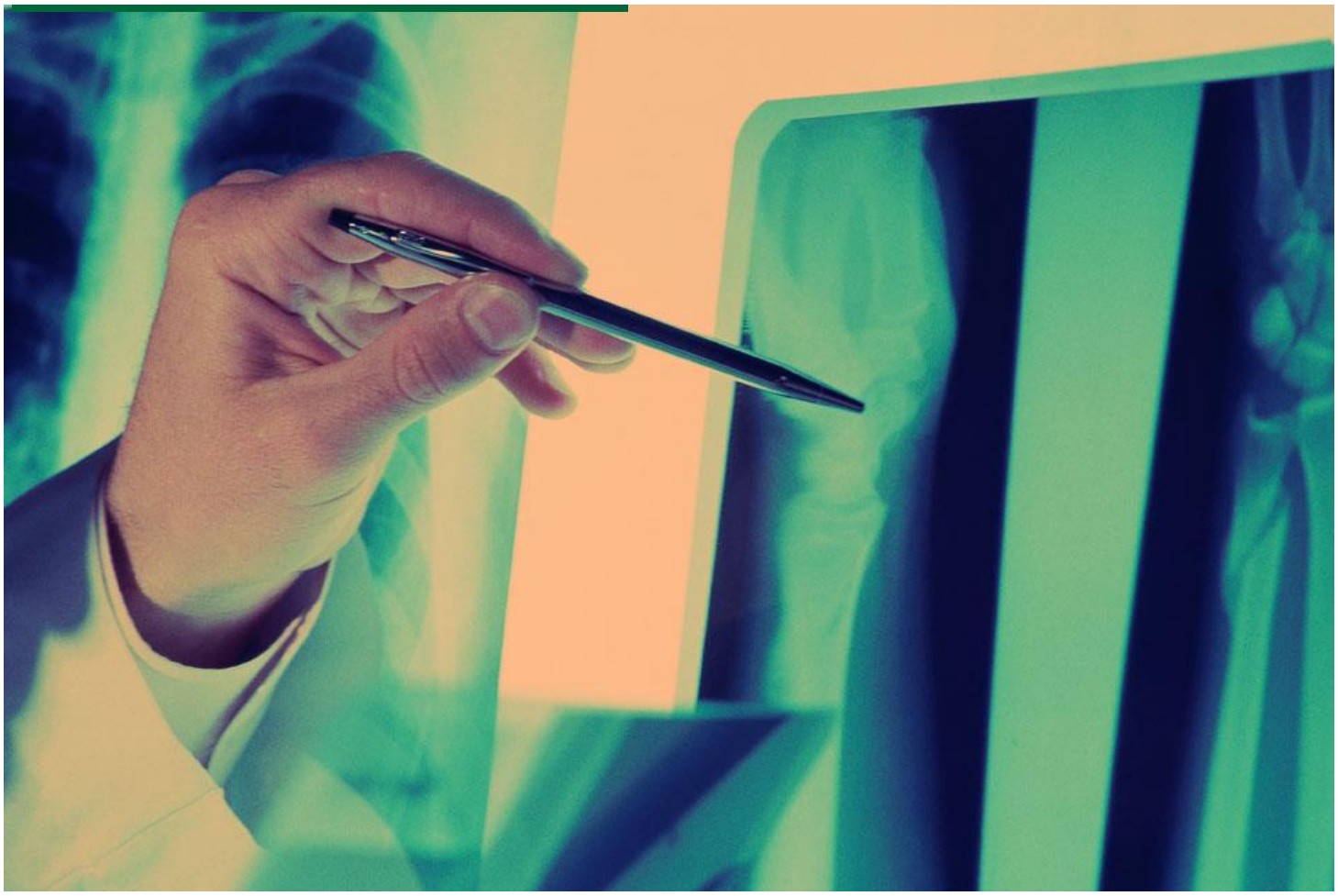
Bone and Joint Research at Rush

2018 Donor Impact Report

Thank You

Today's approaches to bone and joint care — many of which were shaped or pioneered by physicians and scientists from Rush University Medical Center — have improved quality of life for countless people with musculoskeletal problems. In spite of this progress, big breakthroughs are still needed to mitigate the life-altering effects of arthritis, bring relief to the millions of adults with lower back pain and reduce the overall burden of musculoskeletal conditions on both people and society. Patients and providers around the country look to Rush as one of a select few institutions equipped to tackle these challenges and usher in a new era of innovative treatments.

In the following report, we highlight a number of research programs that are disrupting the field of orthopedic medicine and paving the way to better care. Each of these achievements is only possible because of you and our strong community of philanthropic partners. Thank you.



