

A NEW PATHWAY TO PAIN RELIEF

An injectable neural stimulation electrode shows promise in treating a variety of conditions.

FULL STORY, p. 12



FROM THE CHAIRS

EXPLORE

The Biomedical Engineering Alliance at Case Western Reserve University and Cleveland Clinic

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RANKINGS



Case Western Reserve University has moved up in U.S. News and World Report rankings — a reflection of improved graduation rates, selectivity, faculty resources and the academic qualifications of the class of 2023.

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#7 BEST ONLINE MASTER'S IN BIOMEDICAL ENGINEERING DEGREE PROGRAMS



Robert F. Kirsch

Allen H. and Constance T. Ford Professor
Chair of Biomedical Engineering
Case Western Reserve University

 @RKirschCWRU



Geoffrey Vince

The Virginia Lois Kennedy Endowed
Chair in Biomedical Engineering
and Applied Therapeutics
Lerner Research Institute
Cleveland Clinic

 @DGeoffreyVince

Our Spring 2020 BME Alliance newsletter is being issued as the world responds to the spread of the COVID-19 virus. Case Western Reserve University, along with virtually all other universities in the United States, has sent all of our undergraduate students home and has ramped down non-essential, on-campus research and administrative activities. Likewise, research by the Cleveland Clinic members of the BME Alliance, as well as associated investigators at all of our medical center partners, has been substantially reduced as we fight the pandemic on the frontlines. Several of our BME Alliance faculty have quickly pivoted their research to focus on the development of diagnostic testing for the virus. We are proud of these efforts of our faculty and those of our extended community of researchers and medical caregivers.

We are also very proud and gratified to report that our students, faculty and staff have been real champions in adapting almost instantaneously to an "online life." We have maintained ALL of our courses via remote delivery methods – in the space of less than a week! Many elements of our research activities (computational and analysis components, experimental protocol development, manuscript writing, student committee meetings, laboratory meetings, etc.) continue, and all of our administrative operations proceed unabated. Major events, such as our annual Open House for recruitment of PhD students and our Case-Coulter Translational Research Partnership Oversight Committee meeting, were switched from in-person to virtual events in one to two days! You can get a behind-the-scenes look at how our faculty and staff rapidly revamped the Open House to a virtual format on page 17. We hope that the

legacy of the COVID-19 pandemic for the BME Alliance will be our resilience.

While the global pandemic is at the forefront of our minds, many other positive activities within the BME Alliance have taken place, and continue to occur, since our last newsletter. During the fall, Case Western Reserve University hosted two seminal events: the Coulter Investment Forum and the inaugural Artificial Intelligence in Oncology Symposium. During the Coulter Investment Forum, which you can read about on page 16, more than 350 venture capitalists and entrepreneurs heard pitches from start-up companies in the areas of medical devices, therapeutics, diagnostics, healthcare IT and delivery solutions. The Artificial Intelligence in Oncology Symposium, highlighted on page 18 attracted 270 thought leaders sharing ideas on how to use AI to improve cancer care.

The force behind all we do in the BME Alliance is the talented faculty, researchers and students that call Case Western Reserve and Cleveland Clinic Lerner Research Center home. In this newsletter, we present a Q&A with Sarah Carney, a rising star in biomedical engineering. Beginning on page 4, the PhD candidate shares insight on her cutting-edge research and future plans. Our cover story (page 12) focuses on work done by Andrew Shoffstall, assistant professor of biomedical engineering, and other alumni of the Department of Biomedical Engineering, to create an injectable neural stimulation electrode to provide pain relief.

As we all continue to cope with COVID-19 and its ramifications on our daily lives, we sincerely hope that this newsletter finds you healthy. We look forward to reporting to you during brighter days in the fall.

STUDENT SPOTLIGHT

Case Western Reserve University Students Win 2019 Cleveland Medical Hackathon

During the 2019 Cleveland Clinic Medical Innovation Summit last October, teams of students, engineers, developers, designers, researchers and investors participated in the fast-paced Cleveland Medical Hackathon. Each team had 24 hours to come up with an idea, mock up their solution and present it to judges. Hackathon participants focused on one of three key healthcare challenges: clinician burnout, aging in place and mental health. Teams of students from Case Western Reserve University won first and third place in the annual event for their entries related to aging in place.

First Place

Undergraduate students Kienan Ahner-McHaffie (computer science), Amirreza Naderi (biology), Keyvon Rashidi (biomedical engineering) and Josef Scheidt

(biomedical engineering) conceived of a medical pectoral sensor patch that addresses fall prevention and response to a fall.

Third Place

Graduate students Golnoush Asaeikheybari (computer science), Lin Li (biomedical engineering), Syeda Nur-E Saba (physics and entrepreneurship) and Sukanya Raj lyer (biomedical engineering) tackled the problem of social isolation among senior citizens. They developed an IOS application to connect young females with older females based on shared interests using machine learning. Users were vetted with facial recognition technology and matched with geo-location and interest-based matching algorithms. The app also suggested activities or events the users could participate in based on shared interests.



Left to right: First place winners Amirreza Naderi, Keyvon Rashidi, Kienan Ahner-McHaffie and Josef Scheidt

The winning team of Ahner-McHaffie, Naderi, Rashidi and Scheidt shared this first-hand account of their hackathon experience and the future of the product they created:

As a group of friends, once we realized that we were all staying on campus during fall break, we tried to think of fun things to do. Since we are all big-time nerds, we unanimously decided to attend the Cleveland Medical Hackathon. The night before, we began discussing what we wanted to do and finally settled upon a device that we now call "JAKK: FPS." (The acronym stands for the first letter of our names – Josef, Amir, Keyvon, Kienan – and Fall Prevention System.)

The inspiration for the device was personal for Josef, as he recalled a vivid childhood memory of visiting his grandfather in the hospital after he suffered a fall in his home. The family felt the fall should have been preventable. Josef's grandfather is far

from a lone case on elderly falls. But without the ability to predict the future, how can an elderly person living independently or their family make the correct decision about when additional care is needed or when a senior can indeed live on their own with minimal risk of injury?

Our hackathon solution centered around fall prevention. Research conducted by scientists at MIT has determined that factors such as changes in stride length and speed have been associated with an increased probability of falling within a three-week time-frame. Our device, the JAKK: FPS, seeks to solve this problem by predicting a fall before it occurs and seeking appropriate medical attention when a fall does happen.

