

ORTHOPAEDIC
SURGERY
HIGHLIGHTS
2016



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About the Department

Founded in 1953 as a separate department of the University of Pittsburgh School of Medicine, the Department of Orthopaedic Surgery is committed to delivering the highest quality of diagnostic and therapeutic patient care to both adults and children for a diverse spectrum of orthopaedic disorders. To this aim, the department seeks to meet the needs of 21st century orthopaedic care not only by integrating the latest biological and technological advancements in orthopaedic science, but equally by leading the development of novel treatment modalities through distinguished basic science and clinical research programs. In addition, the Department of Orthopaedic Surgery seeks to be a leader in educating the next generation of orthopaedic surgeons through its residency and fellowship training programs, which include comprehensive, in-depth exposure to all specialties of orthopaedic care and advanced surgical experience.

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Freddie H. Fu, MD, DSc (Hon), DPs (Hon)
*David Silver Professor and Chairman,
Department of Orthopaedic Surgery
University of Pittsburgh School of Medicine*



A Message from the Chairman

In this year's highlights report, I am pleased to share with you a selection of some of our most recent research and clinical care advances from across our department. These continuing efforts from our researchers, clinicians, and staff are what drives forward our department.

The work profiled in this report is indicative and representative of the department as a whole. Our Orthopaedic Robotics Laboratory, directed by Richard Debski and Volker Musahl, is engaged in numerous collaborations with surgeons to better understand the effects of anatomic ACL reconstruction techniques, improve outcomes for rotator cuff tears, and many other multidisciplinary investigations.

Rocky Tuan and his Cellular and Molecular Engineering Lab are advancing the understanding and application of stem cell and ortho-biologic treatments, as well as designing new technologies to improve orthopaedic surgery outcomes across a range of conditions.

MaCalus V. Hogan's collaborative research and education efforts in the Foot and Ankle Center, along with the design and application of outcomes platforms and bundled payment models, are evolving our modes and methods of patient care to keep pace with the continually changing health care environment.

Nam Vo and Joon Lee, leaders of the Ferguson Laboratory for Orthopaedic and Spine Research, continue to pursue and clarify the biological and mechanical mechanisms around intervertebral disc degeneration.

And Kenneth Urish, a specialist in hip and knee arthroplasty, is working to solve the problems presented by biofilms and infections, as well as the study of why devices fail and how to improve the engineering of artificial hips and knees.

The talent of our faculty members also is evident in their continuing ability to attract significant funding to continue their groundbreaking research efforts. In an always highly competitive environment, and in uncertain times with a scarcity of dollars available for new research, I am convinced more than ever that our department and UPMC as a system are evolving to adapt to, and excel in, the changing world of health care.

While proud of the accomplishments of our department as a whole, it is our fundamental dedication to improving every aspect of patient care that matters most. Our research, our educational programs for students and fellows, and our quality improvement initiatives are, and will always be, designed to translate our knowledge and expertise in the pursuit of better care and improved outcomes.





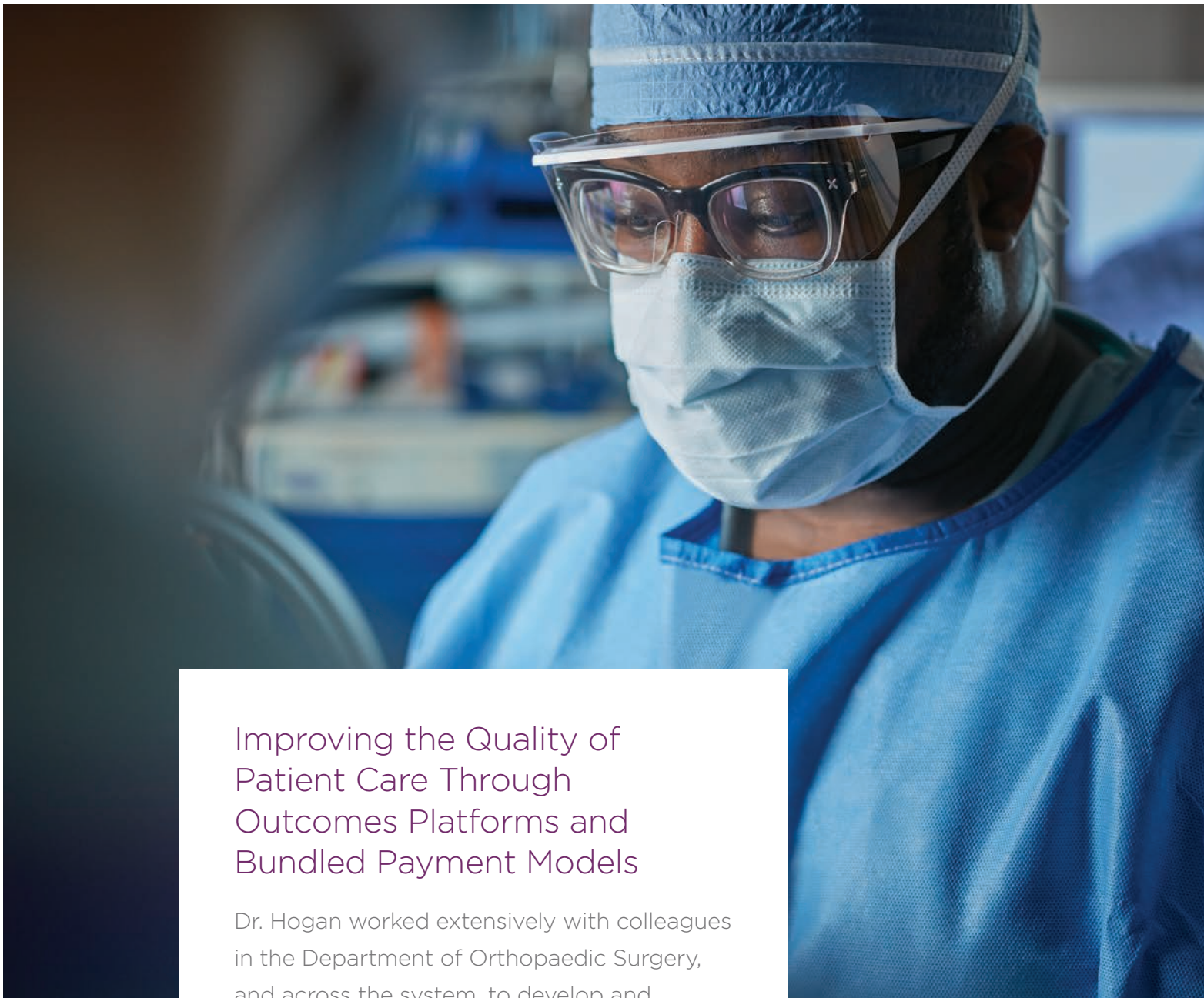
A Collaborative Approach to the Transformation of Orthopaedic Care

The evolution of the health care universe continues at a rapid pace. For orthopaedic surgery, the transformational challenges mirror those of the broader health care environment. For **MaCalus V. Hogan, MD**, the best way to advance the practice of orthopaedic surgery, and expand evidence-based research that drives the progression of health care toward improved quality outcomes is through cross-disciplinary collaboration.

Dr. Hogan juggles multiple roles in the department as an assistant professor, vice chair of education, associate director of the residency program, and chief of the Division of Foot and Ankle Surgery. He is also the director of the Foot and Ankle Injury Group, and along with Hongshai Li, PhD, co-directs the Musculoskeletal Growth Regeneration Lab. In a system-wide role, Dr. Hogan was recently appointed medical director of outcomes and registries at the Wolff Center at UPMC, where he and colleagues are working to implement multidisciplinary registries and outcomes platforms.

While each of Dr. Hogan's roles allows him to explore various realms within research, clinical care, and education, they are all connected by his passion for collaboration and the innovation of better ways to deliver, quantify, and improve patient care.

"These are some of the reasons I felt fortunate to have the opportunity to join Dr. Fu's department and UPMC. The scale and complexity of the work going on here is immense, and it affords me opportunities to work with brilliant surgeons, scientists, and thought leaders in the field of health care delivery," says Dr. Hogan.



Improving the Quality of Patient Care Through Outcomes Platforms and Bundled Payment Models

Dr. Hogan worked extensively with colleagues in the Department of Orthopaedic Surgery, and across the system, to develop and launch a Foot and Ankle Outcomes Platform. This was one of the first physician-led platforms within orthopaedic surgery at UPMC to capture outcome measures, including patient-reported outcomes via a tablet-based application. A collaborative effort with **James Irrgang, PhD, DPT**, director of clinical research and outcomes in the department, the success of the platform and its underlying adaptability is now being used as a model for such outcome platforms for the entire UPMC enterprise.





