be inadequate."

They said that more research is needed to determine the best approach for using anticoagulants in these patients.

Dr. Abraham's research team is designing a clinical trial to identify the optimal anticoagulation routine for patients undergoing intramedullary nailing.

Total Joint Arthroplasty in Cancer Patients

An estimated 13.7 million Americans are living with a history of cancer. Over the past 10 years, cancer death rates have decreased by more than 1% per year and the overall five-year survival rate for cancer increased from 49% in the 1970s to 67% in the past decade.

The number of cancer survivors is likely to grow even more as treatments for various cancers improve. An increasing number of patients with a cancer history will require total joint arthroplasty (TJA), either primary or revision, in the coming years.

It is not clear whether patients with a cancer history should be treated any differently when undergoing primary or revision TJA than patients with no history of malignancy.

Cancer is known to be a promoter of thromboembolic disease and has been demonstrated as a risk factor for venous thromboembolic events (VTE) in both non-operative and postoperative settings. However, the literature is unclear on the extent of risk for VTE and other complications in cancer patients undergoing TJA.

To clarify the issue, researchers from Jefferson and the Sidney Kimmel Cancer Center – including John A. Abraham, MD, Director of Orthopaedic Oncology, and Javad Parvizi, MD, Director of Orthopaedic Research – conducted a review of TJA cases involving patients with a history of cancer. Of 26,415 TJA procedures done at Jefferson between January 2000 and March 2011, 2,211 involved patients with a history of cancer. There were also 300 cases involving patients with active cancer and 25 cases in which TJA was due to an oncologic indication.

The findings, published in *Journal of Arthroplasty* included:

- TJA patients with a history of cancer had a 0.54% risk of an in-hospital ischemic event compared to a 0.26% risk for patients without a cancer history.
- Patients with a cancer history had a 1.72% risk of DVT compared to 0.93% for those without a cancer history.
- When looking at cancer location, the risk of DVT was highest, 6.5%, among patients with a history of head and neck cancer.
- Patients with active cancer had a significant increase in rates of renal and respiratory complications, as well as hematoma or seroma formation. They were also at heightened risk for postoperative mortality (1.33%) compared to patients with no history (0.28%).
- Overall in-hospital complications were highest in patients with cancer of the respiratory system and patients with multiple myeloma (27.3% for each group).
- Both patients with active cancer and those with a history of cancer had significantly higher rates of overall in-hospital complications (8.33% and 5.34% respectively) compared to controls (4.08%).
- The patients whose need for TJA was due to their active cancer had an especially high risk for DVT (12%) and early post operative mortality (2%).

"The demonstrated increased morbidity and mortality in cancer patients undergoing TJA underlines the importance of multidisciplinary management in these patients, and the necessity of active involvement of the medical team in the preoperative evaluation as well as in the perioperative period, to optimize medical status, even if the patient had been in complete remission for a long period of time," the researchers concluded.

Researchers suggested that surgeons may want to consider postponing elective TJA in patients with active disease until their cancer treatment is completed. They also said more stringent use of thromboprophylaxis is probably advised for patients with a history of cancer, even if they have been in remission for many years.

At Jefferson and the Sidney Kimmel Cancer Center, multidisciplinary conferences are conducted to ensure that all treating teams, including medical oncology and radiation oncology, have input into designing the optimal treatment plan for the patient. Careful consideration is given to postoperative anticoagulation regimens and orthopaedic treaments decisions are made keeping in mind the need for patients to return as quickly as possible to their systemic or other cancer therapies.

trauma

As a Level 1 Regional Resource Trauma Center, Jefferson is skilled at treating complex orthopaedic injuries that, if not properly managed, have the potential to cause lifelong disability.

In addition to providing expert care in emergency situations, orthopaedic trauma surgeons conduct research to identify ways to improve treatment for a number of musculoskeletal injuries, including hip and pelvic fractures. Another important area of recent research is compartment syndrome, a dangerous condition that can become a limb-threatening complication to virtually any injury.

Here is what the research has found:

SERVICES

- Treatment of fractures, both simple and complex, using both nonoperative and operative methods, including articular fractures and pelvic/acetabular fractures
- Assessment and treatment of problem fractures, those that have gone on to malunion or nonunion
- Functional treatment of fragility fractures of the elderly
- Treatment of post-traumatic bone infections

Interobserver Variability in the Measurement of Lower Leg Compartment Pressures

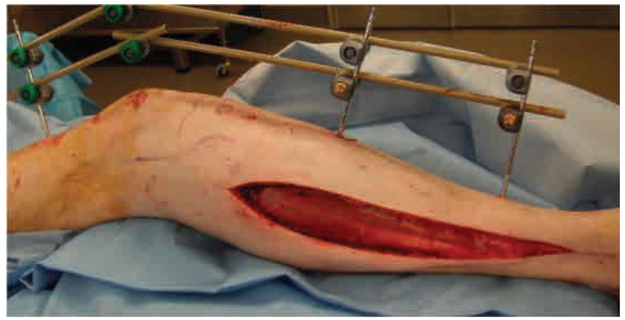
It can be difficult to diagnose acute compartment syndrome. That is troubling because not only is the condition dangerous, but time is of the essence in terms of diagnosis and treatment. Delayed diagnosis can result in contractures and functional loss, infection, renal failure, amputation and, in rare cases, death.

