MAYO CLINIC

2021 • Issue 3

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Letter from the president

As 2021 progresses, there is a renewed sense of coming back to some semblance of normalcy in our lives. Being able to have Mayo Clinic Alumni magazine come out on a normal schedule is something we previously took for granted. I am so glad the magazine is back on track and can again help us connect and bring Mayo Clinic values to the world. The once-in-a-century pandemic that totally disrupted and challenged our usual routines is, thankfully, slowly coming under control as more people are vaccinated.

It feels good to present to our alumni the exciting developments that continue to distinguish Mayo Clinic. I am particularly interested in the progress of the Destination Medical Center initiative, which will transform the landscape of medical care in ways never envisioned by the Mayo brothers. This is just one of the many amazing stories we're happy to bring to alumni. Each quarter, I look forward to seeing the lineup of stories and learning more about the latest goings-on at Mayo Clinic and among alumni. The pandemic truly has fast-forwarded innovation in health care. How's that for a silver lining?

I have said it before — I'll say it again. In the last year, we have been through an unprecedented event that disproportionately affected health care — our chosen profession. The pandemic took a professional and personal toll. I hope in the months ahead you find time for a break to relax, rest and recharge. Our professions are not always stellar examples of self-care. To quote the airline industry, "Put your own oxygen mask on first." We're better physicians and scientists when we are reasonably rested and on even keel. Connections to others is an important part of having balance in our lives. This week, consider reaching out to a fellow alum — someone you trained with, a retired colleague, a former mentor, a friend. A phone call, a text, an email, a meal. I can almost guarantee that you'll feel better as a result.

Something to look forward to — if you don't have the Alumni Association's International Meeting in Lisbon, Portugal, on your calendar, note that it is Sept. 15–17, 2022. I've been to the resort where the meeting will be, Grande Real Villa Itália Hotel & Spa, and it's fabulous. We could all use some time by the sea, reconnecting with old friends, making new friends and bonding over our shared Mayo roots. I hope to see you there!

President, Mayo Clinic Alumni Association

Carl Backer, M.D. (MED '80)
Chief, Section of Pediatric Cardiothoracic Surgery
Professor of surgery
UK Healthcare Kentucky Children's Hospital
Lexington, Kentucky

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About the cover: Anthony Kashou, M.D. (I ’21), one of Mayo Clinic’s young innovators, has created a robust online EKG community and curriculum that’s used around the world.

Illustrations by Federico Gastaldi

Clarification: For the latest information about the Expanded Access Program (EAP) for convalescent plasma featured in issue 1 2021, visit uscovidplasma.org. The data changed before the story was published.

COVID-19 photography disclaimer: Some photos were taken before the pandemic. In others, individuals were alone in nonpatient care, nonpublic settings and were, therefore, in compliance with Mayo Clinic’s COVID-19 safety guidelines while unmasked.

Destination Medical Center

Transforming Rochester

In 2013, the Minnesota legislature passed legislation that included the finance tools and governance to fund the public infrastructure for the Destination Medical Center (DMC) initiative — a 20-year public-private partnership among the state of Minnesota, city of Rochester, Olmsted County and Mayo Clinic. The legislation provided for $585 million in public investment to support $5 billion to $6 billion of private investments. The largest economic development initiative in Minnesota history, DMC is designed to position the state as a global center for the highest quality medical care and to generate high-value jobs, new tax revenue and businesses.

"We are the No. 1 academic medical center in the U.S., but we're never satisfied with that. We keep striving to accomplish great things in new and transformative ways."

– Clark Otley, M.D.

Per the agreement of the partnership, the DMC district must create private economic activity before state funding kicks in. To date, $1.1 billion in private investment has been generated.

According to **Clark Otley, M.D.** (DSRG '96), Department of Dermatology at Mayo Clinic in Rochester and president of the DMC Economic Development Agency board, "Destination Medical Center looks proactively into the future at how to upskill and upscale Rochester as home of the world's leading medical center and the incredible community that supports it. How do we plan for smart economic and structural growth — including accommodations for living, transportation, education and innovation — to support that designation?" ▸

Clark Otley, M.D.

© Photo by Lindsay Nicole Photography

ONE DISCOVERY SQUARE

The economic engine and innovation district of the DMC initiative is Discovery Square — a 16-block area near Mayo Clinic's primary research buildings in downtown Rochester. One Discovery Square, a 92,000-square-foot facility completed in 2019, aimed to attract technology companies to put down roots in the city and partner with Mayo Clinic and others. Mayo Clinic has multiple laboratories in the facility and collaborates with tenants including Philips, Wu-Xi Diagnostics, Exact Sciences and Boston Scientific. These collaborations focus on innovations to better understand complex, serious illnesses that are difficult to diagnose and challenging to treat. The University of Minnesota Rochester also has classroom and laboratory space in One Discovery Square, with students engaging in research in a stimulating ecosystem.

Others in the Discovery Square district include Google, BioSig Technologies and Nference — all Mayo Clinic partner organizations. Four new residential properties have been developed in the area.

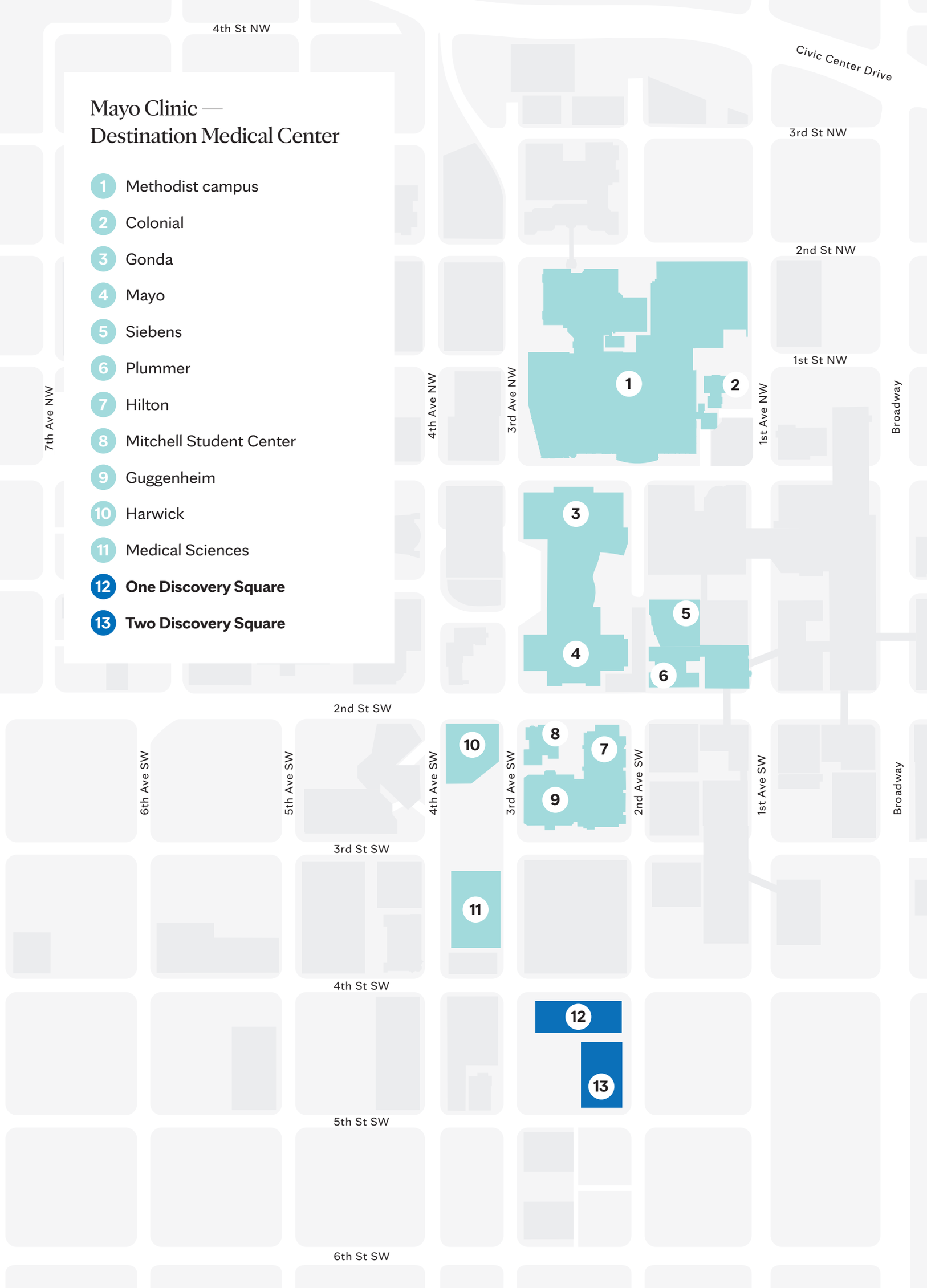
TWO DISCOVERY SQUARE

Leveraging the success of One Discovery Square, Mortenson Construction began construction in September 2020 on Two Discovery Square, a 125,000-square-foot facility that will focus on advancing biomanufacturing, virtual care and advanced analytics. The project is expected to be complete in early 2022.

"The bench-to-bedside advances that will help our patients are occurring every day at facilities on and around Mayo Clinic campuses, including Discovery Square," says Dr. Otley. "Our innovation efforts actually accelerated during the pandemic and are a bright shining reminder of the incredible things we and our world-class collaborators in medical devices, health care information technology, diagnostics and pharmaceuticals do every day. We are the No. 1 academic medical center in the U.S., but we're never satisfied with that. We keep striving to accomplish great things in new and transformative ways. Discovery Square aims to grow the biotechnology giant status of Rochester and Minnesota. We want to attract and work with others who want to partner on furthering our mission for our patients." •

"Discovery Square aims to grow the biotechnology giant status of Rochester and Minnesota. We want to attract and work with others who want to partner on furthering our mission for our patients."

– Clark Otley, M.D.


Mayo Clinic —
Destination Medical Center
1 Methodist campus
2 Colonial
3 Gonda
4 Mayo
5 Siebens
6 Plummer
7 Hilton
8 Mitchell Student Center
9 Guggenheim
10 Harwick
11 Medical Sciences
12 One Discovery Square
13 Two Discovery Square
4th St NW
Civic Center Drive
3rd St NW
2nd St NW
1st St NW
7th Ave NW
4th Ave NW
3rd Ave NW
1st Ave NW
Broadway
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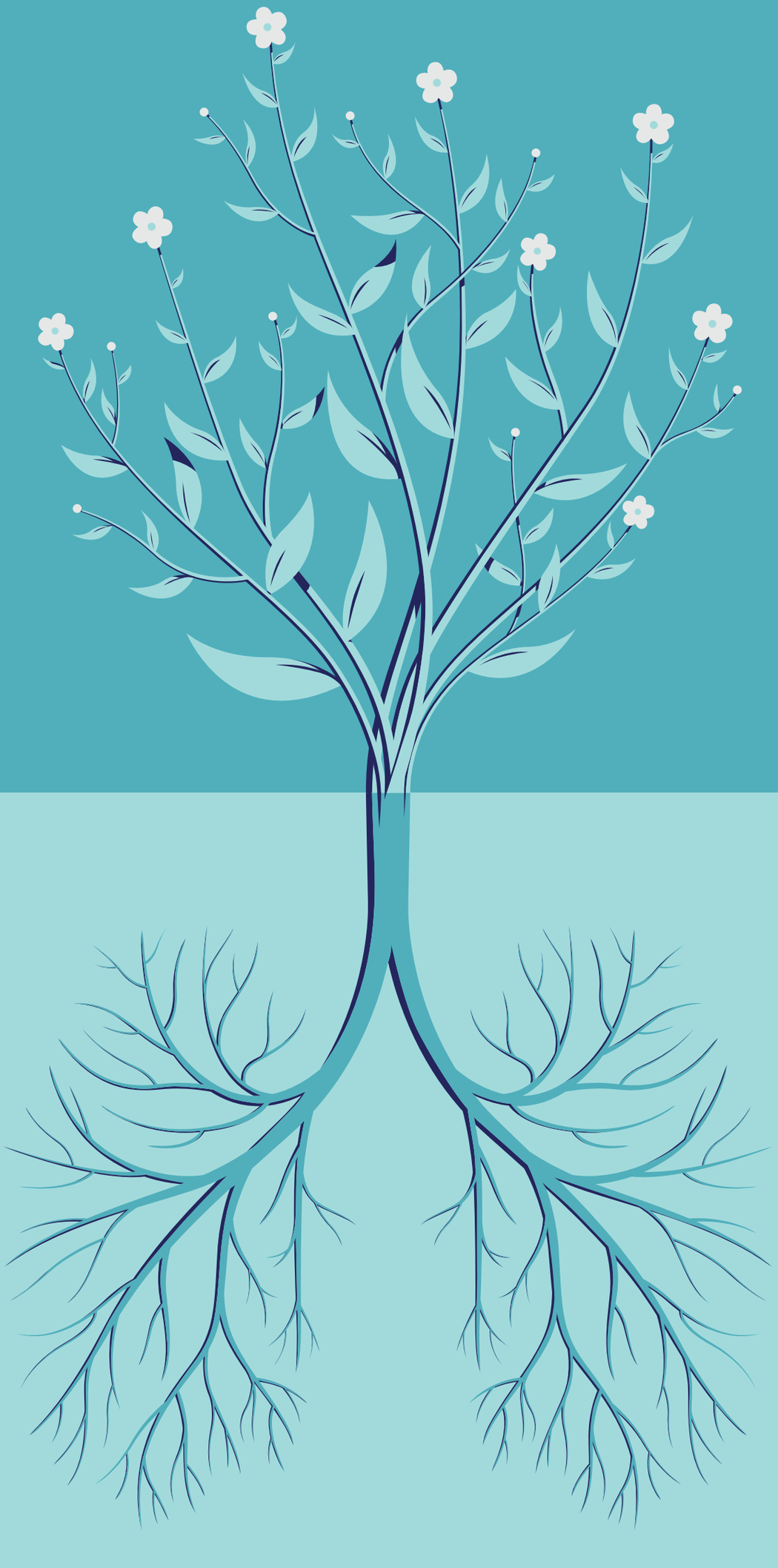
Lung perfusion center