“As an orthopaedic surgeon, MaC has a unique skill set for research that spans basic science, clinical research, and quality improvement. I have had the opportunity to work with him to implement processes for the collection of patient-reported outcome measures, and he has championed these for the Foot and Ankle and Adult Reconstruction Divisions. Moreover, he understands not only the importance of collecting PROs but also using the information to inform discussions with patients to help them better understand their condition and available treatment options.”

James J. Irrgang, PhD, DPT, ATC, FAPTA
Professor and Chair, Department of Physical Therapy
Vice Chair of Clinical Outcomes Research, Department of Orthopaedic Surgery

For Dr. Hogan, the data collected and its utilization should go way beyond mining it for research purposes. “It’s really about using it as a standard of care, as an additional piece to drive us to be better surgeons and take better care of our patients, applying outcomes data at the point of care,” says Dr. Hogan. Dr. Hogan uses this information every day in clinic with his patients, purposely sitting down with them to discuss their goals and what options perhaps make the most sense. “Now, part of the objective is to expand outcomes within the musculoskeletal realm, first across all orthopaedic subspecialties and then working with a large cohort work group towards launching patient reported outcomes, including computer adaptive testing across the enterprise.”

Much of the work that Dr. Hogan, Dr. Irrgang, and their colleagues poured into the development of a successful foot and ankle outcomes measurement platform served as the foundation and model for the implementation of a system-wide bundled payments model for total joint arthroplasty. Combining their work with a Total Joint Pathway already led by Larry Crossett, MD, and a system-wide registry for joint replacement and the reduction of complications and readmissions effort led by Adolph Yates Jr., MD, the stage was set to bring all the other necessary partners together — rehabilitation, post-acute services, finance, and the UPMC Health Plan. This was pivotal to the ability to collaborate timely to build and implement the total joint bundled payment model that could be used throughout the UPMC system to effectively address the changes set in motion by the Centers for Medicare and Medicaid Services (CMS) in 2015.

In the first year, the foot and ankle outcomes platform showed significant success in a number of areas, as well as leading to a recently published paper in *Foot & Ankle International*, discussing the development of performance and assessment platforms.¹



Drs. Hogan, Crossett, and Yates.



“MaC has the unique traits of a talented surgeon, innovative researcher, and balanced administrator. He has been a positive force in advancing the mission of our department. He is a role model for our residents, and a mentor as the residency director. He wears his many leadership hats quite effectively.”

William F. Donaldson III, MD
Executive Vice Chairman for Clinical Services
Chief, Division of Orthopaedic Spinal Surgery



For **Tami Minnier, RN, MSN, FACHE**, chief quality officer of UPMC and co-chair of the total joint replacement bundled payments initiative with Dr. Hogan, the success of the initiative, along with the ongoing outcomes registry work in the musculoskeletal environment, has led to the long-term goal of applying these systems more broadly across the UPMC system. Immediately, however, work is in progress to build the outcomes registry across all of orthopaedic surgery to better collect, visualize, interpret, and apply practically to transform current patient care.

“When MaCalus first came to UPMC, I knew he brought with him a lot of potential and would eventually be a leader within the UPMC system. As co-chair of the bundled payments initiative for total joint replacement, I couldn’t have asked for a better partner. His combination of humility and relationship skills, and his neutrality in the development process was critical to our implementation process. MaC is able to bring people together to work towards a common goal, and moreover, a common goal that will help transform how we deliver care from where it is today to where it will need to be in the future.”

Tami Minnier, RN, MSN, FACHE
Chief Quality Officer, UPMC
Executive Director,
The Beckwith Institute



Teaching and Mentoring Tomorrow’s Surgeons

Dr. Hogan’s passion for teaching new orthopaedic surgeons becomes readily apparent in any conversation about the subject. His roles as residency program associate director and as vice chair of Education speak to how important it is for Dr. Hogan to be a part of how the department trains new surgeons, and how this training must adapt as the broader world of health care evolves. “I’m very respectful of how health care has been and will be delivered. I often tell my residents that the health care of today, and their training today, will be different tomorrow. My early years in practice have been no different. As a discipline, we have to continue to prepare ourselves for this reality,” explains Dr. Hogan.

This past year, Dr. Hogan collaborated with **John R. Fowler Jr., MD**, assistant professor of Orthopaedic Surgery and assistant dean for medical student research, to implement a new musculoskeletal educational and training initiative to all second year medical students within the University of Pittsburgh School of Medicine. Numerous faculty members from the department contributed by leading problem-based learning sessions.

The series of lectures and problem-based case reviews is the first such surgical subspecialty training program within the School of Medicine’s curriculum, and is just one additional aspect of education seen as so important to Dr. Hogan both now and in the future.

With education comes challenges, something Dr. Hogan is primed to meet head on. “Many of the challenges to how we manage care going forward, remain true to our academic mission, and preparing new generations of providers for the future of health care, will be driven by carpooling with the patient. Teaching others how to continue to innovate while being cost conscious, and providing an optimal patient experience will be essential to our long-term success,” says Dr. Hogan.

Research Collaborations: Bench to Bedside and Back Again

Dr. Hogan has a holistic approach to foot and ankle care with numerous research interests that are all part of a larger objective. “Our approach to foot and ankle care and research speaks more broadly to how we collaborate across the field to deliver care, translate our knowledge, and evolve to improve the practice of orthopaedic foot and ankle surgery.”

One primary area of research for Dr. Hogan is in the use of orthobiologics and stem cell therapies, and how these treatment modalities can be translated into effective clinical applications. In essence, this part of Dr. Hogan’s broad research portfolio serves as a foundational element in how the application or use of regenerative therapies can be translated to the bedside. A 2016 publication² in collaboration with Dr. Li and colleagues detailed the use and effectiveness of muscle-derived stem cells for articular cartilage repair.

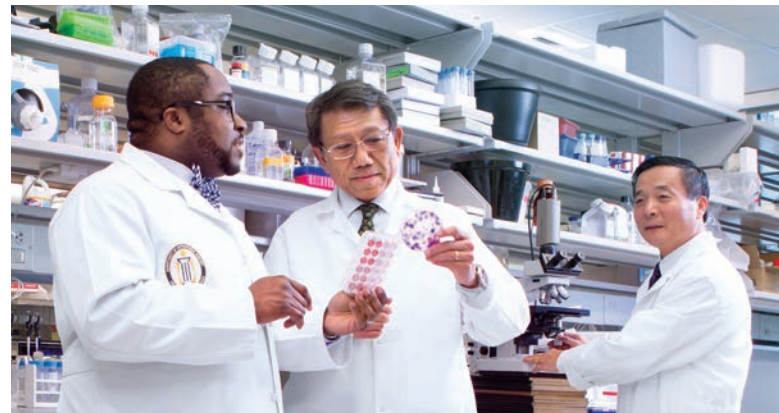
For Dr. Hogan, it’s crucial when applying these orthobiologic treatments and technologies to be responsible in their assessment. “We must be willing to take scientifically driven risk but have the means in place to really assess efficacy,” says Dr. Hogan. With cellular therapies, or orthobiologic treatments, such as platelet-rich plasma or bone marrow aspirate concentrate injections, it is important to collect clinical outcomes to understand how these patients are impacted. Dr. Hogan has several ongoing collaborative efforts on this front.

In one such study in collaboration with **James H-C Wang, PhD**, leader of the Mechanobiology Lab, their team is investigating which factors in human blood and platelets affect outcomes, or their impact in musculoskeletal tissue treatments. “We’re taking tissue samples from patients who undergo surgical intervention with orthobiologic augmentation, or who undergo ultrasound-guided injections to better understand the clinical effectiveness of the treatment, and what specific biological factors are responsible.” Another manuscript³ from Drs. Hogan and Wang’s research team recently published in the *Journal of Tissue Engineering and Regenerative Medicine* evaluated the effectiveness of platelet-rich plasma on the tendon-bone interface healing when co-delivered with a novel compound, kartogenin. “These types of studies are quite interesting in that we’re looking directly at the clinical care with research to validate efficacy,” says Dr. Hogan

Kinematics and Robotics Collaborations

In recent years, Dr. Hogan has worked extensively with the Orthopaedic Robotics Laboratory under the direction of **Richard Debski, PhD**, and **Volker Musahl, MD**, and the Orthopaedic Biodynamics Lab under the direction of **William Anderst, PhD**, to study such conditions as syndesmotic injuries and ankle kinematics following different surgical procedures, including Brostrom-Gould Repair.³

In the in vivo kinematics lab, Dr. Hogan and colleagues perform novel research which is conducted by inserting inert beads into the ankle to aid in the development of modeling ankle injuries and repair techniques. “We are working to develop computational models that can be used to determine how the surgical treatments that we apply to patients change or alter ankle joint kinematics, and how they potentially contribute to ankle joint health and function long-term. Such work is highly translatable and will be helpful in driving how our treatment for certain conditions evolves,” says Dr. Hogan.



Drs. Hogan, Rocky Tuan, and James H-C Wang in the lab.