Signs and symptoms of compartment syndrome include pain out of proportion to the injury; pain with passive stretch of the muscles involved; paralysis of the same muscles; paresthesia in the distribution of the peripheral nerves involved; pallor of the skin; and firmness of the affected compartments. While that list of warning signs is long, the accuracy and reliability of these clinical findings have been shown to be poor. The challenge is that many, or even all, of these signs and symptoms can accompany almost any orthopaedic injury.

To accurately diagnose compartment syndrome, it may be necessary for the clinician to take measurements of the pressure in the affected compartment. The ideal method for obtaining measurements is not clear. As a result, the techniques and instrumentation in use vary.

Deficiencies in taking pressure readings could have clinical ramifications if a diagnosis of compartment syndrome is missed or delayed.

trauma



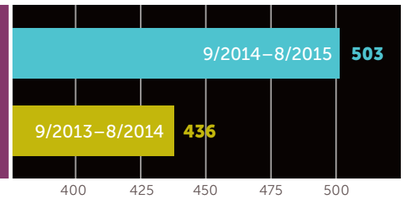
(Top) Above knee cadaver used in lab studies to create a model of lower leg compartment syndrome. **(Bottom)** Demonstration of the Intra-Compartmental Pressure Monitor.

Source: James C. Krieg, MD

Researchers, led by Jefferson faculty member James C. Krieg, MD, conducted a study to determine the variability of measurements when different doctors used the same gauge – the Stryker Intra-Compartmental Pressure Monitor. The hand-held monitor uses a side port needle, a disposable syringe of saline flush and a digital readout monitor. Although the monitor is commonly used and has been tested in lab studies, it had never been tested in a "real life" scenario: real doctors measuring pressure in real limbs.

Trauma Cases

Source: Jefferson internal data



Four above-knee cadaver specimens were used to create a model of lower leg compartment syndrome. Thirty-eight physicians (including 27 orthopaedists) examined the limbs and took four pressure readings each. They were observed for correct assembly and use of the monitor and measurements were compared with known pressures.

The study, published in *Journal of Orthopaedic Trauma*, found that:

- Of the 152 compartment measurements taken, 31% (42) were made with correct technique and 40% (60) were made with less-than-ideal technique. Thirty percent of readings (45) involved catastrophic errors, meaning the technique was quite a deviation from the correct one.
- Only 60% of measurements made with the correct technique were within 5 mm Hg of the standard pressure.
- Accuracy dropped to 42% for measurements taken with small errors in technique and 23% when a catastrophic error was committed.

"Our data support the notion that measurement of compartment pressure in clinical practice is not completely reliable, even when using a commercially available monitor and despite correct technique," the researchers concluded. "We recommend review of correct technique on a regular basis, such as every two years."

The researchers said the decision to perform decompressive fasciotomies should take into consideration that the pressure measurements that were taken may not be completely reliable.

Research such as this has a direct impact on the quality of patient care and the education of medical students and residents. The correct use of the Stryker monitor is now reviewed at least annually with Jefferson orthopaedic residents in an effort to improve its accuracy in clinical practice.

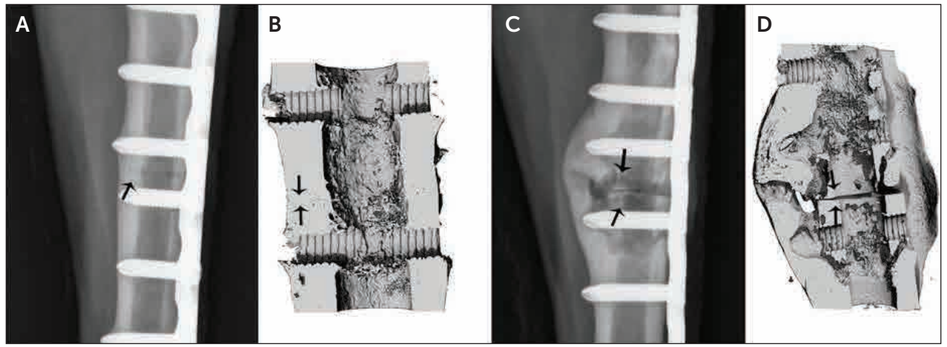
basic **science**

From the Laboratory of Theresa Freeman, PhD, Associate Professor of Orthopaedic Surgery

Repair and regeneration of tissues after injury or wounding is an important area of study that impacts multiple diseases. The development of osteoarthritis can often be attributed to a trauma that occurs in youth, which begins the slow degradation of cartilage. By reducing cartilage damage immediately after an injury, the development of osteoarthritis can be dramatically slowed. Dr. Freeman is studying how inhibition of a protein called Apoptosis signal regulated kinase (ASK)1 can lessen the damage to cartilage by decreasing cell death and pro-inflammatory cytokine production. By reducing tissue destruction, these changes enhance healing and limit cartilage degeneration. In turn, the endogenous cells can activate repair cascades to generate a more robust healing/regenerative response. In addition, Dr. Freeman is working on developing the new discipline of Plasma Medicine. Therapeutic application of a novel non-thermal atmospheric dielectric barrier discharge plasma has shown promise in enhancing cell differentiation, limb development and regeneration of cartilagenous tissue. By generating both ionized species and electric fields, the bioelectrochemical effects of plasma can induce intracellular reactive oxygen and nitrogen species in the tissue that trigger events leading to healing and regeneration.