Rush Department of Orthopedic Surgery

National Acclaim

- **#4**: Current ranking in *U.S. News & World Report*
- **8,000+**: The number of times Rush sports medicine surgeons are cited in scientific publications each year
- **#9:** Orthopedic surgery residency program, as ranked by Doximity
- **#1**: Inpatient leader in the Chicago area for orthopedic surgery

Harnessing the Power of Bone Marrow-Derived Stem Cells

The development of minimally invasive surgical techniques and better rehabilitation protocols has changed the way sports medicine orthopedic surgeons treat many of the most common orthopedic injuries. Nevertheless, tears to the knee's anterior cruciate ligament, or ACL, and meniscus, as well as injuries to the shoulder's rotator cuff, remain characterized by lengthy recovery periods and, occasionally, suboptimal outcomes. A disconcerting percentage of patients in the U.S. who undergo surgery for full-thickness rotator cuff tears require subsequent surgery; ACL and meniscus tears appear to accelerate the development of osteoarthritis in the knee.

Leading physician-scientists at Rush — including **Brian Cole, MD, MBA** (pictured to the right); **Nikhil Verma, MD**; **Adam Yanke, MD, PhD**; and **Brian Forsythe, MD** — are advancing studies utilizing bone marrow-derived stem cells that they hope will fundamentally improve the way surgeons treat these pervasive injuries.

In randomized controlled studies — experiments accepted as the strongest scientific evidence of a new treatment's effectiveness — the physicians are looking to determine if these stem cells can help minimize inflammation, accelerate healing, reduce pain and improve the quality of the surgical repair.

While the patient is undergoing surgery, the physician extracts a small amount of bone marrow from the patient's hip and uses a special centrifuge to separate out mesenchymal stem cells, or MSCs, from the rest of the bone marrow. The MSCs are then delivered back into the patient at the surgical site.

With several patients now one year post-surgery, the researchers are entering an important phase of the study. They have begun collecting MRI evidence and biomarker assessments from subjects to begin determining the effect that these stem cells have on healing and long-term outcomes. **These MRIs and study protocols are not covered by Medicare or insurance; philanthropy makes this data collection and analysis possible.**

Brian Cole, MD, MBA, is leading studies utilizing bone marrow-derived stem cells that could alter the standard of care for many orthopedic conditions.

Leading the Pursuit for Better Solutions to Chronic Back Pain

About half of the 215 million opioid prescriptions filled in the U.S. in 2016 were for chronic back pain, the most common reason for health care visits among musculoskeletal disorders and the leading cause of disability worldwide. While opioids may alleviate pain for some patients — if only temporarily — this relief comes at a significant cost: Current drug formulas are highly addictive and have contributed to a national opioid epidemic.

Put simply, the need for better pain treatments has never been greater, and researchers led by **Howard An, MD**, the Morton International Chair of Orthopedic Surgery, are advancing discoveries to develop a safer way to manage chronic back pain.

Dr. An's team believes that medicines utilizing peripherally restricted kappa receptor agonists, or PRKRAs, would be a more effective therapy for back pain. Unlike conventional opioid drugs which target receptors that enter the brain and central nervous system (making them highly addictive), the PRKRAs may relieve pain without crossing the blood-brain barrier, and recent studies have proven them to effectively reduce pain for women after hysterectomy surgeries. The researchers also hypothesize that with sufficient pain relief from the safer PRKRA drugs, patients could tolerate physical exercise to further reduce their symptoms.

Generous donor support has enabled Dr. An's team to begin its study of PRKRA in a unique rodent model in the lab (a very common precursor to research in patients). The results of these studies will help lay the groundwork for human trials of non-addictive, PRKRA therapy as a viable treatment for chronic back pain.

Continuing a Legacy of Excellence in Joint Replacement Research

Well over 1 million knee and hip replacement procedures are performed each year in the U.S. — a number that will more than double by the year 2030. Faced with this growing need, surgeons from around the country look to the reconstructive experts at Rush to help this rising number of patients reclaim lost mobility and eliminate pain.

Guided by a rich legacy of pioneering research in the area of joint replacement, physician-scientists at Rush actively oversee dozens of study protocols that aim to prevent problems before they happen, preserve natural joints as long as possible, and — when no other options exist — make joint replacements safe and last a lifetime.

Among their many published studies this past year, a team of surgeons including **Craig Della Valle, MD**; **Tad Gerlinger, MD**; **Brett Levine, MD**; **Scott Sporer, MD**; and **Denis Nam, MD**, completed a noteworthy study of two methods for reducing infections after knee or hip surgery.

In this seven-year effort, the team studied the effectiveness of two medicated solutions, a common sterile saline and a diluted betadine formula, to wash out the surgical site before wound closure. To give this study statistical power, the surgeons recruited over 400 patients and ultimately found that the betadine formula was five times more effective than the saline solution at reducing postoperative infection risk.