Tying It All Together

Innovation without explanation, without research, without an understanding and validated assessment of outcome cannot withstand the tests of real-world conditions. “As physicians we have to be part of the discussion, part of the planning phase, and champion the effort to get it done. This means stepping a little bit outside of our normal box of direct clinical care to innovate within our environment and be a part of the innovation happening around us. This has been and always will be key to how orthopaedic surgery advances, this is just the NEXT beginning,” says Dr. Hogan.

References

- ¹ Ferguson CM, Rocha JL, Lalli T, Irrgang JJ, Hurwitz S, Hogan MV. Developing Performance and Assessment Platforms in Foot and Ankle Surgery. *Foot and Ankle International*. 2016; 37(6): 670-679.
- ² Hongshuai L, Aiping L, Ying T, Beckman S, Nakayama N, Poddar M, Hogan MV, Huard J. The Superior Regenerative Potential of Muscle-Derived Stem Cells for Articular Cartilage Repair is Attributed to High Cell Survival and Chondrogenic Potential. *Molecular Therapy – Methods & Clinical Development*. 2016; 3, 16065. Epub ahead of print.
- ³ Zhou Y, Zhang J, Yang J, Narava M, Zhao G, Yuan T, Wu H, Zheng N, Hogan MV, Wang JH. Kartogenin With PRP Promotes the Formation of Fibrocartilage Zone in the Tendon-Bone Interface. *J Tissue Eng Regen Med*. 2017.





Molecules, Cells, and Musculoskeletal Research

At the forefront of cellular and molecular engineering research for musculoskeletal injuries and disease sits **Rocky S. Tuan, PhD**, distinguished professor, vice chair of Orthopaedic Research, and director of the Center for Cellular and Molecular Engineering. Dr. Tuan and his lab are engaged in cutting-edge research across multiple disciplines with numerous individual investigatory projects in the realms of basic science, translational, engineering, and clinical studies.

His collaborations with orthopaedic surgeons in the department, along with colleagues in the regenerative medicine and bioengineering fields, are leading to new discoveries in understanding musculoskeletal biological processes, as well as designing and engineering novel technologies and studies to improve treatments and curative therapies for such things as osteoarthritis, tendon and ligament repair, and tissue regeneration. "An important aspect of my lab is that so much of our work is interrelated, and it truly is a very integrated, multidisciplinary space. We have life scientists, engineers, and clinicians all working together. To pursue the kind of answers we are looking for requires everybody to be mission driven, and that's exactly what we are," says Dr. Tuan.



Stem Cell Research and Therapies

A major area of study for Dr. Tuan and his lab focuses on stem cells and the various technologies for manipulating, growing, and ultimately using them to grow or repair compromised musculo-skeletal tissues such as cartilage, tendons, ligaments, and bone.

Musculoskeletal tissues degrade for a number of reasons, sometimes through injury or trauma, and sometimes as part of the aging process or through disease. Regardless of the causes, the unique aspect of musculoskeletal diseases in general is that structural damage is primary to the cause. And since certain tissues are not able to regenerate or heal on their own after being compromised, finding ways to either help the tissues regenerate or devise ways to grow new, replacement tissues is of great importance. "Stem cells have the ability, by definition, to form whatever tissue you want, but only with the proper coaxing and in hospitable environments. We spend a lot of time on these issues in the lab," says Dr. Tuan.

For stem cell biologists like Dr. Tuan, there are four key problems to face. Sourcing stem cells is the first issue. Where do they come from and how do you keep them viable for use in the future. Increasing the quantities of stem cells — proliferation — while maintaining their potency is the second issue at play. The third issue is differentiating the cells into the tissues that you want them to become so they can be used to repair tendon, cartilage, or bone. Finally, Dr. Tuan says that after differentiation, "You must ensure the cells don't change. If they become tendon or cartilage, keeping them as such is critically important to using them in lab experiments and as therapeutic agents for whatever condition you seek to cure."

Dr. Tuan's lab produces 3-dimensional engineered tissues such as cartilage-bone composite (left) and tendon/ligament (right) using a combination of stem cells and biomaterial scaffolds.



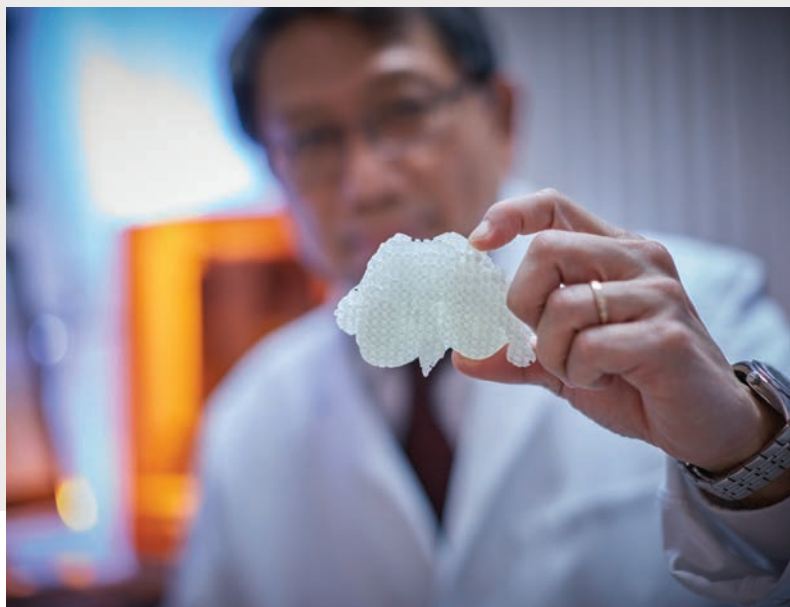
Novel Technologies for Tissue Engineering and Regeneration

Creating an environment in which stem cells can be manipulated or engineered into useful structures is highly important to the technology and end-applications. Biomaterial scaffolds represent one such area in which Dr. Tuan has devoted much attention. "We spend a lot of time thinking about nanomaterials, and about matrix components that can convert immediately or very quickly from a liquid, for example, to a solid."

Photo-crosslinking and 3D printing are technologies that are being employed to create such things as bioscaffolds and microtissues, or tissues-on-a-chip. For example, Dr. Tuan is able to take solutions of matrix materials containing human cells, expose them to light, and convert them into 3D structures with the proper internal architecture. Using 3D printing technologies, Dr. Tuan can create microtissues that are physiologically and structurally similar to the original, native tissue. These tissues-on-a-chip are a representation of the native human environment in which the cells normally exist. Such microtissues, therefore, allow the study of the biology and pathogenesis of a disease condition, potentially enabling screening for therapies without having to use an animal model. "The most important aspect is that we use human cells to make all of these microtissues, so that when we look at the results, they are 'human' results, and not from an animal model."

Practical Applications of Stem Cell Therapies

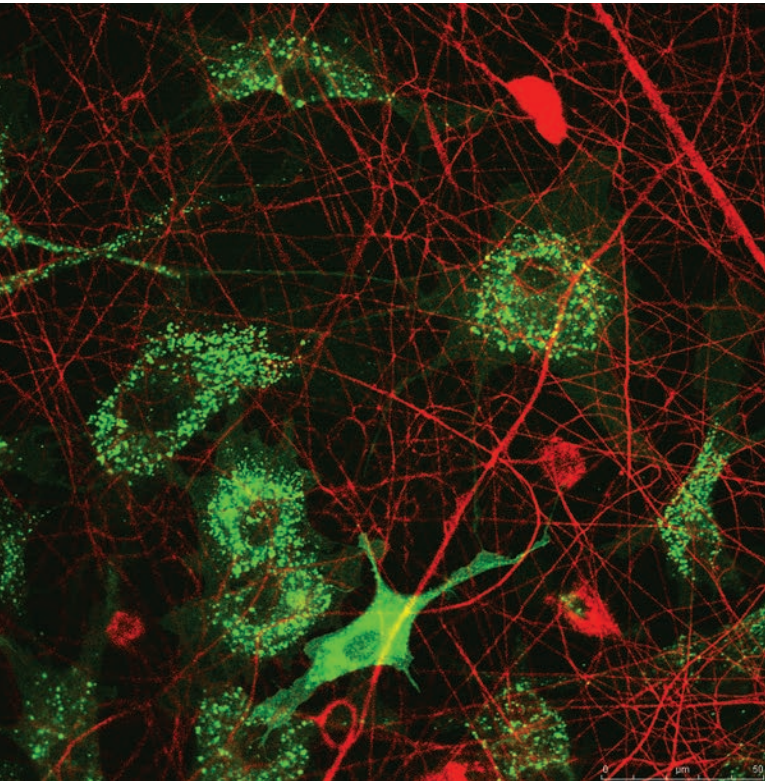
What can stem cells be used for? In Dr. Tuan's lab, a key research study focuses on cartilage resurfacing. Defects in joint cartilage, such as lesions or tears, are problematic and often worsen with time to the point of total failure of joint function, requiring surgical treatment. For Dr. Tuan, cartilage resurfacing using stem cells and novel delivery technologies he and his colleagues have invented are showing promise with potential clinical application. "Essentially, the goal is very simple: repair the hole or defect in the cartilage. With our stem cell work, we are driving toward cartilage formation, and using a delivery scaffold made up of nanofiber material or a photo-crosslinkable 3D gel that we have recently developed to repair the tissue." These patent-protected technologies are showing promising results in Dr. Tuan's studies with cartilage, and investigations are also proceeding with ligaments, tendons, and intervertebral discs. Such technologies may, in the future, allow patients to stave off surgeries, or at least delay the need for surgery for significant periods of time.