From the Laboratory of Noreen Hickok, PhD, Associate Professor of Orthopaedic Surgery

Infection remains a serious complication of every type of orthopaedic surgery. While surgical techniques and materials for joint replacement help ensure that infection rates remain low, implant-associated infections continue to contribute to patient morbidity and healthcare costs. Because prosthetic joint infections are difficult to diagnose and hard to treat, it is critical to find effective prevention strategies. In one such effort, Jefferson researchers are studying how antibiotics work to eradicate infection in the joint environment. Typically, surgeons administer antibiotics before and immediately after surgery to minimize the chances of infection. Dr. Hickok and her colleagues have discovered that the joint environment can mask infection, making it more difficult for antibiotics to eliminate the invading organisms. The researchers are overcoming this problem



A and B - Antibiotic covalent bonded to titanium implant.

C and D - Infected bone.

by making implanted materials antibacterial, including performing surface modifications of titanium hardware with vancomycin, and modifying allograft bone used in spinal fusions with vancomycin or doxycycline. The Jefferson researchers are also testing whether it would be more effective to utilize implant hardware that comes pre-loaded with antibiotics that could be activated if necessary. Ultrasound would then be used to trigger antibiotic release as well as to disperse the locally-released antibiotics into surrounding tissues. This concept has been expanded for use with both joint and spine infections. An additional aspect of the ongoing studies involves the use of light-activated therapy to reduce the risk of infection. Finally, the Jefferson group is exploring the role of the microbiome in the pathogenesis of arthritis and the need for orthopaedic surgery.

From the Laboratory of Rowena McBeath, MD, PhD, Assistant Professor of Orthopaedic Surgery

Tendinosis – a degenerative condition affecting tendons and their insertion into bone – results in painful movement of bones and joints. Current treatment involves physiotherapy, steroid injections and surgery if pain persists; however, the cellular basis of tendinosis development is unknown. Dr. McBeath, a hand surgeon and clinician scientist, studies human tendon cells in culture and the mechanical and intramolecular signaling mechanisms that govern their proliferation and differentiation. Recent studies on tendinosis of the wrist, named de Quervain's tendinosis, has linked disease severity with development of chondroid metaplasia of the tendon compartment tissue. Dr. McBeath's studies on human tendon cells have revealed a capacity of these cells to "transdifferentiate," or change their phenotype from tendon to fibrocartilage. These findings may explain the mechanism whereby tendinosis develops in patients, and suggest further direction into development of cellular and molecular therapies for treatment of these painful conditions.

From the Laboratory of George Feldman DMD, PhD, Assistant Professor of Orthopaedic Surgery

Developmental Dysplasia of the Hip (DDH) is a debilitating condition characterized by incomplete formation of the acetabulum and/or femur. This condition can lead to dislocation of the femur, suboptimal joint function and accelerated wear of the articular cartilage, resulting in a crippling arthritis of the hip. DDH affects 1 in 500 to 1,000 newborns in the U.S. with pockets of high prevalence in Japan, Italy and other Mediterranean countries. The primary goal of current research is to develop a diagnostic DNA test to identify individuals at risk for this disorder. Jefferson researchers studying the DNA of a four-generation family have found a potentially harmful mutation in the CX3CR1 receptor. The presence of this DNA variant has been recently shown by researchers in China to increase the odds of getting DDH by a factor of 2.5. In another family, a potentially harmful mutation in the teneurin-3 gene has been identified. Both of these DNA changes are thought to delay the maturation of stem cells in forming specific regions of the hip joint. To examine the causative relationship between changes in the DNA and changes in the hip socket, similar mutations have been made in mice. Mice with a dysfunctional CX3CR1 receptor appear to show changes in their hip sockets similar to those seen in humans. Similar experiments are underway to demonstrate the function of the teneurin-3 mutation.

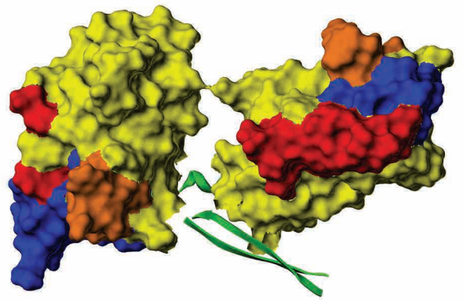
The relevance of these findings has been broadened to include unrelated individuals with DDH. In addition to mutations in both the teneurin-3 and CX3CR1 genes, these severely affected individuals have mutations in genes linked to the pathways in which both of these family-linked, susceptibility-inducing genes reside. Additionally, the research has found potentially harmful changes in the DNA of these sporadic individuals that are in genes linked to the canine version of DDH. Identification of these mutations provides a firm foundation for an accurate diagnostic test in newborns. Early identification and treatment of DDH would prevent hip dysplasia from developing into osteoarthritis.

From the Laboratory of Andrzej Fertala, PhD, Professor of Orthopaedic Surgery

Fibrosis, which results from excessive and disorganized collagen production, can affect almost all tissues. Following knee injury or knee replacement surgery, for instance, arthrofibrosis can cause a painful and debilitating condition known as stiff knee.

