S T A N F O R D

M E D I C I N E

Issue 2 / 2026

special report

# MADE TO MOVE

From musculoskeletal development to peak performance

## Our living framework
Why we're not blobs

## The quest to regrow and repair cartilage
Giving cartilage a voice — and other strategies

## Keeping athletes with disabilities in the game
'All of our bodies are different. Mine just happens to be very different'

## Back in action
Rehab methods honed on elite athletes for the rest of us

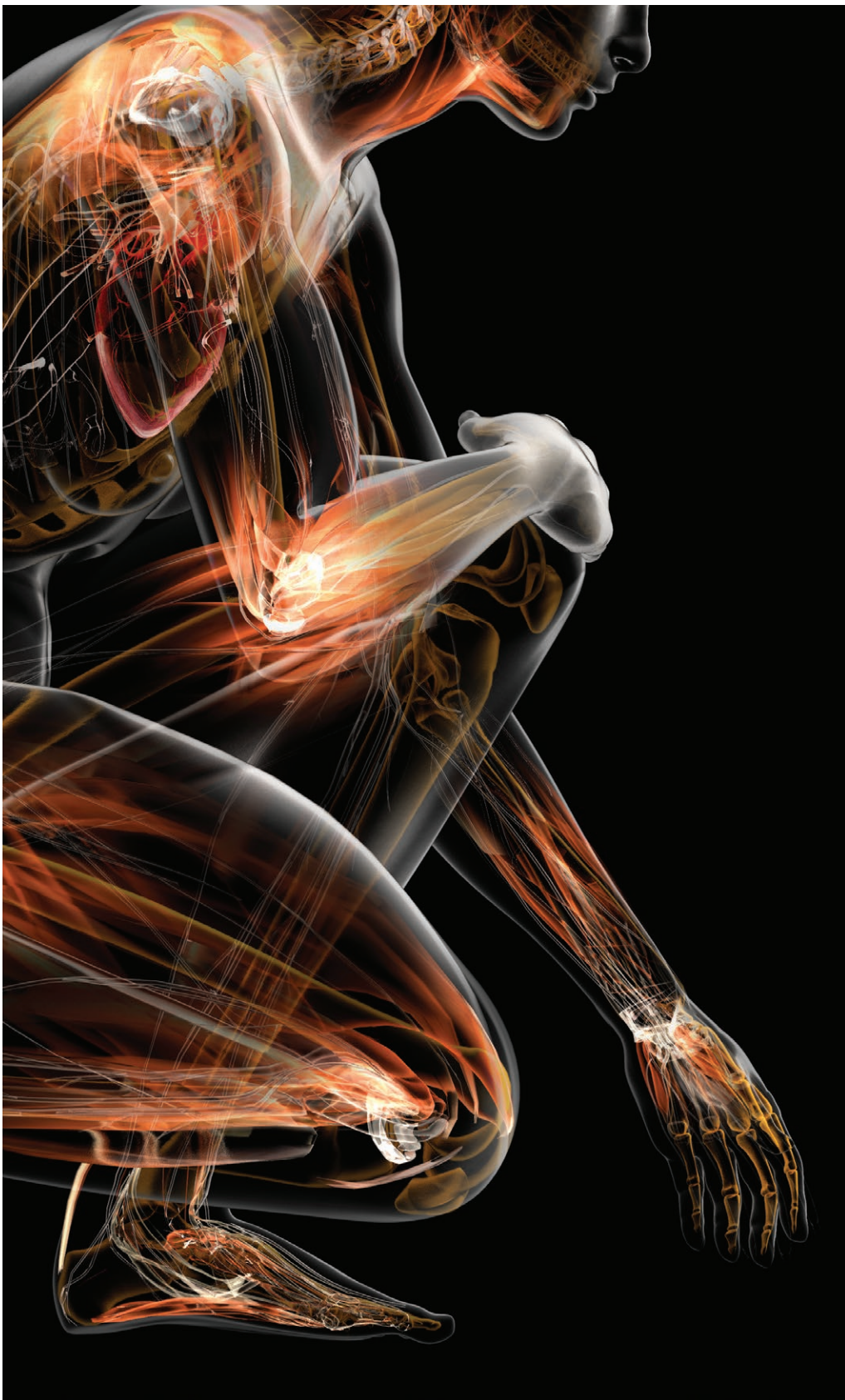
## Why 80 is the new 60
Joint replacements are booming

## The big deal about kids' bones
A conversation with a pediatric bone health expert

plus

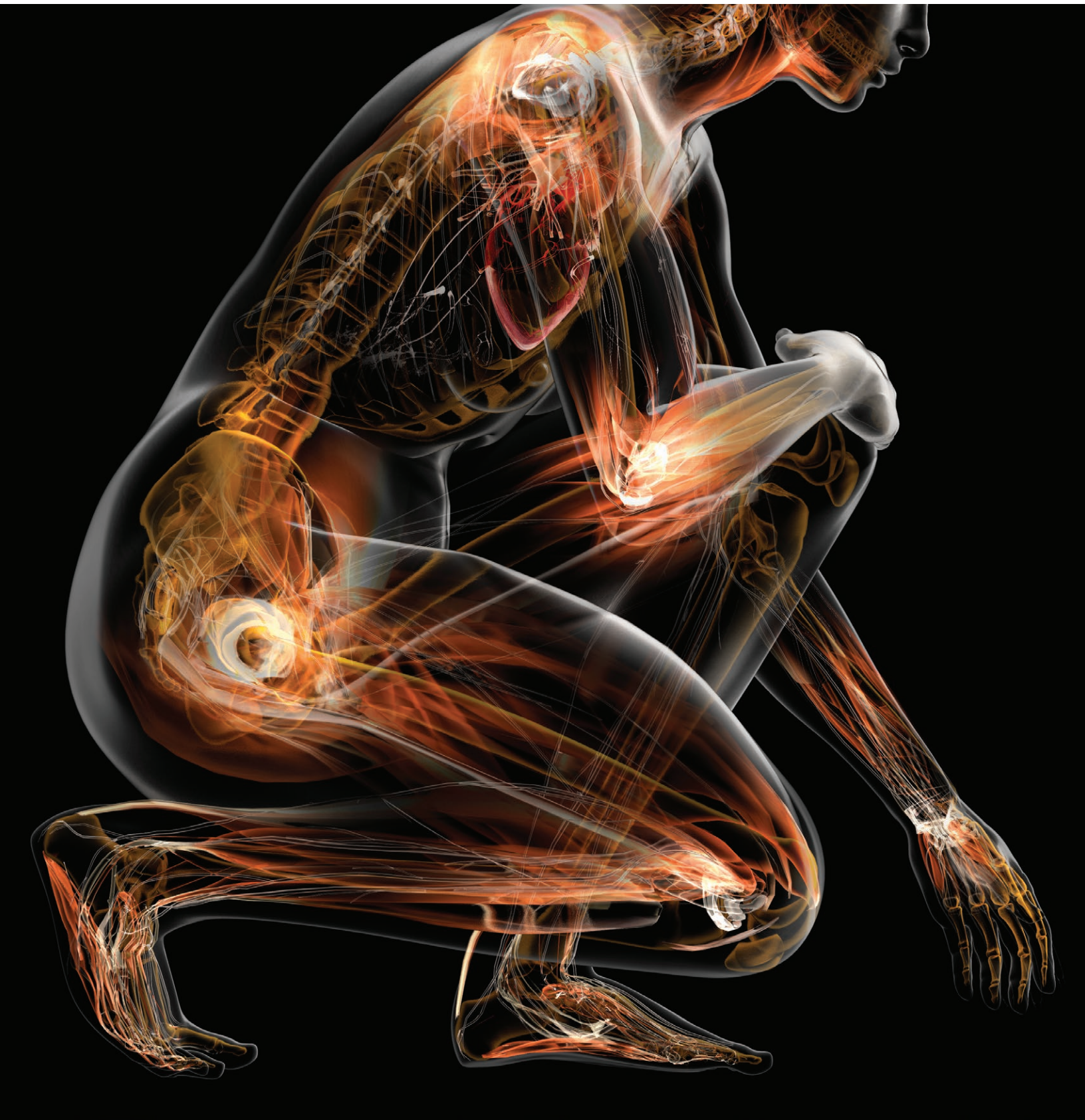
## Ready, set, thesis!
Meet winners of Stanford's 3 Minute Thesis competition

## From a car jack to precision cancer care
Three key radiotherapy inventions



# STANFORD MEDICINE

Issue 2 / 2026



# letter from the dean

**Regrowing cartilage.**
**Personalized joint implants.**
**A device that aligns slipping vertebrae without fusion surgery — allowing the spine to bend and twist as before.**

These pioneering advances, among many others emerging from Stanford Medicine, reflect our long arc of progress in musculoskeletal health.

Orthopaedics stands as one of the oldest medical specialties because diagnosing, treating, preventing and rehabilitating musculoskeletal conditions have a profound impact on human life. Ancient civilizations in China, Egypt, Greece and India chronicled best practices for treating broken bones — an existential injury that threatened livelihoods, diminished quality of life and could lead to death. Millennia later, our priorities are not so different, but the tools we have are.

Modern hip replacement surgeries — a far cry from 19th-century experimental ivory implants — are considered among the most successful and cost-effective procedures ever developed. They relieve pain, rapidly restore function and mobility, and enable patients to enjoy healthy and productive lives for years and even decades more. Stanford Medicine researchers have contributed to this procedure's success, including through a 2021 study that showed that a simple blood test analyzing immune function can forecast how quickly a person undergoing hip replacement surgery will recover.

While hip replacements exemplify orthopaedics' impact on older adults, caring for children involves unique challenges, including protecting bone development and long-term resilience. Researchers at Stanford Medicine, for example, are investigating how weight-bearing exercise and other types of mechanical stress during childhood cause bones to bank strength against osteoporosis and later fractures — and how chronic inflammation, poor nutrition or limited mobility can undermine this critical process.

When bones need treatment, our researchers and clinicians have pioneered new approaches, including the use of magnet-powered implants that internally lengthen bones for people with leg-length discrepancies. This eliminates the need to pierce skin and muscles for months with external bracing. Research-driven advances like these offer lasting gifts to many. Often they go beyond simply treating a condition to expanding healthspan — the number of healthy years people live. We take pride not just in the number of successful operations and treatments but in the stories we hear of retirees resuming hiking, children running alongside classmates without pain and athletes returning to competition after injury — simple joys that might have seemed miraculous just a generation ago.

In this latest issue of *Stanford Medicine* magazine, we document some of these breakthroughs, exploring orthopaedics' profound influence on human health and Stanford's role in shaping the field's future. In these stories, you'll meet the physicians, surgeons and researchers advancing science and redefining standards of care — continuing a tradition that goes back millennia.

Sincerely,

Lloyd Minor, MD
Carl and Elizabeth Naumann Dean of the Stanford School of Medicine
Vice President for Medical Affairs at Stanford University
Professor of Otolaryngology-Head & Neck Surgery

PHOTOGRAPH BY CAROLYN FONG

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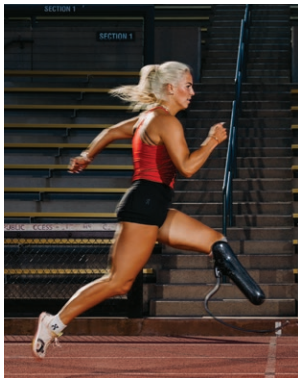
# STANFORD MEDICINE

SPECIAL REPORT

# Made to move

## From musculoskeletal development to peak performance



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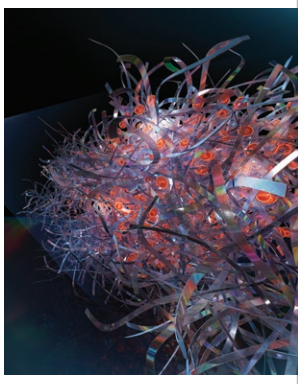

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DEPARTMENTS



COVER: VIOLET FRANCES

# upfront

## About face

CUTS ON THE FACE tend to heal with less scarring than cuts anywhere else — and Stanford Medicine researchers have figured out why. Their findings could one day lead to scar-free healing.

Scars are more than a cosmetic problem. They can interfere with normal tissue function and cause chronic pain, disease and even death. About 45% of deaths in the U.S. are due to some type of scarring — usually of vital organs like the lungs, liver or heart.

"The face and scalp are developmentally unique," said Derrick Wan, MD, the Johnson & Johnson Distinguished Professor in Surgery II.

The researchers compared fibroblasts — the main scar-forming cells — from four body sites and found facial fibroblasts triggered healing pathways.

Activating these pathways — or using a drug to switch off a scar-promoting protein — helped back wounds heal more like facial wounds.

Wan shares co-senior authorship of the mouse-based study, published in January 2026 in *Cell*, with Michael Longaker, MD, the Deane P. and Louise Mitchell Professor in the School of Medicine.

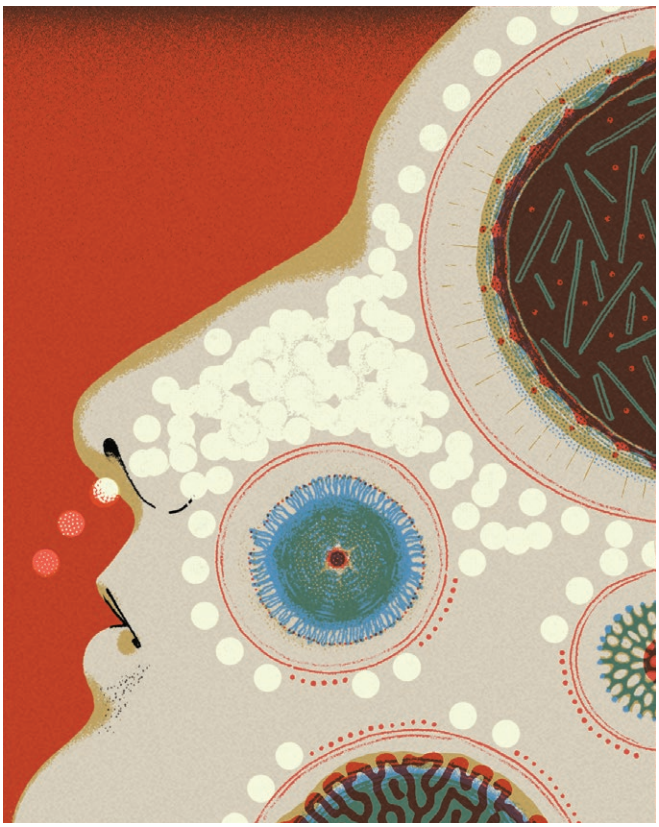
## Blanket immunity

STANFORD MEDICINE researchers and collaborators are a step closer to a universal vaccine — one of medicine's most sought-after breakthroughs.

In a study in mice, researchers developed a vaccine formula that protects against a wide range of respiratory viruses, bacteria and even allergens. The intranasal vaccine provides broad protection in the lungs for several months.

In the study, published in February 2026 in *Science*, researchers showed that vaccinated mice were protected against SARS-CoV-2 and other coronaviruses, Staphylococcus aureus and Acinetobacter baumannii (common hospital-acquired bacterial infections), and house dust mites (a common allergen).

The vaccine is unlike any used today. It doesn't try to mimic any part of a pathogen; instead, it mimics the signals that immune cells use to communicate with each other during an infection. This novel strategy integrates the two branches of immunity — innate and adaptive — creating a feedback loop that sustains a broad immune response.



The vaccine is a "double whammy" against pathogens, said the study's senior author, Bali Pulendran, PhD, the Violetta L. Horton Professor II, a professor of microbiology and immunology.

Against SARS-CoV-2, for example, a prolonged innate response lowers the amount of virus in the lungs 700-fold. And viruses that slip through this initial defense are met with a swift adaptive response in the lungs.

If translated into humans, such a vaccine could replace multiple jabs every year for seasonal respiratory infections and be on hand should a new pandemic virus emerge.

ILLUSTRATIONS BY JUAN BERNABEU

## Gene can lower GLP-1 response

More than a quarter of people with Type 2 diabetes take GLP-1 receptor agonists, but the popular diabetes drugs might not help people with certain genetic variants, Stanford Medicine scientists and collaborators reported in a new study.

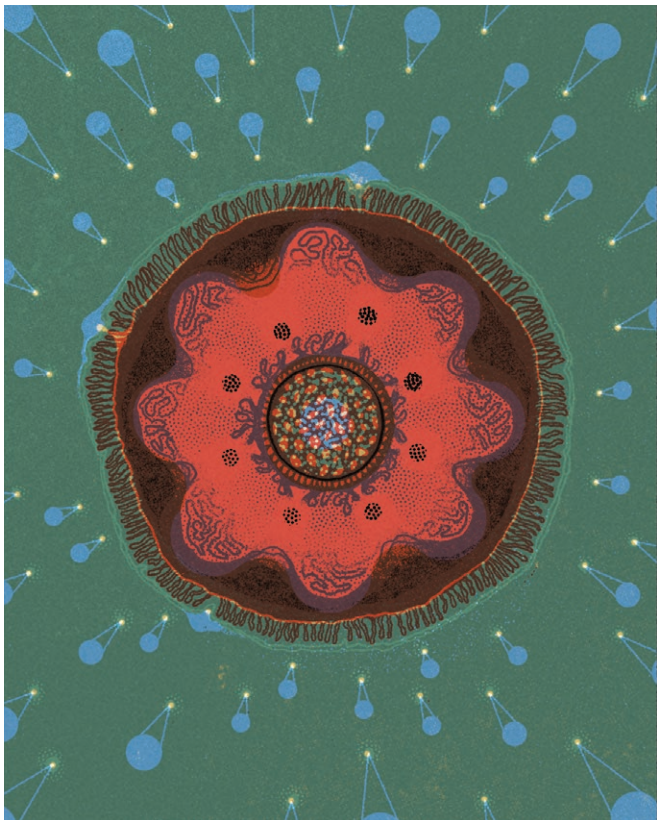
One in 10 people carry genetic variants that handicap PAM, an enzyme that activates many hormones in the body, including GLP-1 (glucagon-like peptide-1), which helps regulate blood sugar.

That causes a still mysterious phenomenon known as GLP-1 resistance, in which levels of GLP-1 are higher but less effective.