Dr. Tuan shows the structural prototype of an engineered knee joint produced by image-guided 3-D printing.

Designing Clinical Therapies for Major Musculoskeletal Conditions

There are numerous clinically relevant aspects of the technologies and devices Dr. Tuan's lab has created, representing research that progresses from basic science and translational studies toward clinically applicable interventions. Two particularly relevant areas of current research revolve around the discovery of disease-modifying osteoarthritis (OA) drugs, and the repair of meniscus tears using tissue engineering and regenerative medicine approaches.



Detail image of nanofiber material.

There are currently no disease-modifying drugs available for osteoarthritis, even as up to a fifth of the total world population is affected by it to one degree or another. And for individuals over the age of 65, there is more than a 50 percent probability of having at least one joint affected by OA. "It is a major quality-of-life disease, and there are no drugs because of a very simple reason. To test a drug, you need to be able to find out how the disease develops so that you can intervene," says Dr. Tuan. And the problem with osteoarthritis is that, with the exception of post-traumatic cases, individuals don't know they have it until it's too late. This makes studying drugs capable of preventing osteoarthritis in the first place exceedingly difficult.

In this situation, how does one go about discovering a drug? This is where Dr. Tuan and his lab's microtissue engineering may bring significant results to bear. "With microtissues, which can be cultured in the lab, we can first develop them so that they begin to display features of joint degeneration, and can then test the effectiveness of many candidate therapeutic agents under different scenarios," explains Dr. Tuan. If a particular agent or chemical is able to slow down or inhibit degeneration in the joint microtissue, it can be considered and pursued as a candidate disease-modifying osteoarthritis drug. This approach will greatly facilitate the drug discovery process for osteoarthritis.

For meniscal injuries — tears — the tissues are unable to heal spontaneously, and the injuries themselves are quite common. A radial meniscal tear will continue to worsen until surgical intervention is required. Dr. Tuan's lab has recently developed a method that utilizes an injectable and photo-crosslinkable material to deliver stem cells and meniscus matrix, guided by a tissue dressing, into the defect. The stem cells then invade the tear and begin to repair the damage. Dr. Tuan is excited about the prospects of this research and indicates, "This is in an early phase right now, but results are promising, and we've just published them in the *American Journal of Sports Medicine*."¹

Stem Cells and Surgical Site Infections

Another clinically relevant line of investigation Dr. Tuan is pursuing is the use of stem cells to mitigate periprosthetic or surgical site infections. These infections, for example in total hip and knee arthroplasty, are quite troublesome and can be difficult to manage if they occur due to issues related to the formation of biofilms. Dr. Tuan and his team have been working to create a new way to use stem cells in the treatment of infections. "It turns out that stem cells, under certain conditions, can have antimicrobial activity. We are developing methods to activate this specific characteristic in populations of stem cells. In the future it may be possible to directly inject such activated stem cells into the periprosthetic or surgical sites to treat the infection."

References

¹ Shimomura K, Rothrauff BB, Tuan RS. Region-Specific Effect of the Decellularized Meniscus Extracellular Matrix on Mesenchymal Stem Cell-Based Meniscus Tissue Engineering. *Am J Sports Med*. 2016; November 28. Epub ahead of print.

Studying Bone Loss Under Microgravity in Space

Dr. Tuan is the principal investigator of a new research grant to study the effects of bone loss related to extended stays in the microgravity environment of outer space. Dr. Tuan is designing experiments that will ultimately be implementable on the International Space Station (ISS), and may have implications not only for individuals exposed to microgravity for long periods (astronauts), but also for individuals suffering from osteoporosis and other musculoskeletal conditions.

Microgravity exposure poses various types of health hazards, one of which is bone loss. Dr. Tuan explains that, based on studies of astronauts on Space Shuttle missions, even short periods of exposure — 10 days to 2 weeks — could result in more than three percent bone loss, with longer periods having a much greater effect. Astronauts on space flights or longer stays on the ISS suffer from this bone loss, "but most of the time, upon returning to Earth, they recover reasonably well, which is also remarkable because if you have an osteoporosis patient with the same kind of bone loss, that individual does not recover. This is potentially a very interesting phenomenon to study," explains Dr. Tuan.

Using micro-bioreactors similar to those used for the osteoarthritis studies, Dr. Tuan is able to create human cartilage and bone microtissues that allow cells to grow and proliferate for extensive time periods, much as they would in a human body. It is expected that once these microtissue samples are brought on board the ISS and exposed to the microgravity of space, they will develop pathologies similar to those seen in the human body. Using these microtissues, it will be possible to test the effectiveness of osteoporosis drugs, such as bisphosphonates, to see if they act in a similar manner on tissues exposed to microgravity as they do for osteoporosis patients on Earth. In addition to having significant implications for those individuals exposed to microgravity for extended periods, these studies should provide avenues of investigation for osteoporosis and other conditions of the musculoskeletal system.







Arthroplasty and Infections: The Role of Biofilms

Kenneth Urish, MD, PhD, is a surgeon-scientist with training in both orthopaedic surgery and bioengineering. Dr. Urish is an assistant professor in the Department of Orthopaedic Surgery, and the associate medical director of the Magee-Womens Hospital of UPMC Bone and Joint Center. With a busy clinical practice focused on primary and revision hip and knee arthroplasty, there are several large challenges that command Dr. Urish's attention in the lab, and drive his basic science and translational studies.

Dealing with implant-related infections in hip and knee arthroplasty is of significant importance given that infection is a leading cause of implant failure. Combating implant infections through a better understanding of biofilm antibiotic tolerance and bacterial persisters are major areas of study for Dr. Urish's Arthritis and Arthroplasty Design Lab.

Dr. Urish is also involved with implant design, and how to address the problems of corrosion and subsequent failure of implants due to this issue. Dr. Urish is a member of the American Society for Testing and Materials (ASTM) medical devices committee, in which he brings his expertise in orthopaedic surgery and bioengineering to help develop the standards used for testing orthopaedic implants. "Half of my time is spent in the clinic because I love taking care of patients and helping them enjoy the best quality of life they can have. And the other half of my time is working on the big problems that we as surgeons see in the clinic. I'm very much an engineer," says Dr. Urish.

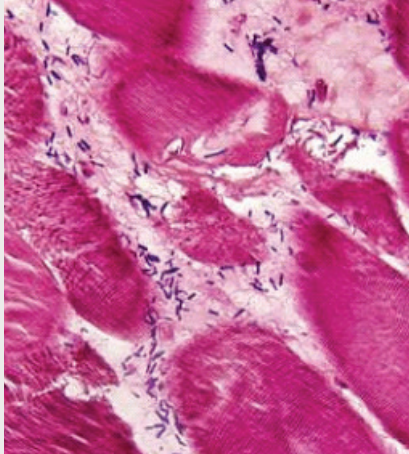
Dr. Urish currently has research support from a number of entities to study biofilms, including awards from the National Institutes of Health, Musculoskeletal Transplant Foundation, and the Orthopaedic Research and Education Foundation.



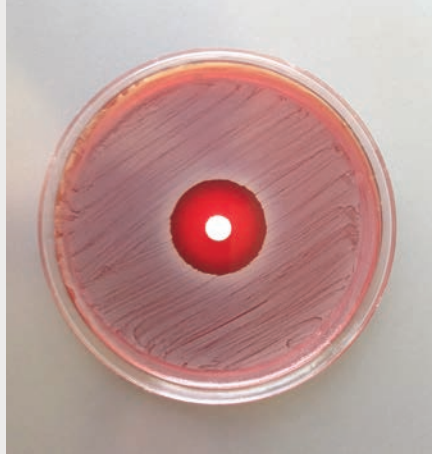
Surgical Infections: Biofilms and Bacterial Persisters

Postsurgical infections are worrisome for every type of surgery, and that is no less true for orthopaedics. The effects on patients who have acquired postsurgical infections can be quite significant in terms of costs, pain and suffering, reduced quality of life, and sometimes the burden of additional surgeries to correct the problem. There are also broader consequences to infections for all of health care. Therefore, preventing infections at all costs is of primary concern to any practicing surgeon. However, there are certain challenges.