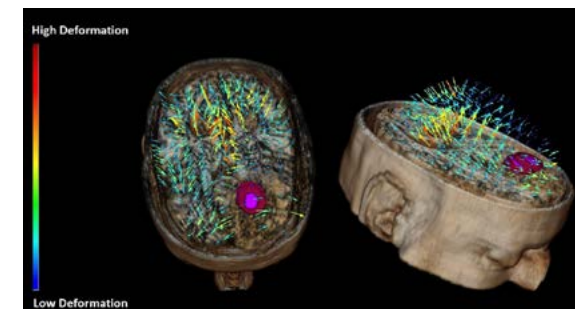
We investigated and prototyped a medical pectoral sensor patch. With the aid of machine learning and artificial intelligence, the sensor establishes a baseline average gait/walking pattern for a person. As the person walks, the device compares the gait pattern to the baseline. We implemented gyroscopes, accelerometers, heart rate detectors and pulse oximeter sensors to obtain the necessary data. The

working prototype demonstrates the function by graphing the data in real time via wireless transmission to a computer application. From this data, various patterns can easily be seen between someone walking normally and someone who has an abnormal gait.

We have also considered future directions and improvements for our device. These include implementation of new sensors, integration of kinematic and fall data with electronic medical records, increased integration with smart phones and possible incorporation of the sensor into other wearable technologies.

We believe our team was particularly strong because of our individual specialties in biology, biomedical engineering and computer science. This allowed us to best use our talents through effective communication between theory (biology), reality (engineering) and practicality (computer programming). We hope to receive additional funding to properly develop the technology beyond the prototype phase and into a consumer product.

Student Project Fund Award



PhD candidates in the Department of Biomedical Engineering, Sukanya Raj lyer and Fnu Ruchika, were funded by the Sears think[box] Student Project Fund to create 3D models of glioblastoma tumor infiltration. They want to study how to provide clinicians with an intuitive understanding of tumor infiltration and help guide personalized treatment options for patients. The Student Project Fund supports a diverse group of individual and team projects, including students from local colleges in the area and international and national institutions.



Graduate Student Honored with Invitation to Trainee Editorial Board

In December 2019, PhD candidate in the Department of Biomedical Engineering, Niha Beig, was offered a 1-year term on the Trainee Editorial Board (TEB) of Radiology: Artificial Intelligence, an online journal that highlights the emerging applications of machine learning and artificial intelligence in the field of medical imaging. As an editorial trainee, she will learn about paper review, research design and journalistic ethics, while reviewing papers for the journal as well.

A RISING STAR IN RESEARCH

Q&A WITH SARAH CARNEY



As a northeast Ohio native, Sarah Carney didn't travel far to attend graduate school in Case Western Reserve University's Biomedical Engineering Department. But with two renowned institutions right in her backyard – the university and Cleveland Clinic Lerner Research Institute – the PhD student was glad to stay put.

In 2017, Carney earned her bachelor's degree in materials science and engineering from The Ohio State University, where she specialized in biomaterials, tissue engineering and drug delivery. She now splits her time between classwork and research on cardiovascular engineering and elastic matrix regeneration in the lab of Anand Ramamurthi, PhD at the Lerner Research Institute.

In this interview, Carney provides insight into her passion for research and the multitude of projects she's worked on in her short career, including a stint last summer in the National Institutes of Health's Graduate Summer Opportunity to Advance Research (G-SOAR) Program.

Q: *Why did you decide to attend Case Western Reserve University for grad school?*

A: As an undergraduate, I participated in a National Science Foundation REU [Research Experiences for Undergraduates] at Cleveland Clinic with Dr. Ramamurthi. I loved my work in the lab, and I knew that I wanted to come back. So when I found out that I could do research for my dissertation in his lab and still get my degree through Case Western Reserve University, it was the best of both worlds. I really benefit from the Biomedical Engineering Alliance between the university and Cleveland Clinic.

Q: *What does your research at the Lerner Research Institute entail?*

A: It's an extension of the work I did the summer between my junior and senior years at Ohio State in Dr. Ramamurthi's lab. My research is on the use of nanoparticles for elastic matrix regeneration to treat abdominal aortic aneurysms. The smooth muscle cells in the abdominal aorta aren't able to naturally regenerate elastin once you become an adult, and elastin is broken down during abdominal aortic aneurysms. My work focuses on the use of a specific gene – called JNK2 – which is upregulated with things like stress and inflammation and becomes overexpressed in the disease I'm working on. I'm silencing this gene using nanoparticles and small interfering RNA (siRNA) to determine the effect on elastin regeneration. Ultimately, I'll be encapsulating siRNA to silence the gene into a lipid-coated nanoparticle and deliver it to the aneurysm wall.

Q: *Was your research at Ohio State in the same area?*

A: No, I worked on a polymeric contraceptive drug delivery vehicle for control of wild animal population. We used electrospinning to make these biodegradable polymer capsules that could be loaded with drugs and implanted into horses. Since my focus was on materials science, we studied a lot of materials and the electrospinning parameters needed to create the capsules.

Q: *So is it fair to say your passion for research began as an undergrad?*

A: It definitely started at Ohio State. I worked with a PhD student who was really helpful and patient. Because

I had such a great introduction to research there, I definitely wanted to continue on in academia.

Q: *What did you do last summer in the NIH's G-SOAR Program?*

My summer internship was in the lab of Tiffany Powell-Wiley, MD, MPH, FAHA. Her group at the National Heart, Lung, and Blood Institute works with African-American women in the Washington, D.C., area who are at risk for cardiovascular disease. Specifically, I studied the intersections of stress, immune response and cardiovascular disease. My work was in vitro with cell culture quantifying human endothelial cell response to different combinations of neurotransmitters, lipids and cytokines. I began correlating the results from cell cultures in the lab to patient outcomes to figure out what factors could potentially be contributing to cardiovascular disease.

Q: *You have certainly participated in a lot of interesting projects during your young career. What draws you to research?*

A: Research gives you an opportunity to look at things that industry may not be interested in if companies can't make money off of it. There's more space and time in academic research – more creative freedom – to figure out the real underlying problem you are trying to solve.

Q: *Midway through your doctoral work do you have any thoughts on what you would like to do after earning your PhD?*

A: I'm not sure yet, but I'm really interested in doing community-based work. My dissertation work and a lot of my experiences have been in cardiovascular disease. However, I'm also really passionate about women's health research. I'm in a collaborative project at the Cleveland Clinic working on pelvic organ prolapse in relation to women's birth and delivery. I would love to do something centered in that area. But I've got a couple years of school left, so that could change.

Q: *When you're not in the lab or classes, what do you like to do?*

A: I love thrift store shopping, and I love to cook. I actually love to read cookbooks more than I like to cook. I think that may be because I don't run the risk of the meal not turning out well!



Reconnecting the Hand and Arm to the Brain

New Research Seeks to Restore Functional Control of Arm and Hand for Those With Quadriplegia

Grant for \$3 million from the U.S. Department of Defense supports the work being done at University Hospitals, Case Western Reserve University and the Cleveland FES Center.

In science, an N of 1 is rarely enough to support any big conclusions — no matter how significant the results. That even applies to the story of Bill Kochevar, the Cleveland man who became the first person with quadriplegia in the world to regain functional control of his arm and hand using technology implanted in his brain and limb.