Give lungs a chance

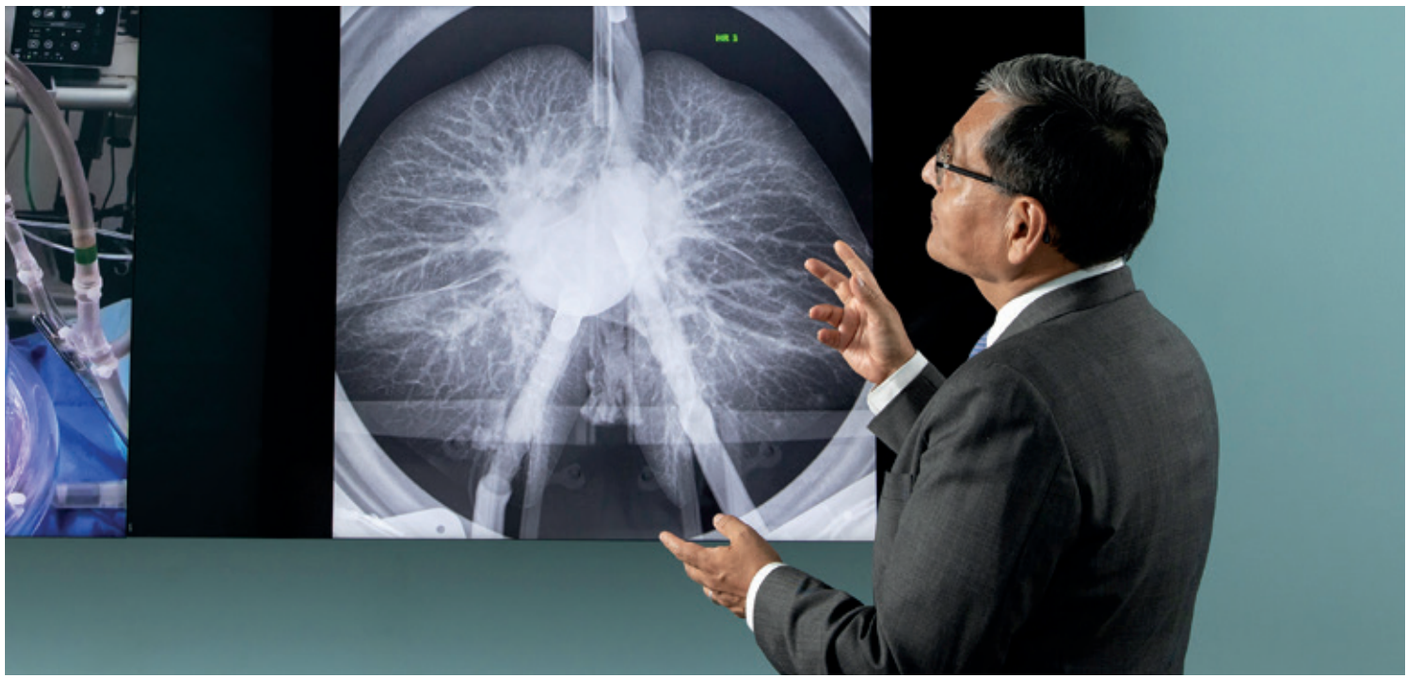
In the first half of 2021, Mayo Clinic in Florida transplanted 26 lungs. Four of them were available for transplantation only after being evaluated with ex vivo lung perfusion (EVLP) in a new facility in the Discovery and Innovation Building on the Florida campus. Seven of the others were procured only because EVLP technology was available in case the lungs didn't meet Mayo transplant surgeons' criteria upon arrival in Florida. One patient had severe lung injury from COVID-19 and was on extracorporeal membrane oxygenation (ECMO) in the ICU until a lung became available via EVLP. ▸



The new facility — a lung perfusion center — is a collaboration with Lung Bioengineering, a subsidiary of United Therapeutics. The facility opened in December 2020. United Therapeutics leases and staffs the center, and Mayo Clinic provides physician oversight and procurement and delivery of lungs in coordination with organ procurement organizations. Mayo has had a relationship with United Therapeutics since 2015, when it was the first center enrolled in the company's EVLP clinical trial.

The goal of the lung perfusion center is to make more donor lungs available for transplantation by gathering additional data on selected marginal donor lungs. EVLP itself is not a new technology; having a centralized facility for organ perfusion is a new concept. Lung Bioengineering has a similar facility in Silver Spring, Maryland — the only two centralized EVLP facilities in the U.S. Both facilities have capacity to provide EVLP support for an ongoing multicenter clinical trial (Increasing Lung Transplant Availability Using Normothermic Ex Vivo Lung Perfusion at a Dedicated EVLP Facility) or as a clinical service using an FDA-approved, commercially available EVLP system. The center in Jacksonville will soon begin working with other transplant programs to offer commercial lung perfusion services to increase the potential of lungs for transplantation in more patients, beyond Mayo Clinic. ▸

The goal of the lung perfusion center is to make more donor lungs available for transplantation by gathering additional data on selected marginal donor lungs.



Jorge Mallea, M.D., evaluates perfused lungs to determine if they're suitable for transplant.

How it works

- When the organ procurement organization contacts Mayo Clinic about an available donor, Mayo sends a team or contracts with a local team to retrieve the lung. Or if another hospital has declined a lung, the procurement organization may contact Mayo Clinic to determine if it would like to consider the lung for EVLP.
- Mayo Clinic reviews clinical data, X-rays and bronchoscopy of the lung in question. If Mayo believes the lung has potential for transplant, Mayo retrieves the organ or contracts with a local team to procure it.
- The lung is flown to the lung perfusion center on Mayo's Florida campus. The facility has room to perform EVLP on two or three lungs at a time, with space for expansion.
- The left atrial cuff and pulmonary artery are cannulated, and an endotracheal tube is placed to connect the lung to the ventilator and allow it to breathe. The lung is connected to the EVLP circuit and slowly warmed. The lung is then perfused with a hyperosmolar solution and ventilated with a protective process for approximately four hours, with constant monitoring of its physiologic parameters.
- Two ex vivo lung specialists and a technician remain in the room with the lung. A Mayo Clinic transplant team conferences in virtually throughout the procedure and makes a decision about the lung's suitability for transplant based on bronchoscopy, blood gases, X-rays and ventilator data.
- If the lung meets Mayo's criteria, it is cooled down, repackaged and transported to a Mayo Clinic operating room.

Why it's needed

- Lungs are vulnerable to damage at the time of the donor's death, resulting in many donor lungs being discarded due to their rapid deterioration.
- Only about 20% of brain-dead donors are able to donate lungs that are suitable for transplant — a lower percentage than other organs.
- EVLP is an option for a portion of lungs initially deemed unsuitable for transplant.
- Survival rates for patients who receive EVLP-treated lungs are similar to those associated with lungs considered acceptable at the time of donation.
- 1,000+ people are awaiting lung transplant in the U.S. — with an upsurge in need due to COVID-19-related illness.
- On average, 75% of patients receive a lung transplant within one year on the wait list; 400 people in the U.S. die each year, waiting for a lung transplant.
- Mayo Clinic physicians perform 54 lung transplants per year across the Rochester and Florida campuses; the Arizona campus is preparing to open a lung transplant program in 2024.
- The survival rate of Mayo Clinic lung transplants exceeds the national average; one-year survival rates at Mayo Clinic are 94% (Florida campus) and 96% (Rochester campus) compared to 89% nationally.

‘TURNING A NO INTO A MAYBE’

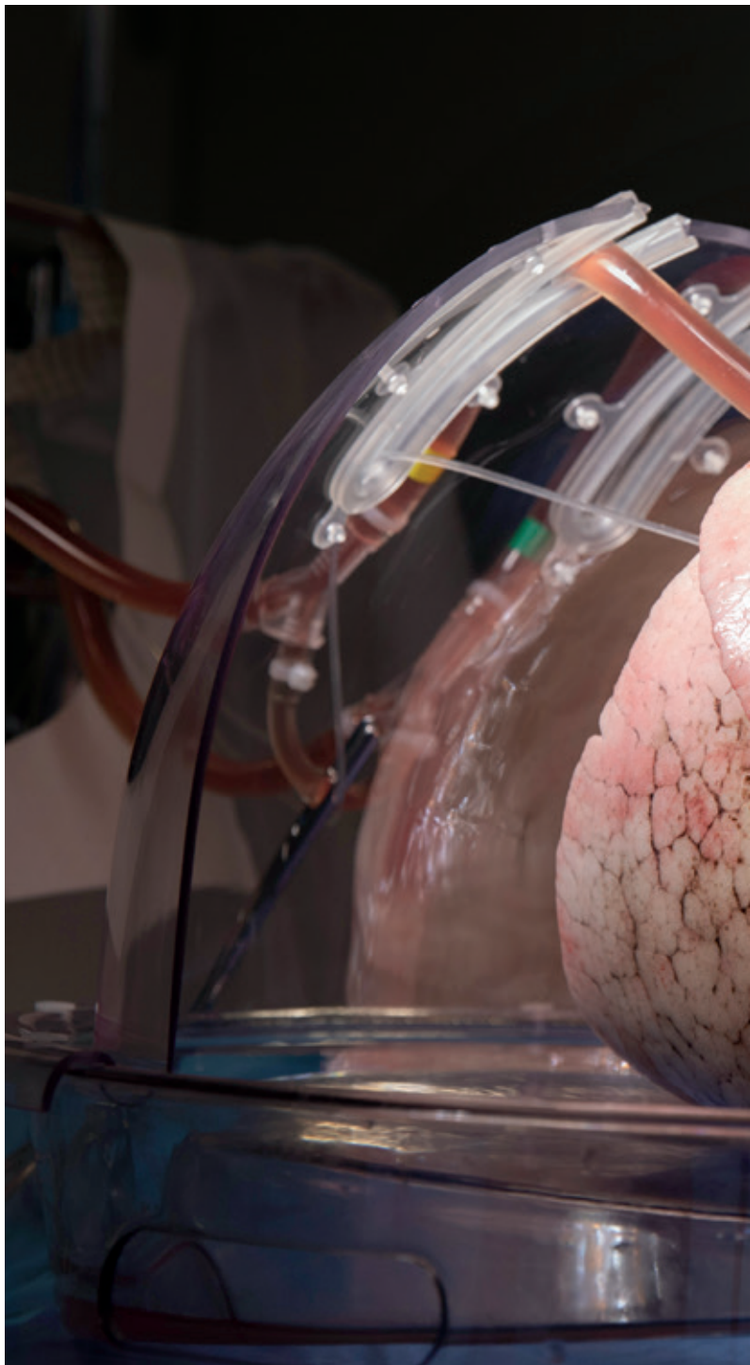
Using an FDA-approved medical device, EVLP involves connecting lungs to a circuit that circulates a protein-rich solution through the lungs and to a ventilator that allows the lungs to breathe. The data collected allows the transplant team to determine if the lungs are fit for transplant.

“EVLP allows us to convert a marginal lung into a lung suitable for transplantation — turning a no into a maybe,” says **Si Pham, M.D.** (S ’17), chair, Department of Cardiothoracic Surgery at Mayo Clinic in Florida. “Right now, some rejected donor lungs are actually acceptable for transplantation. A recent study analyzing UNOS’ (United Network for Organ Sharing) database showed that only 20% of donor lungs are accepted for transplant. An organ has no chance of transplantation if no one evaluates it. EVLP allows us time to assess, analyze and make better decisions about a lung’s suitability for transplant. Mayo Clinic can be more aggressive in saying yes to lungs because we know we have the luxury of a few more hours to thoroughly evaluate them versus make split-second decisions.

“EVLP could significantly shorten the time and reduce mortality on waitlists and improve outcomes for patients with end-stage lung disease. Mayo Clinic has always tried to be in the forefront of applying new technology to provide the best care for patients. Our goal is to change the transplant culture and provide more organs into the system so that nobody dies waiting for an organ.”

Si Pham, M.D. (S ’17)
Department of Cardiothoracic Surgery, Mayo Clinic in Florida

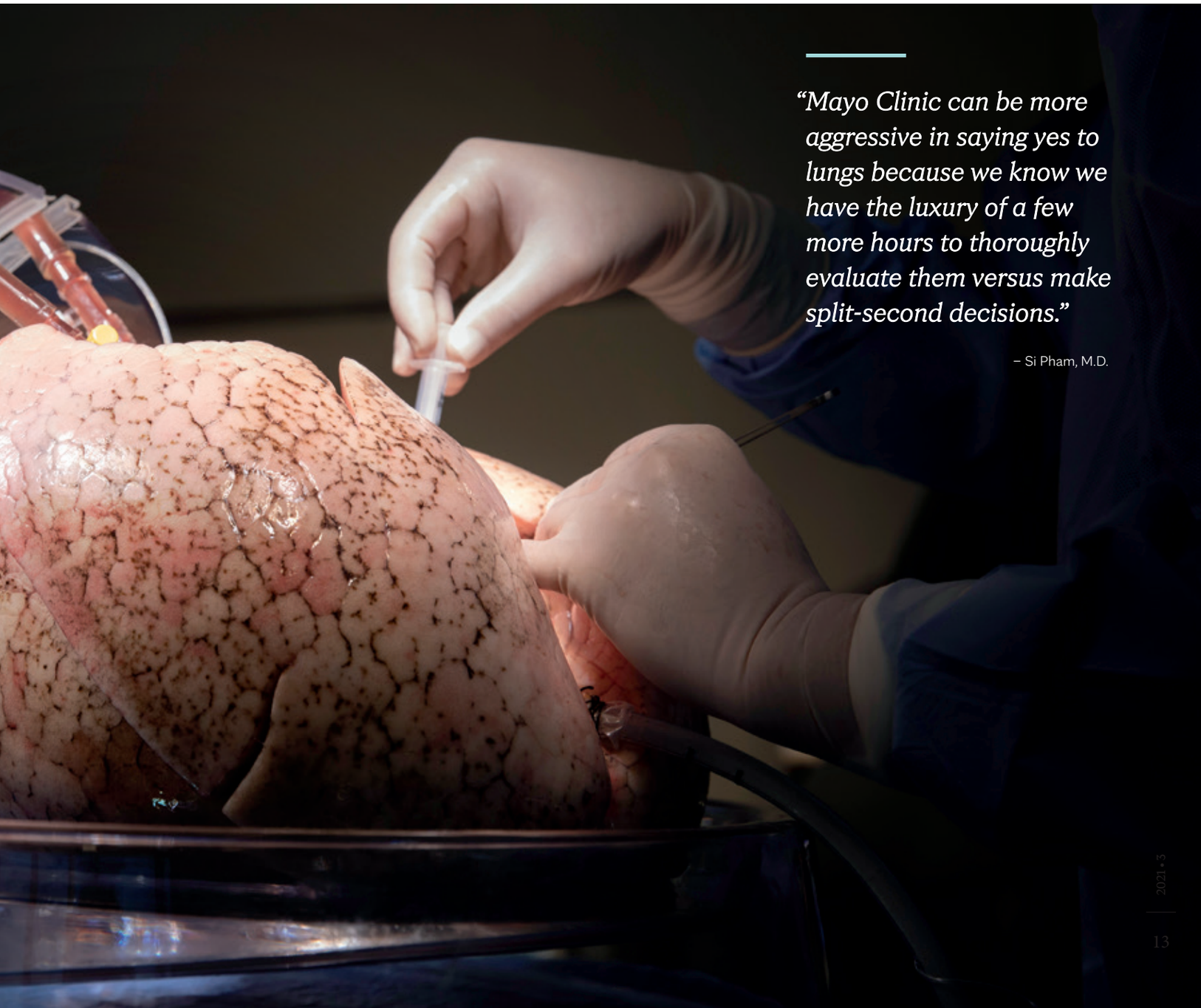
Jorge Mallea, M.D. (TRANM ’11)
Division of Pulmonary, Allergy and Sleep Medicine, Mayo Clinic in Florida



Mayo Clinic and Lung Bioengineering are working to increase awareness about EVLP among organ procurement organization personnel.