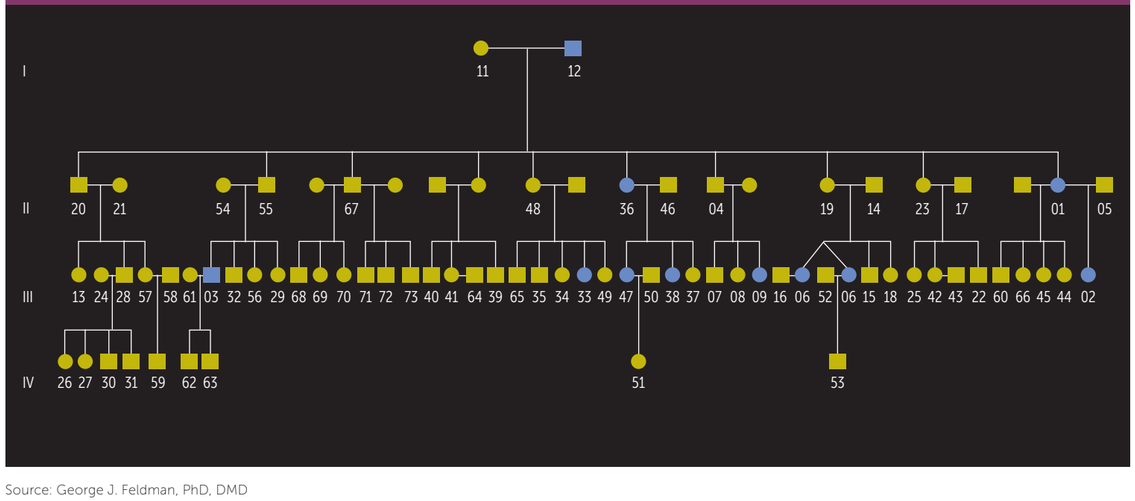
Dr. Fertala and a group of orthopaedic surgeons that includes Pedro Beredjiklian, MD, and Joseph Abboud, MD, are examining novel ways to block excessive collagen production, with the goal of preventing abnormal scarring and improving recovery. Inhibition of the extracellular process of collagen fibril formation represents a new approach to limiting posttraumatic or postsurgical localized fibrosis. Using a newly developed antibody that targets critical regions of the collagen molecule, the researchers demonstrated that this agent prevents interactions between molecules and reduces collagen deposition.

The approach is being tested in a preclinical study with the use of a clinically relevant animal model. Preliminary data indicate that the anti-collagen antibody reduces the amount of newly-formed collagen fibrils in an injured joint capsule, thereby improving the range of motion of an antibody-treated knee. Ongoing studies will define benefits and limitations of the proposed approach to limit post-traumatic stiffness of joints and test its clinical potential.