"Despite people with the PAM variant having higher circulating levels of GLP-1, we saw no evidence of higher biological activity. They were not reducing their blood sugar levels more quickly," said Anna Gloyn, DPhil, professor of pediatrics and of genetics, and a senior author of the study, published in April 2026 in *Genome Medicine*.

In a meta-analysis of three drug trials, totaling 1,119 participants, people with PAM variants were less successful in lowering their HbA1c, a measure of average blood sugar levels.

It's unclear whether the variants affect weight loss from these drugs, which are increasingly prescribed to treat obesity. Some weight loss data from the trials showed no difference, but the data is too limited to be conclusive, Gloyn said.



## Seek and destroy

A TECHNIQUE that transforms immune cells into cancer-seeking bloodhounds may overcome a roadblock that has hampered immunotherapy for solid tumors, a Stanford Medicine study shows.

The approach involves equipping immune cells with surface proteins that detect detritus from cancer cells' abnormal metabolism and encourage the immune cells to migrate toward tumors.

Unlike CAR-T cell therapy, which uses receptors that recognize and target a protein tethered to the surface of a cancer cell, this method responds to small molecules released into the surrounding environment.

Arming immune cells with metabolite-sensing receptors markedly improved their ability to seek out and infiltrate tumors, enhancing survival rates in mice with human breast and ovarian cancers, said Livnat Jerby, PhD, an assistant professor of genetics and the senior author of the study.

CAR-T cell therapy has transformed the treatment of several blood cancers since the Food and Drug Administration approved it in 2017 for treating acute lymphoblastic leukemia. But it's been less successful in patients with solid tumors.

Researchers posit that CAR-T cells become exhausted before they can eliminate solid tumors. Also, it is difficult to identify molecular targets on solid tumors found only on the cancer cells and not on normal tissue.

"The problem with treating solid tumors is also a spatial issue," Jerby said. "Too few T cells are getting into the tumor."

## Real-time fetal monitoring

A TEAM OF researchers is testing a wearable ultrasound patch that allows doctors to monitor high-risk pregnancies more closely than is possible with current technology.

A study of the patch, which gained early validation in several dozen pregnant patients, was published in May 2026 in *Nature Biotechnology*.

"There's nothing similar to our device on the market or in the scientific literature," said Sheng Xu, PhD, a professor of anesthesiology, perioperative and pain medicine.

The patch was developed at Stanford Medicine; Oxford University; and the University of California, San Diego. Xu is the study's senior author, and Geonho Park, PhD, a postdoctoral scholar in anesthesiology, perioperative and pain medicine, is the lead author.

Researchers said it is promising for monitoring high-risk conditions such as intrauterine growth restriction, in which an insufficient amount of blood flows through the umbilical cord, hampering delivery of oxygen and nutrients and causing the fetus to grow slowly.

Current fetal-monitoring options include cardiotocography, to measure fetal heart rate and uterine contractions, and traditional ultrasound, which uses sound waves to capture detailed images of the fetus, including the umbilical cord and placenta.

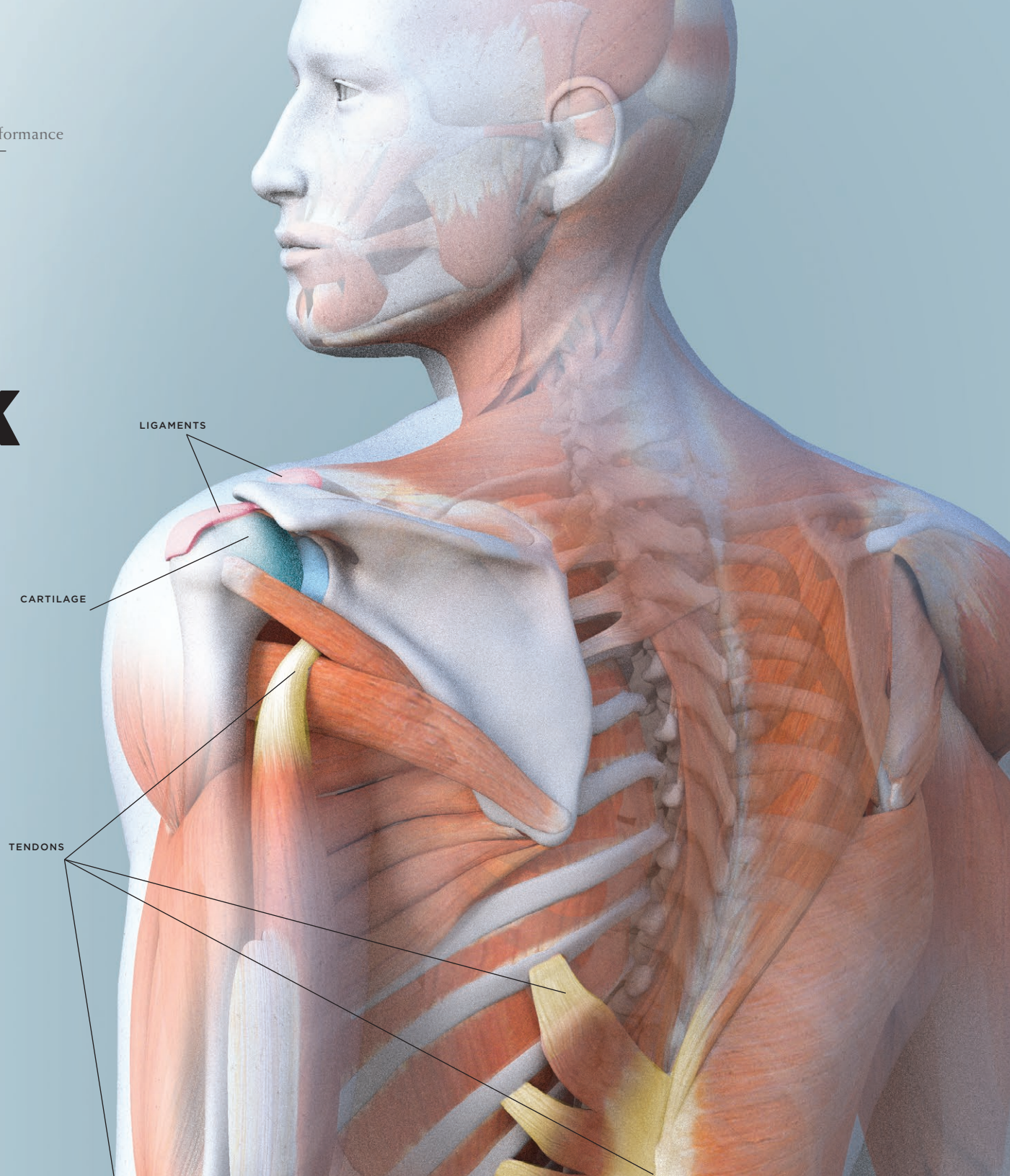
A key element of the patch is an algorithm the team developed to track the major blood vessels in the umbilical cord — two arteries and a vein — in addition to measuring blood flow through a major artery in the fetus, in real time.

# THE LIVING FRAMEWORK

## INSIDE THE GROWING, SELF-HEALING TISSUES THAT MAKE MOVEMENT POSSIBLE

By Nina Bai

ILLUSTRATION BY VIOLET FRANCES



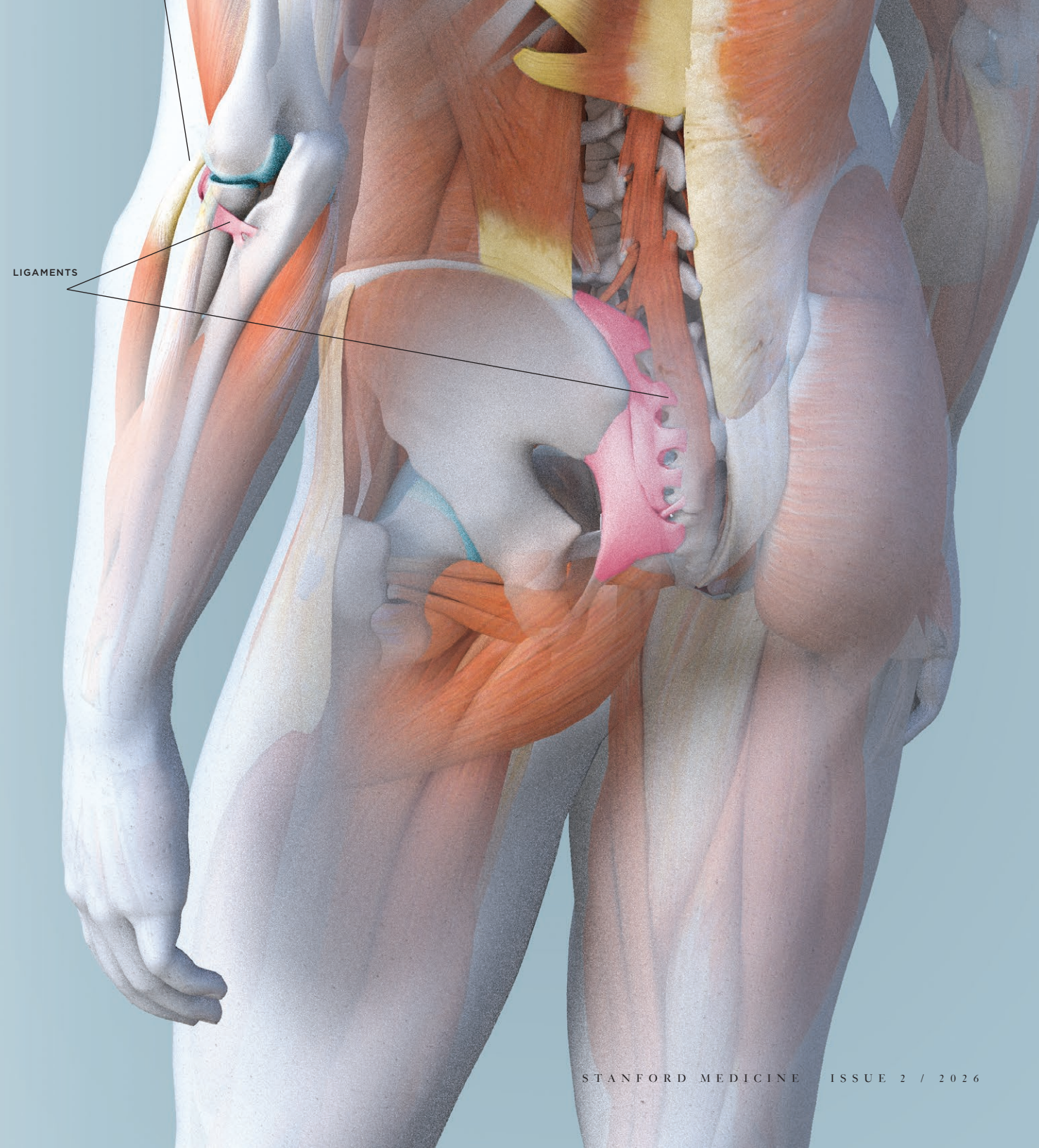
A STANDARD DIAGRAM OF the human musculoskeletal system might evoke the framework of a house — a sturdy construction of muscle and bone, much like the studs, joists and rafters that give a dwelling structure, determine its shape and protect the valuables held inside.

But that image doesn't capture the musculoskeletal system's most remarkable qualities. It's more than a rigid scaffold on which to hang our soft, pliable bodies. It's a collection of living, growing, adapting and often self-healing tissues that enable a stunning range of movement, from tickling piano keys to kicking a soccer ball. Imagine a house rising off its foundation, sprinting and doing a backflip.

A healthy musculoskeletal system is what enables people to move. "The burden of musculoskeletal disease is huge," said William Maloney, MD, the Boswell Chair of Orthopaedics. "It severely impacts people's quality of life, and it affects more people than does cancer or heart disease."

According to the World Health Organization, musculoskeletal conditions affect some 1.7 billion people worldwide — more than 20% of the population — and are the leading contributors to disability. Some 570 million people suffer from low back pain, 528 million from osteoarthritis and 440 million from the acute or long-term consequences of broken bones.

"Mobility is key to life," said Constance Chu, MD, the Elsbach-Richards Professor in Surgery and vice chair of research in the department of orthopaedic surgery. "It's very, very difficult for



the majority of people to work, to maintain social relationships, to exercise, to take care of themselves if they lose mobility or have chronic musculoskeletal pain."

For nearly as long as people have incurred broken bones, people have also tried to mend them. Evidence of healed fractures that likely required splinting and stabilization date back to Neolithic times. Around 1600 B.C., ancient Egyptians inscribed onto papyrus the earliest known instructions for treating bone injuries.

"Orthopaedics is a very broad specialty," Maloney said. "It includes everything from the tips of your fingers to the tips of your toes. It's everything from primary care to highly specialized quaternary care, from people who have routine ankle sprains to people who need half their pelvis taken out for malignant bone cancer."

To maintain mobility, surgery is only part of the story. Physiatrists employ nonsurgical treatments, such as injections and physical therapy, to restore function and manage pain. And researchers in areas ranging from biomechanics to endocrinology to regenerative medicine are venturing into the inner workings of musculoskeletal tissues, learning to keep bones strong, fend off infections in prosthetic joints and coax worn cartilage back to life.


WILLIAM MALONEY, MD, THE BOSWELL CHAIR OF ORTHOPAEDICS, LEADS STANFORD MEDICINE'S DEPARTMENT OF ORTHOPAEDIC SURGERY.

## Main musculoskeletal components

THE ADULT HUMAN BODY has more than 200 bones, some 650 muscles, roughly 900 ligaments, thousands of tendons and about 250 movable joints. Here's a closer look at the main components musculoskeletal specialists heal, repair or replace:

**Bone is a strong yet relatively lightweight** material that is largely an extracellular matrix composed of about 30% collagen and 70% calcium- and phosphorus-rich crystals known as hydroxyapatite. Three types of bone cells live within this extracellular matrix: osteoblasts, which build new bone structure; osteoclasts, which tear it down for remodeling; and osteocytes, mature bone cells that detect mechanical stress.

Healthy bone is in a constant state of reconstruction, with extra fortifications directed to areas of high mechanical stress. Bone is somewhat porous, providing access to networks of small blood vessels that feed the bone cells, and sensory nerves, both inside and on the bone surface, that make a fracture extremely painful. Cavities inside bone also house a gelatinous substance known as bone marrow, which serves as the birthplace of most of our blood cells.

**Muscle — specifically skeletal muscle,** which is the type under our voluntary control — consists of bundles of long, stretchy cells. These oxygen-hungry muscle cells are fed by rich networks of blood vessels and are connected to both motor neurons, which carry instructions from the brain and spinal cord, and sensory neurons, which carry pain and other signals back to the brain and spinal cord.

Each muscle cell is packed with two key types of protein filaments: actin and myosin. When nerves send an electrical signal, the muscle cells are flooded with calcium ions, which trigger actin and myosin to slide against and grip each other, causing the muscle to contract. If muscle is torn, whether through intentional exercise or accidental injury, blood and nearby stem cells rush in to repair the damaged tissue in days to weeks — one of the body's more impressive feats.

**Cartilage is a flexible, slippery,** water-retaining tissue that lines the ends of bones at joints to reduce friction and absorb shock. It's made up of a collagen extracellular matrix filled with large water-trapping molecules known as proteoglycans. Unlike bone and muscle, cartilage lacks blood vessels and nerves — making it a particular problem child for orthopaedics. A few cells interspersed in the collagen matrix, known as chondrocytes, survive on oxygen and nutrients from the synovial fluid that lubricates joints. They help maintain cartilage to a limited extent, but damaged cartilage has essentially no ability to regenerate.

Because cartilage feels no pain and its watery composition

CONTINUES ON PAGE 44

LENNY GONZALEZ

# THE HIDDEN LIFE OF BONES

## OSTEOBLASTS AND OSTEOCLASTS REBUILD BONE THROUGHOUT LIFE

By Erin Digitale

Our skeletons may seem static, but they're quietly animated throughout our lives, with every bone in our bodies under constant (re)construction.

Two specialized types of cells, called osteoblasts and osteoclasts, are responsible for bone assembly and recycling. Physiology teachers tell their students that "osteo**b**lasts **b**uild bone, and osteo**c**lasts **c**hew up bone" to help them keep the roles of the cells straight.

**To begin building**, the osteoblasts manufacture a frame. They lay down many long strands of collagen. This ropelike triple helix is the body's strongest protein. Most collagen ropes run parallel to the length of the bone, with a few cross-linking connectors between strands. We don't understand how the osteoblasts know this pattern, but it's as firmly programmed into them as a web's radial geometry is into the orb spiders dangling outside your window.

**When the matrix is ready,** the osteoblasts pull calcium and phosphorus from the blood, which react with each other and harden into the bone mineral called hydroxyapatite. Bone gets its strength from both the tensile properties of the collagen and the compressive strength of the mineral, meaning it can flex and stand up to heavy loads.

When a bone needs rebuilding or reshaping, the bone-chewing osteoclast cells seal themselves to its surface, making a pocket under their bellies into which they secrete acid and enzymes. The acid dissolves bone mineral, releasing calcium and phosphorus into the blood; the enzymes break down collagen. The resulting bone indentations have the romantic name "Howship's lacunae," after the British anatomist and surgeon who first identified them in the early 1800s.

In adults, whose bones are remodeling, the two processes happen in a tight tango: The osteoclasts chew up old bone, and the osteoblasts build new bone right behind them. This eliminates microfractures and keeps bone healthy.

### How children's bones grow

In kids, the cells work at different times and places: Osteoblasts put up new scaffolding and add mineral on the outside surface of the bone, making it thicker and longer. Osteoclasts then hollow out the inside of the bone, enabling it to expand without getting too heavy. This decoupled process enacts a transformation from the tiny tibias and fibulas of babies and toddlers into the grown-up-sized bones of teens. Depositing plenty of bone mineral in early life, especially during the growth spurt of puberty, provides a bulwark against the bone loss of old age and protection against painful fractures from osteoporosis. Kids' calcium requirements jump around age 11, reflecting their bone-building needs.

