

Letter from the secretary-treasurer

In this issue, we're examining the scientific journey from bedside to bench and back.

You'll find stories of Mayo Clinic innovations that have impacted clinical trials or patient care in the areas of interventional radiology, 3D modeling, transplant and regenerative medicine. In each case, you'll see that the scientific advancements were motivated by patient interactions, and you'll get to meet some of the patients these advancements helped along the way.

This issue also includes our 2025 Early and Mid-Career Award recipients! Their resumes are inspiring; these six individuals have collectively produced algorithms for safer proton therapy, worked with NASA to conduct a sleep experiment on the International Space Station, contributed to seminal discoveries in neurogenerative disease, uncovered drivers of thyroid cancer overdiagnosis, published work that helped reduce hot-air balloon fatalities and illuminated key mechanisms of lipotoxicity. Learn more about their impressive accomplishments on page 42.

For those of you coming to the Mayo Clinic Alumni Association 74th Biennial Meeting on Amelia Island in Florida this Nov. 13–15 — see you soon!



M. Molly McMAhon, M.D.

M. Molly McMahon, M.D. (ENDO '87)
Secretary-Treasurer
Mayo Clinic Alumni Association
Emeritus professor of medicine
Mayo Clinic College of
Medicine and Science
Rochester, Minnesota

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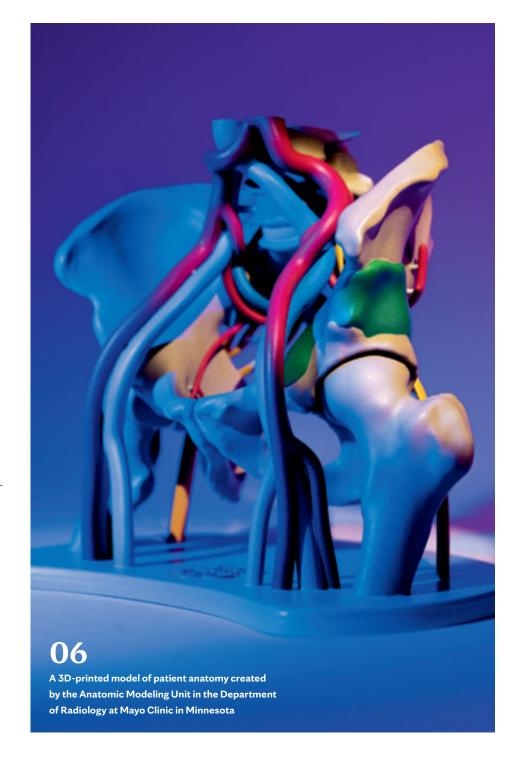
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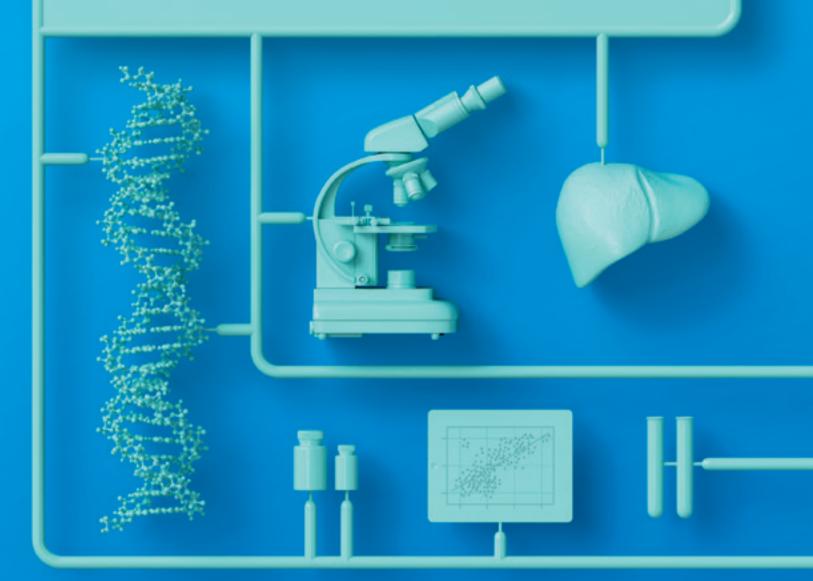
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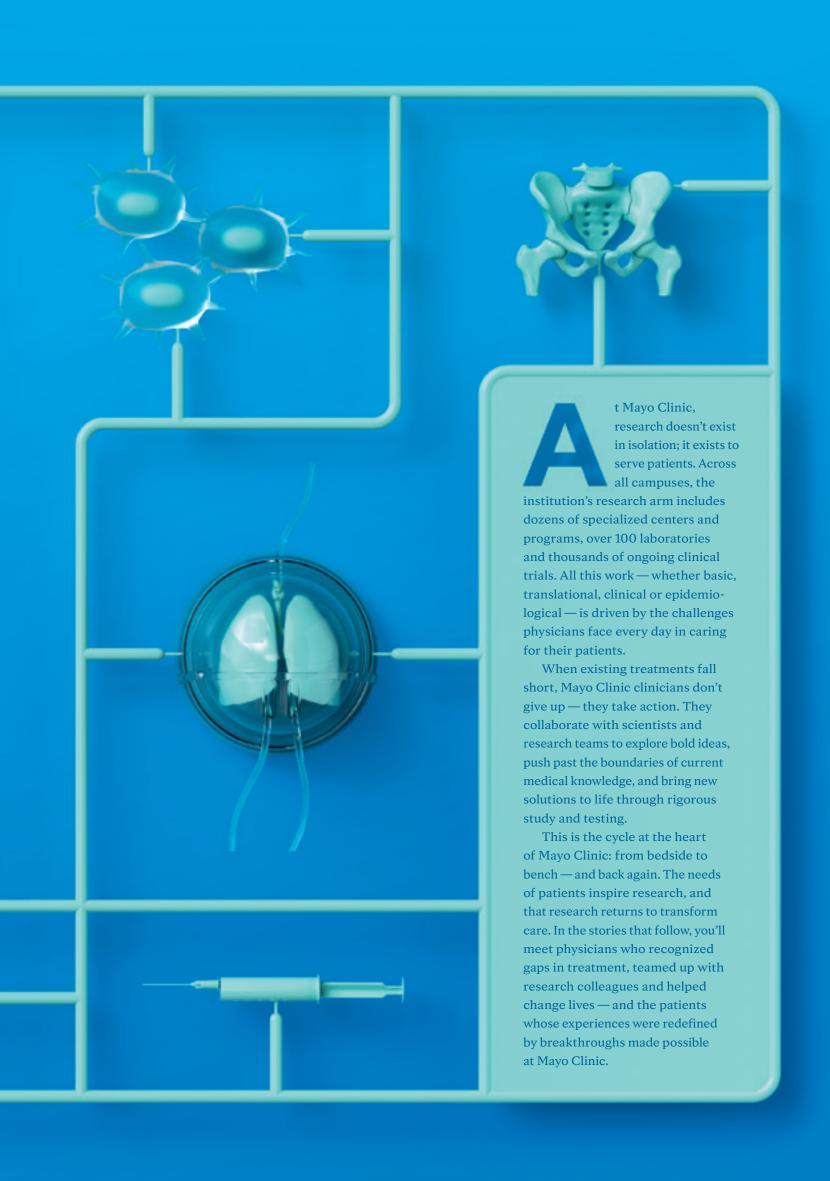
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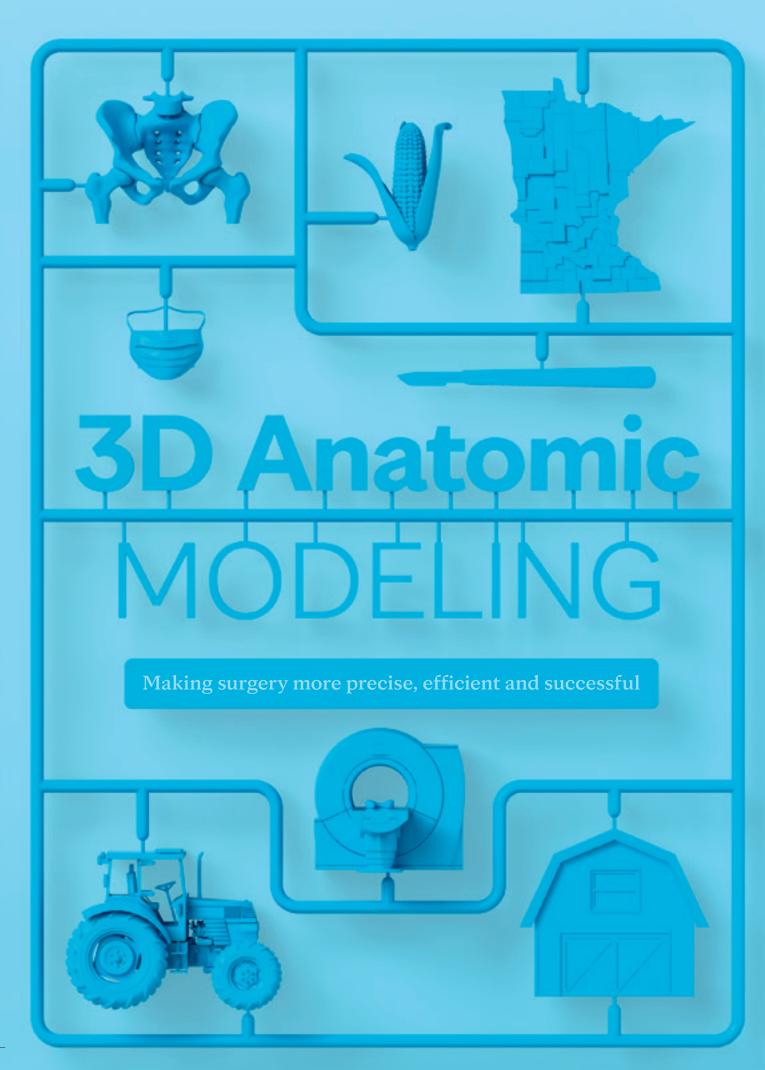


BEDSIDE TO BENCH-AND BACK AGAIN















Robert Spulak, Ph.D., was treated for bone cancer of the pelvis at Mayo Clinic.

obert Spulak, Ph.D., worked for almost four decades as a physicist and manager at Sandia National Laboratories in Albuquerque, New Mexico. He has degrees in physics, astronomy and nuclear engineering. But farming is in his blood.

As a kid growing up in Iowa, Robert loved visiting his grandfather's and uncle's farms in Minnesota. As an adult, he raised sheep, put in an (ultimately unsuccessful) offer on 80 acres of Iowa farmland and started a Master of Agriculture correspondence program. So when an older cousin offered to pass on one of the farms Robert visited as a child, Robert, nearing retirement, was ready to finally dedicate his time to farming.

But Robert's farming dreams came under threat in 2018, when an annoying pain throughout his left leg turned out to be a rare form of bone cancer known as chondrosarcoma in his pelvis. The cancer had not spread, and treatment required surgical resection of the bone. Standard of care would be to remove the entire hip joint, including part of the pelvis and femur, without reconstructing it. After this type of surgery, scar tissue forms in the space and supports weight, creating what's known as a flail hip. But mobility and function are limited — making many of Robert's planned farming tasks implausible.

When researching alternatives, Robert found that Mayo Clinic had been developing metallic pelvic implants to reconstruct the pelvis and hip after removing large amounts of bone.

"Since I was from the Midwest, I already knew of Mayo's stellar reputation," says Robert. "And since Mayo was located in Minnesota, I expected some sympathy for my desire to have enough functionality to farm."

In September 2018, Peter Rose, M.D. (OR '06), chair of the Division of Orthopedic Oncology at Mayo Clinic in Minnesota, and his surgical colleagues Matthew Abdel, M.D. (OR '12), the Andrew A. and Mary S. Sugg Professor of Orthopedic Research, and Karim Bakri, M.B.B.S. (S'10, PLS '12), performed the 14-hour surgery and successfully resected the cancer and reconstructed Robert's hip, pelvis and muscular envelope — preserving Robert's farming dreams.

Dr. Rose is an experienced surgeon, but he had extra help: Mayo Clinic's Anatomic Modeling Unit (AMU) in the Department of Radiology provided a 3D model of Robert's hip anatomy and tumor, created a custom surgical cutting guide to provide an exact resection and worked with an orthopedic implant company to design a custom pelvic implant. Robert's case is just one example of the AMU's huge impact across surgical practice at Mayo Clinic.

Every year, the AMU in Minnesota produces about 1,000 anatomic models and 1,200 cutting guides, often on a tight timeline to accommodate urgent surgeries. These products can help make nearly every type of surgery — especially uncommon or complex surgeries — more precise, efficient and successful.

"A picture is worth a thousand words, and a model is worth a thousand pictures. This technology, it's really all about the patient," says Jonathan Morris, M.D. (RD '06,



RNEU '07), co-founder and medical director of the AMU in Minnesota. "3D printing has changed what we can do for them and how we do it."

THE 3D CATALYST

3D printing at Mayo Clinic goes back to 2006, when surgeons and radiologists were preparing for a surgery to separate twin infants conjoined at the chest and abdomen. Surgeons from different subspecialties had to collaboratively plan the operation — a difficult prospect over 2D images, especially for organs such as a shared liver.

"One of the surgeons said, 'Can we make a physical copy of their liver?' And they said, 'Well, why don't we 3D print it?'" says Dr. Morris.