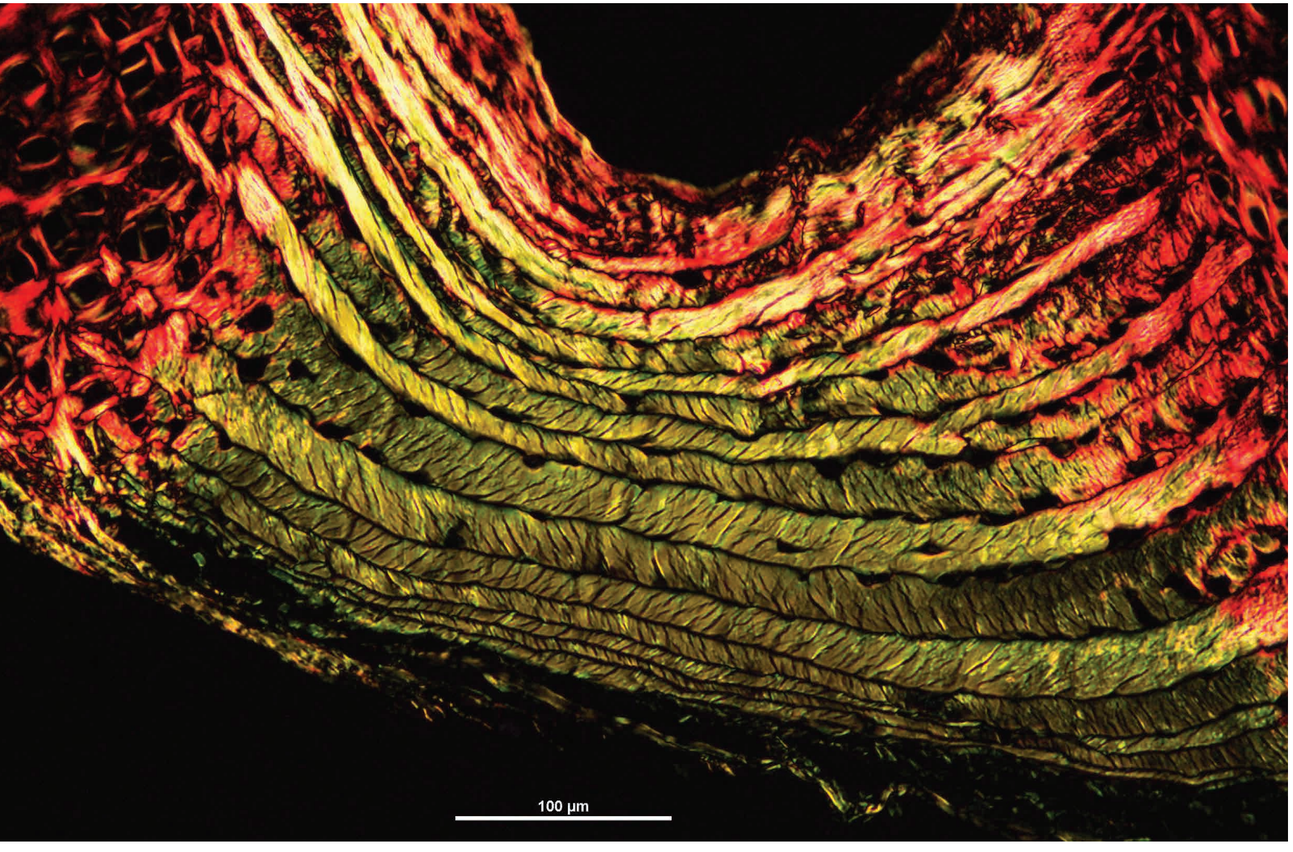


Recombinant Anti-Fibrotic Antibody

Four Generations - Developmental Dysplasia of the Hip



Source: George J. Feldman, PhD, DMD



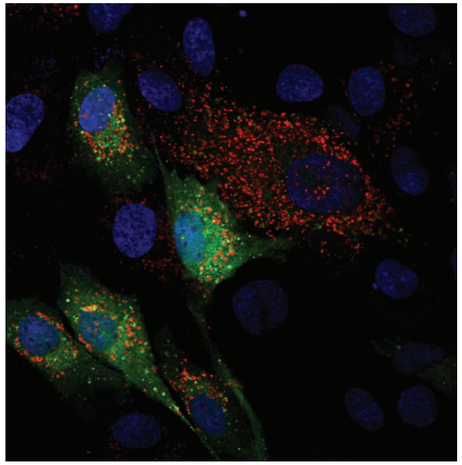
Polarized microscopic image, Outside Annulus Fibrosis

From the Laboratory of Makarand V. Risbud, PhD, Professor of Orthopaedic Surgery and Irving M. Shapiro, BDS, PhD, Professor of Orthopaedic Surgery

The intervertebral disc is a complex structure that separates opposing cartilage-covered bone (vertebrae), permits a range of motions and accommodates high biomechanical forces. The interaction between the semifluid nucleus pulposus and the tight molecular lattice of the annulus fibrosus provides the biomechanical properties necessary for spinal stability. Disturbing this relationship by compromising the stability of the nucleus pulposus, the annulus fibrosus or the endplate cartilage results in disc degeneration, a condition that can lead to excruciating pain and loss of function and often results in costly surgical interventions.

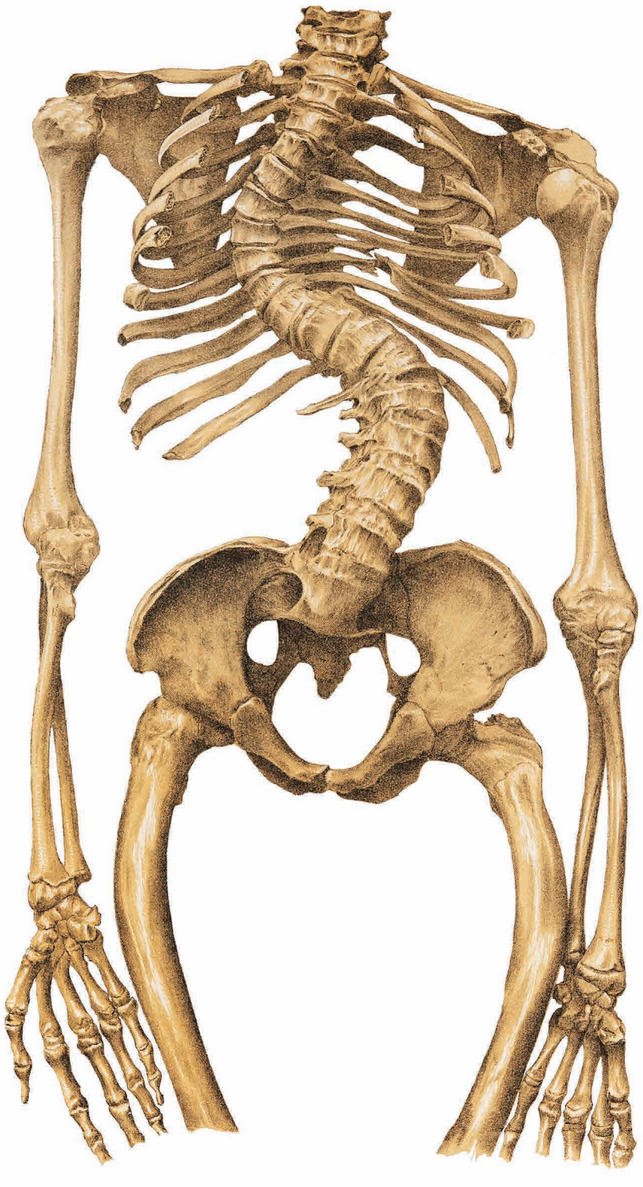
Because the degenerative process is chronic, the nucleus pulposus cells are required to function for long periods in what can be described as a suboptimal microenvironmental niche.