This first-of-its-kind study has made waves in the field of reconstructive surgery, informing better care protocols worldwide. Studies like these are not possible without your support for the tremendous infrastructure needed to enroll patients, collect evidence and conduct statistical analyses.

FAI Studies: Demystifying a Mysterious — and Common — Cause of Hip Pain

In the world of orthopedic surgery, the hip abnormality known as femoroacetabular impingement, or FAI, is considered a recent — and still largely mysterious — condition. First described in 2003, FAI-related injuries are now one of the leading causes of hip surgery (especially in young people) and FAI is understood to accelerate the development of osteoarthritis.

Although estimates of FAI's prevalence in the U.S. population vary widely, somewhere between 40 and 50 percent of Americans are likely to have FAI. The condition presents itself in one of three ways: People with a cam lesion have bone overgrowth on the "ball" part of the hip's ball-and-socket joint; people with a pincer lesion have bone overgrowth at the "socket;" and some people have both abnormalities.

What makes FAI so perplexing is that a great number of individuals with FAI live long, active lives without experiencing problems. When symptoms do develop, however, it usually indicates that there is damage to cartilage and the disease is likely to progress.

To demystify this condition, **Shane Nho, MD, MS** (pictured below), and his Rush collaborators are leading a multi-pronged FAI research effort, including the collection of MRI evidence before and after surgery. Collaborating with experts in computational modeling and scientists in the Joan and Paul Rubschlager Motion Analysis Laboratory, Dr. Nho's team will also determine if patients with FAI-related hip problems exhibit a "movement signature" that may be to blame for their pain.

Dr. Nho's important research, backed by generous donors, may lead to new therapeutic interventions that help patients with FAI prevent pain and damage to cartilage in the hip joint.

Shane Nho, MD, MS, is working with scientists across the Department of Orthopedic Surgery to shed new light on femoroacetabular impingement, or FAI, a hip abnormality that can lead to joint damage and pain.

No Worse for Wear (Particles)? Research Into Artificial Joint Breakdown and Corrosion

The artificial implants utilized in joint replacements are composed of materials such as metal alloys, plastic and ceramics. Unfortunately, all implanted joints break down in the body over time to varying degrees, with microscopic pieces of wear debris called nanoparticles coming off the implant and into other areas of the human body.

Over the years, the design of implants used in surgery and their material composition have undergone improvements to reduce the amount of wear under normal use. Still, some wear debris cannot be entirely avoided. In fact, even under ideal conditions, millions (and perhaps even billions) of nanoparticles are generated each year. In some cases, implants undergo corrosion processes that can create an additional source of foreign particles within the body.

Joint replacement patients are not the only people exposed to nanoparticles — they may be found in food, drinking water, beauty products and even the air we breathe. However, wear particles from artificial implants are a major area of focus for researchers who are just now beginning to understand the health risks triggered by these tiny potential toxins.

Scientists in the Robbins and Jacobs Family Biocompatibility and Implant Pathology Laboratory are uniquely positioned to study these particles and their effects. Over 25 years ago, this lab established a postmortem tissue repository that is now one of the largest in the country, holding tissue samples from hundreds of joint replacement patients, including tissue samples from the joint capsule, liver, spleen, kidney, brain, bone marrow and heart.

Over the past year, scientists in the lab have developed highly sophisticated techniques utilizing infrared spectroscopic imaging to characterize how wear particles get distributed throughout the body. Few institutions have this capability, and the researchers' findings will inform the development of new artificial implants.

Manipulating the Knee Environment to Prevent Osteoarthritis Progression

Osteoarthritis, or OA, is the most common type of arthritis, characterized by progressive damage to cartilage and other joint tissues. In particular, the knee is the most prevalent joint for OA pain, affecting about 20 percent of adults over age 45. On average, people with OA related knee pain suffer for 13 years before receiving knee replacement surgery, and — due to an aging population — the number of these procedures performed each year continues to grow.

A major risk factor for OA is knee injury. Falls, collisions and other types of knee injuries often result in an inflammatory response that accelerates the onset of OA. Physician-scientist **Adam Yanke, MD, PhD,** is looking to

determine what surgeons can do to maintain a healthy knee environment after an injury and if arthritis progression can be stopped in its tracks.

In pilot research studies published this year, Dr. Yanke (pictured below) and his colleagues proved that patients recovering from a knee injury who received an injection of healthy, donor-supplied synovium — the soft tissue in the knee joint that lubricates and nourishes the cartilage — had less inflammation and a more expeditious recovery.