The Mayo Clinic–Lung Bioengineering partnership includes researching ways to restore health to damaged tissues and organs. The EVLP platform opens opportunities to understand biomarkers in donor lungs to determine which ones will respond to the therapy, using stem cells and nanotechnology to treat donor lungs to improve their condition and make them less prone to rejection before transplantation. **Jorge Mallea, M.D.** (TRANM '11), Division of Pulmonary, Allergy and Sleep Medicine at Mayo Clinic in Florida and medical director of the lung perfusion center, says other research possibilities include xenografts and testing bioengineered lungs. Because EVLP is only an evaluation process, it cannot treat severe damage caused by aspiration, infection and trauma, but researchers hope that will be possible in the future.

"Working closely with Lung Bioengineering boosts our expertise in organ perfusion technology and facilitates our research," says Dr. Mallea. While lungs are the initial focus of restoration and regenerative efforts and research, Dr. Mallea says other organs could benefit from the collaboration with United Therapeutics. •



"Mayo Clinic can be more aggressive in saying yes to lungs because we know we have the luxury of a few more hours to thoroughly evaluate them versus make split-second decisions."

– Si Pham, M.D.

Young innovators

Finding a better way

Prolific American inventor Thomas Edison said, "There's a way to do it better — find it."

No doubt, Mayo Clinic physicians and scientists have a long history of finding better ways through invention and innovation. From mallets and masks and syringes and specula to cystoscopes, resectoscopes, proctoscopes and laryngoscopes, Mayo Clinic physicians and scientists have identified ways to improve procedures and practice. Some have been big news — using iodine to treat goiters, insulin to treat diabetes and cortisone to treat rheumatoid arthritis. Others have been behind the scenes — creating the single-file medical record, introducing the first circular nursing station in the U.S.

"If you always do what you always did, you will always get what you always got."

– Albert Einstein

Any invention or discovery is exciting — even more so when the innovator is a trainee. Medical students, residents and fellows are consumed with gaining knowledge, mastering procedures, cramming for exams, passing boards and defending theses. The current Mayo Clinic environment empowers them to explore innovation and supports them in the process.

In the stories that follow, some of those trainee inventors and innovators discuss the solutions they discovered to address areas in need of improvement. They noticed problems and used their own time and resources to engineer fixes. All of these trainees say their only interest was to improve health care for patients. ▸

EYES ON THE PATIENT

Allisa Song (MED '22), a fourth-year student at Mayo Clinic Alix School of Medicine's Rochester campus, already had an invention under her belt when she started medical school. She and a trio of students and recent graduates from the University of Washington and Seattle University invented a screw-on attachment for eye-drop bottles to control the size of drops.

"I read an investigative story about how standard eye-drop containers produce drops that are far too large for the eye to absorb, which means lots of medication is wasted," says Song. "I saw an opportunity to decrease drop size and costs for patients, many who are older, with low vision and dexterity."

The single-use device, the Nanodropper, helps to eliminate medication waste, saves money and empowers patients to get all of the intended benefits out of each bottle. Ultimately, this will improve medication adherence, according to Song.

"Think about patients who use expensive glaucoma eye drops," she says. "When they miss their eye while dispensing the drops, which is very common, they run out of drops before their insurance will cover the next refill. As much as 25% of patients experience 'bottle exhaustion,' which makes it challenging to follow their prescribed medication routine.

"A bottle of eye drops to treat glaucoma costs about $350 without insurance and can cost $75 to $100 with insurance. We want to help patients get the absolute most value from every bottle of drops they purchase. With the Nanodropper, we can improve patient outcomes without increasing cost. It's rewarding to know we're contributing to the push for value-based care."

Song and her team interviewed ophthalmologists and optometrists and conducted a literature search, which revealed that smaller eye drops are just as or more effective than larger drops. Smaller drops have a better safety profile because the extra amount in large drops is absorbed systemically and can have unfavorable side effects.

The Nanodropper is an FDA-listed, sterile Class 1 medical device and is being produced, assembled and sterilized in U.S.-based facilities. The company is partnering with private practice eye care professionals to distribute the device to patients. Nanodropper now has partner clinics in 13 states and Washington, D.C., and has fulfilled hundreds of orders since the product launched in June 2020.

Last year, the company signed a $500,000 contract with the U.S. Air Force and secured seed funding. Nanodropper's co-founders were recognized on the 2021 Forbes 30 Under 30 list in health care.

Nanodropper CEO Song balances company business with her medical studies. "When I hear stories about how the Nanodropper helps people, it motivates me in the classroom and reminds me why I went into medicine," she says. ▸

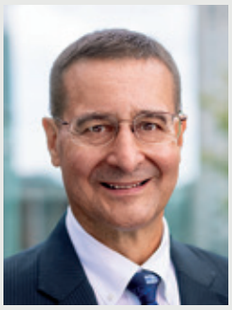
"When I hear stories about how the Nanodropper helps people, it motivates me in the classroom and reminds me why I went into medicine."

– Allisa Song

Illustrious inventors

Four Mayo staff members have been elected to fellow status in the National Academy of Inventors.

2014



Michael Yaszemski, M.D., Ph.D. (OR '96), Department of Orthopedic Surgery at Mayo Clinic in Rochester and the John and Posy Krehbiel Professor of Orthopedics Honoring Bernard F. Morrey, M.D., pioneered use of biodegradable polymers to treat spinal cord injuries.

2016

Richard Ehman, M.D. (RD '85), Department of Radiology at Mayo Clinic in Rochester, the Blanche R. and Richard J. Erlanger Professor of Medical Research, invented magnetic resonance elastography (MRE).

2019

David Ahlquist, M.D. (MED '77, I '80, GI '83, deceased), Division of Gastroenterology and Hepatology at Mayo Clinic in Rochester, invented the technology on which Cologuard — a minimally invasive stool-based assay approved for screening and early diagnosis of colorectal neoplasms — is based.

2020

Samuel Asirvatham, M.D. (CVEP '00), Division of Heart Rhythm Services at Mayo Clinic in Rochester and the James M. and Lee S. Vann Professor of Cardiovascular Diseases, developed a catheter-based navigation system to locally treat brain tissues causing seizures.

"If you have an idea and believe in it, focus on how you can achieve it regardless of what others say is impossible."

– William (Bill) Clifton III, M.D.

MULTIDIMENSIONAL NEUROSURGEON

When he was a resident in the Department of Neurologic Surgery at Mayo Clinic in Florida, **William (Bill) Clifton III, M.D.** (NS '21), was disheartened by some aspects of surgical training.

"Cadavers are expensive to purchase and store, limited in supply and usefulness, not available for pediatric training, not used in all countries, and variable in quality — especially tissue quality," he says. "My dad was an electrical engineer, so we had design-and-build projects going on around the house. Engineering, materials science and math have always been fun to me. I read some blogs and manuals about 3D printing and decided to create tools we could use in neurosurgical training."

Dr. Clifton took out a personal loan to buy a 3D printer that he installed at his home and then spent his free time creating models for surgical trainees. In two years, he created more than 1,200 adult and pediatric models, including skulls, brains, spinal cords, tumors and most organ systems. He has created models of specific patient pathologies to facilitate surgical planning, including a congenital spine abnormality and rare brain tumor.

Dr. Clifton's creations are actually 4D, which means they change form in reaction to factors in their environment including heat, humidity and pressure. In this way, the models replicate the contraction, bending and breaking of human tissue. Dr. Clifton calls his models Biomimetic Human Tissue Simulators.

"4D printing has been around for only a few years," says Dr. Clifton. "I saw a surge of papers about it in the aviation and automobile industries and wondered why we couldn't apply it to the human body. 4D models allow us to see how the surgical landscape will change when we take specific actions."

His first model was a vertebra that performed like bone when screws were drilled into it. Missing were ligaments, tendons, skin, fat and muscles. Dr. Clifton and his collaborator, Aaron Damon, a simulation technologist in the J. Wayne and Delores Barr Weaver Simulation Center at Mayo Clinic in Florida, delved into the organic chemistry of compounds, inventing and patenting a new compound to represent those soft tissue structures.

"The full surgical models I've made for neurosurgery training cost $20 to $100 apiece, compared to $3,000 to $5,000 for a cadaver," he says. "Physicians who evaluated them said they were as good as or better than a cadaver for training. The models also teach very subtle details of surgery that cadavers can't, such as bleeding control and complication management. Our models are biodegradable, water soluble and nontoxic."

Dr. Clifton has authored more than 50 peer-reviewed publications and submitted several patents for neurosurgical devices. Despite his focus in neurosurgery, Dr. Clifton worked with his colleagues in orthopedics, GI and transplant to develop training models.

Dr. Clifton says faculty members were ecstatic about the models because they accelerate the speed with which trainees are ready to perform in the operating room. And Dr. Clifton is ecstatic that surgical trainees don't have to learn on patients.

"If you have an idea and believe in it, focus on how you can achieve it regardless of what others say is impossible," says Dr. Clifton, who is now completing a fellowship in complex surgery at Columbia University in New York City. "Just do it. I hope that, as the ultimate result of my belief in my idea, surgeons training today can acquire even better skills than their predecessors and that Mayo Clinic will be at the forefront of education, research and — most importantly — patient care."

Alfredo Quinones-Hinojosa, M.D. (NS '16), chair, Department of Neurologic Surgery at Mayo Clinic in Florida and a William J. and Charles H. Mayo Professor, has assumed responsibility for Dr. Clifton's lab. ▸

Christine Mehner, M.D., Ph.D. (left), and Marion (Toni) Turnbull, Ph.D.

FLORIDA DUO NAILS IT

When she was an orthopedics resident in her native Germany, **Christine Mehner, M.D., Ph.D.** (BMB '20), noted that the nails used to set fractures didn't provide the best possible outcomes to stabilize fractured long bones, such as the tibia, femur and humerus. In standard surgery to fix a tibia fracture, for example, a surgeon's experience determines adequate positioning of the patient's leg and foot to achieve proper alignment post-surgery. However, in more than 40% of cases, patients have an error in the rotation of the foot after surgery. A rotation error of more than 30 degrees from its original position can negatively affect the patient's knee, hip and ankle over time.

Four years later, when Dr. Mehner was a predoctoral Ph.D. student at Mayo Clinic in Florida, the fracture nail issue resurfaced. She and her colleague **Marion (Toni) Turnbull, Ph.D.,** a New Zealand native who is a research associate in the Department of Neurology, were brainstorming ideas for Mayo Clinic in Florida's Alligator Tank competition in which aspiring entrepreneurs and inventors pitch ideas to a panel of expert judges.

"Too much manual manipulation of the leg and foot during surgery can cause damage, which increases pain and recovery time and detracts from healing," says Dr. Mehner, now a postdoctoral fellow at Mayo Clinic in Florida. "Considering the long-term impact that common rotation errors can have, we thought there must be a better way."

> Employees and staff at all levels are urged to think differently, identify problems and generate solutions to everyday challenges.

Drs. Mehner and Turnbull pitched the concept of an adjustable fracture nail, which has internal rotating mechanisms and components that allow the nail to extend and fine-tune the angle of the fractured limb while in the bone. The patented nail is being prototyped with Mayo Clinic's Surgery Research Center for Excellence. With help from Mayo Clinic Ventures, the inventors hope to find a surgical device company to produce and test the nail in a patient cohort.

"The fracture nails currently in use have been the status quo for decades," says Dr. Mehner. "We believe ours could replace current intramedullary nails and make surgery easier and faster for surgeons. More importantly, the nail could help patients heal faster and with less pain, reduce the risk of permanent injury and chronic pain, and reduce the rate of revision surgery."

An undergraduate class at the University of Minnesota completed a market analysis for the new fracture nail, which has generated enthusiasm from Mayo Clinic orthopedic surgeons. Dr. Turnbull says, "They've said they can't believe it doesn't exist already.

"When you can't believe there's not a better way to do something, look at that as an opportunity for innovation. Mayo Clinic has resources to help with patent disclosures, inventor forums, support and seed funding."

Mayo Clinic in Florida's "I'm In" campaign encourages innovative thinking, continuous improvement and challenging the status quo. Employees and staff at all levels are urged to think differently, identify problems and generate solutions to everyday challenges.

"There's a growing entrepreneurial community on the Florida campus," says Dr. Turnbull. "Once you let people know that innovative ideas will be supported and provide the right culture, more will come. We are already thinking of ideas to improve research and patient care."

The adjustable fracture nail received a 2021 Innovation Accelerator Award from the Mayo Clinic Office of Translation to Practice, which awards projects that aim to develop new products with commercialization potential. ▸

"We believe ours could make surgery easier and faster for surgeons. More importantly, the nail could help patients heal faster and with less pain."

– Christine Mehner, M.D., Ph.D.

PUTTING A RING ON IT

Karim ReFaey, M.B., B.Ch. (NS '16), says his mentor, **Alfredo Quinones-Hinojosa, M.D.** (NS '16), chair, Department of Neurologic Surgery at Mayo Clinic in Florida, tells protégés they must be persistent, dream big and be passionate because their journeys won't be easy.

Dr. ReFaey, a former postdoctoral research fellow in the Department of Neurologic Surgery, is accustomed to persistence. He was a competitive swimmer from an early age, getting up before dawn every day to practice for more than 20 years. "It's a systematic, intense sport with a lot of repetitions, just like science," he says.

Dr. ReFaey was in medical school in his native Egypt when he observed a brain surgery for the first time and wanted to learn more. He found Dr. Quinones-Hinojosa's brain surgery videos online and took the initiative to email him. "I wanted him to train me," says Dr. ReFaey, who joined Dr. Quinones-Hinojosa at Johns Hopkins Hospital in Baltimore, Maryland. When Dr. Quinones-Hinojosa joined Mayo Clinic in Florida to chair the Department of Neurologic Surgery, he asked Dr. ReFaey, then a postdoctoral fellow in neurosurgery, to join him.