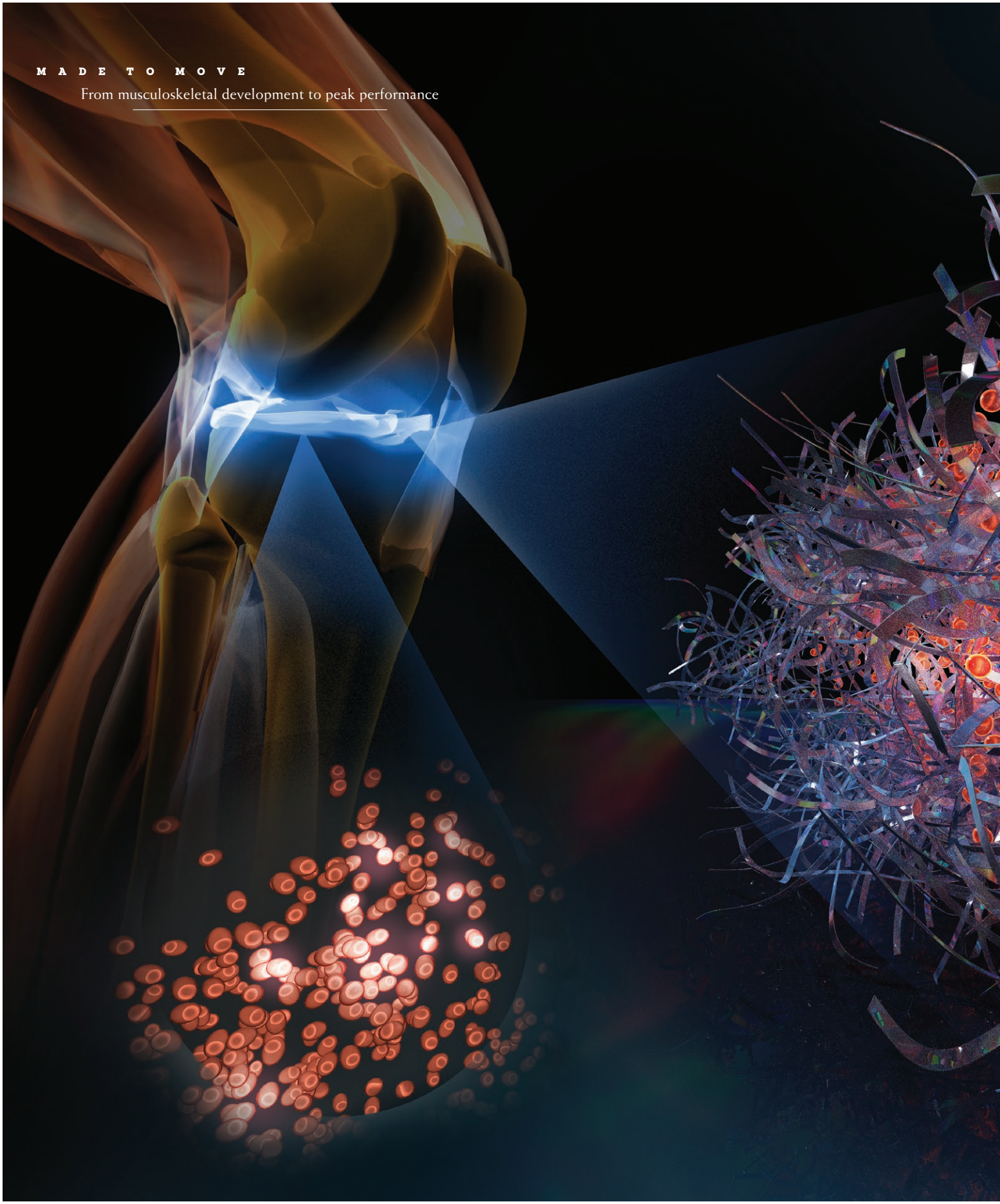
While the osteoblasts and osteoclasts are building and chewing, they're also listening to a complex network of signals from other parts of the body, including the push and pull of muscles — a major stimulus for making bones stronger — and hormones from the kidneys and parathyroid and thyroid glands, which regulate the body's calcium balance. More weight-bearing exercise is good for everyone's bones, and that's especially true in children and teens.

Several fundamental discoveries about bone development and repair have been made at the Stanford Medicine labs of Michael Longaker, MD, the Deane P. and Louise Mitchell Professor in the School of Medicine, and the late Charles Chan, PhD, stem cell researcher and assistant professor of surgery, including:

- The first identifications of skeletal stem cells in mice and in humans, published in 2015 and 2018, respectively. Skeletal stem cells differentiate into the mature cells needed to keep bones healthy, including osteoblasts and osteoclasts.
- The discovery, in 2021, that fracture sites in older bones have fewer skeletal stem cells than fractures in young bones, which helps explain why aging impairs bone healing. This research also identified small molecules that may work as drugs to help old bones heal faster.
- The finding, in 2025, that there are four major subpopulations of human skeletal stem cells, and that imbalances between the four types contribute to genetic diseases that impair bone development and to age-related problems with bone healing.

So, even though they seem unyielding, as sturdy as the I-beams in a skyscraper, our bones are actually complex communities in a constant state of flux. And that's a good thing.

*— Contact Erin Digitale at digitale@stanford.edu*


MADE TO MOVE
From musculoskeletal development to peak performance

NEW SCAFFOLDS, DRUGS AND IMAGING TO REPAIR JOINTS AND PREVENT ARTHRITIS

# CARTILAGE CAN'T HEAL WELL — BUT THAT MAY CHANGE

RUNNING, JUMPING, THROWING OR TYPING.

All involve the vigorous movement of muscles, tendons and bone through joints.

But there's a hidden player: articular cartilage.

This tissue that lines joints is one of the slipperiest surfaces around, and cartilage on cartilage generates less friction than ice on ice.

By Krista Conger

ILLUSTRATION BY VIOLET FRANCES

Without it, joints grind and bone wears away or deforms, making simple movement — like stepping up stairs or raising an arm to reach a glass on a high shelf — painful.

But cartilage is relatively inert. No blood vessels provide nutrients, no true stem cells have been definitively identified and few immune cells patrol healthy joints. As a result, cartilage has little capacity to regrow once it's been lost. This leaves tens of millions of Americans struggling with chronic joint pain (largely due to arthritis), limited mobility and no good treatments.

Stanford Medicine researchers are tackling cartilage loss, from spurring cartilage cells into new cycles of regeneration to designing body-friendly scaffolds to guide their regrowth. They're also devising better imaging techniques to identify the earliest stages of cartilage damage and ways to test interventions on a person's own cells grown in a lab. Looming large, however, are many clinics promoting unproven treatments, including injecting a person's homogenized fat cells or blood plasma into their affected joints. In the absence of effective treatments, desperate people pour money and hope into pipe dreams peddled by would-be miracle workers with few qualifications.

Here's a look at how researchers are attempting the seemingly impossible — regenerating or repairing cartilage that's worn away, damaged or gone entirely.

**CHU'S LAB DEVELOPS HIGHLY SENSITIVE MRI TECHNIQUES CAPABLE OF DETECTING WHAT SHE CALLS 'INVISIBLE CARTILAGE DAMAGE.'**

## CATCHING CARTILAGE DAMAGE BEFORE IT'S TOO LATE

### Identifying invisible damage through powerful imaging and biomarkers

CONSTANCE CHU, MD, the Elsbach-Richards Professor in Surgery and vice chair of research in the Department of Orthopaedic Surgery, has spent more than three decades restoring anterior cruciate ligaments, menisci and cartilage surfaces while growing joint cartilage in the lab. Her patients have ranged from teenagers whose ACL injuries put their seemingly healthy knee cartilage at risk to adults with no cartilage remaining who require joint replacement. Witnessing this progression from vulnerability to pain and degeneration has led Chu to focus her research and clinical practice on preserving joints.

The problem, she believes, is diagnostic. "Cartilage doesn't have any nerves," she explained, "so when you damage or injure cartilage, unless it's a significant injury connected with injury to other tissues, you don't even know about it." Standard imaging — largely relying on joint narrowing visible on X-rays — detects only end-stage disease that is already too advanced to reverse.

Chu's lab develops and evaluates MRI techniques that detect what she calls "invisible cartilage damage" — structural changes that might still be reversible but are invisible to conventional scans. "I call it giving injured and stressed cartilage a voice — or the ability to be seen if not heard," she said.

She has been particularly focused on patients who have suffered ACL tears — a typically young population whose cartilage she finds to be abnormally soft just weeks after injury. Her research shows signs of deterioration long before any symptoms appear. Specialized MRI scans performed one and two years after an ACL reconstruction detect cartilage changes in nearly half of those patients, her research has found; caught at that stage, those changes might be treatable. Left undetected, they likely progress to osteoarthritis just 10 to 15 years later, while most are in their prime work and child-rearing years.

Nidhi Bhutani, PhD, an associate professor of orthopaedic surgery, is trying to close the same diagnostic gap by identifying biomarkers in blood and joint fluid that yield a score of joint health. In collaboration with Chu, she has shown that the immune signatures of osteoarthritis can arise in patients with little to no imaging clues. The findings suggest that osteoarthritis, historically treated as a uniform disease, encompasses distinct forms that genomics could help identify and map. "If you're using the same drug for patients with different subsets of disease, of course the clinical trial fails," Bhutani said. The goal is to bring to orthopaedics the same precision that has transformed oncology: Matching the patient to the treatment, rather than averaging the results among everyone in the room.

## ENGINEERING SCAFFOLDS THAT REGROW BONE AND CARTILAGE

### Microribbons seeded with regeneration-spurring molecules serve as cellular highways into damaged joints

STUART GOODMAN, MD, PHD, the Robert L. and Mary Ellenburg Professor in Surgery, has been operating on joints at Stanford Medicine for over 40 years, focusing on rebuilding those destroyed by infection, failed prior surgeries or injuries that never healed properly. But he became increasingly aware of the limits of the technique. "Putting in more plastic and metal in someone's joint or around their joint, you run out of bone and cartilage and other tissues to work with," he said. "I would rather save the joint than replace it."

For Goodman, the frustration of running out of biological material to work with in the operating room sent him in a different direction: toward the question of what it would take to restore joints rather than replace them. He spent years studying the literal fallout of joint replacement — the plastic particles shed by worn implants that trigger inflammatory cascades, eat away at surrounding bone and force ever more complex revision surgeries. "For 20 years, I focused on the by-products of plastic and metals and how they're not good for cells, and they destroy bone," he said.

He gradually shifted his focus toward a larger ambition: not better artificial joints, but a biological approach that could make artificial joints unnecessary. The lowest-hanging fruit, he found, was bone. Bone's relative capacity for repair — its blood supply, its marrow full of stem cells, its outer membrane that delivers blood and nutrients — makes it tractable in a way that cartilage is not. What resisted solution was not small bone defects, but large gaps — for people, around 2 centimeters or more — that cannot heal on their own. These gaps are often the result of severe trauma, infection or the removal of tumors. He built a lab to study how the immune system and the stem cells found in the marrow interact during bone healing, and how to modulate that interaction to promote repair.

Goodman has collaborated closely with Fan Yang, PhD, an associate professor of orthopaedic surgery and of bioengineering, and director of the Stem Cells and Biomaterials Engineering Laboratory. Yang studies why cartilage and large bone defects are so resistant to repair. "Our body actually has all the necessary cells," she explained. "The question is, how do we get the right ones to come at the right time and do the right things?"

Her answer was to design a scaffold that the body would accept and actively colonize — not a passive structural support, but a biological invitation. She developed what she calls "microribbons" — flat, fettuccine-shaped hydrogel structures that interlock into a porous three-dimensional architecture. Unlike conventional hydrogels, whose pores are too small for cells to migrate through freely, microribbons let cells move in quickly and begin producing their own tissue matrix. The ribbon architecture also gives the scaffold a springlike mechanical resilience — critical for cartilage, which must absorb and release compressive force with every step.

Yang has also focused on the immune environment surrounding the scaffold, developing surface coatings that shift local signaling from pro-inflammatory toward pro-regenerative — particularly important for bone, where immune cells from the marrow are constant participants in the healing process. Goodman loads Yang's microribbon scaffolds with engineered stem cells and tests them in animal models. The combination — an open, mechanically resilient scaffold delivering cells primed to tilt local macrophages from an inflammatory to a regenerative state — has produced promising results in both young and aged mice. But Yang's most urgent message is also about timing. "No regenerative therapy can treat those patients effectively once disease has reached end stage," she said. "The opportunity is to intervene earlier, when it is starting, when we still have a chance to reverse it."

## HOW A 'GEROZYME' INHIBITOR WAKES UP CARTILAGE-MAKING CELLS

### Reversing aging by reprogramming existing cells

CARTILAGE, MEANWHILE, HAS resisted every structural approach that has worked for bone. With no blood supply, no known stem cells and no immune surveillance, there is extremely limited self-repair. Helen Blau, PhD, the Donald E. and Delia B. Baxter Foundation Professor and director of the Baxter Laboratory for Stem Cell Biology, has spent her career studying why some tissues regenerate and others don't. Blau and Bhutani teamed up to show that a fundamental assumption about cartilage — that regeneration would not occur without stem cells — was wrong.

An experimental drug targeting an enzyme Blau calls a "gerozyme" can reprogram the damaged and aging cells already present in the joint, returning them to a healthier, more productive state. "It's a reprogramming of the existing cells," Blau explained. "It's a completely new mechanism of regeneration."

The gerozyme-blocking drug inhibits the age-related destruction of a molecule called prostaglandin E2, which Blau's lab has shown to be essential to the function of muscle stem cells. They wondered whether the molecule might also play a role in aging cartilage and joints.

Bhutani and Blau found that the joints of old mice treated with the drug developed new, young-looking cartilage, and the

animals exhibited less pain and greater function (as measured by gait, weight-bearing and sensitivity to touch before and after treatment). Similar results were observed in animals with joint injuries like the ACL tears that frequently occur in people participating in sports that require sudden pivoting, such as soccer, basketball and skiing. While the tears can be surgically repaired, about 50% of people develop osteoarthritis in the injured joint within about 15 years. A series of injections of the gerozyme inhibitor given twice a week for four weeks after an injury dramatically reduced the chance that the injured mice developed osteoarthritis.

Human cartilage samples obtained during joint replacement surgeries showed a similar pattern: Treated tissue produced more cartilage-building proteins than untreated controls and showed signs of cartilage regeneration. "The fact that you can reprogram injured and diseased cells to cause regeneration is really like an anti-aging or a reverse-aging sort of effect — which I think is very, very promising," Bhutani said. Blau and Bhutani are planning to bring the gerozyme therapy to clinical trials.

PRECISION MEDICINE FOR BUILDING BACK CARTILAGE

### 'Patients' in a dish, on a chip — sussing out what works for you

CHU IS ALSO PIONEERING a precision medicine approach she calls joint avatars. These are miniature organoids — tiny three-dimensional mimics of human tissues or organs — grown from a patient's blood or small tissue samples that allow her to estimate how that individual's cartilage or joint lining tissue responds to different treatments before any intervention is undertaken. She is collaborating with Bhutani and Yunzhi Peter Yang to create organoids specific to the patient and to the treatment being tested. The avatars offer a way to find out what will work for individual patients before subjecting them to it. "You can potentially avoid having someone undergo an expensive, time-consuming procedure that isn't going to work for them," Chu said. "If that proves to be true, it's very powerful."

Goodman is pursuing a different route to the same problem: building the joint outside the body. His lab has designed a "joint-on-a-chip" system — a small plastic wafer engraved with fluid-filled channels that mimic the cellular composition and interactions that make up a functional human joint. "We can take bone cells, cartilage cells, joint cells, immune cells and vascular cells, and connect them up in this microphysiological system," Goodman said. "We can perturb it by adding, let's say, a molecule that causes inflammation, and not only monitor it, but also use it to look at the effects of different drugs on that process."

Where Chu's avatars start from a single patient's cells to predict how that person will respond to a treatment, Goodman's chip is built to model disease itself — re-creating osteoarthritis, joint infection and inflammation in a controlled system where researchers can screen drug candidates long before they reach a clinical trial. Developed with support from the National Institutes of Health's national tissue chip program, in collaboration with the University of Pittsburgh, the project gives Stanford Medicine researchers a way to study how joint disease progresses and to test treatments without waiting on cartilage that, once damaged, still won't regenerate on its own.

FAKE TREATMENTS

### Capitalizing on hope, unregulated clinics promote unproven solutions

ABOUT 1 IN 4 ADULTS in the United States have been diagnosed with some type of arthritis, according to the Centers for Disease Control and Prevention, and about 1 in 10 report that arthritis or joint problems limit their daily activities.

The unproven treatment market — dominated by clinics offering injections of platelet-rich plasma, homogenized fat cells or mesenchymal stem cells into damaged joints — has grown large precisely because so many patients arrive at the end of their options.

The scientific premise behind mesenchymal stem cell injections isn't baseless, and Stanford Medicine researchers are investigating their potential for joint repair. These stem cells are multipotent progenitor cells — found in bone marrow, fat and other tissues — capable of differentiating into cells called chondrocytes that build and maintain cartilage, among other cell types. But that process is slow and exacting: In the lab, coaxing mesenchymal stem cells toward a cartilage fate typically takes weeks of culture with specific growth factors, delivered in a controlled, three-dimensional environment that mimics the

**MICE TREATED WITH THE DRUG DEVELOPED NEW, YOUNG-LOOKING CARTILAGE.**

joint's biochemical and mechanical cues. Skip that step, and the cells have no particular reason to become cartilage at all.

The problem is that most clinics offering "stem cell" injections don't even attempt to isolate or test these cells. They withdraw fat or bone marrow, spin it in a centrifuge and reinject the resulting mixture the same day. That mixture is a slurry in which true mesenchymal stem cells usually make up a tiny fraction of the cells, diluted among blood cells, immune cells and debris. But it has none of the purification, expansion or priming that legitimate research relies on. That gap — between what these specialized stem cells can plausibly do under carefully engineered conditions and what an unpurified, same-day injection can deliver — explains why these treatments so rarely outperform placebo in controlled trials. They are expensive, too. A same-day procedure can cost around $5,000 to $10,000.

Platelet-rich plasma, or PRP — falls into a similar gray area. Platelets are naturally occurring cell fragments in the blood that are packed with proteins that encourage cell growth and tissue repair. Although injection of PRP into damaged or arthritic joints has been shown to provide moderate pain relief and increased function for some people with mild to moderate knee arthritis, clinics marketing the "treatments" often claim much larger, universal benefits. The price at these clinics runs around $1,000 to $4,500 per course of treatment.