Kochevar, who had been paralyzed from the shoulders down in a bicycling accident in 2006, participated in a study at the Cleveland FES Center and Case Western Reserve University, where researchers implanted two micro-electrode arrays in his motor cortex to capture his brain activity and electrodes in the muscles of his

upper and lower arm to stimulate his arm and fingers. A computer interface using mathematical algorithms translated his thoughts into electrical impulses that controlled his muscles.

“We had a lot of success with Bill,” says Robert Kirsch, executive director of the Cleveland FES Center and chair of Case Western Reserve University’s Department of Biomedical Engineering. “We learned that we could do this. We learned a lot of other things as well, including better ways to do [this research] in the future.”

When Kochevar died in December 2017, just a few months after the research was published in *The Lancet* and featured worldwide by the BBC, CBS News, NPR



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Cleveland FES Center

Paralyzed in a biking accident in 2006, Bill Kochevar regained functional control of his arm and hand using a brain-computer interface with recording electrodes implanted in his brain and a functional electrical stimulation (FES) system implanted in his limb that work in tandem to reconnect his brain to paralyzed muscles.

and more, it caused Kirsch and the other researchers to pause and evaluate where to go next. After more than a year of reflecting on the best ways forward, they are poised to launch a feasibility study of the Reconnecting the Hand and Arm to the Brain (ReHAB) System, a greatly enhanced version of the technology used with Kochevar. The study is led by Bolu Ajiboye, an investigator with the FES Center and associate professor of biomedical engineering at Case Western Reserve University.

The research, which builds upon six years worth of work, is being funded with a \$3 million grant from the United States Department of Defense. With Food and Drug Administration approval for up to 12 participants for

initial 13-month trials, the first individual is expected to begin the trial this year followed by additional subjects every nine months or so. “It’s time to start doing this with more people and looking at variations across people,” says Kirsch.

Here is how ReHAB builds upon previous lines of research and hopes to break new ground:

Utilization of Specialized Nerve Cuffs

In Kochevar’s case, researchers implanted electrodes through the skin into neuromuscular junctions using hypodermic needles. This allowed the electrodes to be easily removed, but they were also somewhat imprecise

in their placement. "He was able, by the end, to control his hand and his forearm very precisely," says Jonathan Miller, director of functional neurosurgery at University Hospitals, associate director of clinical affairs at the Cleveland FES Center and professor of neurological surgery at Case Western Reserve School of Medicine. Yet, because the electrodes were inserted directly into the muscle, there were issues controlling the strength of the contractions and limitations on what muscles were able to be activated.

The ReHAB study employs specialized nerve cuffs, developed by Cleveland FES Center investigator Dustin Tyler at Case Western Reserve, which fold around the nerve and offer much greater precision in the placement and intensity of the stimulation. "That leverages the body's own natural organization," says Miller. "By stimulating nerves, we're able to activate muscles the way that the body normally activates them."

Increased Electrode Arrays

Researchers working with Kochevar implanted two 96-electrode arrays in the motor cortex to capture brain activity associated with hand and arm movement. The ReHAB system includes six, smaller 64-electrode micro-arrays placed in both the motor and sensory cortex, and areas associated with intended movement. "The brain doesn't think in one straight line. It's not like information starts one place and then jumps to another place," says Miller. "It happens all at once and in a lot of different places. Everything that happens in the brain is distributed over a widespread area that works together and along these networks."

Creation of a Feedback Loop

By collecting information over a larger area of the brain and tapping into a variety of neural nodes, researchers hope to collect much more detailed information than ever before. In addition, ReHAB won't just gather information

from the brain, but will also return information about touch and spatial alignment back to the brain from the hand and arm. "That's been a major problem with a lot of these prosthetic technologies," says Miller. "There's not adequate feedback to tell exactly how much force is being applied. We're hoping to stimulate the brain to mimic sensation, so participants will be able to feel again and, ideally, even recognize where the arm is in space."

Deeper Pool of Participants

Expanding the number of participants brings its own opportunities and challenges. Work with Kochevar could be individualized, while ReHAB will need to be more consistent in its methods. "Obviously, when you scale a project up, it becomes more complicated," says Miller. Yet, working across individual differences should provide a broader understanding of brain and neural function. Eventually, that knowledge could speed up the pace of development. "We're hoping we can find some more general organizing principles that aren't so sensitive to small differences in where the electrodes are placed or the person's history," says Kirsch. "If we can figure that out, then we can at least have a broad algorithm that we start with."

Expansion Beyond Spinal Cord Injuries

Researchers hope to expand the ReHAB study beyond individuals with spinal cord injuries, which impacts approximately 291,000 people in the United States. So they're recruiting participants beyond that population to possibly include those affected by stroke, multiple sclerosis or spinal cord dysfunction due to tumors or radiation damage. "You need to be able to show that this isn't just something working for one person," says Miller. "There are things that are translatable and potentially generalizable across many people, because eventually our goal is to make this clinical tool."

I AM HUMAN, a documentary featuring the amazing journey of a paralyzed Cleveland veteran and the doctors and researchers who helped him regain control of his hand and arm, made its Cleveland premiere Jan. 30, 2020, in the Hanna Theatre at Playhouse Square.

Directed and produced by Taryn Southern and Elena Gaby, the documentary explores what it means to be human by following three people with implantable brain interfaces. The film prominently features Cleveland veteran Kochevar and the cutting-edge work of the Cleveland FES Center at the Louis Stokes Cleveland VA Medical Center, Case Western Reserve University and University Hospitals Cleveland Medical Center - the same research that ReHAB is built upon.

I AM HUMAN

Cleveland, OH

Thursday, January 30, 2020

Hanna Theatre at Playhouse Square



Here's to you...

We are honored with the sensational turnout and energy for the I AM HUMAN Cleveland Premiere & Panel Discussion. It is a rare occasion that we are able to share a glimpse of FES research with such a strong Cleveland connection.

Thank you for making the evening an extraordinary success! Our greatest appreciation for your continued support of FES research programs goes to the Northeast Ohio community: our families, friends, research partners and collaborators, and everyone who came out to experience I AM HUMAN.

Our sincerest appreciation goes to the I AM HUMAN co-producers and directors, Elena Gaby and Taryn Southern for creating such an incredible film.

We would like to recognize Cleveland veteran Bill Kochevar and his family. Bill was a pioneer in this research, and we appreciate his commitment to this program. Bill's determination and drive made this research and future programs possible.

To follow the future of our work, please visit ReHABstudy.org.