In addition to emphasizing persistence, Dr. Quinones-Hinojosa tells trainees they're more capable than they think they are, according to Dr. ReFaey, who took those words to heart. In 2017, he was in

Karim ReFaey, M.B., B.Ch.

"It's exciting and a little scary to push yourself outside your comfort zone. I'm glad Dr. Quinones-Hinojosa challenged me to truly understand, prioritize and ultimately meet the needs of our patients."

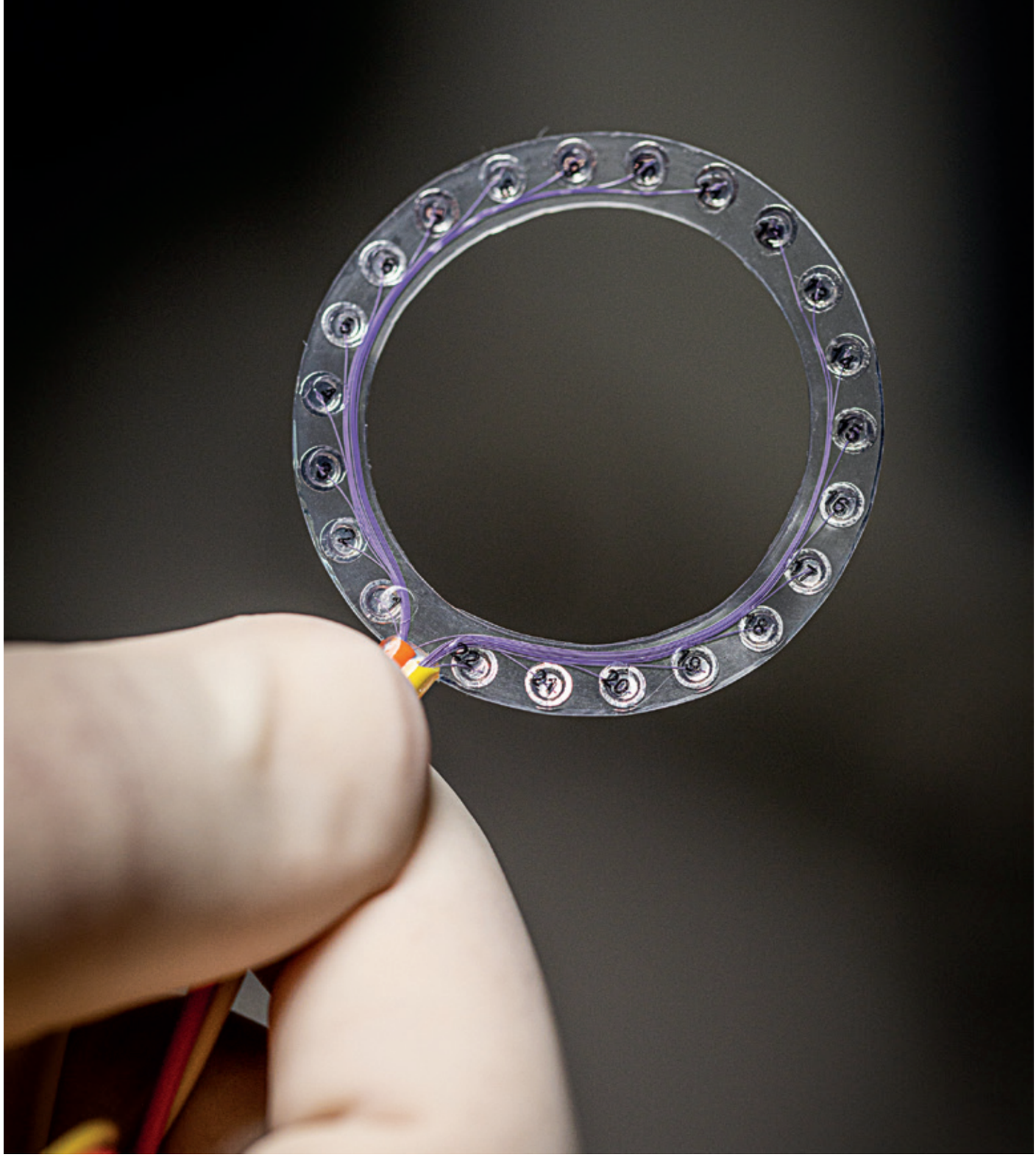
– Karim ReFaey, M.B., B.Ch.

the operating room at Mayo Clinic during a challenging surgery on a patient who had seizures caused by epilepsy. Frustrated, Dr. Quinones-Hinojosa commented that there had to be a better way to map the brain during awake brain surgery. Dr. ReFaey and his neurology colleague **William Tatum, D.O.** (N '09), retired to an office and began brainstorming ideas to improve on the grid electrodes currently used to map brain activity during surgery.

The electrodes that were being used come in strips, and up to four of them were placed on the patient's brain to map electrical activity and assist the surgeon in knowing where to resect tumor tissue. The strip electrodes allowed only for monitoring of epileptogenic electrical patterns in one direction and were challenging to maintain near the surgical resection margin. Using multiple strips also is expensive. Dr. ReFaey conceived a circular grid that covers the surface of the brain, allowing for direct access and ensuring real-time multidirectional, accurate localization of the electrical activity firing from the brain. The ring-shaped electrode assembly enables surgeons to achieve maximized tumor resection safely and real-time electrophysiological data recording from the surface of the brain concurrently. The surgeon can easily move the ring-shaped grid, compared to moving four separate strips.

Within months, the circular grid was patented and a prototype was created and tested in a patient. Four years later, the Mayo Clinic team has published five peer-reviewed papers showing the circular grid's superiority over the traditional electrophotographic tools in patient outcomes. The device has been used in more than 200 patients and is being used in all awake brain surgeries at Mayo Clinic in Florida. Mayo Clinic Ventures will license the invention to an outside company.

"The current brain-mapping concept of electrodes has been in use since the 1940s for awake surgery," says Dr. ReFaey. "It works, but there's a better way. We believe our circular grid is a better way."



Data shows that patients who had surgery with the circular grid have a greater extent of tumor resection and faster recovery by approximately seven days postoperatively, compared to traditional brain-mapping methods. Dr. ReFaey perfected his invention and has presented it to excited audiences at several national neurosurgical meetings.

When Dr. ReFaey initially presented his concept, Dr. Quinones-Hinojosa sent him back to the drawing board. "He said the idea was great but pushed me to make it personal — to think as if these patients were my family or loved ones and ask myself if I'd be willing to use the device on them," says Dr. ReFaey, who is now involved in a start-up company. "Dr. Quinones-Hinojosa said, 'When you have that personal perspective, you don't think about how you're changing the practice, you think about how you're making things better for the patient in the operating room — how you're changing the world.' It's exciting and a little scary to push yourself outside your comfort zone. I'm glad Dr. Quinones-Hinojosa challenged me to truly understand, prioritize and ultimately meet the needs of our patients." ▸

THE EKG GUY

While preparing for exams during medical school at SUNY Upstate Medical University in Syracuse, New York, **Anthony Kashou, M.D.** (I '21), grew frustrated by the state of EKG training resources, deeming them either too basic or too advanced. He took on the task of developing EKG training materials for his fellow students during his fourth year of medical school so they wouldn't have the same struggle.

"As a learner, I had to consult multiple textbooks and the medical literature due to the lack of appropriate resources, which isn't the most effective way to learn," says Dr. Kashou. "Even then, those materials did not always do a good job explaining some clinically relevant material. My classmates liked the content I created and asked for more."

Dr. Kashou, now a final-year resident in the Department of Medicine at Mayo Clinic in Rochester, has created the fastest-growing EKG community, with a million online followers. His curriculum is used by medical providers and programs around the world.

Dr. Kashou realized that medical professionals across the board wanted better EKG learning options. And after only a five-hour weekend session, the learner's improvement in EKG literacy is measurable, he says.

Dr. Kashou is known as The EKG Guy on his website, YouTube channel and social media. He has created more than 500 EKG video lessons and EKG courses including "Ultimate EKG Breakdown," which purports to take someone with no EKG experience to an advanced interpreter level. He recently introduced a more advanced course, "Ultimate EKG Coding Breakdown." His curriculum has earned joint accreditation by the American Medical Association and Accreditation Council for Continuing Medical Education.

"This work is exciting, and the leaps we're making are incredible. We have a chance to truly transform the way we address clinical problems and deliver patient care."

– Anthony Kashou, M.D.

Dr. Kashou is determined to advance EKG knowledge among noncardiac specialists for the benefit of patient care. "Every person who enters an emergency department with chest pain or shortness of breath gets an EKG — one of the most rapid, noninvasive and cost-effective diagnostic tools in modern medicine," he says. "EKG interpretation skills are critical for patient care, yet many providers feel unequipped to achieve proficiency. They struggle to understand why they see what they see on an EKG and often rely on memorizing patterns they need to know to pass exams. I think it's important to be less reliant on an expert or computer's interpretation."

Dr. Kashou's "Ultimate EKG Breakdown" now serves as the primary EKG course

for the electrophysiology technician and physician assistant programs at Mayo Clinic in Rochester. It also serves as a means for Mayo cardiac technicians to improve their skills. On his own time, Dr. Kashou leads seminars for medical professionals at Mayo Clinic who want to improve their EKG proficiency. During the pandemic, his online curriculum served as a learning solution for Mayo Clinic Alix School of Medicine students when clinical duties were suspended.

Dr. Kashou is just as passionate about EKG innovation as he is about EKG education. His research focuses on the development of algorithms to aid in wide complex tachycardia differentiation, the application of artificial intelligence-enabled electrocardiography in clinical practice and the creation of educational solutions to improve EKG literacy among medical providers.

"This work is exciting, and the leaps we're making are incredible," he says. "We have a chance to truly transform the way we address clinical problems and deliver patient care." Dr. Kashou plans to complete a National Institutes of Health-funded combined cardiology and research fellowship track at Mayo Clinic in Rochester. ▸

Inventor launchpad

Budding medical inventors often don't know where to turn to advance their ideas. Enter Mayo Clinic's new Innovation Exchange. This program applies 150 years of experience advancing innovative treatment for serious and complex medical challenges to provide new and seasoned innovators with connections to people, places and resources to accelerate medical breakthroughs.

The Innovation Exchange is a membership-based platform that connects Mayo Clinic's internal innovators and external start-ups throughout the health care industry with premier medical and business insights and introductions to bring innovations to market.

Innovation Exchange offers:

- Expertise and advice from Mayo Clinic physicians, researchers and scientists
- In-person and virtual programmed services and events
- Introductions to funding sources — angel investors, government programs and venture capital firms
- Business strategy consulting, marketing planning and legal advising from a network of business, technology and academic collaborators
- Mentorship matching
- Conference space and makerspace to build prototypes in the Discovery and Innovation Building on Mayo Clinic's campus in Jacksonville, Florida
- Access to research studies, clinical trials and laboratories for qualified firms
- Wet lab space for rent

Charles Bruce, M.D. (I '96, CV '00), medical director, Mayo Clinic Innovation Exchange, chief innovation officer and assistant medical director, Department of Business Development at Mayo Clinic in Florida, has helped create seven start-up companies and has more than 30 patents for medical inventions. "Mayo Clinic routinely collaborates with industry to improve patient care through research agreements, invention licenses and consulting activities — facilitated across the enterprise through our technology transfer office, Mayo Clinic Ventures," he says. "This has resulted in more than 600 invention disclosures, 400 patent filings and 200 issued patents per year. The runway for taking health care innovations to market is long. We're here to help."

"The runway for taking health care innovations to market is long. We're here to help."

– Charles Bruce, M.D.

Innovation Exchange is particularly — but not exclusively — interested in projects related to remote monitoring, virtual care and hospital-at-home concepts; and innovations in oncology, neuroscience, transplant medicine, regenerative medicine and precision medicine.

innovationexchange.mayoclinic.org

BATTLING TRAFFICKING

Fourth-year medical student **Jennifer Talbott** (MED '22) knows a thing or two about human trafficking. Her father is the director of advocacy at the Human Rights Center at the University in Dayton, Ohio. After Talbott enrolled at Mayo Clinic Alix School of Medicine on the Arizona campus, she became curious about how victims of trafficking interact with the medical community. Her curiosity led to research, and research led to enhancing the medical school's curriculum.

As a result of Talbott's initiative — and with support from **Juliana (Jewel) Kling, M.D.** (I '13, CMR '14), a member of the Education Committee at Mayo Clinic in Arizona — the medical school's curriculum now trains students to identify and provide resources to human trafficking's potential victims. The curriculum includes simulations with a standardized patient who exhibits warning signs of sex trafficking, discussions about these encounters and learning from a facilitator.

Because human trafficking has been deemed a growing international public health concern, educational councils and

As a result of Talbott's initiative, the medical school's curriculum now trains students to identify and provide resources to human trafficking's potential victims.

"Health care providers are in a unique position to have an impact on this public health problem. It's incumbent on us to include education about trafficking in the core curriculum for medical students."

– Jennifer Talbott

medical societies recommend that medical students learn to recognize and care for the victims. Health care providers are among the few professionals to interact with sex trafficking victims, who often have poor health. An estimated 88% of victims saw a health care provider while they were being trafficked. The majority were seen in an emergency room or primary care office for chronic medical conditions or acute or traumatic injuries. Yet, according to Talbott's research, most medical students and practicing providers don't feel comfortable identifying victims.

Talbott's research also showed that only four medical schools have published about human trafficking-specific training for their students. She posits that robust curriculum could close the educational gaps and allow for improved identification and treatment of victims of human trafficking.

"Interested medical schools could look to published curricula or consider sharing resources to identify curriculum on sex trafficking that can be integrated into their existing programs," says Talbott, who took a one-year leave of absence from medical school to get a master's in public health from Columbia University. She hopes to incorporate the new curriculum with Mayo Clinic Alix School of Medicine in Rochester. "Health care providers are in a unique position to have an impact on this public health problem. It's incumbent on us to include education about trafficking in the core curriculum for medical students." •

Want to learn more?
Physicians Against the Trafficking of Humans: doc-path.org

Education Services

Creating the medical workforce of the future

Drumroll, please.