The team tried outsourcing the 3D printing, but the result was disappointing: it didn't even look like a liver. Instead,

Mayo's Department of Engineering worked with radiologist **Jane Matsumoto, M.D.** (MED '80), and other physicians to create a 3D model of the twins' fused liver, giving the team a close look at the vascular and biliary anatomy of the organ. The twins were ultimately separated successfully.

"It was the first time that a group of surgeons could hold a patient's liver in their hands outside the body," Dr. Morris says. "That 3D-printed liver was the catalyst of what we've become today."

It spurred the creation of the AMU in Minnesota and, eventually, at Mayo Clinic's campuses in Arizona and Florida. The AMUs rely on collaborations between physicians, researchers, engineers and technologists, and they bring top-tier 3D printing facilities to the hospital, a model known as point-of-care manufacturing.

Getting here required tremendous effort. The Minnesota AMU team had to create custom infrastructure

How it works: 3D anatomic modeling

First, a surgeon decides the clinical case warrants a 3D anatomic model, cutting guide or custom implant. The surgeon orders this from the AMU in the electronic medical record just like any other test at Mayo Clinic.

The patient is then triaged to one of several CT and MRI scanners where radiology protocols have been developed for this purpose, as the protocols are slightly different than those used for diagnostic scanning. The scans are then digitally transferred to the AMU, and specially-trained CT and MRI technologists (segmenters) take the images and convert them into a patient-specific virtual 3D model or "digital twin" of the anatomy and pathology. A single scan may have 13,000 images; technologists — or increasingly, custom Mayo-developed artificial intelligence algorithms — go through each image, segmenting each anatomic and pathologic feature of interest into unique 3D files. These are used to create full-color 3D digital models with each anatomy assigned a different color. For example, coloring the pelvic bone as tan, tumor tissue as green, nerves as yellow, and blood vessels as red and blue.

Then one or more printer technologies are used to print a life-size 3D model of the patient's anatomy layer by layer, a process known as additive manufacturing. Using subtractive manufacturing to create a 3D model would be akin to chiseling away stone to reveal a statue.

The various 3D printers in the AMU use different technologies, including lasers hardening liquid resins, UV light curing photopolymers, lasers melting nylon powders and electron beam melting. Each type of printer has its own strengths and is chosen depending on the job at hand—such as whether it's a model for surgery planning, training or patient education.

THE TUMOR



The 3D model of Robert Spulak's pelvic chondrosarcoma (in green) helped Robert's surgeon Peter Rose, M.D., visualize and plan the surgery to remove the cancer while protecting major blood vessels (in red and blue) and nerves (in yellow). The model was created by the Anatomic Modeling Unit (AMU) in the Department of Radiology at Mayo Clinic in Minnesota.

2005 - Testie 7

for the manufacturing spaces with careful airflow design and anterooms so that powder, polymers and glues wouldn't contaminate the patient areas. The team set up batch contracts for raw materials and off-premise validation testing for biocompatibility, sterilization and cytotoxicity. They hired engineers, healthcare technology maintenance staff and radiology technologists and set up quality control protocols for their 3D printers. Today, Minnesota's AMU contains about 8,000 square feet of manufacturing space — with 18 staff, 15 industrial 3D printers, and a room full of post-processing equipment such as lye baths and vapor smoothing. The Arizona and Florida units each include about 1,000 square feet.

"We have one policy: The door is open," says Dr. Morris.

"Any surgeon or clinician at Mayo Clinic can come in and ask a question about a unique patient problem. And we bring technology to bear on the needs of the patient."



Conjoined twins Abbigail and Isabelle Carlsen before they were successfully separated at Mayo Clinic in 2006 with help from a 3D-printed model of their fused liver.

THE CUTTING GUIDE



The patient-specific cutting guide (in orange) created by the AMU for Robert's surgery was carefully designed to fit the contour of his bone and preserve the femoral and sciatic nerves and as much of the native bone above the tumor as possible.

THE IMPLANT



The AMU and Dr. Rose worked with an orthopedic implant company to design a custom pelvic implant (in silver) that exactly matched the planned cut and guided the fixation screws into the remaining bone. The custom implant reconstructed the pelvis and hip, allowing weight bearing after large amounts of bone had to be removed to resect the chondrosarcoma.



"A picture is worth a thousand words, and a model is worth a thousand pictures."

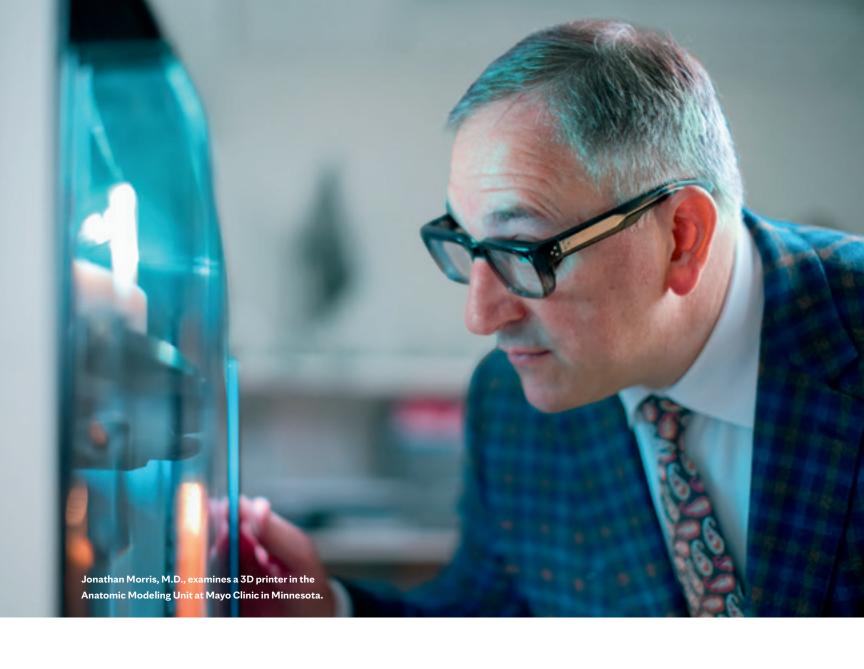
- Jonathan Morris, M.D.

NO MENTAL GYMNASTICS

3D anatomic models help surgeons explain, plan or even practice surgery. Holding an anatomic model before beginning surgery may help a surgeon understand anatomic anomalies and even change the surgical approach. A **systematic review** found that over 80% of studies examining the use of 3D anatomic models in surgical planning noted better clinical outcomes when the models were used.

"It's much easier to give them this than to say, 'Why don't you take these 13,000 images from a CT scan, marry them to 1,500 images on an MRI scan, maybe another 2,000 images on a PET scan and make a complex 3D object in your mind?" says Dr. Morris. "We just hand them the model and, by mixing haptic perception with visual perception, a new understanding develops. There's no mental gymnastics."

In addition, the AMU creates digital "twins" of the patient's anatomy, allowing virtual surgical planning on a computer. Thus, very precise cuts in the bone or soft tissue can be planned outside the operating room before the procedure.



Digital surgical plans can then be transformed into custom, patient-specific designs for cutting guides to precisely resect tumors or cut out exact segments of bone. These are then manufactured with biocompatible, sterilizable materials on one of the AMU's 3D printers.

The digital surgical plans can also be used to create custom titanium implants in partnership with external companies with titanium 3D printing capabilities. Other times, 3D anatomic models created by the AMU are used to pre-bend implants, which can save time in the operating room.

The AMU has conducted studies showing that these services drive surgical confidence and result in less time under anesthesia, less time in the OR and less blood loss. These techniques can also lead to greater organ preservation when resecting tumors involving the kidneys, lungs or liver. In orthopedic oncology surgeries, AMU's services can lead to better bone preservation — sometimes allowing surgeons to spare a limb otherwise slated for amputation.

"We provide a tool that allows the surgeon to understand things in a way that's easy for them — and

then allows them to do what they do even better than they already do it," Dr. Morris says.

A TRUSTWORTHY TUMOR GUIDE

In orthopedic oncology surgery, Dr. Rose says, the name of the game is resecting a bone tumor in one piece with a proper margin.

That's easier in some surgeries than others. For a tumor in a long, straight bone like the tibia, Dr. Rose can use an X-ray camera, find the ankle or knee joint, and use that as the starting point to measure the appropriate number of centimeters to the tumor.

"When you start to get into something like the pelvic bone, which is a bone that curves in multiple planes at once, there are no defined landmarks that we can access well in surgery," he says. "And there's a host of other structures to consider: your bowel, your bladder, your pelvic organs, muscles, nerves, blood vessels — those all make it more difficult."

Years ago, the best Dr. Rose could do to visually collaborate with other surgeons for this type of procedure



was examine the imaging, pull out his pelvis model coated in whiteboard material, take a dry erase marker and sketch out the planned resection.

"Quite frankly, we were successful as far as our ability to get the cancers out reliably, but we were probably taking in some cases more than was necessary, as we had to be safe," says Dr. Rose.

But life-size, 3D-printed, patient-specific models provide a "better intuitive understanding of cancers: where they are and what we can and can't save," Dr. Rose says. In Robert's case, the AMU was not only able to make a 3D model and digital plan to assist with Dr. Rose's surgical planning, but a cutting guide that was carefully designed to fit the contour of his bone and preserve the femoral and sciatic nerves and as much of the native bone above the tumor as possible. The AMU and Dr. Rose also worked with an orthopedic implant company to design a custom-made pelvic implant that exactly matched the planned cut.

Dr. Rose was not the only one considering the 3D model of Robert's pelvis before surgery; Robert himself got to examine the model, cutting guide and custom implant. Seeing that "they could use the models to precisely cut and precisely place the implant," gave Robert "a lot of confidence," he says.

Dr. Rose says these models are invaluable in explaining pathology and upcoming procedures to patients.

"Many of the patients who are referred to us have very rare tumors, and they may not have a good understanding of their extent and relationship to surrounding critical structures," Dr. Rose says. "The ability to sit down with them with a model that shows their exact anatomy can be very valuable to build trust and comfort."

Looking forward, Dr. Rose says that he and his colleague **Matthew Houdek, M.D.** (OR '16), Division of Orthopedic Oncology at Mayo Clinic in Minnesota, will continue to innovate and bring musculoskeletal tumor patients the best hope of cure and restoration of function.

FARMING DREAMS FULFILLED

Robert's recovery was long and, at times, arduous. But his dream of farming motivated him through five weeks in the hospital, seven weeks of frequent outpatient therapy, months of continuing physical therapy at home, and years of exercise to build up his leg and core strength.

His current function is incredible: he walks with a near-normal gait and without a cane, though a bit slower than before. He's in his third year of farming corn and soybeans. He can carry a sack of seed corn, climb up into his tractor, repair large machinery and — with the help of a special back brace — pick up big rocks to clear his fields. While he's still "on the steep part of the farming learning curve," he's enjoying himself.

"There are a lot of problems you have to solve, including mechanical breakdowns and what varieties of seed to plant," he says. "I like figuring out how to overcome these obstacles." •

Want to take a closer look?

In addition to physical models and digital surgical plans, Mayo Clinic's Anatomic Modeling Unit can create interactive models accessible by QR code. Use your phone to scan the QR codes and take a closer look at the models created for Robert.



See the chondrosarcoma in Robert's pelvis.



See the cutting guide used in Robert's surgery.



See Robert's custom pelvic implant.

Interventional radiology

Targeting hard-to-treat tumors

As an interventional radiologist, Rahmi Oklu, M.D., Ph.D. (RD '15), is well aware of **the fallibility of medicine**.