Chu, who led an NIH-funded conference on the responsible use of biologics in orthopaedic surgery, said this "one-injection-fits-all" approach ignores her PRP research finding that its effectiveness is highly variable and not well understood. "Platelet-rich plasma is only as good as what you have to offer based on your age, your health, and your individual ability to repair and heal," she said. In one study, she found that PRP from young, healthy people had an anti-inflammatory effect on cartilage tissue in culture, but PRP from older people with osteoarthritis actually stimulated inflammation, "which is not what you want." Her development of joint avatars will allow her to identify which patients would benefit most.

Blau is direct about what has filled the vacuum of available therapies for joint pain. "People are desperate, so they go anywhere," she said. "There's really no biological basis for the treatments promoted by unregulated clinics working. If you see an effect, it's placebo."

What Stanford Medicine researchers are building — scaffolds that recruit the body's own repair machinery, imaging sensitive enough to catch disease before it declares itself, organoids that let surgeons test what will work for a specific patient, and now a drug that reprograms the cells that were thought to be beyond reach — attempts to close that gap with something more durable. **SM**

*— Contact Krista Conger at kristac@stanford.edu*

## LESSONS FROM ANTLERS

HOW 3D-PRINTED SCAFFOLDS AND ANTLER STEM CELLS ADVANCE BONE REPAIR

Yunzhi Peter Yang, PhD, professor of orthopaedic surgery, envisions a future where surgeons can print the structures needed to rebuild the human skeleton. His lab develops 3D-printing technology to combine biodegradable scaffolds that have bonelike mechanical stability with soft hydrogel components loaded with stem cells or growth factors. He is designing these systems to recapitulate the spatial organization of cells involved in skeleton formation, biological cues within native tissues — including bone, tendon and muscle — and complex tissue interfaces such as bone-tendon and bone-cartilage junctions. He has collaborated with Stuart Goodman, MD, PhD, the Robert L. and Mary Ellenburg Professor in Surgery, for nearly a decade on National Institutes of Health-funded grants to study biodegradable metals — an effort to build implants that do their structural job and then dissolve, leaving nothing behind to complicate future surgery.

This approach has already moved from bench to turf: When a young racehorse in Kentucky developed a life-threatening bone tumor in its jaw and faced euthanasia, Yang's team custom-fabricated a device to fill the defect. Six months later, the bone had healed completely, and the horse raced competitively. The Food and Drug Administration has since given the technology breakthrough device designation — fast-tracking the review process for promising medical devices addressing serious unmet clinical needs.

Yang has also spent over a decade studying deer antlers — among the fastest-growing tissues in nature, capable of adding an inch per day — whose stem cells reside in the periosteum, the same bone-encasing membrane that gives bone its regenerative advantage over cartilage. He believes the mechanisms behind antler growth, which is both extraordinarily rapid and precisely controlled, holds clues for human tissue repair. "If we can discover a mechanism where they grow fast but without forming cancer, that would be huge," he said.

His goal is a hybrid bioprinting system able to fabricate entire limbs — skin, muscle, cartilage and bone together — tailored to individual patients. **SM**

MADE TO MOVE

From musculoskeletal development to peak performance

# BUILT TO LAST

## WHY JOINT REPLACEMENT IS BETTER AND MORE POPULAR THAN EVER

By Mark Conley

ILLUSTRATION BY VIOLET FRANCES

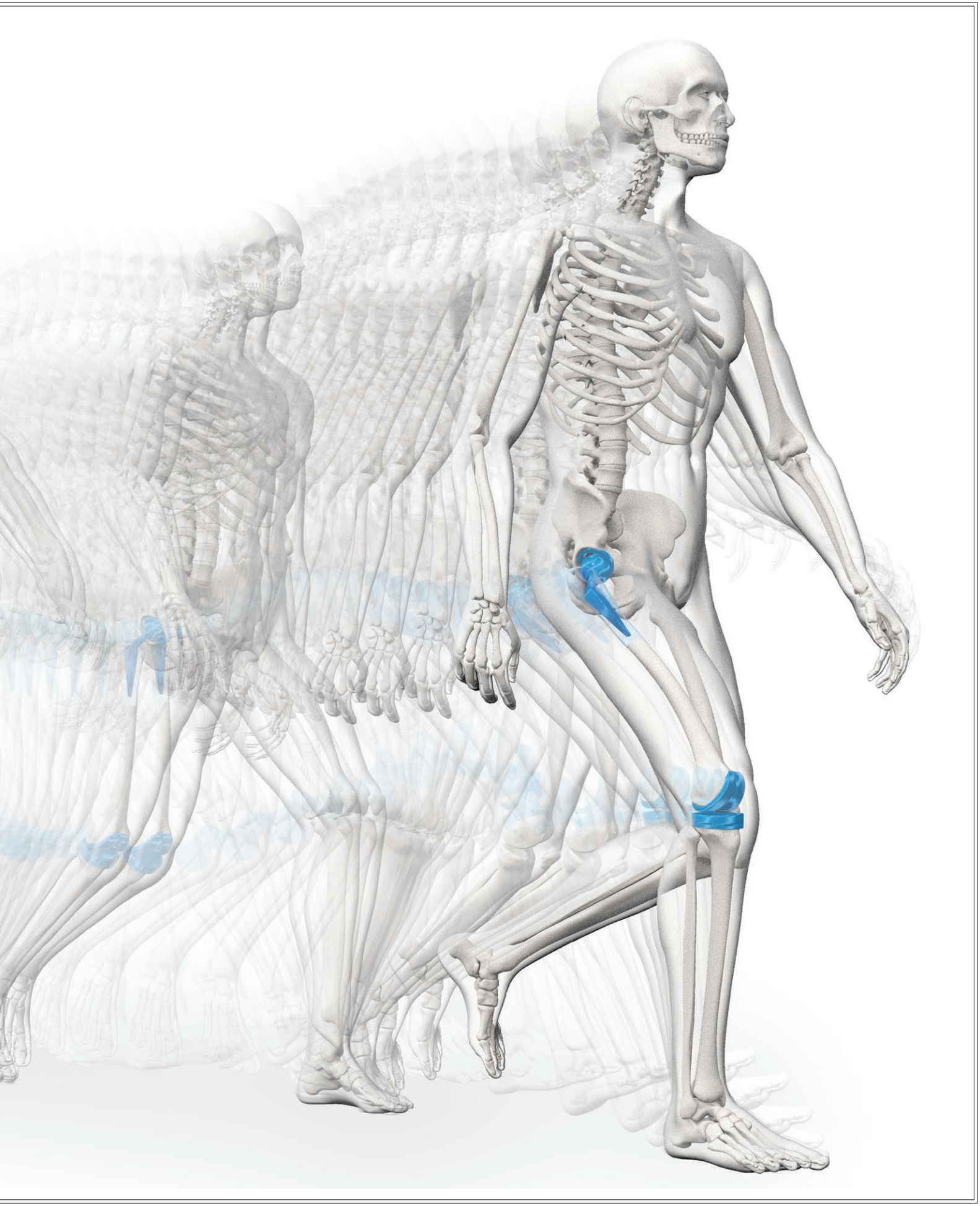
PHOTOGRAPHY BY MISHA GRAVENOR

At age 17, Chloe was suffering from painful osteoarthritis in her right hip, the by-product of a serious childhood joint disorder. That's when her family was referred to orthopaedic surgeon William Maloney, MD, at Stanford Medicine.

Maloney, the Boswell Chair of Orthopaedics, was able to replace the hip with confidence despite the patient's young age, knowing the newly developed plastic-lined joint would have a longer lifespan than its predecessors. That was nearly two decades ago.

"She was finally able to run and play basketball," he said. "I saw her recently and she's got a child of her own. We X-rayed the hip and it looks like the day we put it in. It should last forever."

Chloe, whose name has been changed at her request, received her hip replacement in the early days of this ongoing "polyethylene period" — marked by the advent of a seemingly wear-resistant plastic perfect for replicating the smooth, frictionless movement cartilage naturally provides to a hip socket, knee joint or shoulder. It supplanted earlier



DURING KNEE REPLACEMENTS, THIS CUTTING TOOL PROVIDES SURGEONS WITH HAPTIC FEEDBACK TO KEEP THEIR BONE RESECTIONS WITHIN BOUNDS ESTABLISHED BY A 3D MODEL. THE BLUE DISCS ARE LOCATION TRACKERS.

forms of plastic that often wore down and caused osteolysis — where the immune system's attack on stray plastic particles instead dissolved the surrounding bone and triggered an onslaught of revision surgeries.

Polyethylene is the predominant form of plastic worldwide, a polymer constituting everything from sandwich bags to squeeze bottles to playground equipment. The version used for today's joint parts was strengthened via ionizing radiation, which cross-links the material at a molecular level.

While there is legitimate consternation about plastic's environmental impact, the power of a molecularly optimized piece to fortify a new hip or knee — potentially for a person's remaining lifetime — has altered the joint replacement landscape.

"It's changed the game — there's really no other way to say it," said Jessica Hooper, MD, a Stanford Medicine surgeon and a clinical assistant professor of orthopaedic surgery.

The previous norm for a replacement joint's longevity was 10 to 15 years. Now an implant is expected to last for the rest of most recipients' lives, which explains why the number of people having a hip or knee replaced has surged — younger and older, suffering from a wide range of disability. That growth is expected to accelerate as the next decade dawns.

"We're doing well over a million joint replacements, knees and hips, in the U.S. annually," said Jason Lipof, MD, a Stanford Medicine surgeon and a clinical assistant professor of orthopaedic surgery. "And that number is expected to keep climbing."

## Many roads to a new hip

FORTUNATELY, SAID MALONEY, THE INTEREST of budding physicians in the field of arthroplasty — the term used to encompass surgery that replaces, remodels or realigns joint bone surfaces — is keeping pace with demand, partly thanks to advancements that go beyond materials. Among them are robotics, augmented reality and artificial intelligence, not to mention just fresh approaches to surgery.

A case in point: Anterior hip replacement, a different take on the more standard hip replacement procedures, performed via a small incision at the front of the hip, has gained traction because of its purported improvements in sparing muscle, limiting the risk of dislocation and speeding recovery time. It's also what the new generation of orthopaedists is being taught, which is one reason anterior has so quickly caught up to posterior in annual U.S. surgeries.

It is, however, a more technically demanding procedure with a steeper learning curve that often requires a specialized surgical table. The table looks more like a piece of complex workout equipment and lets the team capture X-ray views of the hip joint from multiple angles.

Posterior, the most common approach for decades, involves an incision at the buttocks, rather than the front of the thigh, as

**'FOR THE MOST PART, I FEEL COMFORTABLE TELLING MY KNEE AND HIP PATIENTS THEY CAN GO BACK TO DOING WHATEVER IT IS THEY DO — CYCLING, HIKING, SURFING, PICKLEBALL, AERIAL ACROBATICS, BEACH VOLLEYBALL.'**

JESSICA HOOPER, MD, CLINICAL ASSISTANT PROFESSOR OF ORTHOPAEDIC SURGERY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**"WE NOW SEE 80-YEAR-OLDS IN OUR CLINIC WHO ARE HIKING AND TAKING 20-MILE BIKE TRIPS AND WALKING 18 HOLES OF GOLF AND PLAYING TENNIS. THE ADAGE THAT TODAY'S 80-YEAR-OLD IS YESTERDAY'S 60-YEAR-OLD IS REALLY TRUE."**

WILLIAM MALONEY, MD,
BOSWELL CHAIR OF ORTHOPAEDICS

patients lie on their side on a flat table. It provides a fuller view without X-rays and is better for muscular and larger people. But it can also necessitate muscle detachment, which increases healing time immediately after surgery.

The consensus: Both versions of the surgery have successful track records. As Maloney noted, there's a reason total hip replacement was dubbed the surgery of the century by the medical community nearly two decades ago: "Either way you do it, it's a great surgery."

Variety of choice is a nice bonus. But advancements in materials, along with precision-aiding technology, are giving surgeons new opportunities to get their patients back to moving the way they used to — particularly patients who want to push the limits with their newly installed parts.

"For the most part, I feel comfortable telling my knee and hip patients they can go back to doing whatever it is they do — cycling, hiking, surfing, pickleball, aerial acrobatics, beach volleyball," Hooper said. "I tell them, 'Don't worry about it — just go back to living your best life.'"

## Same-day joint replacement

HOOPER PERFORMS THE ANTERIOR HIP approach, uses robotics to better understand a joint's natural movement spectrum during knee replacement surgery, and is bullish on the potential of new technology to give surgeons more detailed digital imagery from which to work.

But she's perhaps most impressed by more fundamental advancements she has witnessed: More people of all ages and health levels are getting joint replacements and going home the same day instead of staying in the hospital. Better pain control is a big reason this works, making it possible for patients to recover at home. Close attention is also being paid to the pre- and post-surgery experience, she said.

"We're optimizing patients beforehand — getting them to their healthiest baseline before we go in and do this big surgery," Hooper said. "We also have a director of perioperative medicine for anesthesia, whose job is to look beyond the hospital experience and think about what pain management should look like when the patient goes home."

Hooper said this holistic approach is paying dividends for surgeons and patients alike, limiting complications and allowing safe same-day trips home, where recovery begins in more comfortable surroundings.

"We were headed for more of an outpatient future already, and then COVID took the hospital out of the equation," said Hooper. "So, we've really been trying to optimize the patient's surgical journey, to get them through it as quickly and easily as possible."

Lipof said he thinks a move toward regional anesthesia with light sedation — such as a targeted spinal or epidural pain block — and away from general anesthesia, which can leave patients groggy and nauseated, has also played a big role in getting patients home the same day. "You're up and walking and doing stairs with physical therapy a couple hours after surgery," he said. "Most people do really well."

## Joints are not created equal

WHILE THE BALL-AND-SOCKET MOVEMENT of the hip is simple, and most hip replacement patients are satisfied with their results, the knee provides a more complex equation. According to Lipof, 15% to 20% of total knee replacement patients nationwide express some level of dissatisfaction.

Besides the fact that knees are just "a bit more complicated," Hooper said that attempts to personalize alignment of a knee by matching up imagery of a patient's other knee to the one being replaced are well meaning but still lack precision.

"An X-ray isn't a perfect way to evaluate that," she said. "We don't have good tools to evaluate either a native knee or a replacement in motion, in a reproducible setting. So until those diagnostics become more available, there's a lot of information we're missing."

Lipof and Hooper use a robotic assistant device during knee procedures to help precisely guide their measurements when making bone cuts and aligning the new parts. Akin to a smart version of a handheld power tool, it uses haptic feedback to keep the cutting blade within bounds established by a presurgery 3D model and measures tension in the ligaments so the surgeon can get the new parts into angles that are as natural as possible.

"Something kind of magic happens with the robotics, where it gives you the data and insights into that patient's anatomy,"

Lipof said. "You can use it to understand what their new knee is going to do and how to make it feel more like their own knee."

Along with robotics and advances in materials — not only the improved plastic but also ceramic and metals, including titanium alloys, are used in the knee — new technology is coming down the pike. Computer navigation gives surgeons a 3D map of the joint in the operating room during surgery, and augmented reality smart glasses overlay real-time, patient-specific 3D data onto a surgeon's field of view. And Lipof believes that, in the next year or two, we will see semiautonomous robots helping perform knee replacement with "likely fully autonomous robots coming in the near future to an operating room near you."

The closest thing to that level of futurism now can be seen in what's known as a "smart knee," where a replacement joint includes a sensor that can relay real-time data to a doctor and provide recovery metrics to a patient and their physical therapist.

DEREK AMANATULLAH, MD, PHD, ASSOCIATE PROFESSOR OF ORTHOPAEDIC SURGERY, IS KNOWN FOR PUSHING BEYOND WHAT MOST SURGEONS ARE WILLING TO DO.

## A joint implant that monitors your health

IN MARCH 2026, LIPOF BECAME the first Stanford Medicine surgeon to implant a smart knee. The patient, Barry Mainz, a Silicon Valley executive, learned about the newly available device from a friend in the tech world. Mainz hoped the smart knee, which is essentially an implanted activity tracker, would help him return to skiing, running and hiking as quickly as possible after his failing knee joint was replaced.

"Tons of people use personal activity trackers. This is just one you don't have to remember to take on and off, or charge," Lipof said. "The data it collects, like step count, range of motion, walking stride, gets put into these graphs and shows a patient their progress. So, it's a motivating factor in recovery."

Mainz, immersed in tech and still a dedicated athlete in his early 60s, was perhaps the perfectly motivated first patient. "I wanted my life back," he said. "And with the data you get,


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there's no BSing yourself about your rehab. It's cause and effect right there for you on the screen."

## Beyond disability management

DEREK AMANATULLAH, MD, PHD, an associate professor of orthopaedic surgery, remembers spending much of his early career redoing joint replacements whose materials had worn out, rather than helping patients decide when a new joint would improve their active life. Now, with those types of drastic revisions mostly gone, it's like those days have "totally disappeared," he said, "and it's a huge boon to patients."

The profession has shifted from managing disability to preserving lifestyle. And the material advancement makes it a potential game changer for 80-somethings and 50-somethings alike. "We now see 80-year-olds in our clinic who are hiking and taking 20-mile bike trips and walking 18 holes of golf and playing tennis," Maloney said. "The adage that today's 80-year-old is yesterday's 60-year-old is really true."

Some, of course, are still hoping for solutions that won't leave them feeling foreign-material-laden and bionic. Research on stem cells and other regenerative mechanisms continues, including a promising recent Stanford Medicine study that regrew cartilage in the knee joints of mice and in human tissue.

While biologic resurfacing — a joint-sparing technique to repair or replace damaged cartilage and bone with natural tissues (allografts/autografts) rather than metal and plastic — is an exciting concept being studied, it's not imminent. "That's the holy grail, no doubt, and it'll come. People are working on it," Maloney said. "But it's not like we have to solve the problem tomorrow. Because the outcomes right now are pretty darned good."