After 150 years of fine-tuning medical education and becoming the largest provider of graduate medical education in the world, Mayo Clinic has formalized consultancy services of its education best practices, knowledge and materials to help health care institutions and academic centers create the workforce of tomorrow. Mayo Clinic College of Medicine and Science Education Services applies Mayo Clinic's unmatched expertise and reputation to advance the science of education, according to Mohamad Bydon, M.D. (NS '15), medical director of Mayo's Education Services. ▸

"We believe it is in the best interest of patients everywhere to create institutional cultures around the world that put the needs of patients first," says Dr. Bydon. "Medical education is a critical building block in that process. Our Education Platform offerings will help institutions to develop a strong education 'shield' on their own."

Education Services offered by Mayo Clinic College of Medicine and Science include:

- Undergraduate and graduate medical education program development and enhancement
- Faculty development
- Health care quality education consulting
- Medical simulation consulting

DOING BIG THINGS, FLYING COLORS

Mayo's education consultancy services did big things for NCH Healthcare in Naples, Florida.

The community hospital wanted to establish an internal medicine residency program to address a looming physician shortage — particularly primary care — in its region. And, eventually, retain residents trained in the program. However, NCH lacked experience with graduate medical education and navigating the Accreditation Council for Graduate Medical Education (ACGME) landscape.

When it began working with Mayo Clinic Education Services in 2015, NCH Healthcare had previously sought institutional accreditation and received a number of citations. Within two weeks of engaging with Mayo Clinic Education Services, NCH passed an accreditation survey with flying colors — no citations.

Mayo Clinic alumni Ryan Perdzock, M.D. (second from left), and Kathryn Tapper, M.D. (FM '18) (second from right), both on staff at NCH Healthcare, meet with trainees.

Within two weeks of engaging with Mayo Clinic Education Services, NCH passed an accreditation survey with flying colors — no citations.

Mayo Clinic assisted NCH in developing the residency program, including a recruitment plan, and embedded a graduate of Mayo's own internal medicine residency, **Donnesha Clayton, M.D.** (I '16), as chief resident. Dr. Clayton played a key role in infusing Mayo's education culture into NCH's program from the start.

NCH interviewed 250 applicants for the 12 residency program spots. Mayo helped onboard residents and prepare NCH for the culture shift from a community hospital to academic medical center. The first residents started in 2017.

NCH and Mayo worked hand-in-hand to build the program infrastructure and navigate the first year as an academic medical center. This included establishing policies and procedures, protecting residents' time and space for study, and teaching staff across the institution how to interact with and instruct residents.

Mayo also helped create resident rotations. NCH residents can select rotations at a Mayo Clinic campus, and Mayo Clinic residents and medical students can choose clinical rotations at NCH to gain community hospital experience.

The first class of NCH residents graduated in 2020, with seven of the 12 going on to fellowship programs. NCH retained four of the trainees, and the majority of the class remained in Florida — a benefit for the state. NCH has approval to expand the residency class size from 12 to 16.

"Shifting from a community-based to academic-based hospital is a significant culture change, and who better to link with than Mayo Clinic and the value it puts on education," says Hermes Koop, M.D., designated institutional official, NCH Healthcare. "That relationship has helped our program become what it is in just six years. Now, education is fully integrated in our institution — everyone at NCH understands why residents are here and the benefits of our education programs."

Dr. Koop references programs — plural — because NCH has added a hospice and palliative care fellowship that launched this year, with a Mayo Clinic-trained program director, **Ryan Perdzock, M.D.** (PLM '18). Additions also include a transitional year residency that launched this year and a simulation center with a faculty member who trained in simulation medicine at Mayo Clinic as its director. Mayo Education Services continues to advise on medical education best practices, quality improvement and faculty development.

"Shifting from a community-based to academic-based hospital is a significant culture change, and who better to link with than Mayo Clinic and the value it puts on education."

– Hermes Koop, M.D., NCH Healthcare

To enhance its graduate medical education portfolio, NCH hired Mayo's **Gregory Poland, M.D.** (GIM '88), Emeritus Mary Lowell Leary Professor, as its research director, and he has engaged NCH residents in COVID-19 research that has been published.

Dr. Koop says NCH is considering adding more fellowships, which will improve the quality of residents it attracts. "Word has gotten out among potential applicants that we are linked to Mayo Clinic's strong education reputation, and that's a valuable recruiting tool.

"Since we partnered with Mayo in this endeavor, we've accomplished a great deal, and Mayo Clinic's academic medicine counsel has made it a lot easier. They have helped build our educational foundation, which raises the quality bar for all of the services NCH Healthcare provides." ▸

MAKING IT WORK, BETTER

If you build it, will they come? Not necessarily. Humanitas University in Milan, Italy, built a simulation center as part of its medical school. Despite the university's adjacency to Humanitas Research and Teaching Hospital, the simulation center was underused.

When a Humanitas representative met Mayo Clinic representatives at an International Meeting on Simulation in Healthcare conference in Los Angeles in 2018, a fruitful relationship began. Could Mayo Clinic help Humanitas optimize its simulation center? Yes.

A simulation specialist and clinical engineer from Humanitas spent a month studying Mayo's simulation centers on the Rochester and Florida campuses, and a Mayo Clinic team visited the Humanitas simulation center.

"The simulation center is the first of its kind in Italy. It's beautiful and outfitted with the technology and equipment to facilitate outstanding medical simulation education, but Humanitas wasn't sure how best to use or staff it," says Dr. Bydon. "Mayo was one of the first institutions in the U.S. to develop a multidisciplinary simulation center and is considered a leader in the field. Our simulation practice is directly reflective of how we practice medicine — team training focused on patient needs. We were happy to put our expertise in simulation medical education to work for Humanitas."

The Mayo team determined that there was a lack of awareness about the simulation center at the hospital. In fact, simulation isn't part of traditional medical education in Italy, so greater effort to spread the word was imperative. The center needed documented policies, procedures and a design that facilitated learner flow; and the university and hospital needed a faculty development program that incorporated simulation. Mayo proposed staffing and operational changes and developed simulation education scenarios. Mayo also recommended Humanitas modify its plan to primarily market the simulation center to outside groups as a revenue source and, instead, focus on internal learners.

"Medical education using simulation can improve the quality of care delivery, patient safety, teamwork learning and experiential training," says Dr. Bydon. "Having a simulation center is different from knowing how best to use it for the benefit of an institution's learners and patients."

"We believe it is in the best interest of patients everywhere to create institutional cultures around the world that put the needs of patients first."

– Mohamad Bydon, M.D.

A medical student at Humanitas University interacts with a high-fidelity mannequin and an educator to practice assessing critical care needs of a patient in respiratory distress. Simulation allows students to learn without any risk to actual patients. Photo provided by Humanitas University.

Acting on Mayo's recommendations, Humanitas introduced an awareness campaign to inform hospital faculty, staff and residents about the simulation center and the opportunities it presents; and created a skills lab with simulators in the center that is open 24 hours a day for the convenience of residents.

Fabio Carfagna, Methodology and Technology Development, Humanitas University, says that while pandemic restrictions have delayed some progress, there's much greater awareness of the simulation center now. "The skills lab is our greatest accomplishment so far. Residents can come and go at will, and those who use it are very happy with it. We're measuring to determine if arthroscopy simulation training is improving the skills of residents in the operating room. We've added a simulation scientific coordinator, and a couple of publications have resulted from our simulation work. We hope to establish a fellowship in medical simulation.

"From working with Mayo Clinic, we better understand the true mission of our simulation center, what simulation education entails, what we can expect from it, and how to involve residents and fellows in it."

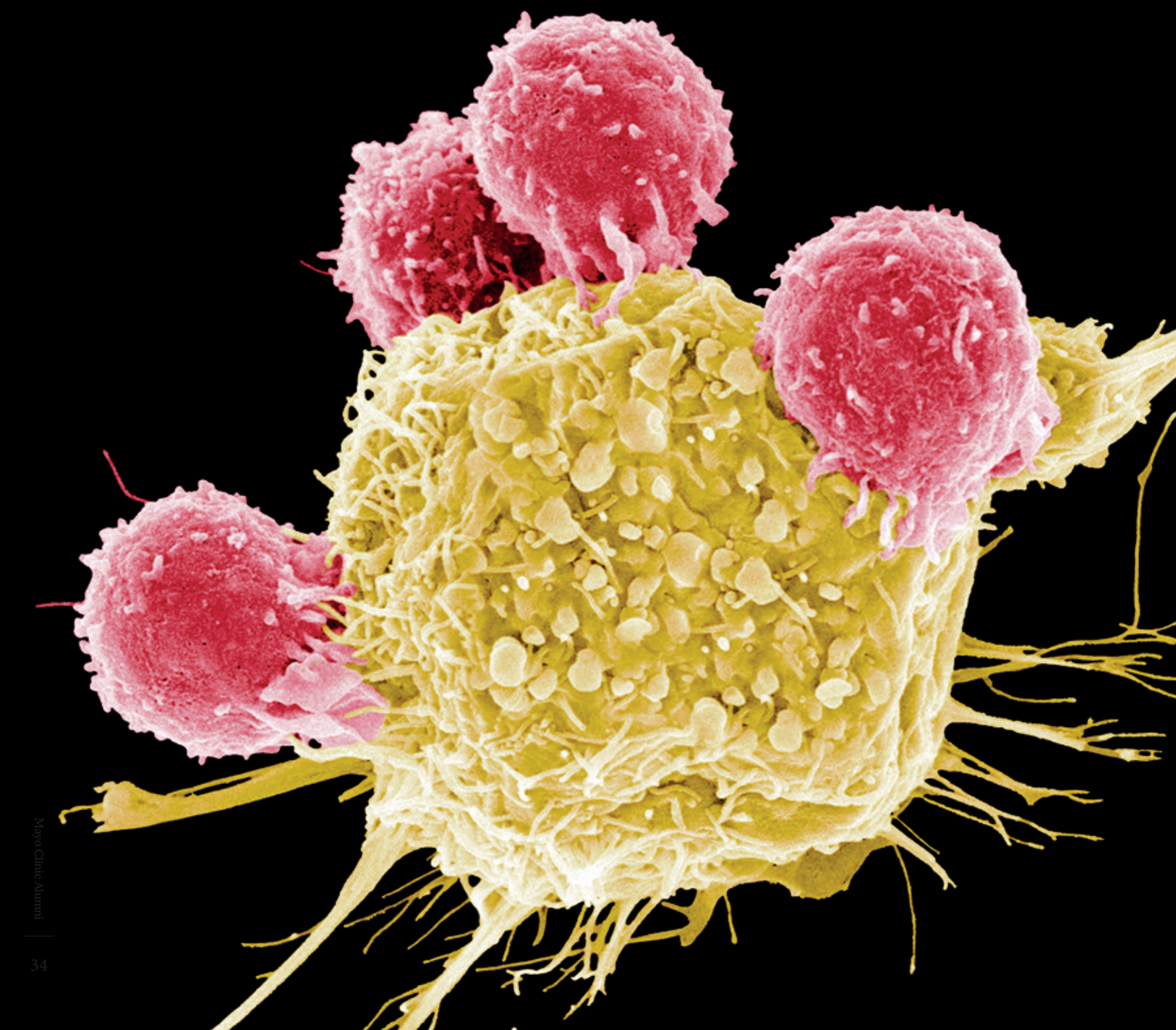
– Fabio Carfagna, Humanitas University

"From working with Mayo Clinic, we better understand the true mission of our simulation center, what simulation education entails, what we can expect from it, and how to involve residents and fellows in it. Shifting our focus inward to our trainees and faculty to improve patient safety and quality has been a cultural change, and we're grateful to have Mayo Clinic as our partner in this work." •

CAR-T cell therapy

Tick-tock, tick-tock

No time to waste



For active tumors that haven't responded to treatment, every week makes a difference. For patients with blood cancers who may benefit from chimeric antigen receptor (CAR)-T cell therapy, expedited evaluation and commencement of treatment make a difference.

Mayo Clinic is one of the top 10 centers in the U.S. providing FDA-approved CAR-T, an individualized cell-based therapy that harnesses the power of the immune system by genetically modifying T cells with chimeric antigen receptors to enable them to recognize antigens and kill cancer. Mayo Clinic's CAR-T cell therapy clinical outcomes are comparable to that reported from the registration study that led to FDA approval.

One of the challenges in providing this highly individualized and potentially curative therapy is shepherding patients through the complex logistics.

What differentiates Mayo Clinic, according to **Yi Lin, M.D., Ph.D.** (I '07, CI '09, HEMO '11), Division of Hematology and medical director of CAR-T cell therapy at Mayo Clinic in Rochester, is patient-oriented care, which starts at the point of first contact with the referral and includes understanding the urgency of care and pulling out all the stops to accelerate the path to treatment. "We schedule all of the specialty visits in a single week, in most cases, so patients can expeditiously proceed to cell collection. To ensure a smooth transition to starting therapy, we work closely with the patient and their local medical team to manage their disease while the CAR-T cells are manufactured. Mayo Clinic excels at complex care that requires collaboration and coordination of multiple specialties." ▸

"We schedule all of the specialty visits in a single week, in most cases, so patients can expeditiously proceed to cell collection."

– Yi Lin, M.D., Ph.D.

Colored scanning electron micrograph of T lymphocyte cells (pink) attached to a cancer cell.

Mayo Clinic infused its first CAR-T cell therapy patient in 2016 after being involved in one of the first multicenter registration studies and was one of the first centers certified to provide all of the FDA-approved CAR-Ts. Mayo offers CAR-T cell therapies on all three campuses. Across locations, Mayo physicians and scientists work together to identify biomarkers to understand who is at risk for more severe complications and who will most likely respond to therapy. This information enables the team to tailor patient-specific management and inform advances in therapeutic development. Patients at all Mayo Clinic locations have access to clinical trials including CAR-T cell therapy earlier in the management of FDA-approved indications, innovative CAR constructs, testing in new cancer types such as solid tumors, and using allogeneic cells. Offering CAR-T cell therapy and clinical trials on all Mayo Clinic campuses expands access for more diverse patients across the country.

The CAR-T cell therapy program on the Rochester campus provides outpatient infusion with remote monitoring. Patients remain near campus but don't have to endure an unnecessary hospital stay.

"We've learned from the outpatient hematology practice and bone marrow transplant program that escalating to inpatient care based on clinical needs reduces nosocomial complications," says Dr. Lin. "We were able to safely adapt that experience with this new therapy. Patients are happier when they can remain with family during their treatment and still have the security of 24/7 support and quick hospital admission if needed. Soon, we will incorporate wearable devices for continuous patient monitoring." •

CAR-T cell therapy & multiple myeloma

Mayo Clinic was a leading site in the first multicenter study of CAR-T cell therapy in multiple myeloma in the U.S. The phase 1 and registration phase 2 studies of idecabtagene vicleucel, an anti-B cell maturation antigen CAR-T cell therapy, showed this agent to be safe and active against relapsed or refractory multiple myeloma. The FDA approved this CAR-T for treatment of relapsed, refractory multiple myeloma in March.