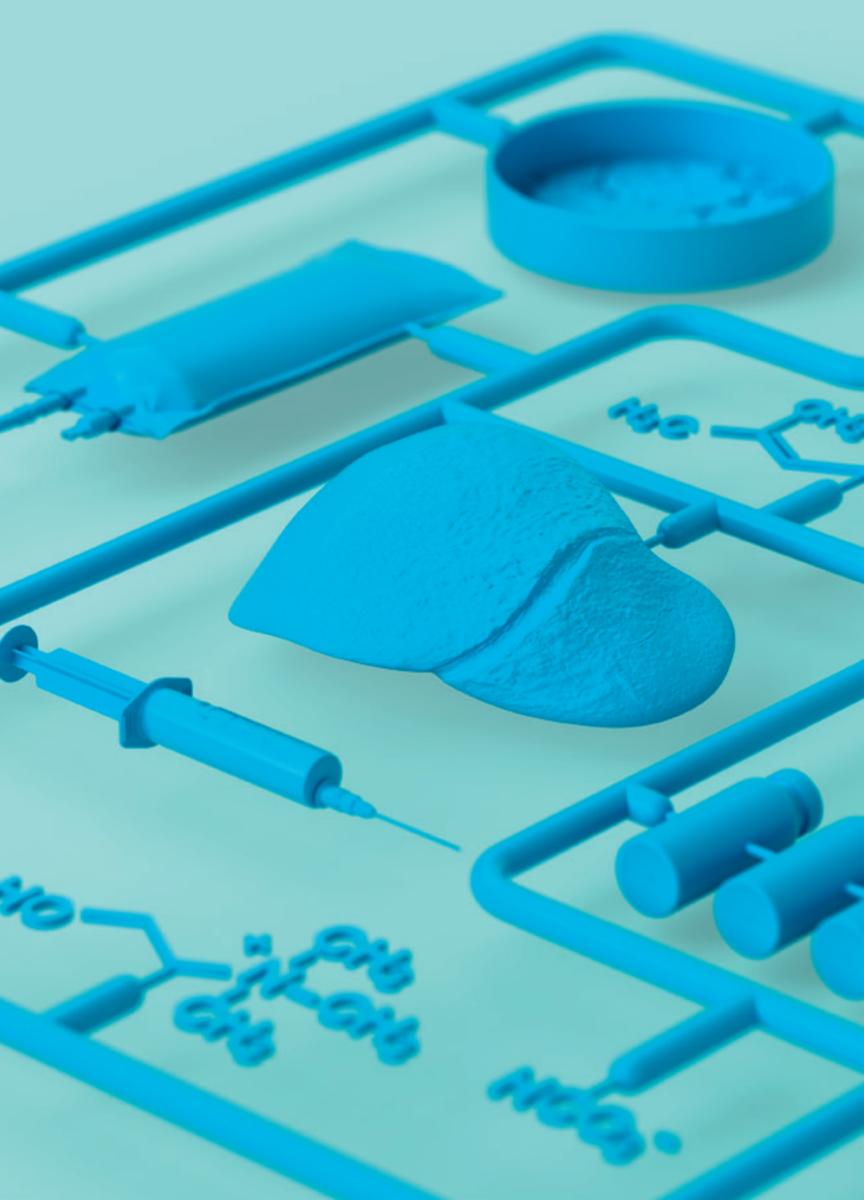
"When you start practicing as a physician, you begin to see firsthand that so many of the procedures and devices we use aren't perfect," he says. "You see patients suffer from complications and outcomes you didn't expect. There are moments where you wish you could have done more. It stays with you. And it drives you to search for something better."

This reality hit Dr. Oklu hard when a patient in his 40s came to the hospital with acute bleeding.

"It was a young patient. We did everything we possibly could," says Dr. Oklu. "The best medicine could not save this patient. The best research, the best hospital care could not save this patient.

"That shook me. If the 'best' we had wasn't enough, then the 'best' had to get better."

The patient's death inspired Dr. Oklu to think outside the box. What followed was a journey that led to multiple National Institutes of Health Research Project (R01) and



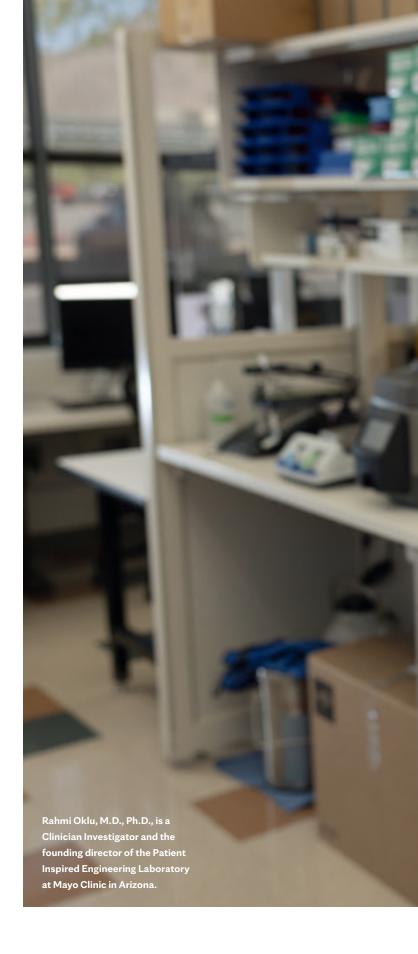
"When you take an idea, build a startup and bring that innovation into clinical practice, you're creating something that can help thousands, even millions. It's a different kind of impact — one that reaches across the globe."

- Rahmi Oklu, M.D., Ph.D.

Small Business Innovation Research (SBIR) grants, five patents, the founding of a startup company, a clinical trial and an arduous path to U.S. Food and Drug Administration (FDA) clearance — all to put a new embolic product known as Obsidio in the hands of physicians around the U.S. Nationally launched in 2024, Obsidio has already been used over 6,000 times and saved numerous lives by stopping life-threatening bleeding.

Even after this exhausting journey, Dr. Oklu isn't slowing down. He's now leading a clinical trial and working toward FDA and European regulatory approvals for a new kind of cancer treatment named inTumo. As a Clinician Investigator and the founding director of the Patient Inspired Engineering Laboratory at Mayo Clinic in Arizona, Dr. Oklu remains at the forefront of medical innovation — turning bold ideas into real solutions that bridge medicine and engineering.

"In medicine, you help people one at a time, and that's incredibly meaningful," he says. "But when you take an idea, build a startup and bring that innovation into clinical practice, you're creating something that can help thousands, even millions. It's a different kind of impact — one that reaches across the globe."



A NEW KIND OF TUMOR ABLATION

Dr. Oklu is a leading interventional radiologist specializing in interventional oncology. He's driven by a mission to transform patient care through minimally invasive, image-guided therapies.

"Dr. Rahmi Oklu is widely recognized for his unique 'patient-inspired engineering' approach, where challenging clinical problems drive his research to develop





groundbreaking medical devices and biomaterials," says **Joseph Hoxworth, M.D.** (RD '07), chair of the Department of Radiology at Mayo Clinic in Arizona. "His inventions have significantly improved clinical procedures, enabling faster, more effective treatments and positively influencing patient outcomes across various conditions."

Today, Dr. Oklu is spearheading the development of a revolutionary liver cancer treatment based on an injectable

biomaterial known as inTumo. As president and CEO of inTumo Therapeutics, Dr. Oklu has an unwavering focus on securing regulatory approval for this product, and he's determined to deliver the potentially life-saving technology to patients worldwide.

For now, inTumo is focusing on patients with hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma. These cancers are often unresectable due





"The beauty of this technology is its speed. Within minutes we know that it has done what it's intended to do."

- Rahmi Oklu, M.D., Ph.D.

to underlying disease, tumor location or patient comorbidities. For select patients, liver transplantation offers the best chance of cure. However, staying within transplant eligibility while awaiting a donor organ is challenging.

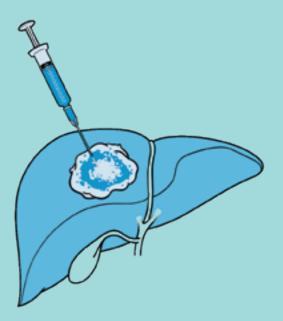
To help maintain these patients within the transplant criteria, interventional radiologists may perform locoregional therapies (LRTs) such as ablation. But ablation may not be viable if the tumor is large, too close to the pancreas or other important structures, or if comorbidities preclude general anesthesia.

Alternatively, some researchers have tried injecting various therapies such as oncolytic viruses, immunotherapy and chemotherapy directly into liver tumors, aiming to deliver a high concentration of the drugs and avoid systemic effects. However, these approaches are still experiental and often fail to achieve uniform distribution or sustained retention within the tumor, limiting therapeutic impact.

Given these limitations, researchers around the world continue to work to expand treatment options. InTumo

How it works: Ionic biomaterial tumor ablation

Dr. Oklu's biomaterial, known as inTumo, is an ionic liquid.



Ionic liquids are thick, syrupy fluids that are liquid at room temperature and do not evaporate. When injected into a tumor, inTumo spreads circumferentially and encircles the tumor.



InTumo ablates tumor cells by precipitating a forceful osmosis, as water tears through cell membranes to equalize the solute concentration.

represents one LRT procedure with great promise for those with liver cancer.

InTumo's therapeutic approach is simpler, easier and faster than current standard medical therapy, Dr. Oklu says. InTumo is a super-concentrated "designer salt" solution comprised of a proprietary formulation that is percutaneously injected into a tumor and, through a physical process, rapidly pulls the water out of the cancer cells, causing instant catastrophic cell death.

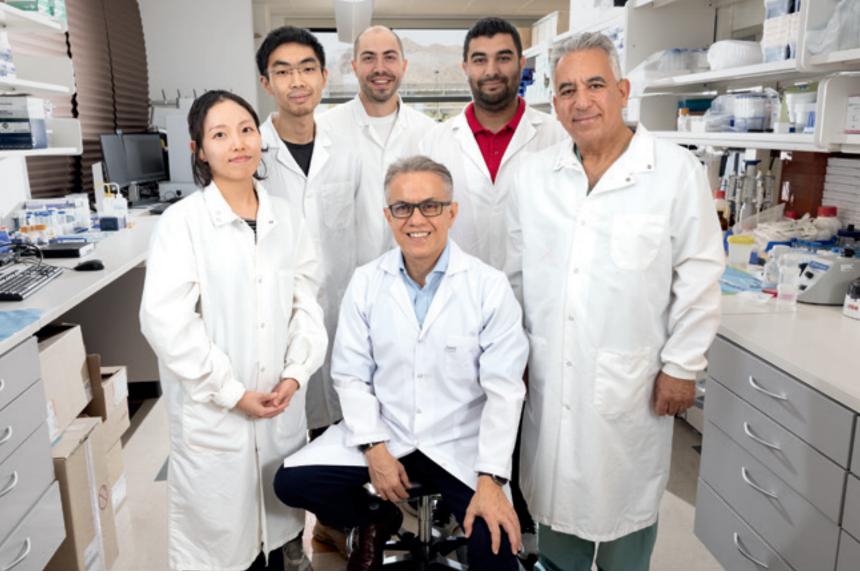
"Picture a tornado; all the fluid gets pulled out of the cell, rupturing the cell membrane," Dr. Oklu says. "So the mechanism of action is physical force."

Dr. Oklu and his team first tested the formulation in small and large animal tumor models, then progressed to testing in resected human cancer tissue. They found inTumo was effective in a variety of tumor types and published their results in peer-reviewed publications, including cover articles in Science Translational Medicine and Advanced Materials.

With successful animal studies completed and the formulation enhanced to achieve human-grade quality, in Tumo advanced to human testing in a clinical trial (ClinicalTrials.gov ID NCT06689670). In the trial, image guidance is used to inject the substance into liver tumors, often under mild sedation and/or local anesthesia. Dr. Oklu and his team have shown that most of this solution flows out from the injected site into, and out of, the blood stream within several hours. An MRI taken as part of the clinical trial immediately after the procedure is used to determine whether the injection successfully ablated the tumor.

"The beauty of this technology is its speed. Within minutes we know that it has done what it's intended to do," he says.

As a physician who treats liver tumors at Mayo Clinic, Dr. Oklu understands firsthand the limitations of current treatments. InTumo, he says, represents a new standard in the ablation of solid tumors.



Members of the Patient Inspired Engineering Laboratory at Mayo Clinic in Arizona who worked on experimental ionic liquid cancer treatment research gather around the lab's founding director, Rahmi Oklu, M.D., Ph.D., at front. Team members include former and current research fellows Jinjoo Kim, Ph.D., Yiyang Tang, M.D., Ismail Altinbasak, Ph.D., and Misagh Sarabi, Ph.D., as well as Hassan Albadawi, M.D., an associate consultant in the Department of Radiology and the Department of Physiology and Biomedical Engineering.

"EVERYTHING IS ABOUT THE PATIENT"

Dr. Oklu was able to witness the life-changing potential of inTumo when his team was contacted by a mother desperate for help for her 24-year-old daughter.

Diagnosed with cholangiocarcinoma, the daughter had undergone a left lobe liver resection. A follow-up surveillance MRI showed that the tumor had recurred, and despite multiple rounds of chemotherapy, her tumor continued to grow. The mother found her way to Dr. Oklu's clinical trial, hoping it could deliver a miracle for her daughter.

The patient's tumor had rapidly grown to 6 centimeters in size, which is substantially larger than tumors typically considered ablatable via percutaneous approaches. But Dr. Oklu decided to include the patient in the trial anyway.

"At the end of the day, I'm a Mayo physician. Everything is about the patient and that's all that matters," he says. "I said, 'If it's not going to help you, then why am I here? What's the sense of pushing this technology?"

An interventional radiologist from Dr. Oklu's team injected inTumo into the patient's liver tumor, a procedure

"Nine months later, she continues to be cancer-free... and is engaged to be married.

We didn't just treat a tumor — we gave her a future."

- Rahmi Oklu, M.D., Ph.D.

that took a matter of minutes. An MRI performed directly after the procedure showed that the approach had substantially ablated the tumor, and the tumor continued to shrink over the next month.

"When I showed her post-treatment scans to the surgical team, they were in disbelief," Dr. Oklu says. "We had successfully down-staged her tumor to the point where surgery became an option — and she underwent a curative resection. Now, nine months later, she continues to be cancer-free ... and is engaged to be married. We didn't just treat a tumor — we gave her a future."

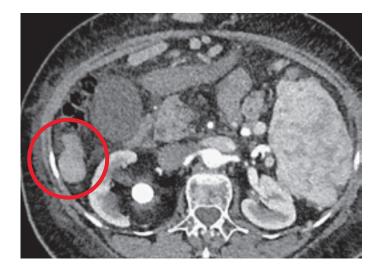
Unfortunately, Dr. Oklu knows that these types of tumors tend to come back. In the case of this patient, he hopes inTumo will be cleared for use to help treat any future recurrence.