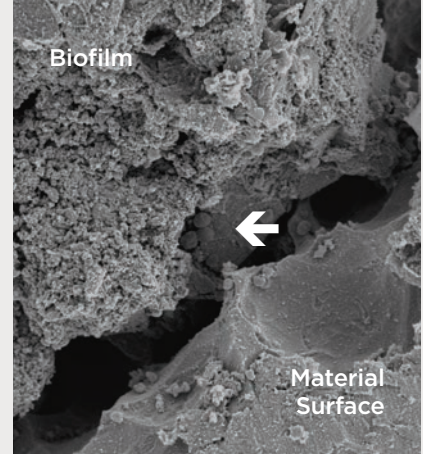




Active bacteria infection infiltrating muscle.



Antibiotic diffusion disc on an agar plate.



Electron microscopy image of biofilm.

Biofilms are communities of bacteria agglomerated into three-dimensional structures, or colonies, that can attach themselves to arthroplasty devices. They are extremely difficult to clear through the use of current techniques, such as irrigation and debridement, or with traditional antibiotic regimens.

Dr. Urish explains that bacterial colonies can form a biofilm on an implanted device relatively quickly after surgery if they are present. "The bacteria secrete polysaccharides, different proteins, and pieces of DNA that, in essence, act as a protective layer or barrier against the outside environment or the host entity in which it is colonizing," explains Dr. Urish. This protective layer, a complex extracellular polymeric substance, is responsible for a number of issues relevant to treating the infection.

The protective layer secreted by the bacterial colony makes it better able to adhere to the surfaces of an implanted device. Its 'sticky' nature means that irrigation techniques or mechanical debridement are not able to totally remove a biofilm from a substrate once established. And the use of antibiotics as a treatment runs into a very challenging feature to overcome in the presence of a biofilm. Dr. Urish explains that within the bacterial colony there are what are called bacterial persisters. "These bacterial persisters behave such that in the presence of any type of stress, for example the introduction of an antibiotic, they have the ability to completely shut down their metabolism." And since antibiotics are based on disrupting some type of metabolic pathway in a bacterium, the bacterial persisters' decreased metabolism renders it highly resistant to antibiotics, even in large doses.

Means to Combat Biofilms

Basic science research by Dr. Urish and colleagues is looking at biofilms and bacterial persisters, and ways to perhaps turn these persisters metabolic systems back on to increase the efficacy of antibiotics. Dr. Urish's lab is also investigating a different approach, using a new compound that does not work directly on the metabolic pathways of bacteria. "If we can disrupt the bacteria's cell wall by punching holes in it, we can kill off these persisters. Their metabolic state in this instance does not matter," says Dr. Urish.

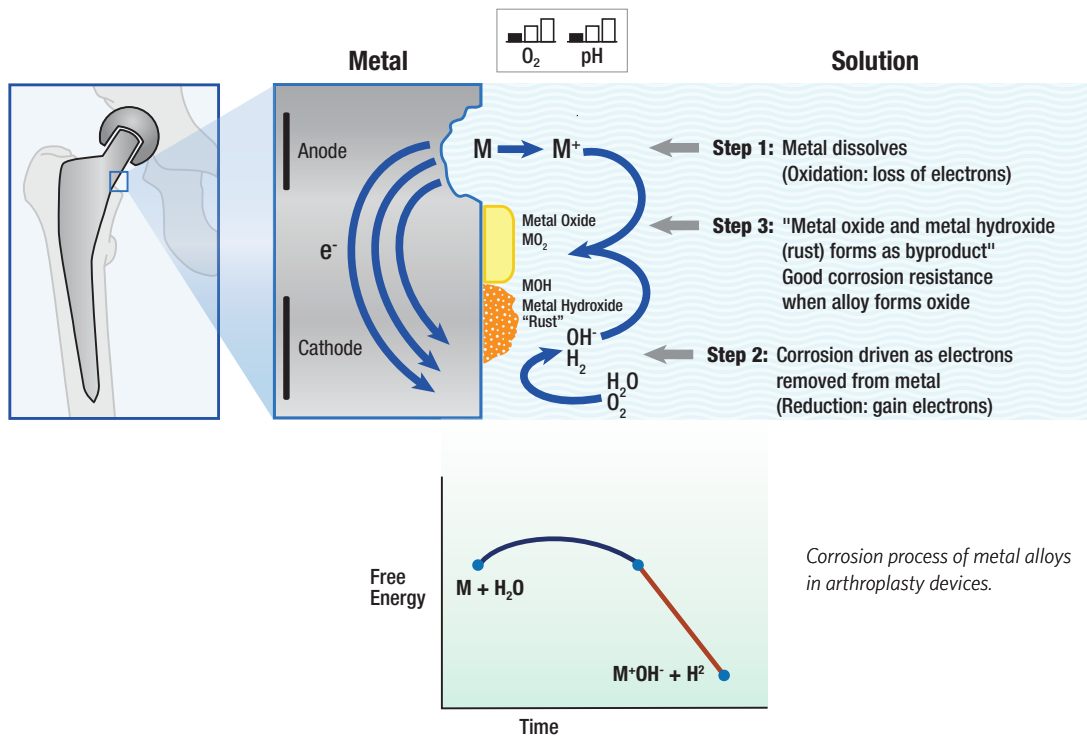
On the clinical side, Dr. Urish is studying outcomes of irrigation and debridement techniques to better understand how they affect the removal of biofilm, and ways to improve these approaches. Dr. Urish explains that approximately 50 percent of cases of infection that use irrigation and debridement techniques fail to completely remove the infection, and as a consequence, the patient's infection continues.

"We're finishing a clinical study now of samples that you should never see any biofilm on because they've been exposed to so much antibiotic, and we're showing that indeed there's a very small biofilm probably there," says Dr. Urish.

Designing Better Devices

As an engineer, Dr. Urish has great interest in the design of arthroplasty devices and combating some of the current issues related to their failure, particularly corrosion and wear of components. Designing devices and analyzing them when they fail in order to find better approaches is at the heart of Dr. Urish's work. "The teamwork between the engineers and the surgeons is what I love about this work. It takes a great design and collaboration to make a device that is going to perform flawlessly for many years. And when you put that device in the patient, it's amazing what they can do," says Dr. Urish.

Conversely, when implants fail, they can cause serious patient health and outcomes issues. For Dr. Urish, one particular area of study has centered around corrosion in orthopaedic implants. Dr. Urish has conducted clinical studies on taper corrosion, trunnion failure, and adverse local tissue reaction in arthroplasty. Understanding why and how devices fail will allow for better design in the future. And with better design comes the potential for better outcomes, lower costs, and higher overall value of care for patients in need.



Reading Resources

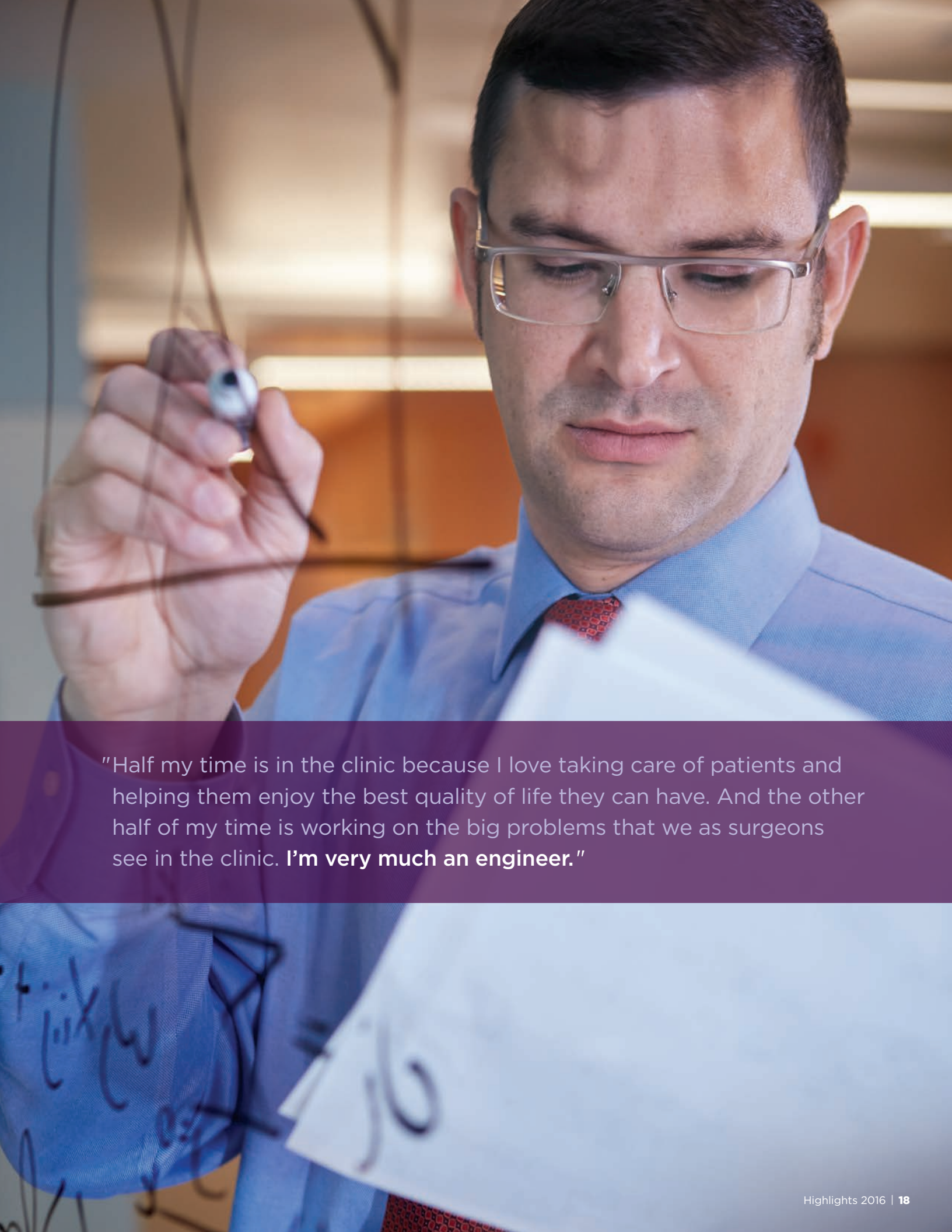
For more information about Dr. Urish's research and clinical work in the areas of biofilms and device design, visit AADLab.org. Additionally, a select list of recent publications on these topics is provided below.