Jefferson researchers are studying those specific conditions that enhance nucleus pulposus cell survival as well as elucidating factors that disregulate the disc microenvironment and promote degenerative disc disease. Since the osmotic pressure within the disc is very high (to offset the biomechanical forces on the spine) the Jefferson researchers are assessing how disc cells survive in this type of environment. They have shown that nucleus pulposus cells respond to changes in osmotic pressure by upregulating a unique transcription factor, TonEBP (tonicity enhancer-binding protein). Once activated, this factor causes transport of osmolytes and water into the disc, thereby maintaining homeostatic conditions. The relationship between the osmotic status of the disc and pain is being examined.



Nucleus Pulposus - Cells within the intervertebral disc

Another characteristic of the disc environment is its low oxygen concentration, which was shown to influence the expression of a critical transcription factor, HIF-1. Subsequent work showed that the stability of this factor is controlled through the coordinated actions of oxygen sensor molecules (PHD). The laboratory has defined several other regulators that control HIF-1 activity, including HSP70 and CCN2, and demonstrated a unique HIF-1 transcriptional program in this hypoxic tissue. Overall, this work has firmly established that HIF-1 is a master regulator of disc cell adaptation to its unique hypoxic niche, thus providing an attractive new therapeutic target to treat disc degeneration.



clinical trials

Funded Clinical Trial	Investigator(s)
A Prospective, Randomized Control Trial of Post-Operative Pain Management Following Primary Single Level Open or MIS TLIF - A Multi-Center ACSR Study Protocol. *Association for Collaborative Spine Research* (01/2015—ongoing)	Mark F. Kurd, MD; Kristen E. Radcliff, MD; Alexander R. Vaccaro, MD, PhD; Christopher Kepler, MD
Association for Collaborative Spine Research (ACSR) Radiation Exposure Registry. *Association for Collaborative Spine Research* (02/2015—ongoing)	Kristen E. Radcliff, MD; Christopher Kepler, MD; Mark F. Kurd, MD; Alexander R. Vaccaro, MD, PhD; Alan S. Hilibrand, MD
A Post-Market, Multi-Center, Prospective Double-Blind, Randomized, Controlled Study to Evaluate the Iovera Device in Treating Pain Associated with Total Knee Arthroplasty. *Myoscience* (04/2015—ongoing)	Antonia F. Chen, MD; Javad Parvizi, MD; William J. Hozack, MD
The Development and Validation of Disease Specific Outcome Instruments for Spine Trauma - International Validation of AO Patient Reported Outcome Spine Trauma. *AOSpine* (07/2015—ongoing)	Kristen E. Radcliff, MD; Christopher Kepler, MD; Mark F. Kurd, MD; Alexander R. Vaccaro, MD, PhD; Alan S. Hilibrand, MD
Cellentra Viable Cell Bone Matrix (VCBM) Anterior Cervical Discectomy and Fusion Outcomes Study (VCBM/MaxAn®) *Biomet* (11/2014—ongoing)	Christopher Kepler, MD
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of a Staphylococcus aureus 4-antigen Vaccine (SA4Ag) in Adults Undergoing Elective Posterior Instrumented Lumbar Spinal Fusion. *Pfizer* (01/2015—ongoing)	Christopher Kelper, MD; Alexander R. Vaccaro, MD, PhD
Post Market Clinical Follow Up Study of the Titan Reverse Shoulder System Used in Primary or Revision Total Shoulder Arthroplasty. *Zimmer* (06/2014—ongoing)	Surena Namdari, MD; Matthew L. Ramsey, MD; Joseph A. Abboud, MD; Charles L. Getz, MD
A Retrospective and Prospective Data Collection Study of the TITAN Modular Total Shoulder System (TSS). *Zimmer* (03/2015—ongoing)	Surena Namdari, MD; Matthew L. Ramsey, MD; Joseph A. Abboud, MD; Charles L. Getz, MD
Retrospective and Prospective Clinical Outcomes of the Zimmer Nexel Total Elbow. *Zimmer* (06/2015—ongoing)	Surena Namdari, MD; Matthew L. Ramsey, MD; Joseph A. Abboud, MD; Charles L. Getz, MD
Prospective Post Market Clinical Follow-Up Study of the Zimmer Trabecular Metal Humeral Stem. *Zimmer* (04/05/2012—ongoing)	Joseph A. Abboud, MD
Retrospective, Post-Market, Clinical and Radiographic Follow-Up Study of the DePuy Delta Xtend Reverse Shoulder System. *DePuy Synthes* (9/24/2013—ongoing)	Joseph A. Abboud, MD; Gerald R. Williams, Jr., MD
A Phase II Randomized, Double-Blind, Placebo Controlled Study to Assess Safety, Tolerability and Effect on Tumor Size of MCS110 in Patients with Pigmented Villonodular Synovitis (PVNS). *Novartis* (10/1/2013—ongoing)	John A. Abraham, MD
Treatment of Plantar Fasciitis with Xeomin: A Randomized, Placebo-Controlled, Double-Blinded, Prospective Study. *Merz* (4/05/2012—ongoing)	Jamal Ahmad, MD
A Prospective, Randomized Clinical Investigation of the Cervitech, Inc. Porous Coated Motion Artificial Disc for Stabilization of the Cervical Spine between C3-C4 and C7-T1. *NuVasive* (02/03/2005—ongoing)	Alan S. Hilibrand, MD; Ashwini D. Sharan, MD
A Multi-Center Prospective Randomized Controlled Clinical Trial Comparing the Safety and Effectiveness of PRODISC-C to Anterior Cervical Discectomy and Fusion (ACDF) Surgery in the Treatment of Symptomatic Cervical Disc Disease (SCDD)—Non Randomized PRODISC-C Continued Access Arm. *Synthes Spine* (04/28/2005—ongoing)	D. Greg Anderson, MD; Todd J. Albert, MD; Alexander R. Vaccaro, MD, PhD