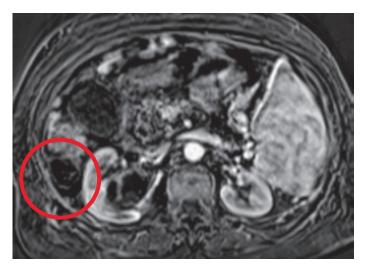
Nearly a dozen other clinical trial participants have also benefited from the inTumo formulation. While not curative, inTumo could play an important role in extending life and maintaining transplant eligibility, providing new hope to patients with liver cancer.

And while the ablative properties of inTumo are promising, they represent just one of its potential mechanisms to treat cancer. Dr. Oklu's team has conducted preclinical animal studies in organs such as the lungs, brain, breast and kidney to explore other potential avenues, including pairing inTumo with chemotherapy, immunotherapy or nanoparticles, and formulating the liquid as a catheter-directed embolic to cut off tumor blood supply and achieve chemical segmentectomy.

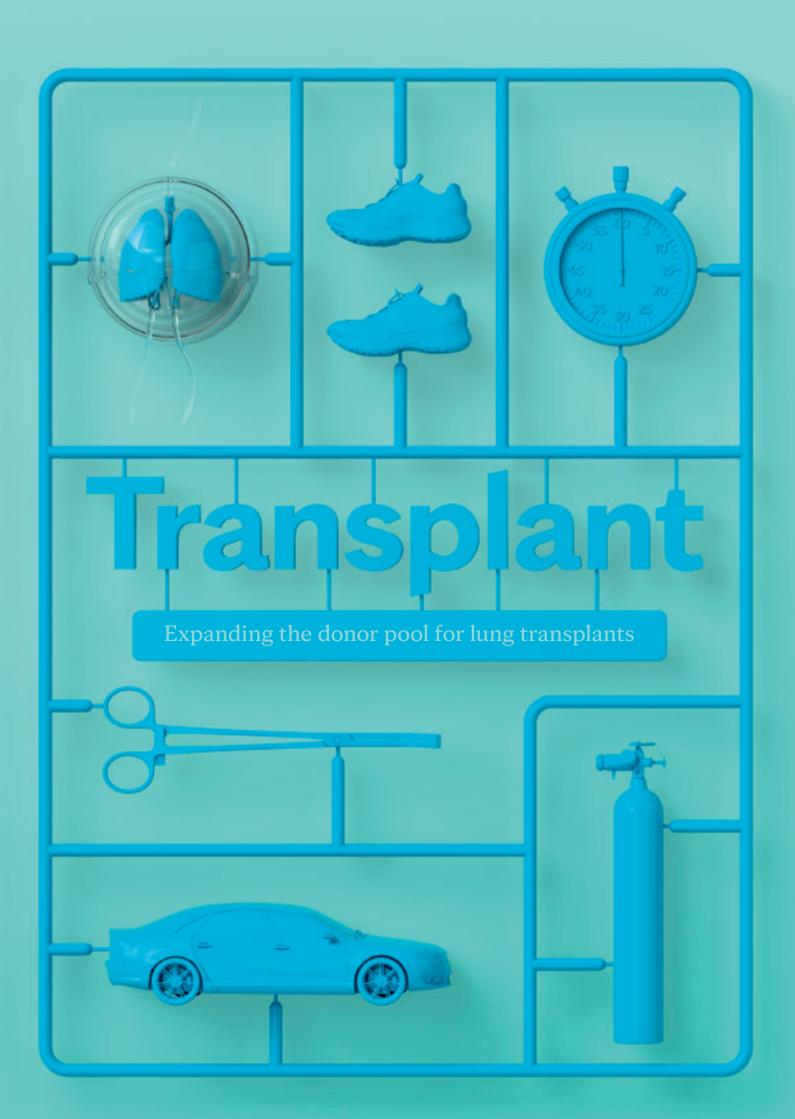
Clearly, Dr. Oklu still has plenty to explore. He'll keep innovating at the bench and working tirelessly to bring these innovations to the bedside. His career is a reminder that innovation is personal; each new idea started with a patient who couldn't wait for progress.

"Bringing an idea from the lab to the clinic and seeing it improve patients' lives is one of the greatest rewards in science and medicine," says Dr. Oklu. •





These images show an example of a patient response to inTumo. The top image shows a hepatocellular carcinoma measuring approximately 4 centimeters. This tumor would have been challenging to ablate via microwave because it extends outside the surface of the liver (known as an exophytic tumor). Using ultrasound guidance, inTumo was injected into the tumor via syringe. This led to instantaneous death of the tumor as shown in the bottom image, a contrast-enhanced MRI showing absence of viability of the tumor taken immediately after treatment. The total procedure time was about five minutes and was performed using local anesthesia and mild sedation.





hen he got the call that a potential lung transplant was available in the fall of 2024, Bill Peterson and his wife, Joellen, were ready.

They got in the car to make the two-hour drive from their home in Eau Claire, Wisconsin, to Mayo Clinic in Rochester, Minnesota. It was snowing, but not heavily enough to deter them. As a man who had never had surgery before, much less a major, lifesaving one, Bill was somewhat anxious — but knew that transplant was his only option.

Upon arriving, Bill was admitted and prepped to go into surgery. After the procurement team assessed the donor lungs, transplant surgeon **Sahar Saddoughi, M.D., Ph.D.** (S '19, TS '21), Division of Thoracic Surgery at Mayo Clinic in Minnesota, came into Bill's room. She had bad news: the lungs weren't deemed good enough for transplant.

"So there I was on the bed getting ready to go into surgery and had to get dressed and go home," says Bill.

Bill returned home to his oxygen tanks and largely homebound life. In 2022, he had been diagnosed with

Mayo Clinic patient Bill
Peterson received a lung
transplant at Mayo Clinic.
Today, he and his wife,
Joellen, benefit from
his vastly improved lung
function and quality of life.

"I'm excited about the type of research we do because we are able to translate from bench to bedside and directly change patients' lives."

- Sahar Saddoughi, M.D., Ph.D.

idiopathic pulmonary fibrosis and had lost weight, muscle and freedom in just a few years.

"The disease progressed to a point where the portable tank didn't give me sufficient oxygen, so I had to lug around a big tank," he says. "I couldn't be very active and couldn't do much of anything."

A few weeks later, Bill got another call for a potential transplant, so he and Joellen again made the drive to Mayo Clinic — only to be told while in admissions that the lungs were again not transplantable. Bill and Joellen drove home, and Bill resumed his place on the transplant waiting list.

As of June 2025, there were over 900 people waiting for a lung transplant in the U.S. Because only about 20% to 30% of donor lungs meet the standard for transplant, there are never enough lungs to go around. This means that every year, patients die waiting for donor lungs or become too sick to receive a transplant — outcomes Dr. Saddoughi finds unacceptable.

So in addition to her clinical practice, Dr. Saddoughi researches ways to expand the donor pool and increase the number of lung transplants. She tests novel transplant therapies and procedures in large animal models, and her lab explores extended-criteria donors, lung rehabilitation and next-generation lungs.

"The availability of high-quality organs for lung transplant is insufficient in the U.S.," says **Cassie Kennedy, M.D.** (I '03, CMR '04, CI '06, THDC '08, CTSA '24), medical director of lung transplantation at the William J. von Liebig Center for Transplantation and Clinical Regeneration at Mayo Clinic in Minnesota. "Science that









"Science that makes 'unusable' organs transplantable will increase the number of transplants and save lives."

- Cassie Kennedy, M.D.

makes 'unusable' organs transplantable will increase the number of transplants and save lives."

In 2023, Dr. Saddoughi used her porcine lab to help clarify some of the controversy surrounding the use of normothermic regional perfusion for lungs — a contribution that would have direct relevance for Bill and could help many others like him.

"I'm excited about the type of research we do because we are able to translate from bench to bedside and directly change patients' lives," says Dr. Saddoughi.

WIDENING THE DONOR POOL

For a long time, transplants from deceased donors were largely limited to transplants resulting from donation after brain death (DBD). Meanwhile, the use of donation after circulatory death (DCD) made up a paltry percentage of total transplants. In 2000, there were just 206 total DCD organ transplants compared to 17,088 DBD transplants in the U.S.

One reason for this disparity had to do with the quality of the donor organs: DBD donors are placed on a ventilator to circulate oxygen and preserve the organs before transplant. For a DCD donor, all life-sustaining measures are stopped; patients then undergo circulatory arrest and asystole. This is followed by a declaration of death and a several minute waiting period before organ procurement — a time when vital organs can be exposed to warm ischemia.

In the case of lung transplant, ex vivo lung perfusion (EVLP) technology can help transplant teams assess whether questionable or marginal lungs — including those from DCD donors — are suitable for transplant. EVLP allows transplant teams to monitor and evaluate post-procurement donor lungs outside of the body for several hours.

In 2019, there were major advances in heart transplant that had big implications for lung transplant in the U.S. Two new technologies revitalized the idea of DCD heart transplant: normothermic regional perfusion (NRP) and the Organ Care System (OCS), an ex-situ perfusion system known as "heart in a box." Both reanimate the heart and allow medical teams to assess heart function before transplant.

NRP and OCS rapidly increased the use of DCD hearts and helped contribute to the rise of DCD organs in general. By 2024, DCD transplants made up 27% of all transplants.

But some in the lung transplantation field began to question NRP's effect on lung graft function.

Marginal lungs can be sent to bioengineering facilities — such as the facility at Mayo Clinic in Florida — for assessment, and these centers were noticing that many post-NRP lungs sent to them were of poor quality, Dr. Saddoughi says. This brought up questions: Was some aspect of the procurement process injuring the lungs? Could the lungs be better protected during procurement?



To help verify whether NRP procurement was damaging lungs, ${\rm Dr.}$ Saddoughi turned to her porcine lab.

"I thought this was a question I could answer for myself through my research," says Dr. Saddoughi.

Her team then established an NRP pig model. Eight pigs underwent circulatory arrest; four were randomized to NRP. The team followed a procedure similar to human NRP procurement: the NRP pigs were quickly placed on bypass for an hour with their head vessels clamped, allowing the heart to start beating again before procurement. As a control, the remaining four pigs went straight to procurement, with no NRP.

All lungs were then placed on EVLP for three hours to evaluate lung function, including oxygenation capacity and airway pressure. The team also looked for gross damage, took X-rays of the lungs, reviewed markers of inflammation, compared metabolic profiles and had an independent pathologist review the lung tissue. All these measures

Top: Lungs undergo ex vivo lung perfusion for monitoring and assessment outside the body. Bottom: As part of ex vivo lung perfusion, blood gas samples are taken from the pulmonary artery.





Mayo Clinic transplant surgeon Sahar Saddoughi, M.D., Ph.D. (left), conducted preclinical research on the effect of normothermic regional perfusion (NRP) on donor lung quality. Her research contributed to greater confidence in NRP, which translated into Mayo Clinic patient Bill Peterson (center) receiving an NRP lung transplant performed by Mayo Clinic surgeon Philip Spencer, M.D. (right).

"The disease progressed to a point where the portable tank didn't give me sufficient oxygen, so I had to lug around a big tank.

I couldn't be very active and couldn't do much of anything."

- Bill Peterson

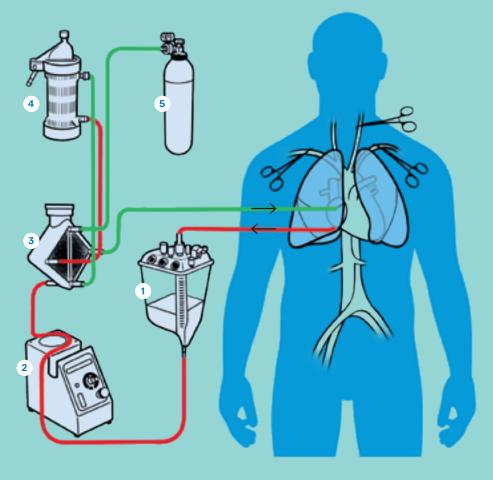
were comparable between the groups, and all lungs were deemed suitable for transplant.

"We found that in this very controlled situation, the lungs seemed to be functioning well," says Dr. Saddoughi. "The outcome was that these lungs after NRP were still in good condition and should be considered for transplant."

The study — along with her research looking at **early national outcomes** of DCD lungs and a meta-analysis comparing DCD and DBD **short- and long-term transplant outcomes** — provided the reassurance Dr. Saddoughi needed to proceed with these types of transplants in her operating room.

"My goal as a lung transplant surgeon is to continue to find ways to open up the donor pool for patients," she says. "I was really comforted by the result. Because I believe in it, and now I can feel confident about that, as both a researcher and a surgeon."

How it works: Normothermic regional perfusion



In NRP, the donor is declared dead after circulatory arrest and asystole. A surgical team then opens the sternum and inserts cannulas into the aorta and the right atrium of the heart, starting the donor on cardiopulmonary bypass. The heart restarts and circulates blood throughout the chest and abdomen, limiting organ ischemia. The vessels to the brain are clamped prior to starting cardiopulmonary bypass, ensuring no blood circulation to the brain. NRP continues for about an hour to revive and assess the organs before procurement.

- 1. Reservoir
- 2. Roller pump
- 3. Membrane oxygenator
- 4. Heat exchanger
- 5. Gas mixer

THE BEST LUNGS FOR BILL

When Bill received his third call about a potential transplant in December 2024, he knew he may arrive in Rochester to be disappointed again. But his previous trips for a potential transplant had actually helped cement Bill and Joellen's trust in the healthcare team.