There remains, though, one risk that every joint replacement patient faces: infection. It's rare, but it can be extremely serious. Amanatullah, who has researched the problem in depth, often presents a graph showing that the five-year mortality of a chronic joint infection rivals that of breast cancer and colon cancer.

It also can seem random. Amanatullah's research suggests that most of the risk comes not from the instruments or the people in the operating room but from the patient's own body. It remains unclear whether bacteria are brought in from the skin surface as surgery begins or whether they are awakened from dormant microbial colonies already living deep within the hip or knee.

Since prophylactic antibiotics, which are taken ahead of surgeries to avoid bacterial infections, became routine roughly 50 years ago, Maloney said, "there's been no improvement in infection rate, so it's really an unsolved problem. The big winner will be whoever can solve or put a dent in the infection problem."

The good news: The risk of infection remains low — 1% to 2% for each joint replaced — which is why the replacement numbers keep climbing.

Amanatullah is known for pushing beyond what most surgeons are willing to do. He operates, for instance, on patients with a high body mass index, a group he believes is marginalized because their surgeries can be more difficult. "Am I supposed to tell you you're too risky, that you have to lose weight to earn surgery from me?" he said, emphasizing that the added risk is lower in absolute terms than patients are often told.

For the million-plus Americans who will get joints replaced in the coming year, the risk-reward quotient has swung far enough in favor of reward. Which also happens to be the word that comes to mind for surgeons thinking how fortunate they are to be in this moment with materials and technology.

"The most rewarding part is just watching people get back to their normal life," Hooper said. "That's really the whole point of doing this."

The 17-year-old patient that Maloney was able to help get back to normal life nearly two decades ago agrees. Chloe has backpacked across Southeast Asia, married, continues to play rec basketball occasionally and is set to give birth to her second child. "The procedure profoundly changed my life," she said. "I have been so grateful that this hip has been able to endure the many chapters of life — and I hope for many more!" SM

*— Contact Mark Conley at mjconley@stanford.edu*

**KEY TAKEAWAYS**

More than 20% of adults in the U.S. suffer from arthritis or chronic joint issues.

Nearly half of those people report that those joint issues limit their everyday activities.

Thanks mostly to advances in materials, the expected lifespan of replacement hips and knees has increased in the past two decades from 10 to 15 years to 25 years or more.

**'SOMETHING KIND OF MAGIC HAPPENS WITH THE ROBOTICS, WHERE IT GIVES YOU THE DATA AND INSIGHTS INTO THAT PATIENT'S ANATOMY. YOU CAN USE IT TO UNDERSTAND WHAT THEIR NEW KNEE IS GOING TO DO... .'**

JASON LIPOF, MD,
CLINICAL ASSISTANT PROFESSOR OF
ORTHOPAEDIC SURGERY

# GAME CHANGERS

## THE INNOVATIONS THAT KEEP COLLEGE AND PROFESSIONAL ATHLETES IN TOP FORM ARE BENEFITING THE REST OF US

By Sarah C.P. Williams

ILLUSTRATION BY JUAN BERNABEU

IT'S A SUNNY SATURDAY IN OCTOBER, and the crowd at Stanford Stadium is roaring as the Cardinal football team pushes down the field. A wide receiver sprints toward the end zone and cuts sharply inward as the ball soars toward him. But before he makes the catch, he grabs the back of his leg and hits the ground.

Within seconds, Stanford Medicine orthopaedic surgeon Seth L. Sherman, MD, is at the player's side. Within minutes, the injury has been assessed; within hours, it has been X-rayed; and by the next day, there is an MRI, a medical plan and a timeline to return to practice.

"The urgency and intensity with which we get to these players' injuries and start working them up and treating them is extraordinarily quick," said Sherman, an associate professor of orthopaedic surgery who has also worked with the Chicago Bulls and Missouri Tigers.

Across town, a 40-year-old dad sustains the same hamstring injury playing soccer in the backyard. He ices it, takes some ibuprofen and props it up on the couch. A week later, still limping around, he visits his primary care doctor. After a normal X-ray, the busy father is told he'll need to try six weeks of physical therapy before insurance will pay for an MRI.

It seems, at first glance, that these two patients are being treated in entirely different worlds. But Stanford Medicine clinicians said the pressure to treat elite athletes with such speed and effectiveness is driving innovation in the universe


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of sports medicine. Over time, that translates to new tools that benefit everyone, from weekend warriors and amateur athletes to average people who sustain a fall.

"This has actually been going on for decades," said Marc Safran, MD, chief of the Stanford Division of Sports Medicine. "If you look back to when Joe Namath tore his ACL playing football in the 1960s, they developed the ACL brace to get him back on the field, and now ACL braces are very common."

Today, braces aren't the only treatment being developed for athletes to return to the field. Minimally invasive surgeries, new drugs and injections to promote healing are increasingly common. Digital technologies that assess movement patterns and an evolving understanding of how the body moves and heals are also in play. All are making their way off the field and into everyday medicine.

At Stanford, this flow of knowledge is deliberate. The Wu Tsai Human Performance Alliance — a research initiative connecting Stanford's sports medicine clinicians, bioengineers and scientists — was built on the idea that elite athletes can provide valuable insights for the rest of us. In sports medicine and orthopaedics, physicians treat college and professional athletes alongside everyone else, carrying what they learn from one patient to the next.

## First, the diagnosis

IN THE EARLY 2000S, SAFRAN BEGAN noticing something unusual in his most flexible patients — ballet dancers, gymnasts and figure skaters. They showed up at his office with pain in their hips but no diagnosis. Their symptoms didn't fit with any known condition, and scans didn't show any obvious problems. Safran suspected that something was causing their hips to shift subtly out of position while they were moving; it reminded him of shoulder microinstability, a condition sometimes seen in swimmers.

"A lot of people in the field didn't think it was possible to have microinstability like this in the hip," said Safran, a professor of orthopaedic surgery.

But the extreme range of motion that dancers and gymnasts put their hips through made the condition stand out, Safran thought. He carefully tracked the athletes' movements and which remedies made their symptoms improve. In 2011, he published his first clinical paper on hip microinstability. It is now a recognized diagnosis with defined treatment options — physical therapy or minimally invasive surgery that tightens a component of the hip joint.

Recently, an active, middle-aged woman came to Safran with hip pain. Other doctors had dismissed her pain or told her she would never return to her previous level of activity. Safran quickly recognized it as hip microinstability and treated her surgically. "I just got a note from her about how incredibly grateful she was that I'd been able to treat her and letting me know that she had just finished a triathlon," Safran said. "That wouldn't have happened if we hadn't started out studying this condition in dancers and gymnasts."

When top-level athletes have a joint, muscle or bone problem, physicians can quickly rule out factors such as obesity, improper training or lack of exercise that might complicate diagnoses in the general public. That makes it easier to notice new patterns of injury and test new treatments.

"We are interacting with elite athletes on a daily basis, and it forces us to keep pushing these boundaries and advancing the field," said Safran, who has served as the chief orthopaedic consultant for the Women's Tennis Association and as a consultant for the NBA and NHL players' associations.

## Then, the treatment

THE SAME DYNAMIC THAT PRODUCES new diagnoses among elite athletes also accelerates new treatments. Once a condition is identified in elite athletes, the pressure to get them back to competition quickly means those athletes are the first to try the latest drug or surgery. That's not only because of resources — teams and coaches willing to put money toward treatments that aren't yet covered by insurance — but also because collegiate or professional athletes might weigh risks and benefits differently than most people do.

"For them, every minute of time loss equates to an impact on their career and future prospects," Sherman said. "Sports medicine is driven by the search for those holy grail treatments that can get athletes back in the action as fast as possible."

The path to platelet-rich plasma therapy is one of the clearest examples of this. The therapy, in which growth factors from the patient's blood are concentrated and injected back into an injury site, had early scientific promise but wasn't widely used. Then, athletes began using it for tendon injuries.

When sports stars like Rafael Nadal and Tiger Woods spoke publicly in the late 2000s about their use of the therapy, known as PRP, to recover from injuries, patients began asking about it.

'WE ARE INTERACTING WITH ELITE ATHLETES ON A DAILY BASIS, AND IT FORCES US TO KEEP PUSHING THESE BOUNDARIES AND ADVANCING THE FIELD.'

**KEY TAKEAWAYS**

The gap between elite and everyday medical care is closing. Analyses of how you move — designed for injury prevention and rehab — once required a $150,000 lab; they can now run on two smartphones.

Physicians are learning how to diagnose and treat sports injuries by working with elite athletes, but their findings have implications for improving care for everyone else.

This could mean more efficient ways to diagnose and treat your orthopaedic injuries and more personalized rehab routines that get you back to everyday life more quickly.

In some ways, the celebrity endorsements outpaced the science. The large randomized controlled trials needed to find out how well it works, and for which conditions, are still ongoing. Today, PRP is commonly used in sports medicine clinics, even as researchers build the evidence base behind it. Most major insurers still classify it as experimental and require patients to pay out of pocket.

"It's not that athletes are trying things that have absolutely no evidence," Sherman said. "It's that they try to be early adopters of new treatments. They start using things before the randomized trials and insurance policies have caught up to the science."

To keep advancing that science, Stanford's orthopaedic team tracks every platelet-rich plasma injection its clinicians deliver, studying how different preparations vary and how well it works for different conditions. The nuanced findings will likely first impact the athletes seen at Stanford Medicine and later move toward personalized treatment for all.

Blood flow restriction followed a similar trajectory. It uses a cuff to restrict blood flow to a limb during light exercise, forcing muscles to work harder than they otherwise would and making it possible to build and maintain muscle that protects and stabilizes a healing injury. It was developed to rehabilitate injured soldiers, then moved into NFL training rooms and collegiate athletic programs. Now, Safran said, it's "kind of everywhere."

But like with PRP, the science of blood flow restriction is still catching up to the hype. Studies show promising results, and physical therapists across the country use it routinely with everyone from elderly patients with muscle loss to recreational athletes recovering from injury. But researchers say more rigorous trials are needed. A Stanford Medicine clinical trial is being conducted to determine whether it can help improve grip strength in people with wrist pain.

Safran and Sherman both hesitate to predict what the next treatment to move from elite athletes to the average clinic might be. Stem cell treatments, new biologics and peptides are all in the pipeline. But they said whatever the next big thing is will likely be tested at Stanford — in athletes and non-athletes alike.

"Stanford is built for that kind of translation," Safran said. "We have 900-plus elite student-athletes and work with a lot of other teams in different sports. But we also have a multitranslational network of researchers from biomechanics, stem cell biology, mechanical biology and imaging technology that allows us, when we're able to collaborate, to be much greater than the sum of our parts."

## After an injury

WHEN A STANFORD CARDINAL ATHLETE finishes formal rehab after an ACL reconstruction, recovery doesn't end there. As they begin attending practices again, coaches and trainers watch their every move. Force plates measure the symmetry of their jump landings. GPS sensors track their motions. The answer to whether they are ready to return to competition — the track, the football field or a court — is predicted by a continuous stream of data.

"There are all these sophisticated tools and technologies that the elite athlete has access to," Sherman said.

For an average person having the same ACL reconstruction, the pathway out of recovery is different. The patient goes home with a set of exercises, a limited number of insurance-covered physical therapy sessions, and a follow-up appointment scheduled for three months out.

The gap between the end of formal rehab and any return to sport — what Sherman called the black box — is managed, for most people, with very little information. A patient may have to rely on gut feelings to decide whether to try going on a run, playing in a weekend pickup game or even something as simple as carrying groceries up a flight of stairs.

That gap inspired Sherman to launch a collaboration with the Wu Tsai Human Performance Alliance's Digital Athlete program. His team is helping test whether smartphone-recorded movements, like squats or jumps, can predict healing and recovery patterns as effectively as in-person trainers.

"This kind of surrogate test on their phone could give someone powerful information about their relative risk of reinjury," Sherman said, "even if they're on a grass field two hours from the nearest clinic."

## Before it happens

TREATING INJURIES IS ONE THING, but the loftier goal of clinicians who work in sports medicine is to prevent injuries in the first place. For elite athletes, that means constant monitoring of their weaknesses and imbalances and staying on the lookout for the earliest signs of overtraining or breakdown.

"An NBA team has 15 athletes and 15 coaches and trainers,"

CONTINUES ON PAGE 44

# KEEPING ATHLETES WITH DISABILITIES IN THE GAME

## INSIDE THE SPECIALIZED FIELD OF ADAPTIVE SPORTS MEDICINE

SYDNEY BARTA'S STRESS FRACTURE WAS NOT PARTICULARLY UNUSUAL.

In 2024, the Stanford University sprinter broke her right foot while training for a race. Foot stress fractures are common overuse injuries among runners, especially young female runners.

"For a long time, I had to modify a lot of workouts because of my foot injury. But I had teammates with similar injuries who also had to modify," Barta said. "All of our bodies are different. Mine just happens to be very different."

That's because the foot Barta broke is her only foot. Barta, who recently graduated with a major in bioengineering, is an amputee who lost her left

By Rachel Tompa

PHOTOGRAPHY BY MISHA GRAVENOR


SYDNEY BARTA,
STANFORD UNIVERSITY
SPRINTER


foot and part of her lower left leg after a metal scaffolding fell on her following a race when she was 6. She is also a Paralympian and the first amputee to compete for the university's track and field team.

Barta has always been into sports — her mother was an athlete and encouraged Barta to try different sports once she was fitted with a prosthetic. She tried softball, basketball, figure skating and water polo, all with nondisabled teams. But she was a young teen before she learned about adaptive sports through other families she and her mother met through the shop where she purchased her prosthetic. A parent told them about an adaptive track program in Indiana, and Barta signed up.

"I ended up falling in love with competing but also competing on the Para side of things. It was really unique for me to have that community," Barta said. "It's not often that you meet people who also love sports, have your same disability and understand that struggle, whether that's the literal struggle of completing the workouts with a disability or the struggle to be included on a team."

That Barta broke her sound foot is not unusual for an athlete with a disability, said Yetsa Tuakli-Wosornu, MD, associate professor of orthopaedic surgery and founding director of the Sports Equity Lab at Stanford, a research group aimed at eliminating inequities in sports.

"Injuries related to bodily asymmetry are higher amongst athletes with physical disabilities," said Tuakli-Wosornu. "That can include overuse injuries on the unaffected side."

Sports can wear down any body — the biomechanics of repeated movement can eventually strain most athletes. But athletes with physical impairments have more bodily stresses from their activities, and those stresses and strains vary depending on the type of disability and the particular sport. Barta, who trains and competes with a specialized flexible prosthesis known as a running blade, can feel the strain of that asymmetry as she runs.

"I have a hard time slowing down because one of my legs is a spring. When I'm slowing down, all that force is going into one of my ankles, one of my knees," she said. "And because all of my force production happens on one side of my body, those joints end up being a lot more sore."

This is the world of adaptive sports. Like sports medicine for athletes without disabilities, adaptive sports medicine entails a constant tension between recovery and well-being versus

performance optimization and competition schedules, Tuakli-Wosornu said. It requires a deep understanding of how different physical and mental impairments intersect with sports' demands. Working or competing in this world also means confronting built-in societal barriers that can prevent athletes with disabilities from fully and joyfully participating in sports.

## Learning from the Games

ALTHOUGH THE FIRST official Paralympic Games took place in 1960 in Rome, sports for athletes with impairments have existed for far longer. The first Olympian with a disability, gymnast and amputee George Eyser, competed in the 1904 Olympic Games.

The Paralympic Games evolved from a rehabilitation sports program at the spinal cord injury center for British veterans of World War II at the Stoke Mandeville Hospital in Buckinghamshire, Great Britain. The program director organized an archery competition for 16 veterans with disabilities to coincide with the 1948 Olympic Games in London.

The most recent summer Paralympic Games, held in Paris in 2024, saw more than 4,400 athletes competing in 549 different events. (The term *Paralympic* derives not from *paraplegic* but from *parallel*, because the Paralympic Games run alongside the Olympic Games. Many use the term *Para* to refer to all adaptive sports or all athletes with disabilities, not just athletes who participate in the Paralympic Games.)

Tuakli-Wosornu, a former long jumper for Ghana's national track team, was the first welfare officer for the International Paralympic Committee, the organization that oversees the Paralympic Games. Since 2012, the IPC has gathered data on injury and illness among competing athletes, representing one of the largest epidemiological datasets of athletes with disabilities in the world.

Athletes competing in the Paralympic Games have more than double the number of injuries as athletes in the Olympic Games. And certain Paralympic sports seem to carry especially high injury burden. For example, Tuakli-Wosornu and her colleagues found that players of Para ice hockey, also known as sled hockey, are prone to femur fractures and other major bone breaks due to high-speed collisions of sleds of various heights. That finding led to a change in the sled equipment used at the Games. Traumatic injury rates plummeted.

The committee also identified gaps in concussion and other brain injury assessments for visually impaired athletes — namely, that the standard assessments involved a visual test. So, the committee developed new guidelines.

"These surveys ... definitely have their place in terms of exposing gaps in our knowledge that could render Para athletes at higher risk of preventable injury," Tuakli-Wosornu said.

**KEY TAKEAWAYS**

Among people with disabilities, participation in adaptive sports is associated with improved mood, new friendships, stronger community bonds and greater employment opportunities.

Athletes competing in the Paralympic Games have more than double the number of injuries as those in the Olympic Games. Many of these injuries are unique to athletes with disabilities and vary depending on the sport and the specific impairment.

**'I HAVE A HARD TIME SLOWING DOWN BECAUSE ONE OF MY LEGS IS A SPRING. WHEN I'M SLOWING DOWN, ALL THAT FORCE IS GOING INTO ONE OF MY ANKLES, ONE OF MY KNEES.'**

## Specialized expertise

"YOU DEFINITELY need a different level of expertise as a sports doctor working with athletes with disabilities," said Michael Fredericson, MD, a professor of orthopaedic surgery and head team physician for the Stanford University track and field and swimming teams.

Fredericson and Tuakli-Wosornu are trained in physical medicine and rehabilitation, a specialty that focuses on optimizing function and quality of life after injury, regardless of whether that injury is permanent. It's the perfect kind of training for working with all athletes, Fredericson said.

"Our training is on how to help people with an injury or disability to maximize their function," he said. "And that's really what we're doing in sports medicine, too."