Urish KL. Biofilm is Persistent. *AAOS Now*. 2016.

Urish KL, et al. Pulse Lavage is Inadequate at Removal of Biofilm From the Surface of Total Knee Arthroplasty Components. *Arthroplasty*. 2015; 29(6): 1128-1132.

Urish KL, et al. Antibiotic Tolerant Staphylococcus Aureus Biofilm Persists on Arthroplasty Materials. *Clin Ortho Res*. 2016; 474(7): 1649-1656.

Liow MH, Urish KL, Preffer FL, Nielson GP, Kwon YM. Metal Ion Levels are not Correlated With Histopathology of Adverse Local Tissue Reactions in Taper Corrosion of Total Hip Arthroplasty. *J Arthroplasty*. 2016; 831(8): 1797-1802.



"Half my time is in the clinic because I love taking care of patients and helping them enjoy the best quality of life they can have. And the other half of my time is working on the big problems that we as surgeons see in the clinic. **I'm very much an engineer.**"



A Hub for Collaborative Research: The Orthopaedic Robotics Laboratory

The Orthopaedic Robotics Laboratory, a joint endeavor between the Departments of Orthopaedic Surgery and Bioengineering, has become a core facility for cross-disciplinary and collaborative research investigating a range of degenerative joint diseases and injuries, as well as pioneering new technologies to aid in injury diagnosis and prevention.

Co-directors **Richard Debski, PhD**, associate professor of bioengineering, and **Volker Musahl, MD**, associate professor of orthopaedic surgery and medical director of the UPMC Rooney Sports Complex, lead the laboratory's investigative efforts into such areas as rotator cuff tears, anterior cruciate ligament injuries, knee joint anatomy, syndesmotic injuries, and other conditions. Many of their studies are performed in their lab on a custom-built robotic testing platform, the only one of its kind in the western hemisphere, and the only one outside of Japan. Dr. Debski points out that their system is able to work with just about any joint in the human body — knees, shoulders, spinal segments, hips,



ankles — as well as those of animal models for certain studies.

“The robot that we use has six degrees of freedom and is able to move two rigid bodies with respect to one another. We have various technologies to help capture additional data, such as an external motion tracking system, pressure sensors, and other technologies depending on what we happen to be studying,” says Dr. Debski.

By applying loads with respect to the bones of the joint in question, the robotic system allows the researchers to determine the contribution of the motion of each bone to the stability of the joint as well as to the soft tissues — muscles, ligaments, tendons — that connect the different

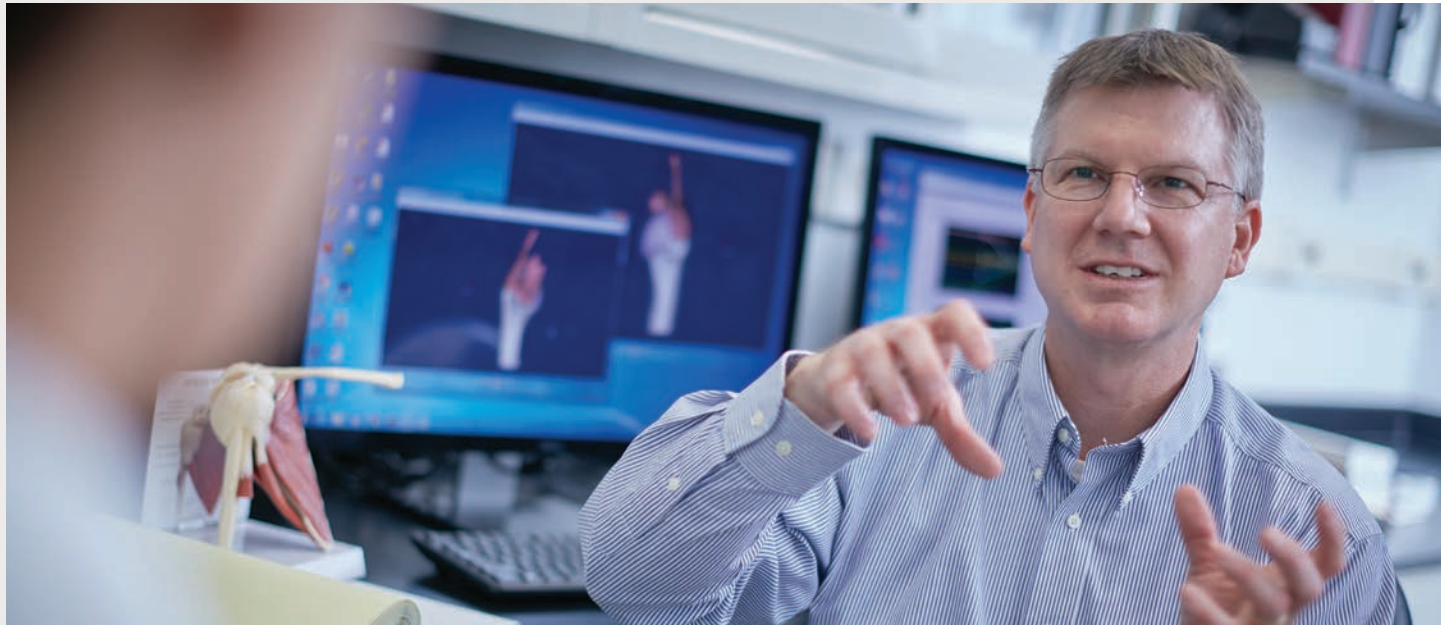
aspects and form the total joint structure. As an example, Dr. Debski explains that he and Dr. Musahl have recently collaborated with **MaCalus V. Hogan, MD**, in his studies of syndesmotic injuries of the ankle. “These injuries involve the motion of the foot, tibia, and fibula. Our robot is able to tell us how the movement of each of these parts, relative to one another and relative to the soft connective tissues, contribute to high ankle sprains.”



Rotator Cuff Tears — New Research

Doctors Debski and Musahl, along with collaborators **James Irrgang, PhD, DPT**, from the Department of Orthopaedic Surgery, and former department colleague **Scott Tashman, PhD**, have recently secured a new NIH R01 grant to study exercise therapy as an initial treatment for rotator cuff tears.





“We are developing some new instruments with ultrasound to help us determine which rotator cuff tears might propagate, or worsen, and which ones could be left alone to heal, or at least not progress any further,”



Continuing from their past studies of rotator cuff tears (see references at the end of this article), the goals of the new study are to better predict which patients can benefit the most from exercise therapy versus surgery as the initial treatment approach, help establish clinical guidelines for treatment approaches, and better understand which factors in exercise therapy — and to what degrees they play — in a successful intervention.

Most patients who are diagnosed with a rotator cuff tear are sent to physical therapy for 6 to 12 weeks, and almost 50 percent of those patients end up having surgery to repair the injury. This new study will attempt to determine — through the use of biomechanical analyses and the individual's anatomical and injury characteristics — whether a patient with a diagnosed rotator cuff tear should have surgery or physical therapy to rehabilitate the injury. Drs. Debski and Musahl explain that additional studies also will involve analyses of cadaveric specimens with materials testing and computational modeling in an effort to try to improve the treatment of tears. “Many patients have these injuries — tears — for an extended period of time — four months, six months, a year, and sometimes longer. This makes it difficult for the orthopaedic surgeon to determine the quality of the tissue and how — or if — the tear might extend,” says Dr. Debski.