"It gave us confidence that they're looking out for us, and they wanted the best lungs for Bill," says Joellen.

If the Mayo Clinic team believed donor lungs to be transplantable, Bill and Joellen were on board — and that confidence extended to DCD lungs. So on Dec. 5, 2024, Bill was successfully transplanted by Mayo Clinic surgeon **Philip Spencer, M.D.** (CS '22), with NRP lungs from a DCD donor.

Recovery from lung transplant was intense, but Bill remains grateful for the lung function the transplant has given him and savors the fact that he's free from the need for supplemental oxygen.

"I still have some work to do to build up my strength and stamina. But I know there's an end result, which will be getting back to some degree of normalcy that I had," Bill says.

Like most areas of science, the issue of NRP lungs is not settled. A 2024 American Association for Thoracic Surgery **consensus statement** says that there are limited data on the effect of thoraco-abdominal NRP on lung function. Dr. Saddoughi, a co-author of the statement, says the practice of NRP continues to evolve.

"There is a lot of uncertainty in lung transplant. There is no such thing as a perfect donor organ," says Dr. Kennedy. "Science that reduces transplant providers' uncertainty about an organ's future performance in the lifesaving tasks of oxygenation and ventilation will improve recipient outcomes and organ utilization."



Philip Spencer, M.D., Department of Cardiovascular Surgery at Mayo Clinic in Minnesota, performs surgery in an operating room.

LOOKING FORWARD

As Dr. Saddoughi looks forward, there are more research questions she wants to help answer, such as whether lung-derived exosomes can help **mitigate ischemia-reperfusion injury** in DCD transplant. She also wants to explore other areas of donor expansion like xenotransplantation, 3D-printed organs, and decellularized and recellularized lungs.

"I feel extremely fortunate to be part of the Mayo Clinic lung transplant team. The program has transformed significantly over the last several years due to the incredible teamwork and leadership. In 2024 alone, we were able to help 84 patients through the amazing gift of lung transplantation," says Dr. Saddoughi. "My hope is to continue my research to ask important questions like: Can we take lungs that are not transplantable and find a way to make them transplantable?

"Ultimately, the goal is to continue to help more patients with end-stage lung disease breathe again."

As for Bill, he exercises every day and takes regular walks with Joellen, extending the distance bit by bit. They're working up to participate in an Eau Claire turkey trot with a fellow local double-lung transplant recipient they met in Rochester.

It's hard for Bill to express what the transplant means to him — a challenge he faced directly when he wrote a letter to the donor family.

"Words can't describe the gratitude I have, and how I feel about this generous gift, really a gift of life," Bill says.

"Our daughter wrote a two-page letter just thanking them, because now she has her dad back and her kids will know their grandfather," Joellen says. •



Regenerative medicine

Offering hope for drug-resistant seizures

Tabitha Wilson began having seizures at the age of 2. Fortunately, they were well controlled with medications — but that began to change during her senior year of high school.

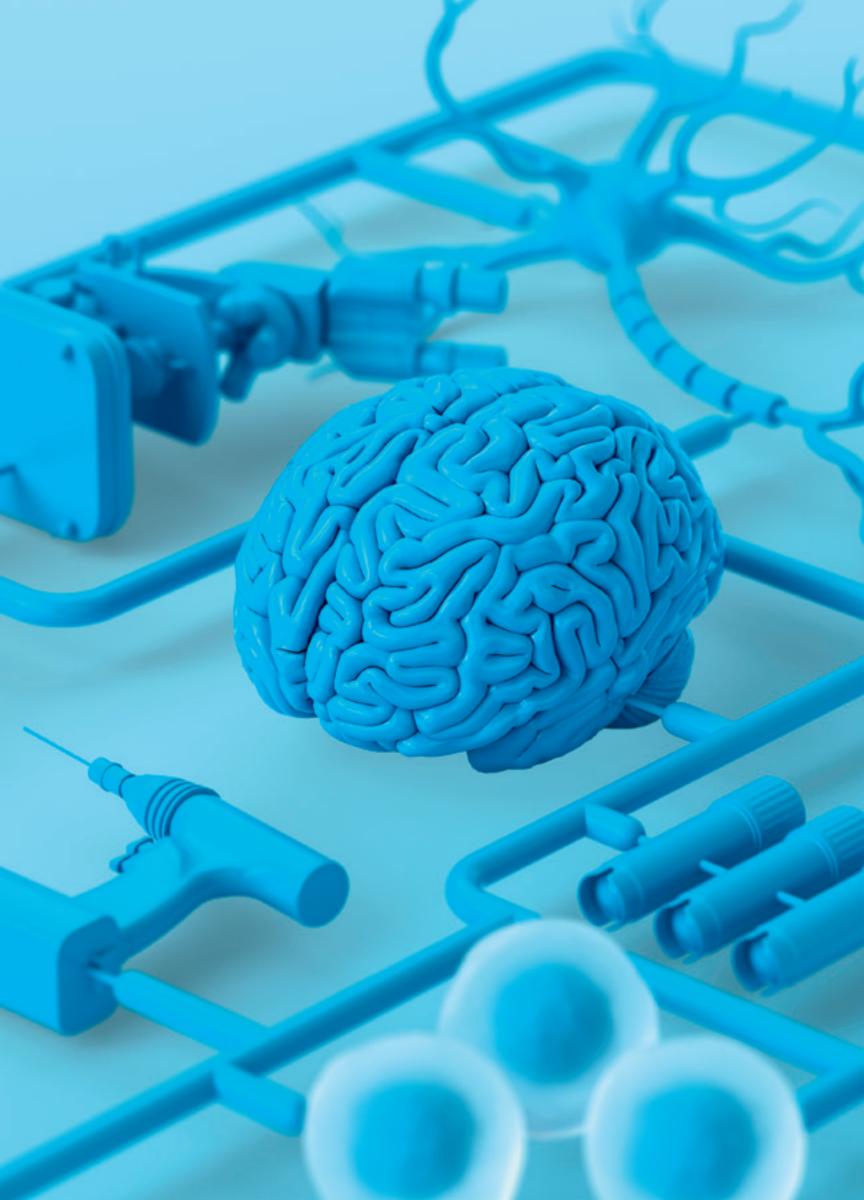
"I was 17 years old sitting in history class when the seizure happened. They had to load me up in an ambulance in front of the whole school," says Tabitha. "It was traumatizing. Something I will never forget."

After that, her seizures worsened. Despite trying multiple medications and undergoing brain surgeries, her seizures became debilitating and dangerous.

"I fell down a flight of stairs, I've burned myself while cooking, I've completely blacked out and don't know where I am," she says. "I can't drive, can't cook or swim alone, I can't take a bath, only a shower, and someone has to be in the house."

Tabitha was desperate for relief for her drug-resistant epilepsy (DRE) — a condition she shares with about 15 million people worldwide.

"I'm willing to try everything and anything to get some sort of control over these seizures because I've been living with this for so long," says Tabitha.









Clinicians like **Sanjeet Grewal, M.D.** (NS '20), Department of Neurologic Surgery at Mayo Clinic in Florida, use every tool in their toolbox to help patients like Tabitha. But at some point, they run out of tools — a heartbreaking experience to witness in patients and frustrating as a physician, Dr. Grewal says. It's a frustration that motivated him to pursue other solutions.

"I've been trained to be a surgeon, take care of people. But I've always had a scientific curiosity," Dr. Grewal says. "As physicians, the moment we wonder why a patient's outcome couldn't be better is the moment science becomes indispensable — because every unanswered question is a doorway to improving care."

In 2024, Tabitha became the first person in the world to receive a new potential therapy for her DRE as part of a phase 1 clinical trial led by Dr. Grewal at Mayo Clinic in Florida. The trial studies the use of deep brain stimulation (DBS) in conjunction with a stem cell implant in the thalamus.

A TEAM EFFORT

Current treatment options for DRE include invasive procedures such as brain resection or laser ablation therapy. While often effective, these surgical approaches carry the risk of side effects such as memory problems, motor deficits and speech impairment. And these options are not available to everyone with DRE.

"There's a subset of patients whose seizures are coming from an area that we can't necessarily resect or ablate," Dr. Grewal says. "Those are the toughest ones for us to help. This trial is for our toughest patients."

Dr. Grewal's clinical trial uses stem cells to attempt a reparative, rather than destructive, approach.

"The paradigm shift here is that we've gone from 'OK, here's a problem in the brain, let's take that problem out or let's disrupt it' to 'Hey, there's part of the brain that's dysfunctional, let's try to fix it," says Dr. Grewal. "So instead of removing or destroying tissue, we're trying to regenerate it and repair it."

"Complex diseases require complex treatment. And the beauty of MSCs is they sense the environment and then, based on that, they respond to it and then secrete the right type and amount of these factors."

- Abba Zubair, M.D., Ph.D.



Sanjeet Grewal, M.D., Department of Neurologic Surgery at Mayo Clinic in Florida, and Abba Zubair, M.D., Ph.D., Department of Laboratory Medicine and Pathology at Mayo Clinic in Florida

DBS is an FDA-approved therapy for DRE and results in median seizure reduction of up to 70% after five years. But it's uncommon for patients to become seizure-free with DBS — and that wasn't good enough for Dr. Grewal.

"We thought, 'Could we make DBS better by adding a regenerative component — adding these stem cells?'" he says.

To accomplish this, Dr. Grewal worked with a team of Florida colleagues, including neurologist **William Tatum, D.O.** (N '09), and neurosurgeon **Alfredo Quinones-Hinojosa, M.D.** (NS '16). Dr. Quinones-Hinojosa is also a William J. and Charles H. Mayo Professor and the James C. and Sarah K. Kennedy Dean of Research at Mayo Clinic in Florida.

The stem cells used in the clinical trial were produced at the Human Cellular Therapy Laboratory at Mayo Clinic in Florida under the leadership of **Abba Zubair**, **M.D.**, **Ph.D.** (LABM '03), a pioneer in cell therapy. Dr. Zubair is also the vice dean of Mayo Clinic Alix School of Medicine – Florida Campus.

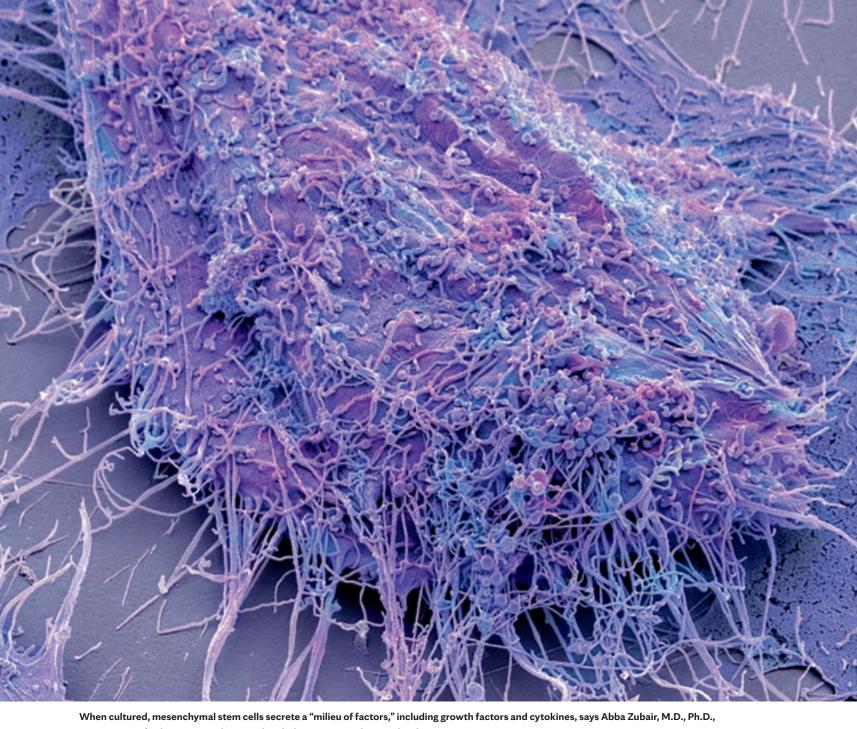
"When it came to which cells to use, there's so many different types," says Dr. Grewal. "That's where Dr. Zubair was very helpful."

Dr. Zubair guided the team toward a type of adult stem cell known as mesenchymal stem cells (MSCs) derived from adipose tissue. When cultured, MSCs secrete a "milieu of factors," Dr. Zubair says, including growth factors and cytokines, some of which are shown to be anti-inflammatory or induce regeneration. Inflammation is thought to contribute to the abnormal firing of neurons that occurs in epilepsy — but there are many possible mechanisms of the condition, Dr. Zubair says.

"Complex diseases require complex treatment," says Dr. Zubair. "And the beauty of MSCs is they sense the environment and then, based on that, they respond to it and then secrete the right type and amount of these factors.

"So it's not like we know what they secrete and could just inject those factors. It's more of a cocktail and the cocktail depends on the situation at the exact time the cells





Department of Laboratory Medicine and Pathology at Mayo Clinic in Florida.

interact with the environment. That makes it really unique and that's why we think the MSCs are a good therapeutic agent in this setting."