Bolu Ajiboye, PhD



Robert Kirsch, PhD



Jonathan Miller, MD

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I AM HUMAN In the News

Read articles at [FEScenter.org/news-and-events](https://fescenter.org/news-and-events)



New technology helps man find freedom despite paralysis



I Am Human Documentary Features FES Center, CWRU



Podcast: "I Am Human"



The real-life bionic people: Cleveland FES Center uses technology to help people with paralysis



Cleveland's Morning News with Wills and Snyder



"I Am Human" Premieres in Cleveland



Documentary Film 'I Am Human' to Have Its Cleveland Premiere on Jan. 30 at the Hanna Theatre



462 Registered Guests

164 VIP Attendees

7 Articles to date

6 Billboards in Cleveland

To read them all, visit [FEScenter.org/news-and-events](https://fescenter.org/news-and-events)

1.1M Impressions



Facebook
January, 2020

33,059
Post Reach

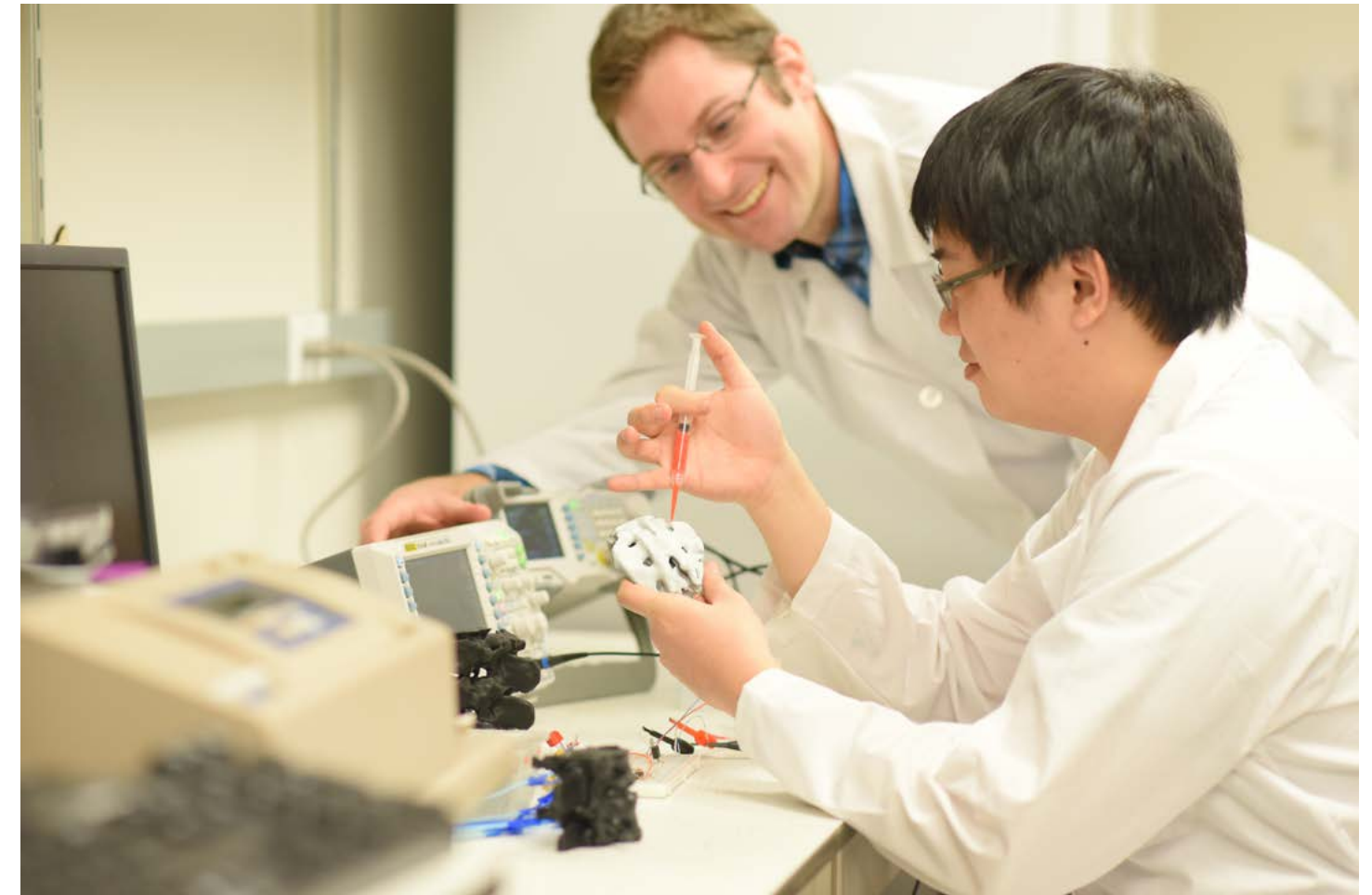
↑416%
Post Engagement

Twitter
January, 2020

10,795
Impressions

A NEW PATHWAY TO PAIN RELIEF

An injectable neural stimulation electrode shows promise in treating a variety of conditions.



Andrew Shoffstall works with PhD candidate Kevin Yang on the insertion site for the injectrode using a model of the sacrum.

The lifetime prevalence of back pain in the United States is approximately 80%, according to the Cleveland Clinic. Low back pain is also one of the leading causes of disability and one of the most common ailments treated with opioids. A team of researchers from across the country, including Andrew Shoffstall at Case Western Reserve University, has created a novel injectable metal electrode that could provide an alternative to traditional drug therapy or surgically-implanted devices for back pain – and a host of other medical issues.

The Injectrode™ is a liquid composite mixture consisting of tiny metal particles mixed with a silicone base similar to surgical glue. When injected, the silicone cures inside the body and molds to the shape of the specific target.

Last fall, collaborators on the Injectrode project received a \$2.2 million grant from the National Institutes of Health (NIH) as part of its HEAL Initiative (Helping to End Addiction Long-termSM), which is focused on improving prevention and treatment for opioid misuse and addiction and enhancing pain management. The team

of researchers will test the Injectrode at the dorsal root ganglion, stimulating the target to alleviate pain.

“The spinal cord is a great potential test bed for this technology,” says Shoffstall, assistant professor of biomedical engineering at Case Western Reserve University. One of his primary partners on the project is Manfred Franke, who earned his PhD in biomedical engineering at the university in 2014. Together with Kip Ludwig, associate professor at the University of Wisconsin, Franke and Shoffstall co-founded Neuronoff Inc. in 2017 to develop medical devices such as the Injectrode. The company now has its R&D arm at the BioEnterprise building at the intersection of Case Western Reserve University and the Cleveland Clinic.

“We hope the NIH grant will prove out, with data, how clinicians can use the Injectrode most effectively to stimulate the dorsal root ganglion or nearby structures to suppress pain and do the entire placement procedure in a much faster, easier way than [neuromodulation] is currently done,” says Franke.



Partnering as PhD Students

In 2009, Shoffstall and Franke first met as graduate students at Case Western Reserve University who shared a curiosity about neuromodulation. Shoffstall worked in the labs of Associate Professor Erin Lavik, now the Associate Dean for Research and Faculty Development at the University of Maryland, Baltimore County. “Her work fused the two areas I have an interest in – biomaterials and neural engineering,” says Shoffstall. As a doctoral candidate, his work focused on creating synthetic platelets that could be injected into the bloodstream at sites of injury to stop bleeding after a spinal cord injury or traumatic brain injury.