Some tears will propagate, while others will not, and this has a lot to do with the integrity and composition of the underlying tissues. Surgical repairs in these instances can be difficult and less successful. Through the use of cadaveric and computational modeling, Drs. Musahl and Debski hope to be able to predict the quality of rotator cuff tissue, and whether or not surgery may be the best option.

For Dr. Musahl, these new rotator cuff investigations are primed to reshape how surgeons diagnose, and ultimately treat these injuries. In addition to these studies, Drs. Musahl and Debski have been collaborating with Rocky Tuan, PhD, distinguished professor and leader of the Center for Cellular and Molecular Engineering, on the use of bio gels, stem cells, and extracellular matrix technologies, and how these therapies can potentially aid in the repair of rotator cuff tears. “These studies will be able to make a real contribution to the science behind, and patient care of, rotator cuff injuries. These injuries are so common, and such a big problem for individuals who sustain them, and there is very little good evidence right now of how best to treat them. I think our research is going to lead to real changes in how doctors approach these injuries, and ultimately how we treat them,” says Dr. Musahl.



Knees, ACLs, and the Anterolateral Capsule

Rotator cuffs and shoulders are not the only joints the Orthopaedic Robotics Laboratory is currently investigating. Because of the robot's flexibility to work with virtually any joint in the human body, the researchers have put it to use in the recent past to look at various aspects of the knee. Dr. Musahl indicates that they have been able to use their technology to examine the anatomy and function of the anterolateral capsule of the knee in relation to joint stability. "Much has been written recently about the anterolateral capsule as a newly discovered ligament, but what we are finding with our studies is that this structure does not behave like a true ligament. This has implications for anterior cruciate ligament (ACL) reconstruction surgery and a number of other areas, and we are continuing our studies to learn more about this aspect of knee joint function and its role in injuries and surgical procedures," says Dr. Musahl.

In terms of the ACL, Dr. Musahl says that they are putting the robot to use to better understand how ACL injuries occur, with the goal of determining how to prevent them in the first place. "Prevention is really a big focus for us in the lab. We are beginning to understand how the shape of the bones — their morphology — influences the degree of instability in the knee after an ACL tear," says Dr. Musahl. These studies, along with new technologies and innovative software in development may ultimately help individuals, and athletes of all levels, understand how to lessen the chances for or prevent an ACL tear while engaged in their activities, and help surgeons make better decisions or modify their techniques during surgical repairs and post-injury rehabilitation plans.

Toward a Better Understanding of Dislocations

A unique, new study under way by Drs. Debski, Musahl, and **Albert Lin, MD**, seeks to understand the nature of dislocations and the impact of multiple dislocations on shoulder joints. “No one has ever dislocated joints with a robot before, and we’re gaining a lot of new data about what it means when an individual sustains a second, or third dislocation to the same joint,” explains Dr. Debski.

For athletes, and in particular football or ice hockey players, these can be very common injuries. “With our robot, we can study what type of injury results from multiple dislocations, and how the injury may change from the first to subsequent dislocations,” says Dr. Musahl. These studies are building evidence that a recurrent dislocation is a very different injury than the first time it occurs.

“What we have created is a portable clinical exam that can quantify how much joint motion occurs in a suspected ACL tear. In the past, the pivot shift test was a very subjective test, but our software has turned it into a quantitative test,” says Dr. Debski.

Understanding the mechanics of multiple dislocations will better characterize the nature of the injuries, how they occur, what damage occurs, and ultimately how best to treat them. Informing treatment modalities — with evidence — will again allow treating physicians to better understand these injuries, and keep the athletes in their care healthier by providing the right treatment at the right time.

Setting a New Standard for the Pivot Shift Test

The pivot shift test has been used for some time by orthopaedic surgeons to assess and diagnose tears to the anterior cruciate ligament. While the test itself can provide useful information, there may exist a high degree of variability based on the technique or individual preference of the surgeon performing the test, and obtaining repeatable results can prove challenging.

To improve upon this, and set a new standard for diagnosis, Drs. Musahl and Debski and colleagues developed software for use on tablet devices that quickly, and with repeatable and accurate results down to a millimeter, can quantify and diagnose the nature of an ACL tear.



Using the custom software app and the native camera in the tablet device, the program is able to measure joint motion by placing markers on the skin of the lateral side of the knee, and then conducting the pivot shift test. Because of the portable nature of tablet devices, the exam can be conducted anywhere — on the field of play, in the exam room, or in the operating suite.

“I don’t think we’re done yet with planning and developing new technologies to help diagnose, treat, and prevent orthopaedic injuries. We have a number of collaborations ongoing. We’re really just getting started. It’s an incredibly exciting time,” says Dr. Musahl.

Reading Resources

For more information about Drs. Musahl and Debski’s research, please see the following published papers.

Gasbarro G, Ye J, Newsome H, Jiang K, Wright V, Vyas D, Irrgang JJ, Musahl V. Morphological Risk Factors in Predicting Symptomatic Structural Failure of Arthroscopic Rotator Cuff Repairs: Tear Size, Location, and Atrophy Matter. *Arthroscopy*. 2016; 32(10): 1947-1952.

Miller RM, Popchak A, Vyas D, Tashman S, Irrgang JJ, Musahl V, Debski RE. Effects of Exercise Therapy for the Treatment of Symptomatic Full-thickness Supraspinatus Tears on In Vivo Glenohumeral Kinematics. *J Shoulder Elbow Surg*. 2016; 24(4): 641-649.

Rahnemai-Azar AA, Miller RM, Guenther D, Fu FH, Lesniak BP, Musahl V, Debski RE. Structural Properties of the Anterolateral Capsule and Iliotibial Band of the Knee. *Am J Sports Med*. 2016; 44(4): 892-897.

The Science of Intervertebral Disc Degeneration

The Ferguson Laboratory for Orthopaedic and Spine Research and its investigators are focused on studying the molecular and cellular biology driving the processes of intervertebral disc degeneration (IDD), as well as developing a range of clinical spinal research and novel biological, cellular, and biomechanical therapies to combat this common condition. Multidisciplinary at its core, the Ferguson Laboratory engages in all aspects of disc and spine research to better understand the complex, interrelated aspects of IDD.

Nam V. Vo, PhD, is an associate professor of Orthopaedic Surgery and co-director of the Ferguson Laboratory along with **Gwendolyn Sowa, MD, PhD**, and **Joon Lee, MD**, who serves as clinical director. Dr. Vo's research is primarily centered around the basic biology mechanisms of how aging impacts the intervertebral disc tissues and spine, and how this in turn leads to spinal pathologies, such as stenosis and chronic low back pain. Specifically, Dr. Vo has spent considerable time analyzing the molecular and cellular mechanisms that regulate homeostasis of the extracellular matrix proteoglycan in intervertebral discs.







The Role of Cellular Senescence in Disc Aging

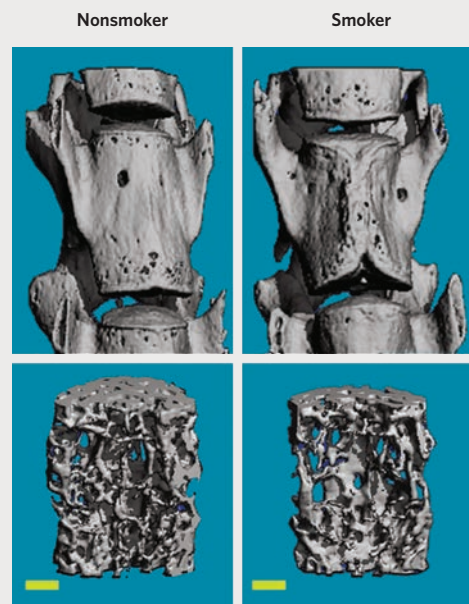
Damage and changes to the spine and intervertebral discs as a consequence of aging are, to varying degrees, inevitable. However, not all individuals with age-affected discs will devolve into full-blown degeneration with progression to disease, or suffer any symptoms as a consequence.

But some patients' age-affected discs do devolve, and it may be in part due to an accelerated pathological aging process. A new area of research for Dr. Vo is understanding the role of cellular senescence¹ in driving the pathological aging of intervertebral disc tissues.

Dr. Vo explains that cellular senescence is largely a consequence of accumulated, unrepaired DNA damage. Anything that promotes DNA damage would, therefore, promote the aging of disc tissue. Each cell in an organism is subjected to tens of thousands of individual DNA lesions each day due to the inherent imperfect replicative fidelity, chemical instability of DNA structure, metabolic byproducts, and environmental exposure to tobacco smoke, UV light, radiation, and so forth. As cells age, they change their behaviors. A subpopulation of aging cells has been identified and characterized as cellular senescence. His lab recently discovered that the senescent disc cells, in addition to losing their capacity to divide, are typically becoming more catabolic, which in turn leads to tissue and matrix degeneration of the disc. "We are trying to figure out how cellular senescence develops and accumulates in the disc with time, as people age, using a cell culture system as well as animal models," says Dr. Vo.