After deciding upon MSCs, Dr. Grewal's team received funding from Mayo Clinic's Center for Regenerative Biotherapeutics for research to ensure that DBS and MSC implants would not interfere with each other. The Practice Advancement Laboratory, under the guidance of Takahisa Kanekiyo, M.D., Ph.D. (NSCI '10), Department of Neuroscience at Mayo Clinic in Florida, conducted in vitro experiments to show that electrical stimulation from DBS would not damage the MSCs, affect their properties or make them more migratory. With the help of senior research technologist Ralph Perkerson, the lab



William Tatum, D.O.



Alfredo Quinones-Hinojosa, M.D.



Takahisa Kanekiyo, M.D., Ph.D.



Alfredo Quinones-Hinojosa, M.D., and Sanjeet Grewal, M.D., and their team implant stem cells into Tabitha Wilson's thalamus at Mayo Clinic in Florida.

"As physicians, the moment we wonder why a patient's outcome couldn't be better is the moment science becomes indispensable — because every unanswered question is a doorway to improving care."

- Sanjeet Grewal, M.D.



Erik Middlebrooks, M.D.

also concluded that MSCs would not interfere with DBS hardware in the brain or decrease its efficacy.

To ensure the cells were precisely implanted in the anterior nucleus of the thalamus, the team relied on the ultrahigh field 7-tesla (7T) MRI expertise of **Erik Middlebrooks, M.D.** (RD '17), Division of Neuroradiology at Mayo Clinic in Florida.

This true team effort highlights the importance of collaboration, Dr. Grewal says.

"I'm inquisitive and want things to get better, but I also know my limitations," says Dr. Grewal. "There are people who have trained for years and years to be scientists and I want to make sure I use their expertise for patients."

Similarly, Dr. Zubair values the perspective that Dr. Grewal and other cross-specialty clinicians bring to his work — especially as it helps facilitate moving innovations from bench to bedside.

"I'm excited about science, but I'm even more excited about solving patients' problems, giving them hope, developing new treatments," Dr. Zubair says. "I'm always thrilled to see the product we generate in my lab taken out either to the floor or to the OR to be injected. It makes my day."

HOPE ON THE HORIZON

There is a long road ahead to determine whether this cell therapy in conjunction with DBS results in clinical improvement for patients with DRE, Dr. Grewal says. Though Tabitha has experienced improvement in her seizure management since the procedure, the initial study simply aims to confirm the safety and feasibility of the operation.

"We wanted to be very cautious initially," says Dr. Grewal.

If proven safe, future steps in researching this therapy would be dose-escalation trials and possible bilateral

How it works: MSC implantation

Seizures are the result of abnormal electrical brain activity; a person with epilepsy has a hyperexcitable brain. This could be due to an excess of excitatory electrical activity and/or a lack of inhibitory activity.

Mesenchymal stem cells (MSCs) are multipotent adult stem cells that can be derived from several sources, including adipose tissue, as in Dr. Grewal's trial. MSCs secrete antiinflammatory and neuroprotective molecules such as interleukin-10 (IL-10) cytokine, brainderived neurotrophic factor (BDNF) protein and vascular endothelial growth factor (VEGF) into nearby brain tissue. The molecules could help mitigate potential contributors to epilepsy by reducing excitability of neurons and repairing damaged cells and tissue - such as by reducing scarring (gliosis), modulating excessive microglial pro-inflammatory activity, or slowing the loss of gamma-aminobutyric acid (GABA)ergic interneurons.

"We feel that the mechanism of action of MSCs is likely multimodal, through paracrine secretion of anti-inflammatory cytokines, secretion of tissue reparative factors such as BDNF, and potentially inducing proliferation, migration and differentiation of the endogenous neural stem cells," Dr. Grewal says.

In this trial, Dr. Grewal's team targeted the anterior nucleus of the thalamus (ANT) for cell implantation. The ANT is a critical hub within

1. Limbic system
2. Anterior nuclei
3. Centromedian nuclei
4. Neocortex
5. Thalamus
6. Hippocampus
7. Cerebellum

thalamocortical and limbic circuits involved in seizure propagation. Its selection was informed by prior success with deep brain stimulation (DBS) in this region, which has been shown to decrease network excitability. It's hoped that MSCs in this location can similarly act synergistically with the DBS as a form of circuit-specific neuromodulation.

implantation of the cells in the brain. In the meantime, researchers like Dr. Grewal and Dr. Zubair remain committed to investigating whether cell therapies could be the solution for the many patients like Tabitha.

"Our tools are getting better and better; cells and genetic therapies are getting more and more sophisticated. That's allowing us to tackle some of these questions we haven't been able to in the past," says Dr. Grewal. "So, whether it's wound healing, neurodegeneration, epilepsy or stroke, there are so many different studies going on investigating the potential of regenerative or reparative therapies."

"We know these products sometimes don't work, but we also do know they generate hope," says Dr. Zubair. "Everybody can have that hope when they come to Mayo, that despite everything else failing, here is something new that can be tried in a safe way." •



Tabitha Wilson and her boyfriend, Steven Montero.

025 • Issue

EARLY AND MID-CAREER AND MID-CAREER

Honoring alumni throughout their professional journeys



any awards honor residents and fellows at the starting lines of their careers. Others celebrate seasoned physicians and researchers nearing their professional finish lines. But there are many Mayo Clinic alumni in the middle of their career marathons, marking the miles with exceptional contributions to medicine.

In 2024, the Mayo Clinic Alumni Association created the Mayo Clinic Early and Mid-Career Alumni Awards to recognize the important accomplishments of this group.

This year, six outstanding recipients were chosen. These individuals have made robust contributions to their areas of expertise in the realms of education, clinical practice, clinical and scientific research, and administration. Beyond their professional output, they demonstrate selfless community service and have consistently acted in a manner that is aligned with Mayo Clinic values.

Early Career

Working in their area of expertise for 10 to 15 years

Mid-Career

Working in their area of expertise for more than 15 years



Mayo Clinic Early Career Award

Keeping the human touch in healthcare



s artificial intelligence (AI) advances and is increasingly incorporated into healthcare, some worry that medicine will lose the essential human touch.

Juan Brito, M.B.B.S. (CTSA '14, ENDO '14), not only guards against a future where healthcare is stripped of humanity, but believes that technology like AI can be used to better serve patients, says **Robert Wermers, M.D.** (I '93, ENDO '96), chair of the Division of Endocrinology, Diabetes, Metabolism and Nutrition at Mayo Clinic in Minnesota.

"While AI is often used to increase efficiency and address information gaps in healthcare, Dr. Brito recognizes its potential to enhance the very essence of patient care — ensuring that technology supports, rather than replaces, empathy, understanding and human connection," Dr. Wermers says.

Dr. Brito is a professor of medicine at Mayo Clinic College of Medicine and Science and a consultant in the Division of Endocrinology, Diabetes, Metabolism and Nutrition at Mayo Clinic in Minnesota.

Dr. Brito has made numerous contributions to research at the intersection of AI and patient care, particularly through his role as director of the Care and AI Laboratory at Mayo Clinic. Through his work in the lab, Dr. Brito has created an AI model to analyze patient-clinician interactions, improving communication and care quality.

As chair of innovation and quality in the Division of Endocrinology, Dr. Brito has led innovations in Al-assisted screening for primary aldosteronism and diagnosis and risk stratification of thyroid cancer. This work includes the Virtual Thyroid Cancer Registry, which automates data extraction, personalizes treatment and facilitates large-scale clinical research. He is also the medical director of Mayo Clinic's Shared Decision Making National Resource Center and has developed tools that enhance shared decision-making, ensuring patients remain active participants in their healthcare.

Outside of the realm of Al, Dr. Brito's research has uncovered drivers of thyroid cancer overdiagnosis and led to the design of a point-of-care tool to guide patients and clinicians in determining whether active surveillance or surgical intervention for small, low-risk thyroid cancer is appropriate. His research on levothyroxine prescribing patterns has helped discourage unnecessary treatment for subclinical hypothyroidism, especially in older adults. He also completed a study comparing brand-name and

"Dr. Brito recognizes (AI)'s potential to enhance the very essence of patient care — ensuring that technology supports, rather than replaces, empathy, understanding and human connection."

Robert Wermers, M.D.

generic levothyroxine in terms of hypothyroidism control, informing and improving patient care. These efforts have led to a reduction in unnecessary treatments and surgeries and reshaped clinical practice guidelines.

Dr. Brito has been internationally recognized by top professional societies with awards such as a Van Meter Award from the American Thyroid Association, an Early Investigator Award from the Endocrine Society and a Rising Star in Endocrinology Award from the American Association of Clinical Endocrinology. He has secured multiple National Institutes of Health grants, including R01 awards and an R37 MERIT Award from the National Cancer Institute, demonstrating his ability to lead high-impact research. Dr. Brito has over 250 peer-reviewed publications, including 100 co-authored with mentees, and over 17,500 citations.

Through it all, Dr. Brito maintains his priority on patient care, says **Victor Montori, M.D.** (I '99, CMR '00, CLRSH '01, ENDO '02), a consultant in the Division of Endocrinology, Diabetes, Metabolism and Nutrition and the Robert H. and Susan M. Rewoldt Professor of Endocrinology Honoring Daniel L. Hurley, M.D., at Mayo Clinic in Minnesota.

"He is a trusted and beloved clinician, who centers himself on the patient before knocking on the exam room door, smiling and greeting the patient," says Dr. Montori. "To patients and families, he is thorough and rigorous. He accompanies patients through their struggles with warmth, kindness, patience and tenacity."

Mei Liu, Ph.D. Algorithms for safer, more effective proton therapy



roton beam therapy delivers precise, finely controlled radiation.

But that narrow focus can also cause problems: small patient motions — even breathing — can lead to radiation being delivered off-target.

Wei Liu, Ph.D. (RADO '13), has helped address this challenge and other difficulties facing proton therapy, including range and setup uncertainties. His research has been revolutionary, producing algorithms that allow physicians to utilize proton therapy with greater safety and efficacy.

"His expertise in computational methods and his biomedical knowledge have contributed greatly to the advancement of translational research in proton therapy," says Steve Jiang, Ph.D., director of the Division of Medical Physics and Engineering at University of Texas Southwestern Medical Center. Dr. Jiang is also the David A. Pistenmaa, M.D., Ph.D., Distinguished Chair in Radiation Oncology and vice chair of the Department of Radiation Oncology at the center. "He has made significant contributions to the field, especially in robust optimization and robustness quantification in intensity-modulated proton therapy."

Dr. Liu is a professor of radiation oncology at Mayo Clinic College of Medicine and Science and a consultant in the Department of Radiation Oncology at Mayo Clinic in Arizona. He is a nationally and internationally recognized expert in medical physics.

In addition to his research designing robustly optimized proton beam therapy, Dr. Liu's algorithm for linear energy transfer (LET) modeling and optimization has already been used in proton therapy to successfully decrease the risk of rectal bleeding in patients being treated for prostate cancer, the risk of brain necrosis in patients treated for brain tumors, and the risk of mandible osteoradionecrosis in patients treated for head and neck cancer. His in-house treatment planning system, Shiva, has been in routine use at the proton center at Mayo Clinic in Arizona for over nine years, benefiting approximately 6,000 patients. More recently, Dr. Liu's team has applied AI, especially generative AI, in the full spectrum of radiation oncology practice to significantly improve the efficiencies of numerous clinical tasks.

Dr. Liu is an associate editor or editorial board member for a dozen journals, including the International Journal of Radiation Oncology - Biology - Physics, IEEE Transactions on Medical Imaging, and Radiotherapy &

Oncology. He currently serves as co-chair of the Thoracic Subcommittee of the Particle Therapy Co-Operative Group, a leading global organization for proton and particle therapy, proof of his significant international stature. Dr. Liu also serves on the National Institutes of Health (NIH) Imaging Technology Development study section and as a reviewer for the Netherlands Organisation for Scientific Research (NWO/ZonMw) and KWF Kankerbestrijding (Dutch Cancer Society).

His research has earned numerous grants from several sources and has provided over \$10 million to further his work as a principal investigator, including two R01 federal grant awards from the NIH.

He is author or co-author of three book chapters and 142 accepted or published peer-reviewed manuscripts, including publications in prestigious journals such as The Lancet Oncology and Nature Medicine. Dr. Liu has 14 patents, and many of his algorithms have found their way into commercial projects that are used to treat tens of thousands of cancer patients worldwide.

Dr. Liu's numerous honors and awards include the John S. Laughlin Early-Career Scientist Award from the American Association of Physicists in Medicine in 2019, a Mentored Quantitative Research Career Development Award (K25) from the NIH and National Cancer Institute, and the naming of the term "Liu Limit" for his pioneering work in plasma astrophysics. He is a fellow of the American Association of Physicists in Medicine.

"His expertise in computational methods and his biomedical knowledge have contributed greatly to the advancement of translational research in proton therapy."

- Steve Jiang, Ph.D.

Derek O'Keeffe, M.B., B.Ch., B.A.O., M.D., Ph.D., M.B.A. Engineering digital health solutions



erek O'Keeffe, M.B., B.Ch., B.A.O., M.D., Ph.D., M.B.A. (ENDO '15), was consulting with a patient who had lost her sight due to diabetes complications when the patient remarked that her assistive cane was cumbersome.

Dr. O'Keeffe could have simply expressed sympathy and carried on. Instead, he set about developing what he calls a "Jedi glove" device using ultrasound sensors and haptic feedback.

"If the wearer gets too close to something, the little finger of the glove starts to vibrate. The closer the wearer gets to an object, the more fingers of the glove vibrate. They can literally 'feel the force' of what's around them," he says.