Some adaptive sports injuries Fredericson and his colleagues treat are similar to those in broader sports medicine, like Barta's overuse injury, but they might be more common or severe in athletes with impairments. For example, head injuries, already prevalent in certain team sports like soccer, are even more common in athletes with a visual impairment.

But other injuries are specific to athletes with disabilities. While athletes without disabilities are most likely to incur lower-body injuries, those who use wheelchairs are more prone

to upper-body injuries, specifically shoulder injuries.

For paraplegic athletes, competing in hot weather can quickly become an emergency because they have difficulty regulating their body temperature and can miss the effects of overheating.

And those who use wheelchairs, prosthetics or other adaptive equipment can develop pressure sores where their bodies meet the engineered devices.

"Sports is a high-risk domain. As long as body parts are moving unpredictably, it's a dynamic, sometimes chaotic system," Tuakli-Wosornu said. "In Para sports, there are additional injuries related to anatomic nuances that are unique to athletes with impairments."

## Athletics at all levels

FREDERICSON RUNS a fellowship program that trains three medical fellows per year in sports medicine with hands-on training as physicians for the university's sports teams. About a decade ago, he and the fellows established an adaptive sports clinic at the VA Palo Alto Health Care System. The weekly clinic brings together physicians, recreational therapists, physical therapists, occupational therapists and psychologists to aid veterans with disabilities who want to participate in sports.

A lot of the clinical work involves matching their patients, who come in at all levels of sport, with accessible activities.

"Some of our vets are Paralympians; some of them don't do any physical activity at all," said Chantal Nguyen, MD, a clinical assistant professor of orthopaedic surgery who recently completed her sports medicine fellowship. "There's no qualification of what an athlete is to use the clinic. The goal is to support them where they are."

They might be an elite athlete in need of specific facilities to practice or a wheelchair user curious about local recreational wheelchair sports leagues. Nguyen and her colleagues are tapped into adaptive sports organizations in the Bay Area and around the nation and can help patients make connections.

Though the benefits of physical activity are well known, less than half of people in the U.S. with physical impairments report doing regular physical activity, as compared with about two-thirds of people without disabilities.

But for these patients, participation in recreational sports is not just a feel-good exercise; it provides other tangible nonphysical benefits.

In 2019, Fredericson led a review of studies examining how organized sports impact quality of life for people with disabilities. These studies show that participating in sports is associated with improved mood, friendships and sense of community belonging, as well as higher employment rates.

"They feel better physically, they have improved social interactions, they tend to stay healthier, they have better energy," Fredericson said. "A lot of folks with disabilities are former athletes — and just knowing that you can still do that is really uplifting."

## Barriers to entry

BUT TAKING PART IN adaptive sports is often not as simple as finding a team and signing up.

Nguyen is conducting a nationwide survey asking athletes with disabilities about their experiences with sports. The answers she has received and the conversations she has had with athletes at sports events for veterans with disabilities have been eye-opening for her.

One athlete told her that the only wheelchair-accessible bathroom was two miles from her event. Another athlete, who uses a catheter to urinate, said that the competitions provided no private place for her to change it. Athletes who use wheelchairs and need to fly to events said their specialized chairs often end up broken by the airlines.

Any one of these experiences can, understandably, put an athlete off from wanting to continue in their sport, Nguyen said.

"Then they stop physical activity altogether. Sports are often an opportunity to enjoy physical activity, and if you take that away, people might not want to do any other form of exercise,"

**'A LOT OF FOLKS WITH DISABILITIES ARE FORMER ATHLETES — AND JUST KNOWING THAT YOU CAN STILL DO THAT IS REALLY UPLIFTING.' BUT TAKING PART IS OFTEN NOT AS SIMPLE AS FINDING A TEAM AND SIGNING UP.'**

MICHAEL FREDERICSON, MD (LEFT)
PROFESSOR OF ORTHOPAEDIC SURGERY AND HEAD TEAM PHYSICIAN FOR THE STANFORD UNIVERSITY TRACK AND FIELD AND SWIMMING TEAMS

YETSA TUAKLI-WOSORNU, MD, (RIGHT)
ASSOCIATE PROFESSOR OF ORTHOPAEDIC SURGERY AND FOUNDING DIRECTOR OF THE SPORTS EQUITY LAB AT STANFORD

WEB EXTRA Watch our video "How a Stanford para-athlete is leveling the playing field," featuring Sydney Barta and Yetsa Tuoakli-Wosornu, MD: stan.md/BartaVideo

she said. "If I didn't talk to the athletes, I wouldn't have realized these things."

There are barriers at all levels and stages of adaptive sports that go beyond infrastructure issues at events. Ableism is deeply woven into our society, and sports are no exception. Many people with disabilities are made to feel — or explicitly told — that they can't be athletes, said Tuakli-Wosornu. And opportunities to participate in adaptive sports are often few and far between. Tuakli-Wosornu was part of a 2024 study that found that only about 20% of NCAA Division 1 universities in the U.S. offer any kind of adaptive sport program, including recreational or club sports.

Perhaps because of all these barriers, disability representation in sports is also lacking. "You can't be what you can't see," she said.

Tuakli-Wosornu and Nguyen are using their positions in the adaptive sports medicine world to continue pushing for better access and care for athletes with disabilities.

"If we want to make sports safer, we have to understand the perspective of the athlete before a person without disabilities starts making rules," Nguyen said. "My goal is to listen to our athletes and to put as much emphasis on following safety regulations for our athletes with disabilities as we do for other athletes."

### From the track to the operating room

BARTA'S EXPERIENCES WITH medical care and competing as an athlete with a disability have spurred her career choices. As a bioengineering major, she conducted research on balance and gait in athletes at Stanford University's Human Performance Lab. In the fall, she's entering a master's degree program in engineering to focus on bone health as a Rhodes scholar at the University of Oxford. After that, she plans to return to the Stanford School of Medicine and specialize in orthopaedic surgery. She's also training for the 2028 Summer Paralympic Games in Los Angeles.

Barta had 21 surgeries after her childhood accident and another when she broke her right foot two years ago. Those experiences inspired her to pursue medicine so she can be the kind of physician she wishes she had.

"I've had a ton of interactions with the medical field," she said. "I've never had a female surgeon; I've never had a Division 1 athlete surgeon. I think I really would have benefited from a surgeon who knew intimately what it means to me to be an athlete and how central that is to my identity." **SM** — *Contact Rachel Tompa at medmag@stanford.edu*

CHANTAL NGUYEN, MD, CLINICAL ASSISTANT PROFESSOR OF ORTHOPAEDIC SURGERY

### BEGINNER'S GUIDE TO ADAPTIVE SPORTS AND STAYING SAFE

HOW TO FIND ADAPTIVE SPORTS NEAR YOU AND PROTECT YOUR BODY WHILE TRAINING

Chantal Nguyen, MD, a clinical assistant professor of orthopaedics at Stanford Medicine who works with athletes with disabilities, offers this advice for getting started in adaptive sports:

**Find programs and equipment loans**

- Search online for adaptive sports and recreation groups and get in touch — many offer tryout sessions, coaching and adaptive equipment loans. National organizations include MoveUnited and the Challenged Athletes Foundation.
- Bay Area adaptive sports organizations are listed on Stanford University's Diversity and Access Office site at stan.md/AthleteAccess.
- Your physician or physical therapist might also know of additional resources.

**Try an adaptive version of a sport you already like**

- Most sports have adaptive options (for example: wheelchair basketball, Para swimming and adaptive cycling). If you're not sure what fits best, try a few activities to see what you enjoy and what works for your body.

**Veterans: Check the VA**

- If you're a veteran, contact your local VA to ask about adaptive sports programs and events. Reach the VA Palo Alto Health Care System at stan.md/VetsAdaptive

**Get a medical evaluation before starting a new sport**

- Consider a pre-participation evaluation with a medical professional.

**Wheelchair athletes: Protect your shoulders**

- Preservation of shoulders is essential because they are used for both daily mobility and sport.
- A home exercise program emphasizing scapular stabilization and rotator cuff strengthening, plus efficient wheelchair propulsion technique, can reduce strain. Remember the importance of regular pressure relief, both at home and at events.

**Athletes with amputations: Check skin and prosthetic fit**

- Do frequent skin checks and make sure your prosthesis fits well during activity to reduce friction, blisters and skin breakdown.

**During puberty, kids' bones fortify themselves at a furious pace, accumulating 40% to 60% of all the minerals they'll ever have.** That lifetime bank of bone-strengthening calcium protects against the bone loss of old age.

"Puberty is a real window of opportunity for boosting peak bone mass," said Mary Leonard, MD, the Arline and Pete Harman Professor for the Chair of the Department of Pediatrics at Stanford Medicine. "But it's also a window of vulnerability for kids with chronic disease. If you're sick during those critical years of really fast growth, you're going to miss it."

Parents can protect growing skeletons by helping their children and teens get enough calcium and vitamin D and encouraging weight-bearing exercise instead of screen time. But the situation is extra challenging if a chronic disease is added to the mix.

In this Q&A, Leonard, the Adalyn Jay Physician-in-Chief at Lucile Packard Children's Hospital Stanford, describes her research on how chronic disease damages children's bones.

MARY LEONARD, MD, CHAIR OF PEDIATRICS AT STANFORD MEDICINE

**MADE TO MOVE**

From musculoskeletal development to peak performance

# WHEN CHILDHOOD ILLNESS HARMS THE BONES

## A PEDIATRIC RESEARCHER EXPLAINS PUBERTY'S CRITICAL WINDOW FOR BONE DEVELOPMENT — AND HOW CHRONIC ILLNESS CAN SLAM IT SHUT

By Erin Digitale

**Unlike the elderly, "these kids are not losing bone," she said. "They are failing to gain bone in the first place, with lifelong consequences."**

### Why do children need different bone care than adults?

Damage caused by chronic kidney disease is a good example.

The kidneys regulate vitamin D and calcium metabolism. When they're working poorly in adults, calcium leaches from the bones to the blood. But physicians avoid giving calcium supplements to adults with kidney disease because these patients have accelerated calcification of their blood vessels.

We've studied children with chronic kidney disease. Their biology is different: Their growing bones take up lots of calcium, and those on calcium-containing medications are much less likely to experience bone fractures. In other words, the way we manage bone health in adults with kidney disease is exactly the opposite of what children need.

### What does the latest Stanford Medicine research reveal about building bone in sick kids?

The majority of medicines we have for adults with osteoporosis block bone loss. We don't have drugs for children who fail to gain bone in the first place. Our only strategy is treating their underlying disease.

My lab has studied whether better treatment for chronic diseases strengthens kids' bones. One project focused on children with Crohn's disease. They had terribly fragile bones because of the effects of inflammatory molecules called cytokines on bone metabolism and the use of steroids to tamp down their gut inflammation. When monoclonal antibody treatment — which blocks cytokines — became available for Crohn's, we showed that kids treated with antibodies recover their bone health quickly, with measurable changes in 10 weeks.

### How do you prioritize bone health when a child is battling a serious illness?

It's an important question. When I first started working with stem cell transplant experts who treat cancer patients, they said, "We're just trying to get these kids to survive."

Stem cell transplants are lifesaving, but we found that long-term survivors had small, fragile bones and very little muscle. Patients who received total body irradiation before their transplants were worst off: In their 20s, some had vertebral compression fractures, in which the spine collapses and patients lose height. Those fractures usually happen in elderly people.

Stanford Medicine researchers are studying how to prepare patients for stem cell transplant without radiation. We think that approach may prevent bone complications and give these patients decades of healthier life.

So why worry about bones? Because it's a pediatrician's job to send young people into adulthood as healthy as possible. **SM**

MISHA GRAVENOR

# STABILIZING THE SPINE WITHOUT FUSION

## NEW IMPLANT HOLDS SLIPPED VERTEBRAE STEADY WHILE STILL ALLOWING MOVEMENT

By Sarah C. P. Williams

In February 2021, Dawn Lissy went to see an orthopaedic surgeon about pain radiating from her back down her leg.

The diagnosis: lumbar degenerative spondylolisthesis, a condition in which vertebrae shift out of alignment, pinching spinal nerves. Her doctor immediately recommended fusion surgery, which permanently locks vertebrae together using screws, rods and bone grafts.

But Lissy, a biomedical engineer, knew that a fusion would mean days in the hospital, months in a brace, restricted movement for life and a higher likelihood of future surgeries as other vertebrae degenerate.

She wanted the LimiFlex Dynamic Sagittal Tether, which restores anatomic stability to the vertebrae while still allowing the spine to bend. Developed at Stanford Medicine for patients with degenerative spondylolisthesis, it was still in clinical trials, but Lissy waited. In April 2026, she flew from her hometown of Colorado Springs, Colorado, to Stanford Hospital and became the second patient in the United States to receive the spinal implant once commercially available.

"When I woke up from the surgery, I had immediate relief," Lissy said. "To not have that constant nerve pain was incredible."

The device is more than 20 years in the making. In the spring of 2004, mechanical engineer Louie Fielding was finishing a master's degree and participating in a program offered by Stanford Biodesign (now the Stanford Mussallem Center for Biodesign) that brings together students and mentors to tackle biomedical innovation challenges. Fielding's team landed on the goal of developing a flexible device to stabilize the spine's vertebrae.

Stanford Medicine spine surgeon Todd Alamin, MD, immediately saw the promise of one of their sketches. A fusion, the standard U.S. treatment, eliminates spinal movement — preventing both vertebra slippage and the bending and twisting of everyday life. For years, Alamin had hoped for a more flexible way to treat the condition.

"To control stability, do you really need to get rid of all the motion?" said Alamin, a professor of orthopaedic surgery. "There's got to be a better way."

Fielding, Alamin, and Biodesign partners Colin Cahill and Ian Bennett developed a pair of small titanium springs with textile bands looping around each vertebra. The design allows bending of the spine but ensures that the posture of that segment of the spine is optimized for stability. It works for patients whose X-rays show their vertebrae have slipped 25% or less out of alignment and who don't need the spine completely realigned.

In 2011, the LimiFlex launched commercially in Europe, where it was used to treat more than 2,000 patients over a few years. In 2014, changes to the German markets made focusing on Europe no longer viable, and Fielding and Alamin pivoted to the United States, founding Empirical Spine Inc. and launching the key U.S. clinical trial.

The trial, which included nearly 300 patients, showed that, compared with a fusion surgery, the spinal implant procedures were no less effective but shorter, avoided an overnight hospital stay in appropriately selected patients, and enabled patients to return faster to work and daily life.

The U.S. Food and Drug Administration gave Empirical Spine approval to market the device in the United States in February 2026. The invention reached another important milestone on April 30, when Alamin used it in Lissy's surgery at Stanford Hospital.

"It's great to see these patients four or five days out from surgery feeling fine, knowing that if they'd had a fusion operation, they'd be in an entirely different place," Alamin said. **SM**

HOI CHAN

# Big ideas, three short minutes

## Meet the finalists who distilled their years of biomedical research into 180 seconds

BY PATRICIA HANNON

PHOTOGRAPHY BY LESLIE WILLIAMSON

**Imagine yourself standing before a panel of judges to defend your PhD thesis** by articulating what you had studied and discovered during your years as a doctoral student. This academic rite of passage usually takes about two hours.

Now try doing it in three minutes — TED Talk-style. In a packed auditorium of faculty, dignitaries, peers, friends and families.

That challenge was put to 10 Stanford University PhD students from various disciplines during the final round of a Three Minute Thesis competition on April 16, 2026, hosted by the Stanford University Office of the Vice Provost of Graduate Education.

Founded by the University of Queensland, the 3MT competition helps graduate students develop the communications skills to showcase and distill their research and explain why it matters for an audience of nonexperts.

Judges assessed the presentations based in large part on how well the audience understood the research and why it matters — all within the three-minute time limit. The winners won bragging rights and cash prizes ranging from $500 for the People's Choice Award to $5,000 for first place.

This year, four of the talks converged on a common theme: human health. From discoveries about the immune system to research enabling smartwatches to detect disease, these medical-focused finalists translated complex science into clear, compelling stories. Below, they share what they study, how they approached the three-minute challenge and what they hope their work will change.

Here are their stories:

### A.J. Phillips

ELECTRICAL ENGINEERING

3MT COMPETITION: First place

PRESENTATION SUBJECT: Teaching neural implants to speak the brain's language

**Watch his video online at stan.md/PhillipsVideo**

A.J. PHILLIPS, who grew up in Las Cruces, New Mexico, came to Stanford University for his PhD in 2020 with a goal of creating algorithms to address brain disorders.

In the lab of his adviser, E.J. Chichilnisky, PhD, a professor of neurosurgery and of ophthalmology, Phillips researched technology to restore vision to people blinded by retinal degeneration.

During his 3MT presentation, Phillips described an electronic neural implant his research team is developing to replicate a healthy retina's behavior as it converts light entering our eyes into patterns that represent what we see.

The challenge, he said, is to match the speed and precision of a human brain doing the same task, a feat tested in many all-night experiments stimulating and recording neural activity from retinas.

Phillips said his decade-long hobby of competing in triathlons informs his approach to research.

"My love for triathlon stems from the defining characteristics of the sport — dedication to long-term goals and tenacity in the face of adversity — which are the same attributes that I try to employ as a scientist," he said.

CLOCKWISE FROM LEFT: PHD RECIPIENT ZIV LAUTMAN AND PHD CANDIDATES COLETTE BENKO, IBUKUN AJIFOLOKUN AND A.J. PHILLIPS LED THE PACK IN BRINGING THEIR HUMAN HEALTH RESEARCH TO LIFE — IN JUST THREE MINUTES.

## Ibukun Ajifolokun

MATERIALS SCIENCE AND ENGINEERING

3MT COMPETITION: Second place and People's Choice Award

PRESENTATION SUBJECT: No antigen left behind: How injectable hydrogels improve combination vaccine delivery

**Watch her video online at stan.md/AjifolokunVideo**

IBUKUN AJIFOLOKUN, a third-year PhD candidate, was born in Lagos, Nigeria, and grew up in Ontario, Canada, before her family moved to Chicago when she was in high school.

Ajifolokun researches polymer science and biomaterials in the lab of her adviser, Eric Appel, PhD, an associate professor of materials science and engineering.

In her 3MT presentation, she described a soft injectable hydrogel the lab is developing to provide sustained release of multiple vaccine components at once, thereby reducing the number of doses needed in a vaccination series.