With philanthropic support, the research team plans to take this innovative research to the next level. Dr. Yanke, who earned his PhD in biochemistry, looks to further evaluate the mechanisms of knee repair after injury and pursue the development of new treatments, such as injections that can be administered at the time of knee injury to accelerate cartilage recovery and maximize repair.

Collaborating to Understand Childhood Obesity's Effect on Osteoarthritis Risk

In addition to their own leading-edge research into kinematics and kinetics of natural and artificial joints, researchers in the Joan and Paul Rubschlager Motion Analysis Laboratory partner with researchers across Rush to advance multidisciplinary studies. **Markus Wimmer, PhD,** the Grainger Director of the Rush Arthritis and Orthopedics Institute, leads the lab and serves as an expert resource to numerous co-investigators with research questions involving gait and movement.

In 2018, Dr. Wimmer collaborated with a group of researchers in the Department of Preventive Medicine to better understand the effect of childhood obesity on walking and increased risk for osteoarthritis. Children ages 6-11 — some with a health body mass index, or BMI, and some with a BMI considered overweight/obese — were brought through the state-of-the-art laboratory. Numerous measurements were collected to understand the forces being exerted on each child's joints.

Preliminary results show that children with a higher BMI exhibit movement patterns that are associated with increased risk of osteoarthritis in adults. Interestingly, the researchers found evidence suggesting that losing weight doesn't necessarily eliminate these learned gait patterns.

This collaborative project was funded through donor support, and the researchers will be using the findings from this pilot study to apply for additional grant awards.

Celebrating Dr. Bush-Joseph, Elevating Research and Education Opportunities for Orthopedic Trainees

In his three decades of practice, sports medicine orthopedic surgeon **Charles Bush-Joseph, MD**, has earned gratitude and admiration from scores of patients. His patient-

centered philosophy has improved quality of life for thousands of women and men overcoming orthopedic injuries. As the associate director of the Rush orthopedic sports medicine fellowship program for 27 years, Dr. Bush-Joseph (pictured below) has imparted this philosophy upon dozens of young physician mentees.

In 2018 grateful patients established *The Charles Bush-Joseph Endowment for Sports Medicine Education* to celebrate his legacy and support the next generation of expert physicians. **Now a fully-vested endowment at Rush University, this fund will begin to provide sustainable resources for sports medicine research,** enabling scientists to pursue independent research, present findings at national and international conferences, and gain exposure to leading-edge treatment techniques.

Uncovering the Mechanisms and Origins of Joint Pain

Preventing osteoarthritis, or OA, and devising new methods to slow its progression are promising areas of research at Rush and other major universities. However, for patients suffering from advanced OA, breakthroughs are desperately needed to help them find relief from their pain symptoms. In fact, scientists' understanding of OA pain, its mechanisms and origins, remains surprisingly limited.

The laboratory of Anne-Marie Malfait, MD, PhD, the George W. Stuppy, MD, Chair of Arthritis, is advancing leading-edge research into OA pain. Dr. Malfait, a longtime scientist at Pfizer, argues that better treatments for OA are dependent on a clear understanding of *how* the condition causes pain — an objective that isn't simple, since cartilage has no neurons to transmit pain signals.

To answer this question, Dr. Malfait's lab has developed a unique rodent model to study OA pain and test novel pain-relieving treatments. In Dr. Malfait's model, the mice receive surgery to destabilize the knee. After eight weeks, these mice begin to show signs of OA pain, such as changes in their locomotion, decreased climbing, traveling, etc. Using a strain of mice who have been genetically modified to express a red fluorescent protein, Dr. Malfait and her team can visualize the neurons and pain pathways in an unprecedented manner.

With this unique model, the lab made a breakthrough finding last year when they identified a peptide called 32-mer that is produced when cartilage breaks down. The researchers suggest that blocking the production of this molecule could lead to better OA pain treatments, but additional support is needed to advance this research.

A long time researcher at Pfizer, Anne-Marie Malfait, MD, PhD, is breaking new ground in the study of osteoarthritis pain.

In Gratitude

Your faithful support of the Department of Orthopedic Surgery at Rush is instrumental to the success of our extraordinary faculty, whose work advances the field of orthopedic medicine in different ways. Some are renowned for their surgical or therapeutic innovations. Others are engaged in high-impact basic or translational research, and many are passionate about resident and fellow education. When these passions align with the aspirations of our profoundly generous donor community, we are able to move the dial in orthopedic care — improving quality of life for patients in our clinics and far beyond.

Thank you. We hope you will continue to share in the success of our program for years to come.

Joshua J. Jacobs, MD

The William A. Hark – Susanne G. Swift Professor of Orthopedic Surgery

Chairperson, Department of Orthopedic Surgery

RUSH

To support orthopedic research at Rush, or to learn more information about the topics covered in this report, please contact:

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