Franke chose Case Western Reserve University for grad school because of its strong history and reputation as a leader in biomedical engineering. “Case Western Reserve is the cradle of neuromodulation,” he says. “Going back to the 1960s with work by Thomas Mortimer [professor emeritus] and others, the university has been on the leading edge of developing neuromodulation treatments for a variety of medical conditions.”

During his time at the university, Franke learned to push the boundaries of neuromodulation alongside innovators such as Dustin Tyler, Kent H. Smith Professor II of Biomedical Engineering, and Kenneth Gustafson, associate professor. “You can do so much with neuromodulation, but very few people truly appreciate and understand it because they don’t think beyond the possible,” says Franke.

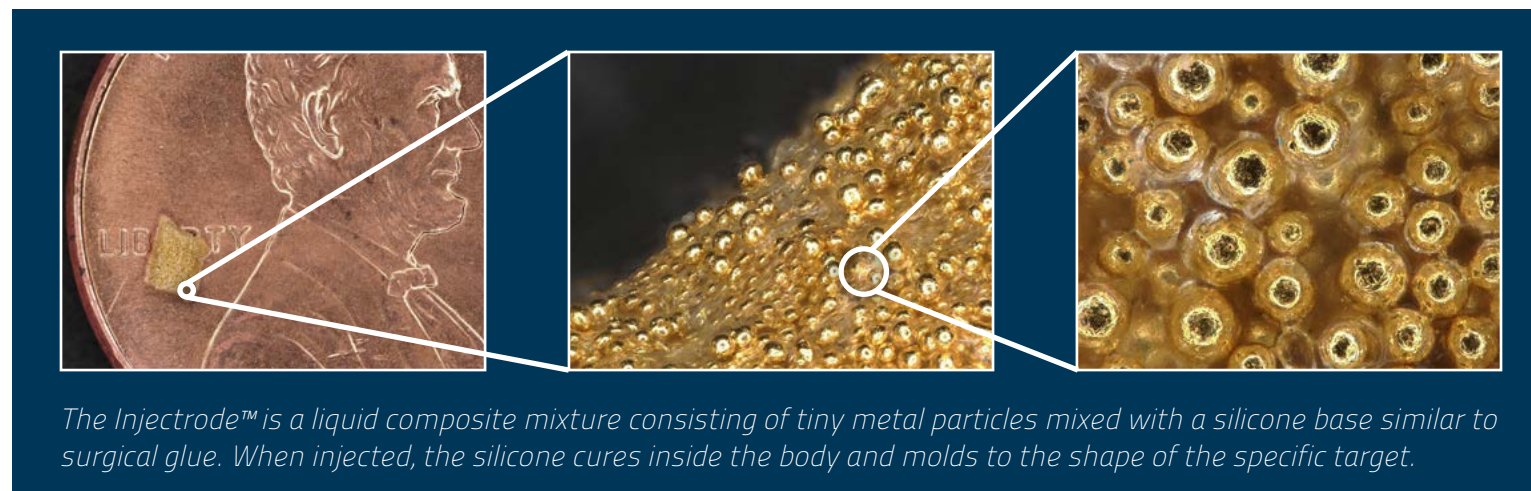
Franke certainly tests the limits of what’s possible: He began filing patents related to neuromodulation technology (currently at 45 granted and counting) in 2012 and earned the Doctoral Excellence Award in Biomedical Engineering in 2014. After surgical training to implant traditional electrodes while at the Case Neural Engineering Center and a stint with a neuromodulation company between 2013 and 2016, Franke conceived of the Injectrode in late 2016 to simplify the process of reaching nerves electrically. Teaming with Shoffstall, whose lab at Case Western Reserve University focuses on the interface of biomaterials with the nervous system, was a natural fit.

Refining the Materials and Delivery Methods

The Injectrode researchers are developing and studying both the biomaterial – what they informally call the “goop” – as well as surgical targeting techniques to guide the liquid to the right spot.

“The composite goop has the consistency of Play-Doh™ and gets extruded out of the syringe when it’s injected,” says Shoffstall. Once injected, it cures to form a highly-conforming, compliant neural electrode in vivo.

The team has tested material mixtures with various amounts of metal particles (such as silver and gold) and different commonly



The Injectrode™ is a liquid composite mixture consisting of tiny metal particles mixed with a silicone base similar to surgical glue. When injected, the silicone cures inside the body and molds to the shape of the specific target.

“If we can get the Injectrode into outpatient procedures, performed by pain physicians instead of neurosurgeons, then it would vastly expand the use of electrical stimulation.”

– Andrew Shoffstall

Assistant Professor of Biomedical Engineering
Case Western Reserve University
Investigator, APT and FES Centers
Cleveland VA Medical Center

used surgical glues and sealants approved by the Federal Drug Administration to ascertain the percolation threshold. “We dope the material with a high enough field of particles to achieve percolation,” says Shoffstall. “The metal flakes or spheres bridge electrical signals from one side of the composite to another.”

At that point, you have a fully-implanted passive conductor – the Injectrode – inside the body extending from the target nerve to approximately one to three millimeters from the surface of the skin. “In some cases, we have been able to pair the Injectrode with a transcutaneous electric nerve stimulation (TENS) unit, which is a standard, inexpensive device, to provide neuromodulation for that nerve,” says Franke.

Neuronoff – a word play on the idea of turning neural systems “on” and “off” – is focused on clinical translation of the minimum viable product. “With the Injectrode, we take all the know-how from 50-plus years of work on electrical stimulation done at Case Western Reserve and bring it to a minimally-invasive level that can be easily commercialized,” says Franke.

Neuronoff’s role in the NIH HEAL grant is to supply Injectrode devices and electrodes to the researchers, while Shoffstall’s lab conducts material analysis and biocompatibility testing. Other collaborators include Doug Weber from the University of Pittsburgh and Scott Lempka, who earned his PhD from Case Western Reserve and is now at the University of Michigan, who are conducting in vivo biologic studies and simulations for injection and stimulation parameter optimization.

Creating the ‘Last-Mile’ Interface

The Injectrode has many potential benefits. It is less invasive than other implanted neural stimulation devices, and it is more targeted than drug therapies. “Even though medications are less invasive than cutting

someone open for surgery, those drugs circulate through your entire bloodstream and touch every cell and organ in your body,” says Shoffstall.

The Injectrode can also conform to a variety of targets to form different neural interfaces. For instance, it can stimulate complex neural structures – such as networks of intersecting nerves – that can be difficult to target with traditional cuff electrodes. “There are areas you can’t interface with today, such as thin fibers in your gut area or near organs, but you can glue some goop to those nerves,” says Franke. “That allows researchers and clinicians to think about new ways of treating conditions because the Injectrode provides this last-mile interface.”