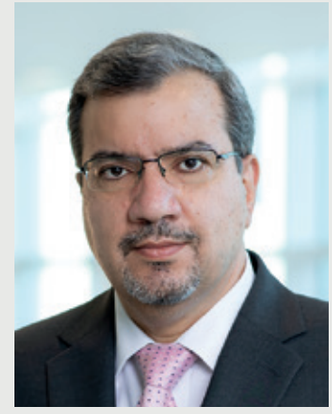
The 128 patients treated in the phase 2 KarMMa-1 study had progressed through most, if not all, standard-of-care therapies. The objective response rate was 73%, including a 33% complete remission or stringent complete remission rate. Median progression-free survival was 8.8 months and close to 12 months for patients who received the highest dose. The median overall survival was 19.4 months. Incidence of severe cytokine release syndrome and neurological side effects was low. The response rate was much higher than the 30% objective response rate found with belantamab mafodotin, approved by the FDA in 2020.

"For multiple myeloma patients who have progressed through the three backbones of conventional myeloma therapy — proteasome inhibitors, immune modulatory drugs and CD38 antibody — CAR-T cell therapy is an exciting, completely novel way to treat the disease," says **Yi Lin, M.D., Ph.D.** "This first FDA-approved autologous BCMA (B-cell maturation agent) CAR-T cell therapy is just the beginning of more transformative immunotherapy in myeloma."

CAR-T cell therapy medical directors

Yi Lin, M.D., Ph.D.
(I '07, CI '09, HEMO '11)
Mayo Clinic in Rochester

Januario Castro, M.D.
(HEMO '18)
Mayo Clinic in Arizona



Mohamed Kharfan Dabaja, M.D.
(HEMO '17)
Mayo Clinic in Florida

"The CAR-T cell therapy practice providers and researchers across Mayo Clinic sites meet regularly to discuss cases and reach agreement on guidelines and medical management so that our care is consistent no matter where patients get care," says Dr. Lin.

This is what expedited evaluation looks like

Monday (day 1): Labs, CAR-T physician consultation, nurse education visit, brain MRI

Tuesday (day 2): Social work visit, neurology consultation, pharmacy visit, financial counselor visit, other diagnostic tests and procedures

Wednesday (day 3): Other consultations as needed (cardiology, pulmonology, nephrology), CAR-T physician return visit to review evaluation results and determine next steps

Thursday (day 4): Central line placement for collection if appropriate

Friday (day 5): White blood cell collection

Cells are delivered to a vendor for manufacturing of T cells, which are engineered to make a new protein called a chimeric antigen receptor (CAR). The CAR enables a T cell to recognize a cancer cell that expresses the antigen. The manufacturing process can take three to four weeks.

The patient returns to Mayo Clinic for repeat tests and procedures, and the physician makes the determination if the patient is eligible to proceed to low-dose chemotherapy and infusion of the engineered CAR-T cells.

"For multiple myeloma patients who have progressed through the three backbones of conventional myeloma therapy, CAR-T cell therapy is an exciting, completely novel way to treat the disease."

– Yi Lin, M.D., Ph.D.

Mayo Clinic Alumni Association Donald C. Balfour Award for Meritorious Research

Curious John

John Giudicessi, M.D., Ph.D.

Divisions of Heart Rhythm Services and Circulatory Failure
Mayo Clinic in Rochester

Fellowship: Clinical, cardiovascular diseases; research, cardiovascular genetics, Mayo Clinic School of Graduate Medical Education, Rochester, Minnesota

Medical school: Mayo Clinic Alix School of Medicine, Rochester

Graduate: Ph.D., Mayo Clinic Graduate School of Biomedical Sciences

When **John Giudicessi, M.D., Ph.D.** (MED '14, MPET '14, I '17, CV '21), was growing up in Des Moines, Iowa, he fueled his incessant curiosity by taking apart unused items in the family's basement. He caught frogs and turtles in a backyard creek. He loved figuring out how things worked. His parents encouraged him to ask questions. Dr. Giudicessi says the burgeoning scientist was evident, but he didn't grow up in a medical or scientific household and, therefore, didn't fully appreciate the career possibilities.

Working with what he knew, Dr. Giudicessi planned to major in biology in college, go to medical school and eventually practice general medicine in his home state.

AN OUTLET FOR CURIOSITY

During college, Dr. Giudicessi learned to channel his curiosity into science. He did an internship in soybean genetics at Pioneer Hi-Bred International, participated in Mayo Clinic's Summer Undergraduate Research Fellowship (SURF) and then served as a research technician at Cold Spring Harbor Laboratory. He loved the research but missed the connection to people — patients. One of his undergraduate mentors, Elizabeth De Stasio, Ph.D., had told him he might get bored with clinical medicine. She urged him to consider an M.D.-Ph.D. Dr. Giudicessi had gotten the Mayo bug during his time in the SURF program and applied to the Medical Scientist Training Program.

For Ph.D. training, Dr. Giudicessi joined the lab of **Michael Ackerman, M.D., Ph.D.** (MDPH '95, PHAR '95, PD '98, PDC '00), Divisions of Heart Rhythm Services and Pediatric Cardiology; Department of Molecular Pharmacology and Experimental Therapeutics; and the Windland Smith Rice Cardiovascular Genomics Research Professor. Dr. Ackerman is a world-renowned genetic cardiologist, and Dr. Giudicessi will soon become Mayo Clinic's next genetic cardiologist with a focus on adults with genetic heart diseases.

"Children with genetic heart disease grow up and need continuity of care," says Dr. Giudicessi. "As one of the first adult genetic cardiologists at Mayo Clinic, I hope to address that need and expand the use of genetics in the adult space."

‘ONE OF THE SPECIAL ONES’

Even though he initially struggled to find a way to fulfill both his people orientation and scientific curiosity, Dr. Giudicessi triumphed — and then some.

“Not only has Dr. Giudicessi excelled in his research career but he also is an incredible clinician,” says **Frank Brozovich, M.D., Ph.D.** (CV ’05), Division of Comprehensive Cardiology at Mayo Clinic and Dr. Giudicessi’s clinical training program director. “There’s a stereotype that clinician-investigators aren’t as good at the clinical side as the typical fellow. Patients love Dr. Giudicessi, and he’s an absolute pleasure to be around. Another consultant sent me a note saying, ‘You better recruit this guy.’ I have no doubt Dr. Giudicessi will make seminal contributions to the scientific literature and be the go-to person to have your family members see when they need cardiovascular care.”

Dr. Giudicessi’s research focuses on using precision medicine to improve the diagnosis, risk stratification and clinical management of patients with sudden cardiac death-predisposing genetic heart disorders. His efforts have spanned the research spectrum from the discovery and functional characterization of new disease-susceptibility genes and genetic modifiers to the development and prospective assessment of artificial intelligence-enabled approaches to identify these disorders in settings not amenable to conventional 12-lead electrocardiography.

“I want to utilize precision medicine proactively to identify those individuals with a genetic predisposition for cardiovascular disease so we can provide appropriate counseling and treatment before the onset of severe and potentially life-threatening manifestations,” says Dr. Giudicessi.

His work has resulted in more than 60 peer-reviewed publications and young investigator and career development awards — including the 2021 Mayo Clinic Alumni Association Donald C. Balfour Award for Meritorious Research.

Interestingly, Dr. Giudicessi’s research mentor, Dr. Ackerman, received the Balfour award in 2000. “The Balfour Award is very special — Mayo Clinic Alumni Association’s highest recognition of scholarly research by a trainee,” says Dr. Ackerman. “Dr. Giudicessi is incredibly deserving of it. I’m fortunate that our relationship has moved to the next phase as colleagues and partners. He is one of the truly special ones, and his career will be exciting to watch.” •

“He is one of the truly special ones, and his career will be exciting to watch.”

– Michael Ackerman, M.D., Ph.D.

2020 Balfour Award recipient

The 2020 recipient of the Balfour Award wasn’t featured in the magazine, which was on hold at the time. The Mayo Clinic Alumni Association wants to make sure **Christopher Graffeo, M.D.** (CTSA ’19, NSSB ’21), gets his due. Dr. Graffeo’s research has focused on improving clinical and translational science for the treatment of complex cranial disease — focusing on the development of novel strategies to improve efficacy, safety and evidence-based study of stereotactic radiosurgery.

CHRISTOPHER GRAFFEO, M.D.

Fellow, cerebrovascular and skull base surgery

Barrow Neurological Institute

Phoenix, Arizona

Residency: Department of Neurologic Surgery, Mayo Clinic in Rochester

Postgraduate: Postdoctoral master’s degree in clinical and translational science, Mayo Clinic Graduate School of Biomedical Sciences

Medical school: New York University School of Medicine, New York City

Undergraduate: University of Virginia

Read more about Dr. Graffeo:
alumniassociation.mayo.edu/news

Mayo Clinic Alumni Association Edward C. Kendall Award for Meritorious Research

Now unstuck, the world is her oyster

Sara Ranjbar, Ph.D.

Research fellow

Mathematical Neuro-Oncology Laboratory

Precision Neurotherapeutics Innovation Program

Department of Neurologic Surgery

Mayo Clinic in Arizona

Postgraduate: Ph.D., biomedical informatics, Arizona State University, Tempe; master's degree, biomedical engineering, Amirkabir University of Technology, Tehran, Iran

Undergraduate: Biomedical engineering, Amirkabir University of Technology

Sara Ranjbar, Ph.D. (NS '21), has spent the last nine years unlearning what she'd practiced her whole life. Dr. Ranjbar is from Iran and learned from an early age to not speak up, challenge others or ask too many questions. As a graduate of one of the top engineering schools in Iran and working to implement a surgical navigation system for skull-based surgeries, Dr. Ranjbar concluded that cultural constraint wasn't helpful for advancing fast-paced science.

"I was painfully aware that I had ideas to contribute, and not speaking up was impeding my progress," she says. "Every time I didn't speak up, I felt bad and ended up in a negative confidence loop. I was stuck and had a vague sense of being lost and invisible. I needed to be brave enough to proceed in a different way."

A DIFFERENT WAY

Dr. Ranjbar moved to the U.S. in 2012 and enrolled in the Ph.D. program at Arizona State University. Her thesis showed that using quantitative image analysis and machine learning can help improve the specificity of breast cancer diagnosis, predict HPV status in head and neck tumors, differentiate benign and malignant head and neck tumors, and stage cognitive decline in Alzheimer's disease.

In 2018 she joined the Mathematical Neuro-Oncology Laboratory at Mayo Clinic in Arizona to train in neuroimaging and neuro-oncology under the supervision of **Kristin Swanson, Ph.D.** (NS '15), Department of Neurologic Surgery and the Vasek and Anna Maria Polak Professor of Cancer Research, who has built a career around designing mathematical approaches for personalized glioblastoma (GBM) treatment.

While artificial intelligence (AI) is male-dominated, Dr. Swanson's lab is not. "It's the first time I've had a woman mentor and majority women group," says Dr. Ranjbar. "Seeing how women support each other, present research in a convincing way and speak up freely has helped me do the same and take more leadership roles. I recently agreed to present at four conferences without feeling nervous about it. I don't feel stuck anymore."

Dr. Swanson says it's common for women scientists to be reluctant to speak up. "As a woman leader at Mayo Clinic, I create a culture where everyone is emboldened to speak and know their voice is valuable and heard. Dr. Ranjbar has had a remarkable path and demonstrated resilience while excelling in her pursuit of a career in science."

A SWEET REWARD

Overcoming this cultural burden has made Dr. Ranjbar's receipt of the 2021 Mayo Clinic Alumni Association Edward C. Kendall Award for Meritorious Research even sweeter.

"I'm so honored and happy that Mayo Clinic sees value in my research," she says. "I'm a first-generation college student, and my mom is so excited. When I was young and she figured out that I was good at math, she encouraged me. She's my biggest supporter; I'm pretty sure she's telling everyone she knows in Iran about the Kendall Award."

Dr. Ranjbar's work with GBM focuses on MRI-based machine learning models. She has built models that characterize MRI types, extract brain tissue from MRI, outline tumor extent, identify cystic GBMs, estimate missing MRI images for patients and noninvasively predict tissue heterogeneity across entire tumors. Her efforts have resulted in two accepted first-author papers, another submitted and another in preparation; two first-author, two second-author and five co-author published abstracts; and one co-author paper submitted and one in preparation. Her long-term goal is to be a scientific leader working at the cross-section of imaging and AI at a high-profile research institute.

A RARE INTUITION

Dr. Swanson has no doubt her protégé will accomplish that goal. "Dr. Ranjbar wants to affect positive change for patients and is an exceptionally intuitive researcher. She has a natural gift for having insights into the data before it reveals itself. Rather than just plot out the data without deep understanding of what it means, she peels away the layers of noise, hears the signal and picks out the important part that will be useful to the patient. This is a rare quality. In 20 years of mentoring students, I find Dr. Ranjbar to be one of the most persistent and effective researchers I have trained. The world of AI is hungry for expertise and intuition like hers. The world is her oyster." •

"The world of AI is hungry for expertise and intuition like hers. The world is her oyster."

– Kristin Swanson, Ph.D.

2020 Kendall Award recipient

The 2020 recipient of the Kendall Award wasn't featured in the magazine, which was on hold at the time. The Mayo Clinic Alumni Association wants to make sure Yang Chen, Ph.D. (BMB '18), is recognized. Dr. Chen's pioneering research has significantly advanced the field of natriuretic peptide physiology and therapeutics for cardiovascular and renal injury and disease.

YANG CHEN, PH.D.

Research fellow

Cardiorenal Research Laboratory

Department of Cardiovascular Medicine

Mayo Clinic in Rochester

Graduate: Ph.D., Mayo Clinic Graduate School of Biomedical Sciences, Rochester, Minnesota

Undergraduate: Huazhong University of Science and Technology, China

Read more about Dr. Chen:
alumniassociation.mayo.edu/news

Ann Benassi, M.D., cared for Rochester-area school children with orthopedic problems, 1973. A school principal said, “It is most rewarding to see the miracle performed with some of these children through proper therapy.”

SPOTLIGHT ON THE ’40S THROUGH ’60S

Women at Mayo Clinic

Periodically, Mayo Clinic Alumni highlights the contributions of some of the early women physicians and scientists at Mayo Clinic. Today, Mayo Clinic has 10,766 living women alumni (physicians and scientists) around the world.

Join us in celebrating these women who blazed trails for other women at Mayo Clinic.

Mary Giffin, M.D., and colleagues in the Sections of Neurology and Psychiatry, 1953.