It's just one example of why Dr. O'Keeffe calls himself a physicianeer; he regularly combines his skills in clinical care and engineering to solve patient problems. He holds dual first-class honors degrees and doctorates in medicine and engineering. The caliber of his Ph.D. work led to a Fulbright Scholarship at Harvard University, and his medical training included time as a scholar at the University of Oxford and a visiting resident at Mayo Clinic. He then completed a fellowship in endocrinology at Mayo Clinic.

Today, Dr. O'Keeffe is an attending endocrinologist at University Hospital Galway and a professor of medical device technology at the University of Galway in Ireland. He is also the founder and director of the Health Innovation via Engineering (HIVE) lab at the university.

The HIVE lab has raised over 10 million euros in funding, produced patent applications and publications in journals such as the New England Journal of Medicine and The BMJ, and impacted national policy in digital health. Projects include using drones to fly lifesaving medicines to island communities and developing AI-driven avatars to assist in patient education. Through HIVE, Dr. O'Keeffe has also developed a virtual hospital concept that encompasses a clinical and technical framework to address admission avoidance in patients with chronic diseases such as diabetes, heart failure and COPD.

"Dr. O'Keeffe's diverse research portfolio is characterized by innovation, collaboration and development of imaginative technological solutions for real-world problems," says colleague **Matthew Griffin, M.B., B.Ch., B.A.O.** (I '94, NEPH '96), a professor of transplant biology and the head of the Discipline of Medicine at the University of Galway School of Medicine.

Dr. O'Keeffe is a leader in not only clinical practice innovation, but health policy in Ireland. He has served as the Irish public healthcare system's national clinical lead for diabetes and contributed to the development of clinical practice guidelines and models of care for people living with diabetes in Ireland. He also successfully advocated for Ireland's health service to provide free access to continuous glucose monitors and led the creation of Ireland's first national diabetes strategy.

In addition, Dr. O'Keeffe has also strongly contributed to education. He developed a Masters of Diabetes program to ensure a high-quality pipeline of specialized healthcare professionals and researchers for people living with diabetes, as well as a postgraduate diploma in digital health for healthcare professionals.

Along the way, he has produced over 100 peer-reviewed publications and garnered awards. Dr. O'Keeffe's awards include the St. Luke's Medal from the Royal College of Physicians of Ireland and Outstanding Young Person of the World from Junior Chamber International for his work—including a collaboration with NASA to successfully put a sleep experiment on the International Space Station.

"Dr. O'Keeffe's diverse research portfolio is characterized by innovation, collaboration and development of imaginative technological solutions for real-world problems."

- Matthew Griffin, M.B., B.Ch., B.A.O.

Nilüfer Ertekin-Taner, M.D., Ph.D.

Research

motivated by

human resilience



ilüfer Ertekin-Taner, M.D., Ph.D. (NSCI '03, 11 '04, N '07, NBN '08), is a Clinician Investigator, enterprise chair of the Department of Neuroscience and the Roy E. & Merle Meyer Professor of Neuroscience at Mayo Clinic. She leads the Genetics of Alzheimer's Disease and Endophenotypes Laboratory at Mayo Clinic in Florida, and is a popular mentor and a frequently invited speaker.

Yet, she maintains a busy clinical practice for patients with dementia and cognitive impairment.

"Each of these patients teaches me something unique about human resilience," she says. "I think about my patient, a music teacher who continues to play piano for others. I think about a young mother with early-onset dementia who continues to go and cheer her young kids at their sports games. And I also think about the 80-year-old grandma who is still able to form a connection with her grandkids long after losing the ability to speak. I'm amazed and humbled to see this human grace and grit."

These patients teach her and motivate her, she says: "There's so much to be done in these conditions."

Dr. Ertekin-Taner's research is focused on the discovery of molecular disease mechanisms, new treatments and biomarkers for Alzheimer's disease (AD) and Alzheimer's disease related dementias (ADRD). By combining multiomics and deep endophenotypes in large human cohorts and validations in model systems, her research has led to seminal discoveries in the fields of neurodegenerative diseases and precision medicine.

A few examples: She has completed some of the largest published multi-omics studies in human brains and blood for AD/ADRD, uncovered novel disease pathways, nominated hundreds of therapeutic targets, and is developing novel treatments and biomarkers for these conditions. She has served as principal investigator on 38 grants with total extramural grant support of over \$80 million since 2008. She has over 220 publications with nearly 20,000 citations.

As a clinician and scientist, Dr. Ertekin-Taner has the expertise to counsel and manage her patients and their families according to the most up-to-date clinical trials and practices related to genetic testing, biomarkers in AD/ADRD and neuroimaging. She also attends caregiver sessions, gives out media interviews, and participates in workshops, webcasts and seminars to disseminate clinical and scientific knowledge to caregiver families and the public.

"Dr. Ertekin-Taner is a servant and transformative leader, who has the ability to engage and energize diverse groups to tackle complex challenges."

– Vesna Garovic, M.D., Ph.D.

Dr. Ertekin-Taner is a sought-after mentor, as evidenced by over 80 clinical and research mentees ranging from high school students to junior faculty. Many of her trainees come to her lab without any prior research experience and are subsequently accepted to highly competitive postgraduate programs.

As enterprise chair for the Department of Neuroscience at Mayo Clinic, she oversees its 30 research laboratories, nearly 300 staff and over 80 Ph.D. students across the organization. She has also served on many advisory boards and committees, including a select committee of the National Academies of Sciences, Engineering and Medicine requested by the U.S. Congress to provide research recommendations for the treatment and prevention of dementia. She is also frequently invited by prestigious academic institutions to give presentations as a visiting professor.

Her many awards include the 2018 Mayo Clinic Florida Investigator of the Year and the 2022 Zenith Fellows Award from the Alzheimer's Association, considered to be one of the most prestigious awards in Alzheimer's disease research worldwide.

"Dr. Ertekin-Taner is a servant and transformative leader, who has the ability to engage and energize diverse groups to tackle complex challenges," says **Vesna Garovic, M.D., Ph.D.** (NEPH '99), chair of the Division of Nephrology and Hypertension at Mayo Clinic in Minnesota. Dr. Garovic is also the Penske Foundation Professor of Clinical Medicine in Honor of Ian D. Hay, M.D., Ph.D., and J. Eileen Hay, M.B., Ch.B.

Clayton Cowl, M.D., M.S.

Serving patients in the sky and on the road



layton Cowl, M.D., M.S. (THDC '00), is widely recognized as an expert in pulmonary, aerospace and transportation medicine with all the requisite degrees, clinical experience and publications to prove it.

But as a clinician serving professional pilots and commercial drivers, Dr. Cowl wanted to fully understand the demands of their jobs. So he is also a commercially-rated pilot, flies hot-air balloons and holds a commercial driver's license that allows him to operate semi-trucks.

"When I talk to my patients who drive, I don't just say, 'Do you drive a truck?' I say 'Oh, do you drive a reefer (refrigerated trailer) or dry van? Are you a 'tanker yanker'?'" he once told Minnesota Public Radio. "And all of a sudden there's a bond there. They go, 'Wow, this guy actually knows something about what I do."

Dr. Cowl is an associate professor of medicine at Mayo Clinic College of Medicine and Science and chief of the Section of Transportation Medicine in the Division of Public Health, Infectious Diseases and Occupational Medicine at Mayo Clinic in Minnesota. He also has a joint appointment in the Division of Pulmonary and Critical Care Medicine.

Among his contributions to transportation medicine, Dr. Cowl has served as a senior Federal Aviation Administration (FAA) Aviation Medical Examiner for more than two decades and is particularly skilled at assisting and assessing pilots with highly complex medical conditions being considered for medical waivers. He is a fellow of the Aerospace Medical Association and a past president of the Civil Aviation Medical Association. He developed a live and online course for providers performing Federal Motor Carrier Safety Administration medical certification exams on commercial truck and bus drivers — and is the editor of the definitive textbook reference on the subject.

During his nine years as chair of the Division of Preventive, Occupational and Aerospace Medicine at Mayo Clinic, he oversaw the launch of an aerospace medicine training program, the expansion of services in the hyperbaric and altitude medicine facility, and the development of a webbased online consultation service for commercial pilots with medical conditions called Mayo Clinic Clear Approach.

In his occupational lung disease and inhalational toxicology practice, Dr. Cowl evaluates and treats patients who have experienced exposure "(Dr. Cowl has made) robust contributions to all three Mayo shields in the areas of transportation medicine, clinical toxicology and occupational lung disease."

– Philip Hagen, M.D.

to various toxic substances, fumes and gases such as asbestos, silicone and anhydrous ammonia. Dr. Cowl has also served as the president of the American College of Chest Physicians, one of the largest international professional organizations dedicated to chest medicine, critical care and sleep medicine.

Dr. Cowl's research areas include epidemiological work on aviation crash data and altitude physiology, including using Mayo Clinic's altitude chamber facility to test and validate emergency oxygen delivery systems for Boeing and the Department of Defense. His study of injuries and fatalities in hot-air balloons published in JAMA resulted in balloon manufacturers transitioning to an alternate load cable material in new balloon models, resulting in fewer deaths. He is a co-principal investigator of the Minnesota Retaining Employment and Talent After Injury/Illness Network (RETAIN) program that investigates strategies to improve return-to-work paths for ill or injured workers, including those in safety-sensitive roles like commercial driving.

"(Dr. Cowl has made) robust contributions to all three Mayo shields in the areas of transportation medicine, clinical toxicology and occupational lung disease," says **Philip Hagen, M.D.** (MED '83, I '86, PREV '88), emeritus assistant professor of medicine at Mayo Clinic College of Medicine and Science in Minnesota. "He also has contributed within the framework of community service and advocacy for pilots and commercial truck and bus drivers, all with character and tireless work."

Harmeet Malhi, M.B.B.S.

Asking the right questions about **liver disease**



uring her childhood in the foothills of the Himalayas, **Harmeet**Malhi, M.B.B.S. (I '04, CI '06, GI '07, HEPT '08), was relentless: she wanted answers and she wanted to discover new things—as quickly as possible. She asked her family members question after question until she was satisfied. She would run up mountain paths ahead of everyone in the family.

"The first day of kindergarten, I reassured everyone that I was fully capable of finding my way to and from school, which was over a mile away," she says.

Today, she's translated her energy and curiosity into a career as an internationally recognized expert in liver disease, particularly metabolic dysfunction-associated steatohepatitis (MASH).

Dr. Malhi is a professor of medicine and professor of physiology at Mayo Clinic College of Medicine and Science and a consultant in the Division of Gastroenterology and Hepatology at Mayo Clinic in Minnesota. She is an associate director of Mayo Clinic's Center for Cell Signaling in Gastroenterology and vice chair of the Division of Gastroenterology and Hepatology.

Dr. Malhi pioneered the concept of using extracellular vesicles as biomarkers for liver injury. Her research has also illuminated key mechanisms of lipotoxicity, endoplasmic reticulum stress and inflammation, paving the way for novel therapeutic approaches and research lines in the field. More recently, she has helped develop novel epigenetic inhibitors for the therapy of alcohol-associated hepatitis. She has also deepened understanding of liver injury due to hepatic steatosis, the most common form of chronic liver disease in western societies. Her research has received continuous NIH funding since 2012.

Dr. Malhi is also a clinically-trained transplant hepatologist, one of only about 1,000 physicians trained in transplant hepatology in the country. She participates in the care of pre- and post-transplant patients in outpatient practice and performs endoscopic procedures. She has also helped organize and strongly supports a specialized clinic in hepatology taking care of patients who have metabolic dysfunction-associated steatotic liver diseases.

"I have had the privilege of witnessing firsthand Dr. Malhi's robust contributions to the field of hepatology, her leadership in translational research, and her commitment to fostering innovation and education," says Nataliya Razumilava, M.D., assistant professor of internal medicine at University of Michigan Medical School. "She has an unparalleled ability to translate complex basic science findings into clinically relevant applications."

Dr. Malhi chaired the basic research committee for the American Association for the Study of Liver Disease (AASLD), the premier North American society dedicated to the prevention and cure of liver disease, and currently serves on the Governing Board of the AASLD as a councilorat-large. She is also deputy editor of Hepatology, the AASLD's flagship journal, where she has played a pivotal role in elevating the journal's impact and ensuring the dissemination of cutting-edge research. She has given approximately 75 extramural presentations and is known for the breadth and depth of her knowledge, her ability to clarify difficult concepts and the informative nature of her seminars.

Dr. Malhi says the most rewarding aspect of her work is mentoring the next generation of physician-scientists. In this role, she passes along her accumulated wisdom—some of which reflects the bold, inquisitive child she once was.

"Ask an important question and answer it well," she says. "Many smart people may have the same ideas as you. Move fast."

"I have had the privilege of witnessing firsthand Dr. Malhi's robust contributions to the field of hepatology, her leadership in translational research, and her

commitment to fostering innovation and education."

- Nataliya Razumilava, M.D.



Mayo Clinic announces \$1.9B investment in Arizona

ayo Clinic announced a nearly \$1.9 billion investment in the continued transformation of its Phoenix campus as part of its Bold. Forward. strategy to Cure, Connect and Transform healthcare for the benefit of patients everywhere.