While the NIH HEAL grant focuses on treating low back pain, the Injectrode has potential for multiple indications, including post-amputation neuropathic pain, migraine, overactive bladder, epileptic seizures and sciatic pain. “We want to demonstrate that the Injectrode works in one thing first – chronic back pain,” says Shoffstall. “But as we build out the tools, get more comfortable with the biomaterials and get more data, then we can start testing the Injectrode in a variety of places.”

That, in turn, would open up opportunities to move neuromodulation beyond usage by a small group of highly-trained neurosurgeons. “They are the specialized of the specialized,” says Shoffstall. “If we can get the Injectrode into outpatient procedures, performed by pain physicians instead of neurosurgeons, then it would vastly expand the use of electrical stimulation.”

BIOMEDICAL START-UPS CONNECT WITH INVESTORS AT THE COULTER INVESTMENT FORUM



Last October, more than 350 venture capitalists and entrepreneurs attended the Coulter Investment Forum on the opening day of Cleveland Clinic's Medical Innovation Summit. They heard pitches from 29 start-up companies in the areas of medical devices, therapeutics, diagnostics, healthcare information technology and delivery solutions.

The event, now in its fifth year, is invaluable for budding companies. "The Coulter Investment Forum provides fast-growing companies the opportunity to showcase their technologies to a number of thought leaders within the biomedical ecosystem," says John Zak, MD, president and CEO of XaTek. "It is that rare opportunity to address the scientific, commercialization and investment communities all at once."

Cleveland-based XaTek was one of the companies invited to participate in the forum. Its ClotChip™ system is an in vitro diagnostic assay delivered in a handheld, point-of-care device with full connectivity that can assess a patient's bleeding profile in minutes and with sensitivity to clinical conditions.

Participating companies were nominated by one of The Walter H. Coulter Foundation's 16 university partners. The foundation's university-based translational research grant programs establish a business-like process to accelerate academic innovations to the marketplace. Two companies chosen by Case Western Reserve University through its Case-Coulter Translational Research Partnership (CCTRP) were part of the pitch competition: XaTek and Exotome. The latter developed a proprietary ligand PSMA-1 that binds to the cell membrane receptor PSMA, which is overexpressed in some types of cancer. "The Coulter Investment Forum takes advantage of the sheer volume of investable technologies that are coming out of the different Coulter programs to attract investors to a single site," says Steve Fening, CCTRP director

and associate professor of biomedical engineering at Case Western Reserve University. "It allows us to attract a different caliber of investors to look at these technologies than we would be able to do individually, school by school."

Last fall was the first time the Coulter Investment Forum was held in Cleveland in close proximity to Case Western Reserve University. Previous host universities have included Stanford University, Boston University, University of Michigan and Duke University. Next fall, Drexel University in Philadelphia will host the event.

The eight-minute pitches presented by competing companies in October, which included 10 start-ups selected by Cleveland Clinic in addition to the Coulter-vetted companies, were evaluated by a panel of 10 judges comprising venture capitalists and medical practitioners. The judges selected the C-HEART technology by Atlanta-based Covanos as the 2019 platinum prize winner. C-HEART uses advanced, proprietary mathematical methods and computational fluid dynamics to identify non-invasively whether blockages in coronary arteries require a medical intervention, such as surgery or stent.

While it's an honor to win the platinum prize, the primary goal of participating companies is to attract the attention of funders. The 2019 Coulter Investment Forum provided the ideal venue to do just that.

"The most exciting part of the event was witnessing the energy of the assembled venture capitalists we attracted. That was particularly important for schools like Case Western Reserve University in the Midwest, where we don't have a ton of venture capitalists just down the street from us," says Fening. "The quantity and quality of venture capitalists that the forum attracted to the region was something I've never seen before."

BME PIVOTS TO A VIRTUAL OPEN HOUSE IN RESPONSE TO COVID-19

[BME.CASE.EDU/OPENHOUSE2020](https://bme.case.edu/openhouse2020)



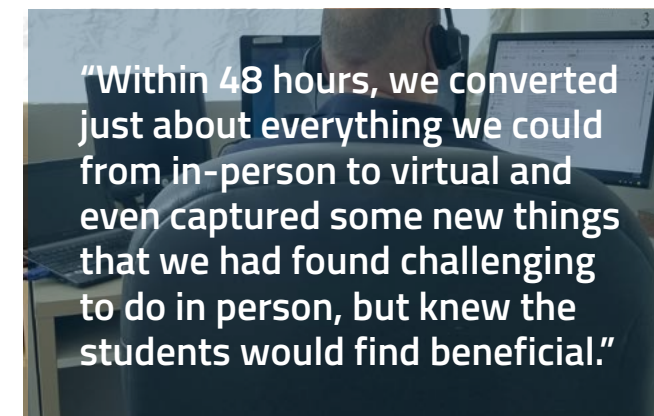
Faculty and staff from the Department of Biomedical Engineering at Case Western Reserve University and Cleveland Clinic spent weeks planning the annual Open House for prospective PhD students to be held March 13 – 15. But as the coronavirus rapidly spread around the globe, it became clear to members of the Open House Committee that the event would not go off as planned. On Wednesday, March 11 – the same day the World Health Organization declared COVID-19 a global pandemic – the committee decided to forgo the in-person event and shift to an online Open House.

"Within 48 hours, we converted just about everything we could from in-person to virtual and even captured some new things that we had found challenging to do in person, but knew the students would find beneficial," says Horst von Recum, professor of biomedical engineering at Case Western Reserve University and a member of the Open House Committee.

Traditionally, the Open House includes in-person orientations, mixers, sessions with current PhD candidates and one-on-one interviews with 40 to 50 prospective graduate students. Faculty and staff brainstormed creative ways to turn these events into virtual ones. The online Open House included the following:

- **The Webinar** – A primary component of the event was a webinar that introduced prospective students to Case Western Reserve University, the Department of Biomedical Engineering and its major research thrusts, and Cleveland.

- **The Interviews** – One-on-one interviews that were typically conducted in-person between students and faculty with matched research interests were held via Zoom video conferencing. von Recum created a series of YouTube videos to teach faculty how to use Zoom for the webinar and interviews and another video to explain to students how to interface virtually and what was expected of them.



- **The Hangouts** – In place of mixers and networking between sessions, the Open House Committee created a Zoom meeting room where prospective students could "hang out" between events and meet one another, chat and leave notes.
- **Meet the Lab Sessions** – A new idea generated for the virtual Open

House, these sessions allowed attendees to meet with members of the labs they would potentially join via Zoom.

- **The Landing Page** – The committee created the Landing Page, another new addition to the Open House, where prospective students could not only obtain resources about the Department of Biomedical Engineering, but also take a look inside research labs and facilities at the university via virtual tours and videos. The resource page remains online at: bme.case.edu/openhouse2020.

The virtual Open House was a resounding success, says von Recum. "We received many comments about how impressive it was that we put together something so comprehensive on such short notice," he says. "It was definitely a team effort."