Mary Giffin, M.D.

(I '45, NPSY '48)

Born in Rochester, Minnesota | Died 2002

- Father, **Herbert Z. Giffin, M.D.** (I '06), Mayo Clinic physician, first chair of Mayo Clinic Emeritus Staff
- Undergraduate, Smith College; medical degree, Johns Hopkins University; master's degree, neurology and psychiatry, University of Minnesota; postgraduate studies, psychiatry, Phipps Institute, Johns Hopkins University
- Internship, Strong Memorial Hospital, Rochester, New York; residency, internal medicine, neurology and psychiatry, Mayo Clinic
- Staff member, Mayo Clinic Sections of Neurology and Psychiatry, 1949
- Assistant professor, University of Minnesota/Mayo Clinic
- President, Illinois Council of Child Psychiatry
- Specialized in child psychiatry; wrote and lectured extensively on collaborative research technique in study of juvenile delinquency, schizophrenia, and psychiatric backgrounds in criminality
- Co-authored book on teenage suicide, "A Cry for Help"
- Wrote "Her Doctor Will Mayo: A Child's View of Dr. Will Mayo of Mayo Clinic," recounting childhood relationship with Dr. Will Mayo
- Left Mayo Clinic in 1958 to become medical director, Josselyn Clinic, Highland Park, Illinois; work recognized by resolution of General Assembly of Illinois Senate; retired to private practice through 2002

Gertrude Pease, M.D.

(PATH ’46)

Born in Fort Harrison, Montana | Retired 1967 | Died 1998

- Father was a physician
- Undergraduate, Montana State University; master’s degree, bacteriology, University of Washington; medical school, Creighton University College of Medicine; master’s degree, pathology, University of Minnesota
- Internship and residency, pathology, University of Illinois Research and Educational Hospitals; residency, pathology, Mayo Clinic
- Staff member, Mayo Clinic Section of Clinical Pathology, 1946
- Associate professor of clinical pathology, Mayo Clinic/University of Minnesota
- Conducted studies in Mayo Clinic special hematology laboratory
- Known for pioneering work in procedure of critical pathologic review of sections of bone marrow

Lillian (Lila) Elveback, Ph.D.

(STAT ’52)

Born in Sidney, Montana | Retired 1983 | Died 2004

- Undergraduate and Ph.D., statistics, University of Minnesota; master’s degree, mathematical statistics, Columbia University; fellowship, statistics, Mayo Clinic
- Professor, Division of Biostatistics, School of Medicine, Tulane University
- Chief statistician, Department of Epidemiology, Public Health Research Institute, New York
- Staff member, Mayo Clinic Section of Medical Statistics, Epidemiology, and Population Genetics, 1965
- Professor of biostatistics, Mayo Clinic
- Assisted in development of Rochester Epidemiology Project
- Developed Mayo Clinic statistics teaching program and medical school courses
- Board of directors and co-founder, American College of Epidemiology
- Co-author of textbook “Epidemiology: Man and Disease”
- Consultant, World Health Organization, American Association for the Prevention of Blindness; Epilepsy Section, National Institute of Neurological and Communicative Disorders and Stroke
- Research in statistical methods in clinical laboratory studies, stochastic models in medicine and epidemiology, design of experiments

Cynthia Stoltze Hardison, M.D.

(I ’56)

Born in Lethbridge, Alberta, Canada | Retired 1968 | Died 2020

- Mother was a nurse
- Undergraduate, Wellesley College and Stanford University; medical degree, Northwestern University Medical School; master’s degree, University of Minnesota
- Internship, Evanston Hospital; residency, internal medicine, Mayo Clinic
- Staff member, Mayo Clinic Section of Medicine, 1956
- Published extensively on Sjögren’s syndrome
- Left Mayo Clinic to establish Raleigh (North Carolina) Internal Medicine Associates with husband **Joseph Hardison, M.D.** (I ’64); specialized in hematology and oncology
- Hematology consultant, Journal of American Medical Association
- President, American College of Gastroenterology Women’s Auxiliary

Jenifer Jowsey, Ph.D.

(OR ’63)

Born in London, England

- Undergraduate, master’s degree and Ph.D., Oxford University
- British American Cancer Society Exchange Fellow, University of Chicago
- Research associate, Argonne National Laboratory Department of Radiological Physics
- Research assistant, Royal National Orthopaedic Hospital, London
- Research associate, Albert Einstein Medical Center
- Staff member, Mayo Clinic Section of Surgical Research, 1963 — the first Mayo Clinic orthopedic Ph.D. scientist; joined bone biology lab
- Head, Orthopedic Research Laboratory, Mayo Clinic
- Professor of physiology, Mayo Clinic
- Executive Committee, Orthopaedic Research Society
- Research in bone tissue; performed seminal work on osteoporosis, metabolic bone disease and bone histomorphometry
- Married to **Fenwick Riley, M.D.** (OPH ’67)
- Left Mayo Clinic for Seattle in 1978
- Department of Orthopedic Surgery at Mayo Clinic gives the Jenifer Jowsey, Ph.D., Award for Excellence in Research by a Research Fellow in Orthopedic Surgery

Left: Staff members in Pathology's Gross Specimen Laboratory in the 1914 Building, 1941. Above: Jenifer Jowsey, Ph.D., director of orthopedic research at Mayo Clinic, 1973.

Ann Benassi, M.D.

(PMR '64)

Born in Kenton, Ohio | Retired, lives in Rochester, Minnesota

- Father and grandfather were country physicians
- Undergraduate and medical degrees, Ohio State University
- Residency, physical medicine and rehabilitation, Mayo Clinic
- Medical officer, Public Health Service, North Dakota; consultant, St. Luke's Hospital, Neuropsychiatric Institute, St. John's Hospital and Veterans Administration Hospital, Fargo
- Staff member, Mayo Clinic Department of Physical Medicine and Rehabilitation, 1969
- Associate professor of physical medicine and rehabilitation, Mayo Clinic
- Research in postoperative management of total knee arthroplasty, treatment of cerebral palsy, rehabilitation of paraplegia and quadriplegia, juvenile rheumatoid arthritis, rehabilitation of traumatic injuries to the hand, prosthetic replacement in hands, spinal cord injury in children, rheumatoid arthritis of the hand
- Advocate for children with functional loss from disease and trauma; relationship with Minnesota Crippled Child Association led to travel for consultation and therapy in rural areas of the state
- Collaborator in developing Mayo Clinic rehabilitation program for hand dysfunction
- Vice president, Minnesota Medical Association; Women's American Medical Association Rochester branch
- President, Minnesota Physiatric Society
- Distinguished Clinical Physician Award, American Academy of Physical Medicine and Rehabilitation
- When asked in 1974 story why she "joined a man's world of medicine," she said: "I made a choice, and I've had to fight for it. I want to make it easier for the girls coming up in medicine. They have a right to be more than lady doctors. They have a right to be doctors." •

Mayo Clinic Update

Reverse-order heart-liver transplant helps prevent rejection for highly sensitized patients

Patients who have high levels of antibodies face major challenges getting a transplant. These highly sensitized patients have a much higher risk of death while waiting for suitable organs they are less likely to reject. An innovative surgical approach at Mayo Clinic offers an option for highly sensitized patients in need of a combined heart and liver transplant.

Traditionally, surgeons transplant the heart first, followed by the liver. A team of Mayo Clinic heart transplant surgeons decided to reverse the order for highly sensitized patients to determine if the liver would absorb some of the patient's antibodies, removing them from circulation and lowering the risk of antibody-mediated rejection. The strategy worked, according to a study published in the Journal of the American College of Cardiology.

"This unique approach to heart-liver transplant opens the door to more highly sensitized patients getting the transplants they desperately need," says **Sudhir Kushwaha, M.D.** (CV '00), Division of Circulatory Failure at Mayo Clinic in Rochester and the study's senior author.

An estimated 20% of people waiting for a transplant are highly sensitized. People can become sensitized due to blood transfusions, pregnancies and previous transplants.

The Mayo Clinic team was inspired to try the heart-after-liver transplant procedure after noting that patients who had traditional heart-liver transplant were much less likely to experience rejection than those who had a heart transplant alone. Previous research has shown a similar phenomenon for patients having a simultaneous kidney-liver transplant.

Mayo Clinic began offering the pioneering heart-after-liver transplant surgery in 2011. The study reviews the outcomes for seven patients who had the procedure. The patients were ages 33–51; six of the seven were women. All experienced a significant drop in antibodies after the procedure, and none of the patients had experienced rejection within four years after surgery. The study's limitations include its small sample size and younger age of typical transplant patients.

This new procedure is promising but has major challenges. The heart is usually transplanted first because it is more time-sensitive than other organs. The reverse-order procedure requires complex choreography between the heart and liver transplant teams. Additional research is needed to see whether transplanting a portion of a donor's liver would offer the same protective benefit for highly sensitized heart transplant patients.

Alum named executive director, Mayo Clinic Cancer Programs

Cheryl Willman, M.D. (MED '81, PATH '81), was named executive director of Mayo Clinic Cancer Programs and director of the Mayo Clinic Comprehensive Cancer Center. Dr. Willman comes to Mayo Clinic from the University of New Mexico Comprehensive Cancer Center, where she served as executive director and CEO for 20 years.

Dr. Willman will lead the expansion and strategic development of Mayo Clinic Comprehensive Cancer Center sites in Arizona, Florida and Minnesota, as well as newly developing Mayo Clinic global cancer programs in London and Abu Dhabi, United Arab Emirates.

Dr. Willman is a pioneer in cancer precision medicine. Her research focuses on the use of genomic, next-generation genome sequencing and computational technologies to discover novel cancer-causing genomic mutations that can be translated to better cancer diagnostics and therapeutics. She has been continuously funded by the National Institutes of Health, National Cancer Institute and Leukemia & Lymphoma Society for more than 30 years.

Dr. Willman received her medical degree from Mayo Clinic Alix School of Medicine. She completed residency and postdoctoral training in pathology and cancer research at Mayo Clinic, the University of New Mexico and University of Washington.

Mayo Clinic & Kaiser Permanente announce investment in Medically Home

Mayo Clinic and Kaiser Permanente have partnered to allow more patients to receive acute-level care and recovery services in the comfort, convenience and safety of their homes.

Beginning with significant strategic investments in Medically Home Group, a Boston-based, technology-enabled services company, Mayo Clinic and Kaiser Permanente seek to expand access to this unique model and encourage health systems and care providers to adopt it. By building capacity to meet rapidly increasing demand while addressing regulatory and legislative barriers, the partnership will allow more patients to safely receive care in their homes.

Medically Home's one-of-a-kind technology and services platform enables providers to address a significant range of clinical conditions safely in a patient's home. This includes routine infections and chronic disease exacerbation, emergency medicine, cancer care, acute level of COVID-19 care and transfusions.

Key features of Medically Home's virtual and physical care delivery model include a 24/7 medical command center staffed by an array of clinicians and an integrated care team in the community who deliver care to patients at their bedside. Patients hospitalized using the Medically Home model have a lower need for recurring hospitalization at 30 and 90 days after a care episode.

"Patients expect and deserve high-quality care and excellent outcomes in a convenient and comfortable setting, even when faced with complex medical challenges," says **Gianrico Farrugia, M.D.** (I '91, GI '94), president and CEO of Mayo Clinic. "Our partnership with Kaiser Permanente and Medically Home will create the next generation of patient-centric, compassionate health care that seamlessly integrates advanced technology with clinical expertise. By bringing best-in-class clinicians and services to patients in their homes, we'll be able to provide more people with individualized care that's tailored to meet their specific needs."

Both Mayo Clinic and Kaiser Permanente are successfully using Medically Home's scalable care delivery model today. Mayo Clinic launched its Advanced Care at Home program last summer at Mayo Clinic in Florida and Mayo Clinic Health System in Eau Claire, Wisconsin.

Lack of diversity in genomic databases may affect therapy selection for minority groups

Yan Asmann, Ph.D.

Low representation of minority groups in public genomic databases may affect therapy selection for Black patients with cancer, according to Mayo Clinic research.

Researchers investigated the use of genomic databases and found that tumor mutation burden was significantly inflated in Black patients compared to white patients.

As a result of the study, clinicians who use public genomic databases need to be aware of the potential for inflated tumor mutation burden values and how that may affect therapy selection and outcomes, especially for patients from underrepresented groups.

Clinicians use biomarkers to determine whether patients might benefit from immunotherapy. One of those biomarkers is tumor mutation burden, the number of mutations within a tumor compared to normal cells. Most of the time tumor mutation burden is calculated, normal cells are not used, and genomic databases of mutations or algorithms are used to filter results.

The research team collected data from 701 patients who were newly diagnosed with multiple myeloma, including 575 self-reported white patients and 126 self-reported Black patients. The team analyzed DNA from patients' tumor cells and healthy cells to determine the differences. The team paired tumor and germline exome sequencing data to analyze differences between the two sources of DNA. They used public databases to filter mutation variants from the tumor sequencing data.

"The FDA has approved a threshold of more than 10 mutations per megabase of DNA to select patients to receive immunotherapy," says **Yan Asmann, Ph.D.** (GI '00, LABM '01), Department of Quantitative Health Sciences at Mayo Clinic in Florida and first author of the study.

Because the autoimmune toxicities with immune checkpoint inhibitors can be severe, it is critical to have an accurate tumor mutational burden as a biomarker to improve the ability to predict the optimal treatment for patients.

"Determining tumor mutation burden becomes difficult when you do not have DNA from a patient's normal cells," says **Aaron Mansfield, M.D.** (I '09, CI '11, HEMO '13, CTSA '18), Division of Medical Oncology at Mayo Clinic in Rochester and corresponding author of the paper. "For this reason, reference genomes are used for comparisons to tumors to estimate the burden."

Based on his experiences with patients, Dr. Mansfield was concerned that this type of approach to determining tumor mutation burden was inaccurate, especially in patients with ancestral backgrounds that are not well represented in the reference genome databases.

"At the level of an individual patient, our findings suggest that when we sequence tumors, it is also important to sequence paired normal tissues to accurately identify differences," says Dr. Mansfield. "At the level of the research community, we need to continue to improve the representation of patients with diverse ancestral backgrounds in reference genome databases."

According to Dr. Mansfield, accurate tumor mutational burden is particularly important in cancers treated with immune checkpoint inhibitors, including breast, bladder, cervical, colon, head and neck, liver, lung, renal cell, stomach and rectal cancers, as well as Hodgkin's lymphoma, melanoma and any other solid tumor that is not able to repair errors during DNA replication.