Funded Clinical Trial	Investigator(s)
A Prospective, Randomized, Double-Blind, Controlled Investigation Evaluating the Intracept Intraosseous Nerve Ablation System for the Reduction of Pain in Patients with Chronic Axial Low Back Pain. *Relievant* (04/2012—ongoing)	D. Greg Anderson, MD; Kristen E. Radcliff, MD
Post-Market Clinical Follow-Up Study of the Zimmer Vivacit-E Highly Crosslinked Polyethylene Liner Used with the Continuum Acetabular Shell. *Zimmer* (10/1/2013—ongoing)	William V. Arnold, MD, PhD; Javad Parvizi, MD
Prospective Post-Market Clinical Follow-Up of the Zimmer Trabecular Metal Reverse Shoulder System. *Zimmer* (08/2011—ongoing)	Luke S. Austin, MD; Matthew D. Pepe, MD; Bradford S. Tucker, MD
Prospective Clinical Evaluation Treating Subchondral Bone Marrow Lesions with Subchondroplasty for Pain Relief. *Knee Creations LLC* (3/15/2012—ongoing)	Steven B. Cohen, MD
Trabecular Metal Femoral Hip Stem Used within the Zimmer Hip Registry. *Zimmer* (02/09/2012—ongoing)	Carl Deirmengian, MD
Prospective Post-Market Clinical Follow-Up of the Zimmer Trabecular Metal Reverse Shoulder System. *Zimmer* (08/23/2011—ongoing)	Charles L. Getz, MD; Matthew L. Ramsey, MD
Ascension Radial Head. *Integra Life Sciences* (09/2012—ongoing)	Charles L. Getz, MD; Matthew L. Ramsey, MD; Joseph A. Abboud, MD
Mult-Center Trial of the Sidus Stem Free Shoulder Arthroplasty System. *Zimmer* (7/18/2013—ongoing)	Charles L. Getz, MD; Matthew L. Ramsey, MD; Joseph A. Abboud, MD
Post-Market Study of the Stryker Orthopaedics Triathlon TS Total Knee System. *Stryker Orthopaedics* (4/1/2012—ongoing)	Fabio R. Orozco, MD; Alvin C. Ong, MD
Persona Outcomes Knee Study (POLAR). *Zimmer* (3/1/2013—ongoing).	Matthew S. Austin, MD
Retrieval of Discarded Surgical Tissue. *National Disease Registry Institute* (1/12/2004 – 6/30/2013)	Javad Parvizi, MD; Peter F. Sharkey, MD; James J. Purtill, MD; William J. Hozack, MD; Richard H. Rothman, MD, PhD
Multi-Center Trial of the Continuum Ceramic Bearing System in Total Hip Arthroplasty. *Zimmer* (08/05/2010—ongoing)	Javad Parvizi, MD; William J. Hozack, MD; Matthew S. Austin, MD
American Joint Replacement Registry (12/23/2010—ongoing)	Javad Parvizi, MD
A Phase II Study to Determine the Efficacy and Safety of Allogeneic Human Chrondrocytes Expressing TGF- β1 in Patients with Grade 3 Chronic Degenerative Joint Disease of the Knee (09/01/2011—ongoing)	Javad Parvizi, MD; Marc I. Harwood, MD; Peter C. Vitanzo, Jr., MD
Evaluation of In-vivo Wear of Ceramic Femoral Head Against Highly Cross-Linked Polyethylene: A Comparative Study. *Ceramtec* (11/2011—ongoing)	Javad Parvizi, MD
A Prospective, Randomized, Controlled, Multi-Center, Pivotal Human Clinical Trial to Evaluate the Safety and Effectiveness of Augment Injectable Bone Graft Compared to Autologous Bone Graft as Bone Regeneration Device in Hindfoot Fusions. *BioMimetic* (4/7/2011—ongoing)	Steven M. Raikin, MD
Skelkast Surpass Post-Approval Active Surveillance. *Skelkast* (10/2012—ongoing)	Peter F. Sharkey, MD; Rob Good, MD
Characterization of Bone Marrow Lesions in Retrieved Tibial Plateaus. *Knee Creations LLC* (8/3/2011—ongoing)	Peter F. Sharkey, MD
Outcomes of Patients following Primary Total Knee Replacement. *Stelkast* (6/7/2013—ongoing)	Peter F. Sharkey, MD
Comparing Pain Relief between Exparel® Injection Versus On-Q Catheter as the Postsurgical Analgesia Following Total Knee Arthroplasty (TKA). *Sharpe-Strumia Research Foundation* (07/01/2013—ongoing)	Eric B. Smith, MD; Jess H. Lonner, MD; Peter F. Sharkey, MD