"Bold. Forward. Unbound. in Arizona is the final major building block of Bold. Forward. Unbound., our complete reimagining of our physical infrastructure to enable all of Bold. Forward.," says **Gianrico Farrugia, M.D.** (I '91, GI '94), president and CEO of Mayo Clinic. "Through this work, we are physically and digitally transforming healthcare and blurring the lines between inpatient and outpatient care to support Category-of-One healthcare for our patients, a Category-of-One workplace for our staff and to serve as a blueprint for the world."

Bold. Forward. Unbound. in Arizona will enable new innovative care concepts, physical spaces and integrated technologies to create seamless care experiences for patients and a better workplace for staff.

The 1.2-million-square-foot expansion includes the construction of a new procedural building, a four-floor vertical and horizontal expansion of the Mayo Clinic Specialty Building, the integration of leading-edge technology, the addition of 11 new operating rooms and two new patient units supporting 48 additional beds, and an enhanced arrival experience for patients and visitors.

The plan calls for a two-story, indoor promenade that wraps around the front of the campus, creating cohesion and convenience for patients and visitors as they move from building to building. Another prominent feature in the new design will be the development of care neighborhoods that cluster complementary clinical services for a more intuitive and connected patient experience.

"This incredible investment will forever change the patient and staff experience in Arizona as Mayo Clinic grows and reinvents its nationally recognized clinical care, research and education," says **Richard Gray, M.D.** (S '00), CEO of Mayo Clinic in Arizona. "Bold. Forward. Unbound. in Arizona will increase clinical space on the Phoenix campus by nearly 60 percent, allowing us to care for more patients than ever before. We look forward to setting new standards for patient care and medical innovation."

Bold. Forward. Unbound. in Arizona is part of Mayo Clinic's Bold. Forward. Unbound. physical plan to achieve seamless integration of physical spaces and digital capabilities to meet patients' unmet and evolving needs across all sites. Projects are underway in Rochester, Minnesota, and Jacksonville, Florida, and Mayo Clinic Health System recently completed projects in Mankato, Minnesota, and La Crosse, Wisconsin. Design for the Arizona expansion begins this year with completion slated for 2031.

very year, some mothers die due to preventable heart problems after giving birth. The ability to screen for heart weakness before pregnancy could play a crucial role in identifying women who may need additional care to improve maternal outcomes.

Mayo Clinic researchers, led by **Anja Kinaszczuk, D.O.** (FM '20), Department of Family Medicine at Mayo Clinic in Florida, and **Demilade Adedinsewo, M.B., Ch.B.** (CV '20), Department of Cardiovascular Medicine at Mayo Clinic in Florida, tested artificial intelligence (AI) tools, using recordings from an electrocardiogram (ECG) and a digital stethoscope, to find unknown heart problems in women of childbearing age seen in primary care.

Study findings published in the Annals of Family Medicine show high diagnostic performance of these technologies to detect left ventricular ejection fraction below 50%, indicating heart muscle weakness. These tools were tested on two groups of women aged 18 to 49:

- Group 1: 100 women already scheduled for an echocardiogram. They also had a standard clinical ECG and digital stethoscope recording of the heart's electrical activity and heart sounds.
- Group 2: 100 women seen for routine primary care visits to see how often the AI tools would find heart problems.

The AI-ECG demonstrated an area under the curve (AUC) of 0.94 while the AI digital stethoscope, Eko DUO,

achieved an even higher AUC of 0.98, indicating strong diagnostic accuracy. In the second cohort, the prevalence of positive AI screening results was 1% for the AI-ECG and 3.2% for the AI-stethoscope.

"Statistically, nearly half of pregnancies in this country are unplanned, and approximately 1% to 2% of women may have heart problems they don't know about. Our research findings suggest that these AI tools could be used to screen women before pregnancy, allowing for improved pregnancy planning and risk stratification, early treatment and better health outcomes, which addresses a critical gap in current maternal care," says senior author Dr. Adedinsewo.



Anja Kinaszczuk, D.O.



Demilade Adedinsewo, M.B., Ch.B.

This research builds upon
Dr. Adedinsewo's earlier published
studies, including a pilot prospective study evaluating AI
digital tools to detect pregnancy-related cardiomyopathy
among obstetric patients in the U.S. and a pragmatic
randomized clinical trial of women in Nigeria who were
pregnant or had recently given birth. Collectively, this
research highlights the potential of AI to modernize
cardiovascular screening, enabling earlier identification
and management of heart muscle weakness in women
of reproductive age. Further research is underway to
explore the potential of using these technologies to
screen for heart weakness in broader populations.

Lyell Jones Jr., M.D., named dean of Mayo Clinic School of Graduate Medical Education

yell Jones Jr., M.D. (I1 '01, N '04, NEMG '05), has been named dean of Mayo Clinic School of Graduate Medical Education following the retirement of former dean Annie Sadosty, M.D. (EM '99).

Dr. Jones has been a dedicated member of the Mayo Clinic community since 2009, serving in various capacities, including consultant and professor of neurology, vice chair of education in the Department of Neurology, and Enterprise Medical Director of Contracting and Payer Relations.



Lyell Jones Jr., M.D.

His extensive background in education, combined with his enterprise leadership roles, have positioned him as a thought leader in training the

next generation of clinicians for a dynamic and challenging healthcare environment. Throughout his career, Dr. Jones has demonstrated a commitment to innovation and excellence in medical education. He has developed novel curricula for trainees at Mayo Clinic and nationwide, founded the Health Disparities Initiative (NeuroHDI) and established an award-winning Residency Wellness Program.

After 26 years of distinguished and exemplary service, Dr. Sadosty retired from Mayo Clinic in June 2025. She launched several strategic initiatives aimed at advancing medical training, and is lauded for her tremendous passion, energy, expertise and leadership during her time as dean.

Mayo Clinic Alix School of Medicine rated a top U.S. medical school

ayo Clinic Alix School of Medicine has again been rated as a top national medical school for research by U.S. News & World Report. The ratings place medical schools into one of four tiers; Mayo Clinic Alix School of Medicine is in Tier 1 for 2025 Best Medical Schools: Research.

"This rating is a direct result of the unwavering commitment of our entire medical school community. We congratulate our medical school faculty and staff for their talents, hard work and commitment to the Mayo values," says **Fredric Meyer, M.D.** (NS '87), Juanita Kious Waugh Executive Dean of Education, Alfred Uihlein Family Professor of Neurologic Surgery and dean of Mayo Clinic Alix School of Medicine.

Dr. Meyer underscored how, as an academic medical center, the medical school exemplifies the integration of education with research and clinical practice. It's part of the culture at Mayo Clinic — one that encourages students to collaborate with and learn directly from renowned practicing physicians and scientists.

A tiered rating system has replaced the ordinal ranking system used by U.S. News in previous years. Tiers were calculated based on data related to research activity, student selectivity and faculty resources.

The ratings and data for these disciplines were derived from

survey data that schools reported to U.S. News in 2024, in some cases combined with



Fredric Meyer, M.D.

third-party-sourced information.

Mayo Clinic is top-ranked in more specialties than any other hospital and has two hospitals recognized as Honor Roll members — the highest honor — in U.S. News & World Report's 2024–2025 "Best Hospitals" rankings. U.S. News continues to rank hospitals numerically within states. In the most recent report, Mayo Clinic once again holds the No. 1 position in Minnesota and Arizona.

Lichen planus patients show response to targeted treatment

ayo Clinic researchers have identified a targeted therapy that could bring relief to people living with lichen planus, a chronic inflammatory skin condition of the skin, hair, nails, mouth and genitals. Researchers described the findings from their first-in-human, phase 2 clinical trial in an article published in the Journal of Clinical Investigation.

The researchers identified unique molecular and cellular changes in the skin with lichen planus, particularly an overactive immune response involving specific types of T cell.

The researchers then used baricitinib, a medication that selectively blocks the specific inflammatory pathways of lichen planus, to treat patients in the study. Baricitinib is an oral Janus kinase (JAK) inhibitor that interrupts the signaling pathway of interferon-gamma. Interferongamma is a critical signal in normal antiviral responses and aberrant in lichen planus, which leads to immune cells attacking normal cells.

Patients with treatment-refractory disease experienced early and sustained clinical response to the treatment, resulting in an 83% improvement in symptom respon-



Aaron Mangold, M.D., Department of Dermatology at Mayo Clinic in Arizona, and former senior research technologist Alysia Hughes examine tissue samples.

siveness within 16 weeks of treatment, a marked improvement over baseline. The therapy also rapidly reduced interferon activity, a key signaling molecule in the disease, and reduced the specific, pathogenic T cells.

"This research is an important step in connecting the dots in understanding — and treating — autoimmune and inflammatory diseases," says **Aaron Mangold, M.D.** (TY '12, DERM '15), Department of Dermatology at Mayo Clinic in Arizona and senior author of the study. "These findings provide a potential new, effective, disease-specific treatment option for lichen planus and therapeutic targets for other inflammatory diseases."

Mayo Clinic uncovers brain cell changes that could explain Tourette syndrome

new Mayo Clinic study finds that people with Tourette syndrome have about half as many of a specific type of brain cell that helps calm overactive movement signals as people without the condition. This deficit may be a key reason why their motor signals go unchecked, leading to the involuntary tics that define the disorder. Published in Biological Psychiatry, the study is the first to analyze individual brain cells from people with Tourette syndrome.

"This research may help lay the foundation for a new generation of treatments," says Alexej Abyzov, Ph.D. (QHS '16), a consultant in the Department of Quantitative Health Sciences at Mayo Clinic in Minnesota and co-author of the study. "If we can understand how these brain cells are altered and how they interact, we may be able to intervene earlier and more precisely."

Tourette syndrome is a neurodevelopmental condition causing repeated, involuntary movements and vocalizations such as eye blinking, throat clearing or facial grimacing. While genetic studies have identified



Alexej Abyzov, Ph.D.



Yifan Wang, Ph.D.

some risk genes, the biological mechanisms behind the condition have remained unclear.

To better understand what's happening in the brain with Tourette syndrome, Dr. Abyzov and his team analyzed more than 43,000 individual cells from postmortem brain tissue of people with and without the condition. They focused on the basal ganglia and analyzed how changes in the brain's genecontrol systems might trigger stress and inflammation.

First, in people with Tourette syndrome, they found a 50% reduction in interneurons, cells that help calm excess signals in the brain's movement circuits. They also observed stress responses in two other brain cell types. Medium spiny

neurons make up most of the cells in the basal ganglia and help send movement signals. These medium spiny neurons showed reduced energy production. Microglia, the brain's immune cells, showed inflammation. The researchers found a close link between the two responses, suggesting the cells may interact in Tourette syndrome.

"We're seeing different types of brain cells reacting to stress and possibly communicating with each other in ways that could be driving symptoms," says **Yifan Wang, Ph.D.** (QHS '20), a research fellow in the Department of Quantitative Health Sciences at Mayo Clinic in Minnesota and co-author of the study.

The study points to changes in DNA regions that control when genes turn on and off as a possible cause of brain cell changes in Tourette syndrome. Next, the researchers plan to study how these brain changes develop over time and look for genetic factors that may help explain the disorder. The researchers conducted the study in collaboration with the lab of Flora Vaccarino, M.D., at Yale University.

Obituaries

Ann Benassi, M.D. (PMR '64), died May 12, 2025.

James Burke, M.D. (S '91), died July 28, 2024.

Richard Collins II, M.D. (I '76, CV '78), died May 2, 2025.

Dimitris Daskalopoulos, M.D. (PDC '82, PHYS '83), died May 29, 2024.

Manuel Galofre, M.D. (S '63, ENDO '71), died January 27, 2025.

Charles Michael Johnson III, M.D. (S '75, RD '78), died June 19, 2025.

Gerhard Johnson, M.D. (I '69, HEMO '70), died March 28, 2025.

James Jordan, M.D. (I '69, P '72), died June 30, 2025.

Clyde Lamp Jr., M.D. (ENT '52), died November 4, 2024. James Larson, M.D. (PATH '77), died May 31, 2024. Fred Nobrega, M.D. (EPID '68, I '69), died May 11, 2025. Richard Sampson, M.D. (PATH '71), died February 6, 2025. Richard Siebert, M.D. (NS '71), died May 24, 2022. Steven A. Smith, M.D. (ENDO '88), died April 21, 2025. Shelby Wilkes, M.D. (OPH '80), died December 28, 2024.

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CORRESPONDENCE AND ADDRESS CHANGES

Mayo Clinic Alumni Center Siebens 7, Mayo Clinic 200 First Street SW Rochester, MN 55905 mayoalumni@mayo.edu 507-284-2317

ABOUT THE MAGAZINE

Fax 507-538-7442

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EXECUTIVE EDITOR

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WE ASKED

What's one aspect of your education or training that you wish every medical learner could experience?



"Why, throughout my residency at the Mayo Clinic, the emphasis was on the physical exam after a detailed history. Inspection or observation was first! This is why they were superb diagnostic clinicians!!"

Morton Brookler, M.D.
 (1'62 RHFII'63) retiree

"The annual internal
medicine board review preparation
course. I tried not to miss a lecture and
went every year during my residency. It
was excellent preparation for the boards!
I describe my education at Mayo
being, 'like a baby pelican — I just
opened my beak and the education
poured in!"

Patricia Walker, M.D. (MED '81, I '84), professor
 of medicine at the University of Minnesota
 and HealthPartners Institute
 distinguished scholar