"We performed this proof-of-principle study in patients with multiple myeloma. However, the findings of racially disparate tumor mutation burden inflation might be generalizable to all cancer types," says Dr. Mansfield.

The lack of representation of diverse backgrounds in genomic research is well known. Of more than 60,000 people genotyped and sequenced, only 8.6% are of African ancestry, while 54.9% are of non-Finnish European ancestry.

"Investigators around the world are looking at ways to improve the ability to select patients to receive immunotherapy," says Dr. Mansfield. "We have identified a problem with one approach and have recommended a solution for it."

Aaron Mansfield, M.D.

Alum named president of Mayo Clinic Health System

Prathibha Varkey, M.B.B.S. (CCMI '01, PREV '02), is the new president of Mayo Clinic Health System. She succeeds **Bobbie Gostout, M.D.** (MED '86, I '87, OBG '91, BIOC '93, GYNO '96), who retired from Mayo Clinic last year.

Dr. Varkey will lead the strategy and operations of Mayo Clinic Health System's 17 hospitals and almost 50 community clinics across Minnesota, Wisconsin and Iowa.

Dr. Varkey previously practiced medicine at Mayo Clinic in Rochester for 11 years. She left Mayo Clinic in 2013 to serve as CEO of Seton Clinical Enterprise in Austin, Texas. Dr. Varkey served as president and CEO of Northeast Medical Group at Yale New Haven Health in New Haven, Connecticut, from 2016 until rejoining the Mayo Clinic staff.

Dr. Varkey received her medical degree from Christian Medical College, Vellore, in Tamil Nadu, India. She completed internal medicine residency at Yale New Haven Health's Hospital of St. Raphael. She has a master's in public health from Harvard T.H. Chan School of Public Health, a master's in health professions education from the University of Illinois Medical Center and an M.B.A. from the University of Minnesota.

Prathibha Varkey, M.B.B.S.

Mayo Clinic ranks among 'Best Children's Hospitals' by U.S. News & World Report

Mayo Clinic Children's Center again ranked as a top-performing children's hospital in U.S. News & World Report's 2021–2022 "Best Children's Hospitals" rankings.

Mayo Clinic Children's Center in Rochester is ranked the No. 1 hospital in Minnesota and the five-state region of Iowa, Minnesota, North Dakota, South Dakota and Wisconsin.

Mayo Clinic Children's Center ranked as a top-performing children's hospital in 8 of 10 pediatric specialties. The rankings identify the top 50 children's hospitals in each of 10 specialties considered. Only 89 children's hospitals of the 193 considered in the rankings were ranked in at least one pediatric specialty in 2021.

Chetna Mangat, M.D. (PD '14), Department of Pediatric and Adolescent Medicine

Mayo researchers, collaborators identify gene associated with Alzheimer's disease

Mayo Clinic researchers and collaborators report the protein-coding gene SERPINA5 may worsen tau protein tangles, which are characteristic of Alzheimer's disease, and advance disease. By combining clinical expertise, brain tissue samples, pathology expertise and artificial intelligence, the team clarified and validated the relevance of the gene to Alzheimer's disease.

The researchers used tissue samples from 385 brains donated to the Mayo Clinic Brain Bank. The samples were from people who were diagnosed with Alzheimer's disease and lacked co-existing diseases found in the brain.

The team used the samples to classify the pattern of protein tangles associated with Alzheimer's and used digital pathology and RNA sequencing to identify gene expression in the samples, measuring gene changes responsible for instructing proteins.

"We looked at an entire disease spectrum and found gene changes that may really influence the hippocampus," says **Melissa Murray, Ph.D.** (NSCI '10), Department of Neuroscience at Mayo Clinic in Florida and lead author of a paper about the research. "That means we may have targets that indicate why some people have relative preservation and others have relative exacerbation of memory loss symptoms."

Using a machine learning algorithm, the authors narrowed the genes of interest from about 50,000 to five. The top candidate, SERPINA5, was strongly associated with tau tangle progression in the hippocampus and cortex of the samples. The researchers plan to investigate how SERPINA5 interacts with tau protein to develop an inhibitor.

"Much of the focus of therapeutics is on abnormal proteins — amyloid and tau — used to biologically define Alzheimer's disease," says Dr. Murray. "But we hope to take a step back to look at a new interacting partner that may accelerate tau or push tau accumulation past the tipping point."

New research building grows to 11 floors

The Anna-Maria and Stephen Kellen Building on Mayo Clinic's Rochester, Minnesota, campus, set to open in the fourth quarter of 2023, will feature 11 floors and 176,000 square feet of flexible laboratory space. The building will be located at the intersection of 3rd Street SW and 4th Avenue SW, with underground connectors to the Opus and Baldwin buildings. The building was announced in 2019 as a four-story building.

The energy-efficient structure was funded, in part, through a gift from the Anna-Maria and Stephen Kellen Foundation as well as other generous benefactors. The new facility will enable Mayo's team-based scientists to continue finding care solutions for patients.

"Research is a key pillar of our 2030 strategy," says **Gianrico Farrugia, M.D.** (I '91, GI '94), president and CEO of Mayo Clinic. "We're committed to advancing more cures, connecting more patients to our expanded expertise and transforming health care for people everywhere. And that transformation starts with research."

Mayo study finds colon cancer driven by hereditary gene mutations in 1 in 6 patients

A Mayo Clinic study bolsters evidence that colorectal cancer is often imprinted in family genes and passed on from one generation to the next.

Researchers in the Mayo Clinic Center for Individualized Medicine found 1 in 6 patients with colorectal cancer had an inherited cancer-related gene mutation that likely predisposed them to the disease. The researchers also discovered that 60% of these cases wouldn't have been detected if relying on a standard guideline-based approach.

"We found that 15.5% of the 361 patients with colorectal cancer had an inherited mutation in a gene associated with the development of their cancer," says **Niloy Jewel Samadder, M.D.** (GIAE '11), Division of Gastroenterology and Hepatology at Mayo Clinic in Arizona and the study's senior author. "We also found that more than 1 in 10 of these patients had modifications in their medical or surgical therapy based on the genetic findings."

The patients were tested with a sequencing panel that included more than 80 cancer-causing or predisposing genes. In comparison, standard panels for colorectal cancer include only 20 or fewer genes.

The patients with colorectal cancer were part of a larger cohort of 3,000 patients involved in the two-year Interrogating Cancer Etiology Using Proactive Genetic Testing (INTERCEPT) study and were newly diagnosed with various cancers at Mayo Clinic Cancer Center locations in Arizona, Florida and Minnesota.

"Through the INTERCEPT study, the Center for Individualized Medicine has addressed a question of relevance to all cancer patients," says **Aleksandar Sekulic, M.D., Ph.D.** (IMM '99, DERM '00, CI '03, DERM '06), associate director of the center, Mayo Clinic in Arizona. "These findings shed a new light on the role our genes play in the development of colon cancer."

The colorectal cancer study emphasizes that uncovering hidden inherited genetic mutations using a universal testing approach and broader gene panels could lead to opportunities for cancer management in families and targeted cancer therapies that can save lives.

In the study, researchers examined gene variants with which the patient was born and that predisposed them to developing cancer. Although many mutations that cause colorectal cancer happen by chance in a single cell — including from environmental factors, diet, smoking and alcohol use — the study confirms many are inherited mutations that set off a cycle of events that can lead to cancer.

Niloy Jewel Samadder, M.D.

Aleksandar Sekulic, M.D., Ph.D.

"Though the most common mutations were found in genes typically associated with colorectal cancer, we found that a substantial number of mutations were present in genes typically associated with breast and ovarian cancer," says Dr. Samadder. "This may lead to novel targeted therapies based on the cancer's unique genetic basis. For example, where a breast cancer drug can be used in a patient with colon cancer."

Equally important to the discovery of a patient's inherited cancer mutation is the potential for patients to share the heritable cause of their disease with their blood relatives, allowing family members to pursue care for earlier disease detection and cancer management.

"The power of genetics is that we can foresee the cancer that will develop in other family members," says Dr. Samadder. "This can allow us to target cancer screening to those high-risk individuals and, hopefully, prevent cancer altogether in the next generation of the family."

In the study, all blood-related family members of patients found to have a genetic mutation were offered free genetic testing. Only 16% of these family members had testing, which may suggest there are nonfinancial barriers to genetic testing.

Dr. Samadder says the next steps will be to incorporate the study findings into the care of all patients with cancer at Mayo Clinic. "Steps are being taken to ensure all patients are offered genomic sequencing to better understand the genes that led to the development of their cancer, and how to precisely target treatment and improve survival."

Trial demonstrates early AI-guided detection of heart disease in routine practice

Some types of heart disease, such as asymptomatic low ejection fraction, can be difficult to recognize, especially in the early stages when treatment would be most effective. The ECG AI-Guided Screening for Low Ejection Fraction (EAGLE) trial set out to determine whether an artificial intelligence (AI) screening tool developed to detect low ejection fraction using data from an EKG could improve the diagnosis of this condition in routine practice.

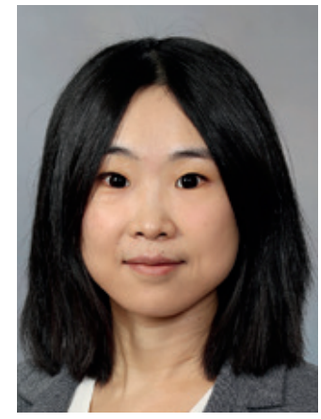
An echocardiogram can readily diagnose low ejection fraction, but this time-consuming imaging test requires more resources than a 12-lead EKG, which is fast, inexpensive and readily available. The AI-enabled EKG algorithm was tested and developed through a convolutional neural network and validated in subsequent studies.

The EAGLE trial took place in 45 medical institutions in Minnesota and Wisconsin, including rural clinics and community and academic medical centers. In all, 348 primary care clinicians from 120 medical care teams were randomly assigned to usual care or intervention. The intervention group was alerted to a positive screening result for low ejection fraction via the electronic health record, prompting them to order an echocardiogram to confirm.

"The AI-enabled EKG facilitated the diagnosis of patients with low ejection fraction in a real-world setting by identifying people who previously would have slipped through the cracks," says **Peter Noseworthy, M.D.** (CV '13), Division of Heart Rhythm Services at Mayo Clinic in Rochester and senior author on the study.

In eight months, 22,641 adult patients had an EKG under the care of the clinicians in the trial. The AI found positive results in 6% of the patients. The proportion of patients who received an echocardiogram was similar overall, but among patients with a positive screening result, a higher percentage of intervention patients received an echocardiogram.

Peter Noseworthy, M.D.



Xiaoxi Yao, Ph.D.

"The AI intervention increased the diagnosis of low ejection fraction overall by 32% relative to usual care. Among patients with a positive AI result, the relative increase of diagnosis was 43%," says **Xiaoxi Yao, Ph.D.** (HSR '15), Department of Health Sciences Research at Mayo Clinic in Rochester and first author on the study. "To put it in absolute terms, for every 1,000 patients screened, the AI screening yielded five new diagnoses of low ejection fraction over usual care."

"With EAGLE, the information was readily available in the electronic health record, and care teams could see the results and decide how to use that information," says Dr. Noseworthy. "The takeaway is that we are likely to see more AI use in the practice of medicine as time goes on. It's up to us to figure how to use this in a way that improves care and health outcomes but does not overburden front-line clinicians."

Obituaries

Hubert Ashman, M.D. (I '48), died April 11, 2021.

Mary Atkins, M.D. (PD '70), died May 10, 2018.

Grover Bynum Jr., M.D. (I '60), died Jan. 29, 2019.

Domenick Cover, M.D. (NEPH '87), died Dec. 22, 2018.

Guy Fessler Jr., D.D.S. (OMS '59), died Jan. 10, 2014.

John Hastings, M.D. (N '69), died April 28, 2021.

David Healow, M.D. (ANES '84), died Jan. 11, 2020.

Richard Hempstead, M.D. (U '52), died Jan. 30, 2016.

James Hunt, M.D. (I '58), died May 1, 2021.

Quentin Knauer, M.D. (S '62), died Sept. 8, 2016.

Myron Krueger, M.D. (I '70), died May 17, 2021.

Thomas Lake, M.D. (RD '70), died May 3, 2021.

Mark Mathison, M.D. (U '73), died Jan. 21, 2021.

John Ramsdell, M.D. (S '59), died Feb. 9, 2021.

Alumni Center

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alumniassociation.mayo.edu

Alumni meetings & receptions

alumniassociation.mayo.edu/events

Alumni philanthropy

Doctors Mayo Society
800-297-1185 | 507-284-9101
doctorsmayosociety@mayo.edu

Physician referral

Arizona 866-629-6362
Florida 800-634-1417
Rochester 800-533-1564
mayoclinic.org/medicalprofs

Refer a friend

alumniassociation.mayo.edu/resources/refer-a-friend

Education verification

Mayo Clinic College of Medicine
college.mayo.edu/academics/residencies-and-fellowships/contact-and-verifications

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About the magazine

Mayo Clinic Alumni magazine is published quarterly and mailed free of charge to physicians, scientists and medical educators who studied and/or trained at Mayo Clinic, and to Mayo consulting staff. The magazine reports on Mayo Clinic alumni, staff and students, and informs readers about newsworthy activities at Mayo Clinic.

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Then and now. Facing south on 2nd Avenue. Today, Kahler Hotel on the left and Gonda Building on right. Inset photo circa 1940s.

ALUMNI CENTER
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FIND MAYO CLINIC

Mayo Clinic ranked

No. 1 hospital in the nation by U.S. News & World Report

Mayo Clinic has again been ranked the No. 1 "Best Hospital" nationwide by U.S. News & World Report in its 2021–2022 "Best Hospitals" rankings, for the sixth consecutive year.

Mayo Clinic in Rochester has also been ranked No. 1 in Minnesota since 2012, when U.S. News & World Report first published state rankings. Mayo Clinic in Arizona has ranked No. 1 in Arizona for nine consecutive years, and Mayo Clinic in Florida has ranked No. 1 in Florida for five of the last six years.

Mayo Clinic in Arizona is ranked No. 15 on the "Best Hospitals" Honor Roll rankings, which marks the fifth consecutive year that Mayo Clinic in Arizona has been named a top 20 hospital.

"Mayo Clinic is honored to be the No. 1 ranked hospital in the nation for the sixth consecutive year, and we are truly grateful to our extraordinary staff for always putting our patients' needs first in the exceptional care that they provide," says **Gianrico Farrugia, M.D.** (I '91, GI '94), president and CEO, Mayo Clinic. "At Mayo Clinic, each patient receives specialized care from an innovative, collaborative and highly talented team that is committed to both treating serious or complex disease and advancing new and better cures through innovative research."

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