clinical trials

Funded Clinical Trial	Investigator(s)
Efficacy of Riluzole in Patients with Cervical Spondylotic Myelopathy Undergoing Surgical Treatment, A Randomized, Double-Blind Placebo-Controlled, Multi-Center Study. *AOSpine North America* (02/16/2012—ongoing)	Alexander R. Vaccaro, MD, PhD; Todd J. Albert, MD; Alan S. Hilibrand, MD; D. Greg Anderson, MD; Jeffrey A. Rihn, MD; Kristen E. Radcliff, MD
Surgical Versus Nonoperative Treatment of Metastatic Epidural Spinal Cord Compression (MESCC). Quality of Life and Cost-Effectiveness Outcomes. *AOSpine North America* (02/14/2008—ongoing)	Alexander R. Vaccaro, MD, PhD, Todd J. Albert, MD; Alan S. Hilibrand, MD; D. Greg Anderson, MD; Jeffrey A. Rihn, MD; Kristen E. Radcliff, MD
An Assessment of P-15 Bone Putty in Anterior Cervical Fusion with Instrumentation Investigational Plan. *Cerapedics* (06/07/2007—ongoing)	Alexander R. Vaccaro, MD, PhD; Todd J. Albert, MD; James S. Harrop, MD; Ashwini D. Sharan, MD; Srinivas Prasad, MD; Jack Jallo, MD, PhD, FACS
Addendum to Investigational Plan 1003 Version 5.3 IDE Protocol G050178: An Assessment of P-15 Bone Putty in Anterior Cervical Fusion with Instrumentation. *Cerapedics* (03/11/2010—ongoing)	Alexander R. Vaccaro, MD, PhD; Todd J. Albert, MD; James S. Harrop, MD
Bacterial Colonization With and Without Iodophor-Impregnated Adhesive Drapes in Hip Surgery: a Prospective, Randomized, Multi-Center Trial *3M Corporation* (6/2014-present)	Javad Parvizi, MD; Antonia Chen, MD
Retrospective and Prospective Data Collection Study of the TITAN Modular Total Shoulder System (TSS) *Integra* (8/2014-present)	Surena Namdari, MD; Matthew Ramsey, MD; Joseph Abboud, MD; Mark Lazarus, MD; Gerald Williams, MD; Charles Getz, MD
Prospective Post Market Clinical Follow-Up Study of the Zimmer® Trabecular Metal™ Total Ankle System. *Zimmer* (8/2014-present)	Steven Raikin, MD; David Pedowitz, MD
The Influence of a Natural Anti-Inflammatory Product on Levels of Inflammatory Markers in Cases of Osteoarthritis of the Knee. *PRN Neutriceuticals* (3/2013-present)	Peter Sharkey, MD; Javad Parvizi, MD
A Multi-Center 2x2 Factorial Randomized Trial Comparing Sliding Hip Screws Versus Cancellous Screws AND Vitamin D versus Placebo on Patient Important Outcomes and Quality of Life in the Treatment of Young Adult (18-60) *Femoral Neck Fractures. McMaster University* (8/2014-present).	James Krieg, MD; Asif Ilyas, MD; Gregory Deirmegian, MD; Sommer Hammoud, MD; John Abraham, MD; Jamal Ahmad, MD
Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY): A Multi-Center Randomized Controlled Study Comparing Alternative Antibiotic Regimens in Patients Undergoing Tumor Resections with Endoprosthetic Replacements. *McMaster University* (2/2014-present)	John Abraham, MD; Barry Kenneally, MD
Basal Joint Arthroplasty Pain Management – Prospective Comparative Study. *Pacira* (8/2013-present)	Fred Liss, MD; Asif Ilyas, MD; Charles Leinberry, MD; Pedro Beredjiklian, MD
Triathlon Tritanium Knee Outcomes Study. *Stryker* (4/2014-present)	Fabio Orozco, MD; Alvin Ong, MD; Zachary Post, MD
Post Market Study of the Stryker Orthopaedics Triathlon PKR Knee System. *Stryker* (11/2013-Present)	Fabio Orozco, MD, Alvin Ong, MD, Zachary Post, MD
Comparing Pain Relief between Exparel® Injection Versus On-Q Catheter as the Postsurgical Analgesia Following Total Knee Arthroplasty (TKA). *Sharpe-Strumia Research Foundation* (07/01/2013-ongoing)	Eric B. Smith, MD; Jess H. Lonner, MD; Peter F. Sharkey, MD
Outcomes of Patients following Primary Total Knee Replacement. *Stelkast* (6/7/2013-ongoing)	Peter F. Sharkey, MD

Funded Clinical Trial	Investigator(s)
Prospective Randomized Control Trial Investigating the Effect of Patient Education on Post-Operative Opioid Consumption Following Common Hand and Wrist Surgeries	Jacoby SM
Trends in Post-Operative Opioid Prescribing Among Hand Surgeons: National Survey of Members of the American Association for Hand Surgery	Jacoby SM
Prospective Double-Blinded Randomized Placebo-Controlled Trial Comparing a Novel Topical Analgesic with Placebo for Treatment of Lateral Epicondylitis.	Jacoby SM
Prospective Single-Blinded Randomized Controlled Trial Comparing Outcomes and Revision Rates Following Tenolysis with and without AlloWrap® Amnion Membrane Barrier	Culp RW
Can Carpal Tunnel Release Surgery Also "Cure" Insomnia? A Prospective Therapeutic Intervention Series	Jacoby SM
Long-term Outcomes of Interosseous Membrane Reconstruction of the Forearm	Osterman AL
Patient Use of Internet Rating Systems for Choosing Care Providers: A Survey of Consecutive Hand Surgery Patients Seen at a Specialty Hand Clinic	Jacoby SM

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