"It means a mother from a rural village doesn't have to choose between multiple clinic visits to vaccinate her child or going to work and feeding her family," Ajifolokun said. "It means fewer missed vaccinations and more lives saved."

She said she envisions a career in developing biomaterials for clinical use, but she also wants to teach and mentor others to help them understand science.

"I love being with people because I'm reminded that the ultimate goal of research is the betterment of humanity," Ajifolokun said.

## Colette Benko

DEVELOPMENTAL BIOLOGY

3MT COMPETITION: Third place

PRESENTATION SUBJECT: Cellfies: Understanding how cells communicate with the immune system

**Watch her video online at stan.md/BenkoVideo**

COLETTE BENKO, a fourth-year PhD candidate, was born and grew up in Calgary, Alberta. In the lab of her adviser, Andrew Fire, PhD, a professor of pathology and of genetics, Benko explores how cells communicate with the immune system.

Her 3MT presentation drew an analogy between how people select photos for social media and how cells select peptides — tiny bits of protein — to display on their surface as antigens to update the immune system. This constant updating allows our immune cells to quickly determine if something isn't right.

"Understanding how our cells select antigens could be instructive in the development of immunotherapies for a wide variety of illnesses," Benko said.

CONTINUES ON PAGE 43

# From a car jack to precision cancer care

## Three Stanford Medicine inventions that made radiotherapy safer and more precise

BY ERIN DIGITALE

ILLUSTRATION BY HOI CHAN

**It was early 1956 when Henry Kaplan, MD,** the first chair of the Stanford University School of Medicine's department of radiology, ran an unusual errand.

After years of hard work, Kaplan and his colleagues were almost ready to fire up their new invention, the country's first medical linear accelerator. The machine transformed a beam of speeding electrons into a stream of high-energy X-rays capable of penetrating deeply into the body to irradiate tumors, offering the hope of vastly improved cancer treatment.

But as they prepared to treat the first patient, the doctors realized they needed one more piece of equipment. So, Kaplan set out from the teaching hospital — located, like the medical school, in San Francisco at that time — to visit a nearby auto garage.

"I will never forget the puzzled look on the face of the garage owner down on Fillmore Street when I asked him to borrow a heavy-duty automobile jack," Kaplan said in an interview later quoted in *The World of Stanford Radiology*, a history book published in 2006, after his death. "I explained that it was to carry a large block of lead with a pinhole in it."

The block of lead — and the pinhole — worked with the new Stanford Medicine linear accelerator technology to deliver radiotherapy as precisely as possible. The physicians needed them because their patient was a baby boy with an eye tumor. To preserve his vision, they wanted to administer a narrow stream of X-rays to miss the lens and cornea of the child's eye. Hence, the odd errand.

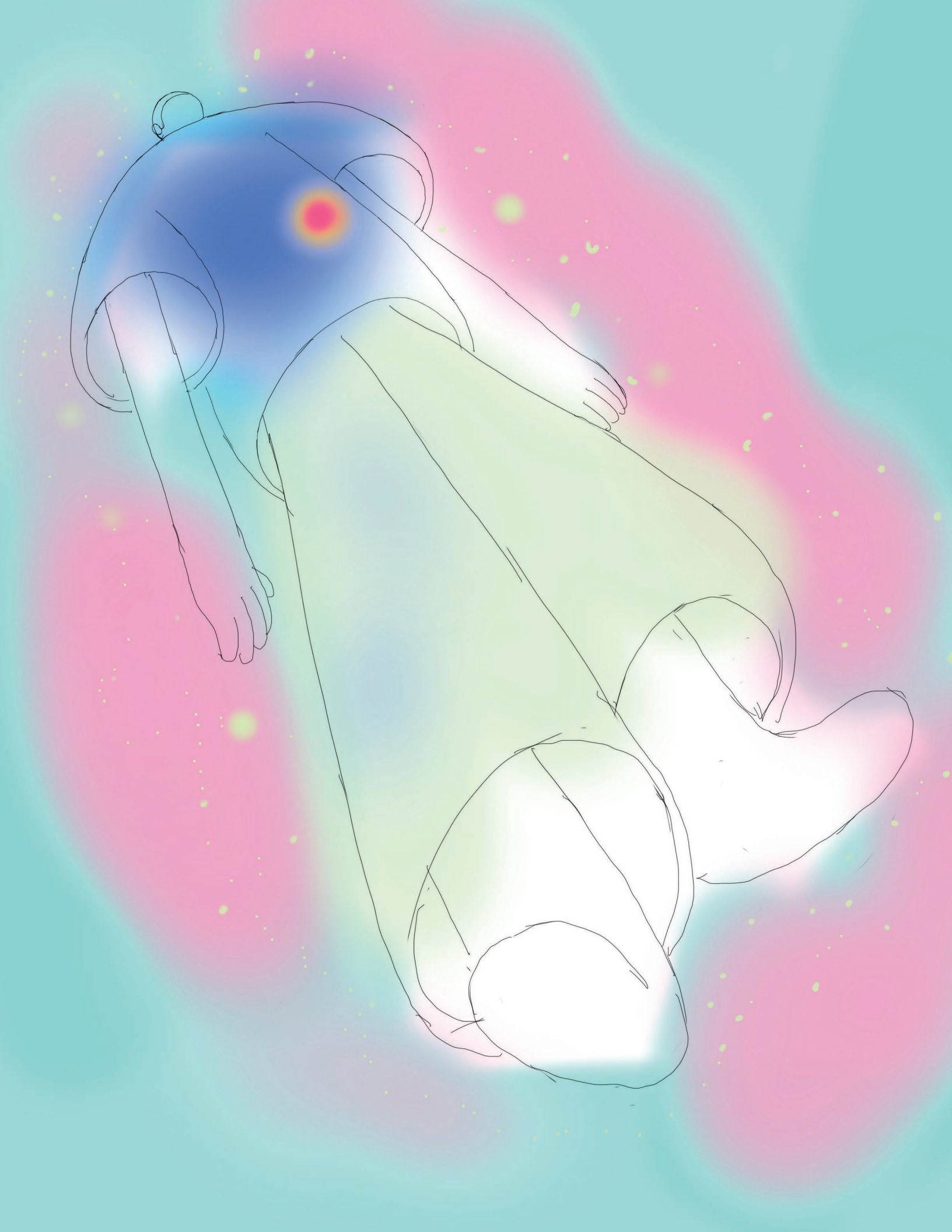
Kaplan's trip to the local garage was an early step in establishing a tradition of outside-the-box decision-making that many Stanford radiotherapy innovators would follow, to the benefit of generations of patients at Stanford Medicine and around the world.

For decades, Stanford has pushed radiotherapy toward tighter targeting and fewer side effects — starting with the first klystron-powered medical linear accelerator, later with the first image-guided radiosurgery, via CyberKnife, and now a way to broaden access to proton therapy.

### Targeted radiotherapy, with fewer side effects

SINCE THE EARLY DAYS of their field — which began with parallel efforts at Stanford and in England to develop the world's first two medical linear accelerators — radiation oncologists, neurosurgeons and others who rely on radiotherapy have faced the same challenge: how to deliver radiation exactly where it needs to go, with as few off-target effects as possible.

Radiation kills cells by damaging their DNA. It's good at eliminating malignant cells, especially those buried inside delicate body structures that would be damaged by surgery. It can also be used to destroy other harmful tissues, such as the tangled blood vessels in an arteriovenous malformation, which can rupture and cause strokes if left untreated, or neurons that trigger focal seizures in people with epilepsy.



But radiation also poses risks. If it hits healthy tissue, radiation can cause short-term injury as well as long-term problems such as secondary cancers and organ damage from inflammation and scarring.

Here are three key Stanford radiotherapy inventions that have advanced the precision, accessibility and applications of radiotherapy, each reflecting an approach to making radiation treatment safer, more versatile and available:

### LA-1: North America's first medical linear accelerator

KAPLAN ARRIVED AT Stanford in 1948, drawn in part by the university's research on particle accelerators. Stanford University engineers and physicists, experts in the nascent fields of microwaves and radar, had already made discoveries used in radar systems that defended Great Britain from World War II air raids. A key innovation was the invention in 1937 of a microwave power amplifier, the klystron, by brothers Russell and Sigurd Varian working with Stanford University physics professor William Hansen, PhD.

Microwaves could also be used to speed up electrons to very high energy levels. Hansen, working with physics department colleagues including Edward Ginzton, PhD, invented novel designs of particle accelerators called linear accelerators, using klystrons as the source of microwave power, for high-energy physics research.

Kaplan sought out Ginzton to turn linear accelerator technology into a medical device capable of zapping cancer cells. Radiologists were already treating cancer with lower-energy X-rays or by directly administering radioactive substances to tumors (through tubes, hollow needles and other devices). But these methods made it hard to treat tumors deep inside the body and exposed patients to a lot of off-target radiation. Aiming the sped-up electrons from a linear accelerator at a metal target transformed them into high-energy X-rays that could penetrate more deeply into the body.

Kaplan and Ginzton raised funds for the project; supervised construction of equipment in physics labs at the university campus in Palo Alto; and oversaw installation of the machine, dubbed LA-1 (for Linear Accelerator 1), in a concrete bunker built into a San Francisco hillside, adjacent to what was then Stanford's hospital. (Plans to move the medical school to Palo Alto were underway, so the bunker was designed with a hatch that would allow the machine to be lifted out later.)

Their first patient was a 7-month-old boy who had a genetic form of retinoblastoma that affected both eyes. Before Kaplan's team met him, surgeons had removed his right eye. The radiologists wanted to do everything possible to spare his remaining vision.

The linear accelerator-based X-ray therapy, precisely shaped by the block of lead pierced with a pinhole, worked: The team irradiated the child's tumor while avoiding the lens and cornea of his left eye, and he lived for decades after treatment with his vision intact. LA-1 was moved to the Palo Alto campus in 1959 and used to treat patients until 1972, when it was decommissioned and acquired by the Smithsonian Institution. The most recent medical linear accelerator to be installed at Stanford Medicine Cancer Center, LA-20, is a descendant of the original LA-1 design.

### CyberKnife: Image-guided radiotherapy with submillimeter accuracy

AS RADIOTHERAPY continued to evolve, experts around the world developed better and more specialized ways to deliver radiation. One such innovation, the Gamma Knife, was invented in Sweden in 1967 by Lars Leksell, MD, PhD, to treat diverse brain disorders. The patient's head is stabilized in a frame, then positioned inside a fixed, dome-shaped array of many cobalt-60 radiation sources.

The physician uses imaging data about the location of the problem to guide beams of gamma radiation from the radioactive cobalt, which converge from multiple angles on the tumor (or other surgical target). The target receives a high radiation dose, but because the beams arrive from many directions, other parts of the head get much lower doses.

In the 1980s, John Adler, MD, then a young neurosurgeon studying with Leksell in Stockholm, was so struck by this concept that he decided to become a medical inventor himself.

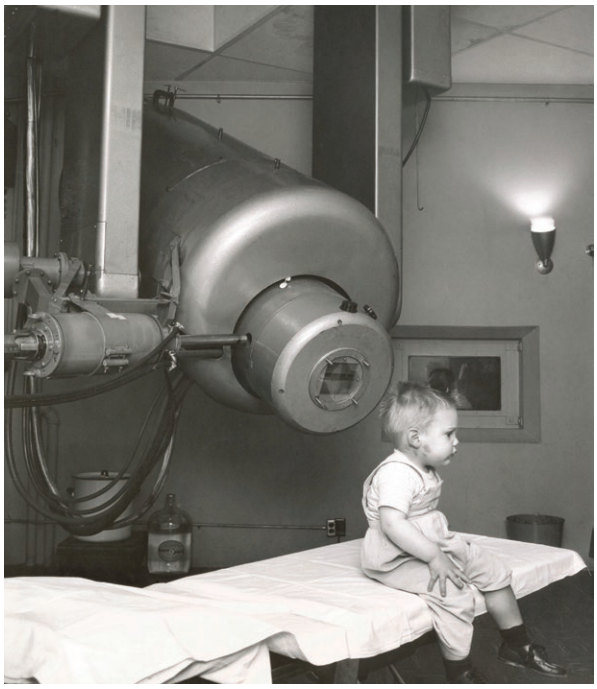
"I knew I wanted in on this new thing," Adler said recently. He is now a professor of neurosurgery, emeritus at Stanford Medicine. "I thought it was the coolest thing I ever saw."

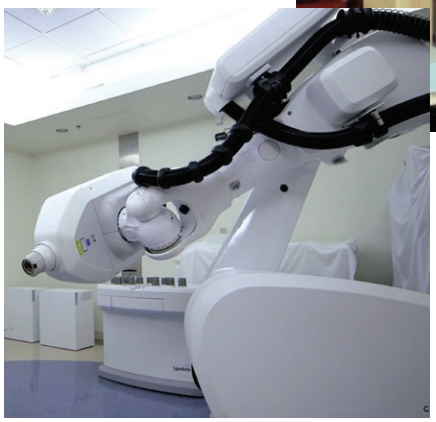
The Gamma Knife reminded him of the way a magnifying glass can focus sunlight. Its relative noninvasiveness soon had him thinking of difficult surgical problems he wanted to use it to tackle. But it had a big drawback: The shape of the Gamma Knife and associated head brace meant you couldn't treat anything outside a patient's head.

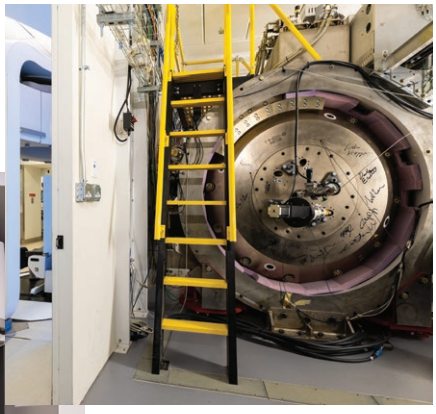
"I thought, if this concept of convergent beams works so well, might it not work anywhere in the body?" Adler said. "That was my inspiration." Instead of using several fixed radiation sources to generate convergent beams, he tried moving a single radiation source around the patient.

Adler came to Stanford University in 1987 to put his idea into action. It was the right place for his complex project to come together because there were so many experts here who had elements of the knowledge he needed.

"Perhaps most lucky of all was the proximity to people who knew how to make linear accelerators," Adler said. He also began working with experts at Stanford University's School of Engineering on a new approach for noninvasively localizing a target inside a patient's body, the principles of which would start the field of image-guided radiation therapy.








**Radiotherapy innovations at Stanford**
Clockwise from top right:
This child, who had retinoblastoma, was the first patient treated with LA-1, Stanford's first medical linear accelerator, in 1957; a synchrocyclotron, which accelerates protons to near-light speed to treat tumors with proton therapy at the Stanford Medicine Cancer Center; Tricia and Stephen De La Torre try out the new proton therapy chair; the CyberKnife, a noninvasive robotic radiation therapy system invented at Stanford to treat tumors; an early version of the CyberKnife with inventor John Adler, MD.

The new machine — eventually named the CyberKnife — was designed around a new computational method for using simple skull X-rays to precisely aim the radiation beam at a surgical target deep inside a patient. The concept is similar to the way the brain merges images from our two differently positioned eyes to give us accurate depth perception.

"You acquire X-ray images from two different directions, computationally compare those images and compare them with the CT scan," Adler said. "Today, it's almost instantaneous. You can determine where the patient's head is positioned, and should their head move even slightly, a new and different X-ray projection enables retargeting. It became the first viable means to do precision image-guided tracking within the field of radiation."

Advancing the CyberKnife from early concepts to a working device took several years, many rounds of fundraising, and resilience to withstand the skepticism of other neurosurgeons and radiation oncologists. (Its inventor jokes that the device was known for a while as "Adler's folly.") Stanford Hospital patients were the first to be treated with CyberKnife, in 1994.

Gradually, the machine came to be

recognized as a valuable addition to surgeons' and radiation oncologists' tool kits. The CyberKnife can be aimed with less than a millimeter of error when delivering radiation, minimizing side effects. It enables noninvasive radiosurgery, which has revolutionized treatment for conditions where conventional surgery would cause a lot of damage to healthy tissue. The top applications include metastatic tumors and arteriovenous malformations of the brain and spinal cord, as well as cancerous and noncancerous conditions of the head and neck, heart, lungs, prostate and abdomen — such as liver and kidney tumors.

Today, hundreds of CyberKnife machines have been installed in hospitals around the world.

## Proton radiotherapy arrives at Stanford Medicine

ON APRIL 7, 2026, Stanford Medicine radiation oncologists cut the ribbon on the latest example of their innovative prowess: a first-of-its-kind facility, formally known as the Sridhar B. Seshadri Proton Therapy Suite.

Proton therapy enables oncologists to deliver cancer-killing radiation precisely to a tumor with minimal damage to healthy tissues. Although it was developed in the San Francisco Bay Area in the 1950s, this therapy has been hard for Northern California patients to obtain. The football-field-sized footprint of traditional equipment and its high cost prevent most hospitals from offering the treatment.

Stanford Medicine's innovation — in collaboration with two medical technology companies — was to drastically shrink the size and cost of the machinery used to deliver proton therapy. This will expand access to the benefits of protons.

"The key is being able to eliminate cancer without causing unacceptable collateral damage," said Billy Loo, MD, PhD, professor of radiation oncology and co-director of particle therapy at Stanford Medicine, who played a key role in the innovation. "With protons, we can deposit the dose of radiation in a more controlled way."

Protons are the positively charged particles in the center of an atom. Their charge and mass allow them to be maneuvered with precision. Especially for patients with tumors near critical structures — such as the brain, heart, spinal cord, or nerves involved in speaking and swallowing — protons offer advantages over traditional X-rays. Although they aren't appropriate for all cancers, protons can be used for a wide variety of tumors, including those in the head and neck, spine, lungs, liver, and prostate.

"We can use magnets to send small bits of the beam of protons in various directions to shape the dose, even for tumors with irregular shapes," said Yuan James Rao, MD, associate professor of radiation oncology and co-director of particle therapy. Protons can also be targeted to stop inside a tumor, with little to no exit dose. In contrast, X-rays travel through a tumor and keep going, exposing tissues behind it to radiation.