EXPERTS CONVENE AT THE ARTIFICIAL INTELLIGENCE IN ONCOLOGY SYMPOSIUM

Above: Pallavi Tiwari, Hugo Aerts, Brian Hobbs, Donna Plecha and Satish Viswanath.

On October 24, 2019, the Case Comprehensive Cancer Center and the Center for Computational Imaging and Personalized Diagnostics (CCIPD) hosted the inaugural Artificial Intelligence in Oncology Symposium. Held on the campus of Case Western Reserve University, the event attracted 270 attendees from 12 states and eight countries, with an additional 50 tuning in to a livestream.

"The potential for artificial intelligence to improve cancer care is extraordinary," said Pamela Davis, MD, Dean of the Case Western Reserve University School of Medicine in her welcome message (pictured left). "Cancer is incredibly complex, and that complexity really lends itself to the kind of analytics you can derive from AI. The gains that could be possible with AI could be life-transforming for patients." A leader in the field, the Case Comprehensive Cancer Center has investigators on more than 10 projects in AI in oncology funded by the National Cancer Institute.

The symposium featured an impressive lineup of speakers and panelists, organized into four sessions that focused on developments and opportunities for AI in radiology, pathology and genomics, immuno-oncology, and policy and ethics. The gathering of a variety of stakeholders at the intersection of oncology and artificial intelligence was timely given that the National Cancer Institute named AI one of the three pillars of its strategic plan for 2020 and beyond.

"Artificial intelligence could have a profound and transformative impact on the management and care of cancer patients, but it's not just about AI for diagnosis and detection of the disease," said Anant Madabhushi in his opening remarks. Madabhushi is director of the CCIPD and F. Alex Nason Professor II of Biomedical Engineering at Case Western Reserve University. "There is a huge opportunity for the role of AI in prognosticating disease outcome – for stratifying noninvasively with imaging data the more aggressive cancers from the less aggressive cancers. There is also a clinical role for AI in



Pamela Davis, MD, Dean of the Case Western Reserve University School of Medicine, delivers the welcome message.



Sohrab Shah, the Nicholls-Biondi Endowed Chair in Computational Oncology at Memorial Sloan Kettering Cancer Center, delivers the keynote address.

predicting therapeutic response to identify which patients will respond to specific therapies in advance of that treatment." Since its inception in 2012, the CCIPD has developed more than 80 technologies utilizing computer analytics and big data in oncology and other medical specialties.

One of the highlights of the symposium was the keynote address by Sohrab Shah, the Nicholls-Biondi Endowed Chair in Computational Oncology at Memorial Sloan Kettering Cancer Center, who shared insight into the computational methodologies he has developed and applied in cancer genomics. "In the lab, we view cancer as a dynamic disease, and that means the cancer diagnosis is often very different than the cancer that achieves relapse or resistance to treatment or undergoes metastatic spread to different parts of the anatomy," he said. "Ultimately, these processes are driven by changes in the genome, so we think of cancer as a disease of the genome." Shah's address focused on the co-evolution of malignant and immune cells in high-grade serous ovarian cancer.

Throughout the keynote address, speaker presentations and panel discussions, a few overarching themes emerged as experts discussed the roadmaps for successful translation and clinical adoption of AI tools:

- **AI in oncology requires vast, validated datasets.** "Cancer is a computational problem," said symposium speaker Kevin White, chief science officer



Opening remarks by Anant Madabhushi, director of the CCIPD and F. Alex Nason Professor II of Biomedical Engineering at Case Western Reserve University.

at Tempus, a Chicago-based biotechnology company. "Over the next decade, the greatest progress in technology will be made by those who have access to the deepest and most comprehensive datasets."

- **Datasets must be shared over multiple sites.** "It is incumbent on us to push our health systems to develop data models and data marts that allow us to take all of the transactional data we generate on a day-to-day basis and mobilize it in shareable ways," said symposium speaker Michael Feldman, MD, a professor of pathology and laboratory medicine and director of the Office of Pathology Informatics at the University of Pennsylvania.
- **Experts must breakdown professional silos and work together.** "Having a data dump where we place all the data and think something beautiful will drop out is not realistic," said Shah. "But if we integrate the clinicians, oncologists and surgeons and ask them to articulate the pressing clinical problems that can be solved through integrating multi-modal data points, then we will likely get somewhere."

Though the road ahead for AI in oncology is challenging, attendees at the Artificial Intelligence in Oncology symposium were upbeat about the field's potential to ultimately make a difference in the lives of cancer patients. "I think in the next decade we will see a huge growth area in integrated multi-modal systems," said Shah. "It's an exciting time because data are ubiquitous."

BUILDING THE FIRST HOLOGRAPHIC BRAIN 'ATLAS'

HoloLens to define and visualize pathways in the human brain



A team of researchers, led by Case Western Reserve University scientists and technicians using the Microsoft HoloLens mixed reality platform, has created what is believed to be the first interactive holographic mapping system of the axonal pathways in the human brain.

The project, described by researchers as a “blending of advanced visualization hardware, software development and neuroanatomy data,” is expected to have a wide range of scientific, clinical and educational applications and further a collaborative interaction between neuroanatomists and brain-imaging scientists.

For starters, it almost instantly becomes “the foundation for a new holographic neurosurgical

navigation system” for Deep Brain Stimulation (DBS) and is being dubbed ‘HoloDBS’ by the team, says lead researcher Cameron McIntyre, the Tilles-Weidenthal Professor of Biomedical Engineering at the Case Western Reserve University School of Medicine.

“More than 100 clinicians have had a chance to beta test this so far, and the excitement around the technology has been exceptional,” McIntyre says, adding that the method is already dramatically advancing scientists’ understanding of the complexities associated with certain targeted brain surgeries.

The new research incorporates decades of valuable, but disconnected, neural data from dozens of sources and transforms them into a fully three-dimensional and interactive visualization. Users of the technology,

including neural engineers, neuroanatomists, neurologists, and neurosurgeons, are able to see both the animated “atlas” of the brain via the HoloLens headset — and the axonal connections in front of them.



Neurosurgeons and CWRU researchers use an interactive HoloLens model to plan electrode trajectories for 14 electrodes that will be placed in a single study subject's brain.

“The cool thing about this is that we have been able to integrate decades of neuro-anatomical knowledge into the context of the most modern brain visualization techniques,” McIntyre says. “We’re taking all of that anatomical knowledge and putting it into the hands of users in an entirely new and useful format.”

McIntyre worked alongside radiology professor Mark Griswold, who is faculty leader of Microsoft HoloLens education-related initiatives and directs the Interactive Commons, a university-wide entity that aims to help faculty, staff and students use a range of visualization technologies to enhance teaching and research. Griswold also led the team that developed the HoloAnatomy app.

Others on the project included Mikkel Petersen, a postdoctoral fellow in the McIntyre Lab, and world expert neuroanatomists from the University of Rochester, Université Laval in Quebec City, Quebec, Emory University and the University of Pittsburgh.