Dr. Vo and Gwendolyn Sowa, MD, PhD,
co-directors of the Ferguson Lab.



Detail scans of vertebrae in smokers versus nonsmokers.

Knowing that in some individuals this aging process is accelerated while in others it is not motivates Dr. Vo to determine what factors are contributing to the rate of age-related disc degeneration. "It's damage to the DNA that we are most interested in, since unrepaired DNA damage is most detrimental to cell structure and function, and is what drives cells to undergo senescence," says Dr. Vo. Anything that causes DNA damage, for example oxidative or genotoxic damage, can accelerate the aging process of disc tissues. In past experiments, we have shown that mice deficient in DNA repair, or mice exposed to ionizing radiation or chemotherapeutic drugs that crosslink or damage DNA, seems to accelerate aging of the disc tissues." As cells age, they tend to accumulate molecular damage in their proteins, lipid membrane, DNA, and subcellular organelles, such as mitochondria. "We have some leads we are pursuing with our research. Excessive loading forces or chronic exposure to stress, and oxidative or inflammatory stresses, are things we believe are driving these damages leading to accelerated aging and degenerative changes," says Dr. Vo.

Factors That Can Accelerate Disc Aging

As noted previously, Dr. Vo is pursuing, in ongoing studies, the major factors that regulate the aging process of intervertebral discs and associated degenerative changes. Some of these factors may prove to be protective in nature, such as moderate exercise and proper diet. And then there are those external or environmental factors that can play a role in upsetting disc biology, leading to degeneration. These include tobacco smoking, obesity, and spinal injury resulting from excessive stress with a high magnitude and duration seen in athletes or certain occupations, such as a jackhammer operator.

With regard to tobacco smoke, a past study² by Dr. Vo and colleagues showed a very strong correlation between chronic exposure to tobacco smoke and IDD in a mouse model. Dr. Vo indicates that results of the study showed "chronic exposure to tobacco smoke, known to contain numerous potent genotoxins and oxidants, causes disc degeneration. It causes loss of vertebral bone, disc matrix breakdown, and it accelerates cellular senescence within the disc in our mouse model of human tobacco smokers."

Tough, But Not Indestructible Tissues

Intervertebral disc tissues are robust, tough tissue, mechanically active and under constant dynamic compressive and tensile loading forces. Intervertebral disc biology is somewhat unique compared to other types of tissues in the body in that they are largely avascular and aneural. While the discs are quite good at their job and remain so for much of an individual's life, their ability to regenerate or heal themselves after an injury is limited. It is thought that this is largely due to the avascular nature of the disc and the constant mechanical stresses they bear.

Since disc tissues are, by and large, unable to heal themselves of damage from age or injury, developing therapies that can facilitate or boost what little native healing capacity exists, or finding ways to reduce or slow the age-related changes that do occur, are some inquiries Dr. Vo and his colleagues are pursuing in the lab. These areas of research cover the mechanobiology

A Surgeon's Perspective

As an orthopaedic surgeon specializing in spinal surgery, **Joon Lee, MD**, sees the possibilities and practical applications of Dr. Vo's research and that of the entire Ferguson Laboratory firsthand as its clinical director. While much in the lab and with Dr. Vo's work is focused on the basic science of IDD, the research also lays a solid foundation for future studies to develop biologic and treatment interventions to prevent or minimize IDD in the first place.

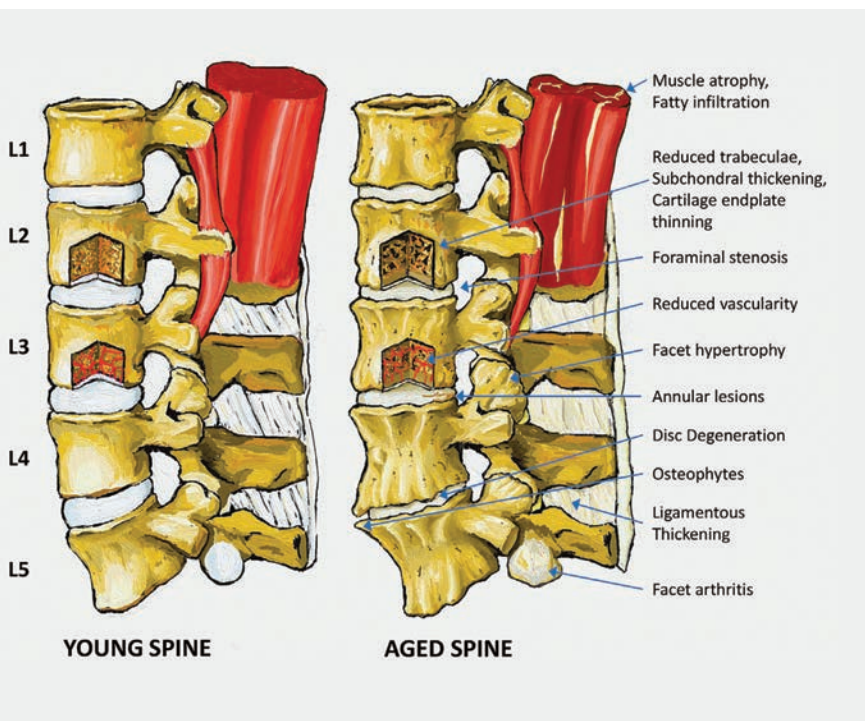
"From a clinical standpoint, the way we currently treat IDD surgically is typically more reflexive than preventative in nature. The damages are already done in the patient, either through injury or age, or a combination of the two, and our current surgical procedures are able to only correct and remedy the problem after the fact," says Dr. Lee. Of course, great strides have been made in spinal surgical repair for degenerative disc disease over the years, but Dr. Lee is honest in the assessment of current surgical techniques and how they are used to treat individuals with severe degeneration and symptoms, including pain.

In terms of pain, and how pain manifests in individuals with IDD, Dr. Lee indicates that new animal models in development by Dr. Vo are being investigated to try and answer the questions about how disc degeneration causes pain, the pathways it travels, and what therapeutic interventions can be tested at the bench to reduce or eliminate debilitating pain.

Not everyone with IDD will develop pain or symptoms. Some individuals with severely degenerated discs as seen in scans are completely asymptomatic when it appears as if they should be in a great deal of pain. "And then there are patients with what we would define as minor looking injuries who are experiencing intractable pain and significant disability," indicates Dr. Lee. The reasons for this are largely unknown, why one patient with IDD has pain and symptoms and a similar individual does not. Understanding how these

mechanisms work through both in vitro and in vivo animal modeling is part of Dr. Vo's current research.

"It's an ambitious project, but I think it will have some important clinical translational findings. By developing a good working model, we can translate some of this into benchtop in vitro studies to test various therapeutics in our current clinical armamentarium," says Dr. Lee.



of intervertebral discs to learn more about beneficial or therapeutic loading conditions to aid in recovery after injury, gene and cellular-based therapies to treat IDD, biomarkers research for diagnostic and prognostic purposes, and biomechanical studies to help improve existing treatment modalities.

Another major area of research is the exploration and testing of biologic therapies to minimize the development of disc cellular senescence to restore disc matrix homeostasis.

An example of one such study by Dr. Vo and colleagues found that pharmacological and genetic inhibition of NF- κ B,³ a central stress response pathway that is required for the formation of cellular senescence, mitigates age-associated IDD in a novel mouse model of human progeria.⁴



The Answers Will Come

Given that aging is the biggest risk factor for the development of IDD, elucidating the cellular, molecular, and mechanistic changes brought on by advancing age and environmental stresses — both internal and external — will be critical to developing therapies or interventions that can slow down age-related changes to disc tissues, or point to preventative strategies that can help protect individuals and reduce their chances of developing full-blown degeneration and disease.

Reading Resources

Additional information about Dr. Vo's research and the Ferguson Laboratory can be found at fergusonspinelab.com, as well as these recently published papers.

¹ Vo N, et al. Molecular Mechanisms of Biological Aging in Intervertebral Discs. *J Orthop Res.* 2016; 34(8): 1289-1306.

² Wang D, Nasto LA, Roughley P, Leme AS, Houghton AM, Usas A, Sowa G, Lee J, Niedernhofer L, Shapiro S, Kang J, Vo N. Spine Degeneration in a Murine Model of Chronic Human Tobacco Smokers. *Osteoarthritis Cartilage.* 2012; 20(8): 896-895.

³ Nasto LA, et al. Inhibition of NF- κ B Activity Ameliorates Age-Associated Disc Degeneration in a Mouse Model of Accelerated Aging. *Spine.* 2012; 37: 1819-1825.

⁴ Vo NV, et al. Accelerated Aging of Intervertebral Discs in a Mouse Model of Progeria. *J Orthop Res.* 2010; 28(12): 1600-1607.

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