## Smaller equipment expands proton therapy access

ABOUT FOUR YEARS AGO, after failing to find a location in Palo Alto to build a traditional proton therapy facility, Loo and his team realized that they knew of two medical device companies taking different spins on smaller equipment.

Mevion Medical Systems offered the most compact cyclotron, which is the machine that generates the protons. These machines shrank proton therapy facilities to around half the size of a basketball court. But the smaller cyclotron still required a three-story building. This was because, during treatment, patients would generally lie flat while the radiation source rotated on a gantry around them, moving one story above or below a treatment room.

Meanwhile, Leo Cancer Care took a different space-saving approach, developing a system that positioned patients upright for treatment in a specialized chair that swivels in the path of a stationary proton beam. "It's much easier to rotate the patient, rather than having to rotate a big machine around them," Loo said. His team wondered if the two innovations could be merged.

"Once we brought the companies together, the light bulbs went on," he said. Combining the world's smallest cyclotron and the rotating chair would make a very small proton therapy setup, which could fit inside an existing 1,200-square-foot X-ray treatment vault in the Stanford Medicine Cancer Center. There would be no need to construct a new building. "They said, 'OK, we will make this product,' and Stanford Medicine agreed to be the first customer."

The equipment makes proton therapy accessible to many Northern California patients who would have struggled to relocate hundreds of miles for the six to eight weeks often needed for treatment. Twelve other medical centers around the world are installing the new system.

## Proton therapy research: upright treatment and FLASH

LOO AND HIS team will conduct research on their new setup that includes testing the advantages of delivering radiation to patients sitting upright. Evidence suggests that, for certain diseases such as lung cancer, sitting up may be safer — the lung is more stretched out and moves less when someone is upright than when they're lying down, which should spare healthy tissue from radiation exposure. Upright positioning also provides flexibility in how to deliver radiation. "It's a new mindset of planning proton therapy using continuous arcs or even spirals of radiation, instead of beams from a few angles," Loo said.

The Stanford Medicine team also plans to study an approach called FLASH treatment, giving the same dose of radiation in a much shorter time period than usual. Stanford Medicine experts began

WEB EXTRA For a closer look at Stanford Medicine's proton therapy facility, watch our video: stan.md/ProtonTherapy

exploring this idea to improve the precision of dose delivery, because the body shifts even when someone is holding still. While they were developing technology to deliver radiotherapy in a fraction of a second, researchers elsewhere demonstrated that very fast radiotherapy has the same impact on tumors but causes less damage to surrounding healthy tissues.

"It's a really surprising scientific finding that we're working hard to understand," Loo said. "We plan to develop clinical trials of FLASH for our proton system."

### Pediatric radiotherapy that protects developing brains and bodies

THE MINIMIZED SIDE effects of proton therapy make an especially profound difference for children.

"Because kids are growing and developing, various parts of the body are more sensitive to even low doses of radiation," said Susan Hiniker, MD, associate professor of radiation oncology and director of pediatric radiation oncology and associate director of particle therapy (pediatric) at Stanford Medicine Children's Health.

Treatments for childhood cancers have vastly improved since Henry Kaplan's day, giving survivors decades of life after cancer — and making it especially important to minimize their risk of long-term side effects.

In a serendipitous parallel to the experience of Kaplan's team, Hiniker, Loo and their colleagues realized this spring that the best candidate for their first proton therapy patient was a young boy who could benefit from a novel, minimally invasive treatment.

Seven-year-old Stephen De La Torre was diagnosed in early 2026 with an ultrarare brain tumor known as a papillary tumor of the pineal region. The tumor, about the size of an AA battery, was blocking drainage of cerebrospinal fluid from his brain, causing swelling that led to headaches, vision problems, nausea and lethargy. On March 9, Stephen had surgery at Lucile Packard Children's Hospital Stanford to excise the tumor.

"Our surgeons told us that his tumor was located really close to the brain stem, so they removed what they could safely," said Stephen's mom, Tricia De La Torre. "He needed radiation to eliminate the rest."

When Stephen began radiotherapy treatment, the new proton therapy facility was in its final stages of calibration.

"Dr. Hiniker told us that he could receive protons for the last few radiation treatments, and that it would be good for the surrounding tissue not to get that extra radiation because the tumor is so close to his brain stem," De La Torre said.

Stephen's first proton treatment, which took about half an hour, was on June 4, three months after his surgery. He had six additional treatments in the following days, and in mid-June the team sent him home to Lakeport, California, where his family threw him a big party to celebrate his return.

Stephen was very brave about his entire medical journey, his mom said, adding that he kept reassuring his family he would be OK.

When it came to his role in Stanford Medicine's tradition of innovation, "He's really excited about it," De La Torre said. "He's been telling everybody, 'I'm the first patient!'" SM

*— Contact Erin Digitale at digitale@stanford.edu*

PLUS

### Big ideas, three short minutes

CONTINUED FROM PAGE 37

When she's not in the lab, Benko is exploring nature. "Whether it's volunteering as a docent at Año Nuevo State Park or trekking into the Bwindi Impenetrable Forest to see gorillas," she said, "I love being surrounded by wildlife and sharing the diverse biology found in nature with my community."

### Ziv Lautman, PhD

BIOENGINEERING

3MT COMPETITION: A finalist

PRESENTATION SUBJECT:
Dr. Smartwatch: What your wearable knows could change your life

**Watch his video online at stan.md/LautmanVideo**

ZIV LAUTMAN, a native of Israel, grew up in a family that emphasized the importance of community and making an impact. He came to the San Francisco Bay Area in 2015 to lead American operations of an environmental pollution-monitoring company he co-founded.

In 2019, an interest in joining the AI boom brought Lautman into the Stanford Medicine lab of structural biology associate professor Adam de la Zerda, PhD, where he earned a master's in bioengineering.

In the lab of his PhD adviser, genetics professor Michael Snyder, PhD, Lautman researched the potential of wearable technology and AI-driven technology to transform early disease detection.

In his 3MT presentation, Lautman described an early-warning AI system he built to close the gap between data collected from patients' health trackers and their clinicians. Lautman believes that kind of data might have prevented the sudden cardiac death of his research partner had it been available and analyzed by his doctors.

"Disease does not arrive suddenly. It whispers first," he said. "And no matter if the storm is brewing in your body or your mind, wearables can hear it coming before it is too late." SM

*— Contact Patricia Hannon at phannon@stanford.edu*

FEATURE

## The living framework

CONTINUED FROM PAGE 6

doesn't show up well on imaging, many people discover their cartilage is gone only when they feel joint pain from bone scraping on bone.

**Tendons and ligaments** are essential accessories to muscle and bone, like the screws and brackets that hold the whole assemblage together. Both consist of strong bands of collagen maintained by cells known as fibroblasts. Tendons connect muscle to bone, translating muscle contractions into movement. The Achilles tendon, for example, connects the calf muscles to the heel bone.

Ligaments are a bit more elastic and connect bone to bone, stabilizing movement at joints. (Joints, the confluence of bone, cartilage, tendons and ligaments, arguably account for the most significant orthopaedic problems, Chu said.) The anterior cruciate ligament, or ACL, for example, connects the femur to the tibia and helps prevent the knee from twisting.

These tough, sinewy connective tissues (sinew is, in fact, an old term that refers to both tendon and ligament) undergo constant mechanical stress and are among the most frequently injured components of the musculoskeletal system. Unfortunately, a relatively poor blood supply to these tissues means injuries are slow to heal.

### New frontiers

ORTHOPAEDIC SURGEONS TODAY ARE ADEPT AT fixing catastrophic failures of the musculoskeletal system, and demand has never been higher. "The types of problems we treat often have immediate results," said Raffi Avedian, MD, an associate professor of orthopaedic surgery and vice chair of education for the department. "If someone has an injury, say they have broken bones and can't walk, their life changes fundamentally. But within a defined treatment course, we can have folks back on their feet and get their lives back."

Every year, more than half a million people in the U.S. undergo total hip replacement surgery (one consequence of worn-out joint cartilage). What used to require a weeklong stay in the hospital is often an outpatient procedure now, thanks to faster, less invasive techniques. "It's a life-changing operation that works very well," Avedian said.

But the most challenging frontiers of orthopaedic medicine are the underlying aging and disease processes that gradually weaken bone, muscle, tendons, ligaments and cartilage — the fissures that lead to the faults. Osteoporosis occurs when osteoclasts reabsorb bone faster than osteoblasts can replace it, causing bone to become hollow and brittle. Sarcopenia is age-related loss of skeletal muscle mass and its regenerative abilities. Osteoarthritis, the most common of the three, is the weakening and wearing down of joint cartilage from use, leading to inflammation and painful friction at joints and often immobility.

The hope is to slow or even reverse these conditions before they lead to broken bones and worn-out joints that require surgical intervention. But truly disease-modifying treatments have yet to reach the clinic. Success will likely depend on matching each patient with the right regenerative treatment for them, Maloney said.

Our musculoskeletal system was made to move. In utero, without adequate fetal movement, joints do not form properly or even at all. Throughout life, bone and muscle gain strength from use. And increasingly, innovations in orthopaedic surgery and research are extending people's mobility past injury, illness and well into old age.

"The average age of my patients has grown 10 or 15 years over the last 20 years," Maloney said. It's not unusual for an 80-year-old today to seek out a knee replacement so they can keep hiking, biking, playing tennis and walking 18 holes of golf. "People no longer tolerate not being able to be active and travel and exercise. They don't accept being sedentary."

Now, with some help, this old house can keep moving. SM

*— Contact Nina Bai at nina.bai@stanford.edu*

FEATURE

## Game changers

CONTINUED FROM PAGE 25

said Scott Delp, PhD, director of the Wu Tsai Human Performance Alliance. "Your average high school athlete or casual runner doesn't have that kind of individual attention."

Delp wants to change that, with technology. "The goal is to have an Olympic-level coach in your pocket," he said. "You shouldn't have to be a professional athlete to get that insight."

Toward that end, Delp is leading the development of OpenCap, a tool that uses two ordinary phone cameras to generate the kind of three-dimensional motion analysis that typically requires an advanced lab and technician. It captures a person's movement patterns — their running gait, how they shift from sitting to standing, or how their knee buckles when they land a jump.

Using video of that movement, the program creates a kind of digital double of the person, then models biomechanical data, such as how much force their bones and muscles are experiencing. That data, in turn, can be used to assess injury risk or to help a physical therapist figure out how to adjust someone's movements to take pressure off a damaged joint.

The tool runs more than 1,000 analyses a day for researchers worldwide, in clinics that could never have afforded the technology it replaces. Delp uses his technology to screen the Stanford football players for hamstring injury risk, and Ger-

many's national volleyball team has used it to evaluate injuries. But Delp is quick to point out that, by sheer number, most injuries don't happen to elite athletes but to ordinary kids on rec league fields.

A 10-minute test on a smartphone could change that, making it easier to identify kids and adults who aren't moving their bodies optimally or are at higher-than-usual risk of an injury. Today, the setup isn't designed for consumers, but clinicians and researchers can use the open-access software for free.

"If we can solve the problem of identifying injury risk for the elite athlete, we've solved it for everybody," said Delp, the James H. Clark Professor in the School of Engineering, and a professor of bioengineering and of mechanical engineering.

## Evening the playing field

HISTORICALLY, THE GAP IN SPORTS science hasn't only been between elite athletes and amateurs but also between genders. A study of six leading sports and exercise medicine journals over a six-year span found that 34% of study participants were women and 6% of studies focused on women.

Emily Kraus, MD, is among the Stanford Medicine physicians most focused on those gaps. A clinical assistant professor of orthopaedic surgery, she directs the Wu Tsai Performance Alliance-supported program FASTR, Female Athlete Science and Translational Research.

Early in her career, Kraus worked on a study of bone stress injuries in collegiate runners that was led by Michael Fredericson, MD, a professor of orthopaedic surgery and director of physical medicine and rehabilitation sports medicine at Stanford Medicine. The project found that female runners were sustaining bone stress injuries at unusually high rates. The data revealed that the pattern was linked to undereating: When female athletes didn't consume enough calories to support their training, their hormones were disrupted and their bones were weakened, a condition called the female athlete triad. Researchers now understand it as one piece of a broader syndrome, relative energy deficiency in sport, or REDs, in which chronic underfueling ripples out to affect many body systems beyond bone.

The starting point for treatment was surprisingly straightforward: Many of these athletes simply weren't eating enough to support their training. Correcting that with a team that typically includes a physician, a dietitian and a mental-health professional is the foundation of care, and studies link better-fueled athletes to healthier bones and fewer bone stress injuries. Now, Kraus — who co-chairs the U.S. Olympic and Paralympic Committee's REDs expert panel — screens for the condition in all active females she sees.

"This is not just information for the elite 1% of the athletic population," she said. "A lot of these takeaways are super important for all women, whatever level they compete at or whether they compete at all."

But evening the playing field doesn't mean erasing every difference. Sherman was careful to note that even with the same information, the calculus of how much risk to take often differs between elite athletes and everyone else. A recreational skier recovering from an injury might postpone a weekend trip to Tahoe. An Olympic hopeful who may not get another shot at the Games might chose to get back on the mountain more quickly.

Risk tolerance aside, the knowledge that elite athletes use in their training to prevent, diagnose and treat their injuries is slowly making its way to the rest of us. As Kraus put it, the goal is simply to help people move better, "whether it's going out on a stroll around the block or running your fastest hundred-meter sprint in the Olympics." SM

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# FEAST AND FAMINE

## METABOLISM CHANGES THAT OCCUR AS PYTHONS GORGE THEN FAST PROVIDE INSIGHT INTO POTENTIAL WEIGHT LOSS OPTIONS

Pythons don't nibble. They chomp, squeeze and swallow their prey whole in a meal that can approach 100% of their body weight.

But despite stealthy slithering, months or even a year may pass between massive mouthfuls. This pattern of extreme feasting and fasting taxes their metabolism far beyond what humans experience on a day-to-day basis.

Researchers at Stanford Medicine and the University of Colorado Boulder have found that a metabolite called pTOS, which spikes a thousandfold in pythons after a large meal, causes obese laboratory mice to shun their food pellets and lose weight — mimicking the effect of semaglutide drugs such as Ozempic and Wegovy. The research was published in March 2026 in *Nature*.

Although it's too soon to tell whether pTOS will translate to a new weight loss drug in humans, the research solidifies the power of studying extremes in the animal kingdom.

"Obviously, we are not snakes," said Jonathan Long, PhD, an associate professor of pathology and senior author of the study. "But maybe by studying these animals we can identify molecules or metabolic pathways that also affect human metabolism."

Reptiles have repeatedly gifted humans with useful drugs. Snake venom is chock-full of biologically active compounds that have been developed into blood pressure medications and anticoagulants. And semaglutide arose from the discovery of a hormone in the Gila monster that regulates blood sugar levels.

"Mammals have a relatively narrow physiologic and metabolic range,"said Long, a member of the Wu Tsai Neurosciences Institute. "Humans, for example, eat around 1% to 2% of their body weight each meal, and we eat about three times a day," unlike snakes, who eat rarely and whose physiology changes drastically after a meal.

Within hours after eating, the pythons' organs, including their hearts, begin to expand in size by 50% or more, and cells that don't normally divide, like the insulin-producing beta cells in the pancreas, explode in number.

Although more research needs to be conducted into the possible use of pTOS in humans to curb appetite, the pythons gave the researchers a plethora of additional molecules to study.

"We're generating a landscape of molecules that vary in prevalence after eating in all organs of these snakes," Long said. "We already found many that look like hormones but that have no similarity with any known hormones in mice or humans. This is a form of natural product discovery."

Long and his colleagues speculate that some of these molecules could be clinically useful. "Maybe a patient with Type 1 diabetes due to defective beta cell function could benefit from a snake molecule that stimulates cell division, or a person with liver disease could take a snake-derived drug that facilitates organ remodeling," Long said. BY KRISTA CONGER

ILLUSTRATION BY JUAN BERNABEU

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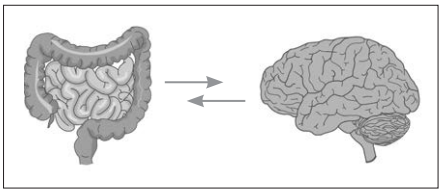
# Your microbiome may be aging your brain

SCIENTISTS FIND A LINK IN MICE BETWEEN GUT BACTERIA AND AGE-RELATED COGNITIVE DECLINE

**The sight of a delectable plate of lasagna** or the aroma of a holiday ham is sure to get hungry bellies rumbling in anticipation of a feast to come.

We've all experienced the sensation of "eating" with our eyes and noses, but much less is understood about the information superhighway, known as the vagus nerve, that sends signals in the opposite direction — from your gut straight to your brain.

These signals relay more than just what you've eaten and when you are full. A new study in mice from researchers at Stanford Medicine and the Palo Alto, California-based Arc Institute has identified a critical link between the bacteria that live in your gut — your gut microbiome — and the cognitive decline that often occurs with aging.



"Although memory loss is common with age, it affects people differently and at different ages," said Christoph Thaiss, PhD, who shared co-senior authorship of the study, published in March 2026 in *Nature*, with Maayan Levy, PhD. "We learned the timeline of memory decline is not hardwired; it's actively modulated in the body, and the gastrointestinal tract is a critical regulator of this process." Thaiss and Levy are both associate professors of pathology and investigators at the Arc Institute.

To test their theory that the gut microbiome plays a role in our "senior moments," the researchers housed young (2-month-old) mice with old (18-month-old) mice. Living (and pooping) in close proximity caused the microbiomes of the young mice to more closely resemble those of the older mice.

When the researchers compared the mice's ability to recognize a novel object or to find the exit in a maze, the young mice with "old" microbiomes performed significantly more poorly than their peers — showing less curiosity about the unfamiliar object and bumbling about the maze.

Strikingly, treating these mice with antibiotics for two weeks restored their cognitive abilities, causing them to avidly explore unfamiliar objects and zip through the maze as well as their control peers. The findings may extend to humans.

"Our study emphasizes that processes in the brain can be modulated through peripheral intervention," Levy said. "Since the gastrointestinal tract is easily accessible orally, modulating the abundance of gut microbiome metabolites is a very appealing strategy to control brain function." BY KRISTA CONGER

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