Neuron Paper Details Project

The process is described in “Holographic Reconstruction of Axonal Pathways in the Human Brain,” published online in the journal *Neuron*. Full text

of the article is available online on [cell.com](https://www.cell.com).

The project focuses on visualizing the precise axon pathways in the brain. Axon pathfinding is a subfield of neural development which researches how neurons send out axons to reach the correct targets in the brain.

Researchers focused on the subthalamic region of the brain, a common surgical target for deep brain stimulation, but an area of the brain that has been highly problematic for the current best technology, known as tractographic reconstructions.

Tractography, known for revealing colorful “rainbows” inside the human brain, has been used in hospitals for about 20 years. It visually represents the nerve tracts in the brain by using data collected by diffusion MRI, presenting the information in two- and three-dimensional images called tractograms.

The Case Western Reserve team advanced that technology not only by making it truly three-dimensional, but interactive by asking a group of expert neuroanatomists to “interactively define axonal trajectories of the cortical, basal ganglia and cerebellar systems” while wearing the HoloLens headset.

“In doing so, we have produced what is the first anatomically realistic model of the major axonal pathways in the human subthalamic region,” McIntyre says. “This is just the first step and can be repeated throughout the brain.”



The HoloLens model allows researchers to estimate which axonal pathways are likely to be stimulated at different electrode locations.

FACULTY HIGHLIGHTS



Jay Alberts

Jay Alberts, Lerner Research Institute Department of Biomedical Engineering, was awarded a \$2 million grant from the Department of Defense to create augmented reality assessment modules that will help determine when military personnel who have sustained a mild traumatic brain injury can return to duty. The Troop READY project, a collaboration between Alberts and military experts, will test and use a "ruggedized" (fit for combat environments) version of the Microsoft HoloLens augmented reality system to create return-to-duty modules that objectively measure a service member's performance of duties and activities. The modules will assess motor and cognitive demands that military members are likely to encounter in training and on the battlefield, and can also be used to make return predictions and recommendations.



Jillian Beveridge

Jillian Beveridge, Lerner Research Institute Department of Biomedical Engineering, was awarded a three-year, \$736,000 grant from the NIH entitled "The Effects of Reduced ACL Stiffness on Dynamic In Vivo Joint Function." In addition, Beveridge was selected to receive the 2019 Early Career Award from the Journal of Orthopaedic Research at the 2020 ORS conference in Phoenix. The award comes with a \$2,000 unrestricted grant sponsored by the publisher, Wiley.



Aaron Fleischman and Courtney Shell

Lerner Research Institute Department of Biomedical Engineering was awarded two annual fund awards: Aaron Fleischman received \$98,500 for "Micro Pressure Sensors" and Courtney Shell received \$37,500 for "Reducing Pain and Anxiety During Needle Stick Procedures."



Andrew Janowczyk and Anant Madabhushi

Case Western Reserve University researchers in the Center for Computational Imaging and Personal Diagnostics (CCIPD) have released a new tool to ensure the quality of digital pathology images being used for diagnostic and research purposes. HistoQC is an open-source quality-control tool that helps users flag low-quality images while preserving those that can help clinicians make accurate diagnoses. The creation of HistoQC was spearheaded by Anant Madabhushi, director of CCIPD and F. Alex Nason Professor II of Biomedical Engineering, and Andrew Janowczyk, a research faculty member in the Department of Biomedical Engineering.



Vinod Labhassetwar

Vinod Labhassetwar, Lerner Research Institute Department of Biomedical Engineering, received a 5-year, \$2,081,476 grant to investigate the use of a tissue plasminogen activator (tPA) nanoconjugate for stroke therapy. While tPA is the only FDA-approved therapy to re-establish cerebral blood flow, it is associated with an increased risk of hemorrhage, which means that few stroke patients are helped by tPA. Labhassetwar's earlier studies demonstrated that the nanoconjugate performed better than tPA alone and did not cause neurotoxicity. With this grant, Labhassetwar hopes to develop the tPA nanoconjugate as a safe and effective treatment for stroke, with the goal of reducing the degree of disability after a stroke.



P. Hunter Peckham

P. Hunter Peckham, Donnell Professor of Biomedical Engineering and Orthopaedics at Case Western Reserve University, has had a noteworthy year. He was honored by election to the International Academy for Medical and Biological Engineering, awarded a \$6 million grant from the NIH/NINDS CREATE program

and was selected for the 2020 Robert A. Pritzker Distinguished Lecture Award from the Biomedical Engineering Society.



Anand Ramamurthi

Anand Ramamurthi, Lerner Research Institute Department of Biomedical Engineering, received a 3-year, \$300,000 grant from the National Science Foundation entitled "Collaborative Research: Design and Development of a Multifunctional Nanoplatforam for Augmented Elastic Matrix Repair."



Pallavi Tiwari

The V Foundation – named after former basketball coach Jim Valvano, who died from cancer – awarded Pallavi Tiwari, assistant professor of biomedical engineering at Case Western Reserve University, a three-year, \$600,000 grant to bring her "GPS maps" to clinical testing. So far, the approach has done well in retrospective cases, and Tiwari is hopeful those results will translate to the clinic. In addition, Tiwari and Prateek Prasanna, researchers in the Center for Computational Imaging and Personalized Diagnostics, received accolades from the European Society of Radiology (ESR) Board of Directors and the European Radiology editorial team for co-authoring the ninth most cited article, according to the recent impact factor calculations. The October 2017 article is

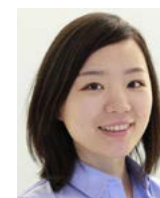
entitled "Radiomic features from the peritumoral brain parenchyma on treatment-naïve multi-parametric MR imaging predict long versus short-term survival in glioblastoma multiforme: Preliminary findings."



D. Geoffrey Vince

D. Geoffrey Vince, Virginia Lois Kennedy Chair in Biomedical Engineering and Applied Therapeutics, Lerner Research Institute Department of Biomedical Engineering, has received a four-year, \$4.34 million grant from the Department of Defense to study the relationship between the composition of carotid artery plaque and the risk of a future cerebrovascular accident and stroke. The investigators will study the combined power of ultrasound together with a new machine learning algorithm to better, and non-invasively, assess plaque composition. In this study, 1,500 patients with carotid artery stenosis from Cleveland Clinic and the Louis Stokes Cleveland Veterans Affairs Medical Center will undergo ultrasound of their carotid arteries. In tandem, a new program called the Compositional Analysis System by Machine (CASM) learning algorithm will create three-dimensional reconstructions of the plaques. The investigators will test the CASM algorithm's ability to accurately determine the degree of stenosis and predict the precise plaque composition. Vince has also been elected to the Cleveland Clinic Board of Governors for a five-year term.

Welcome New Faculty



Dan Ma

The Department of Biomedical Engineering at Case Western Reserve University welcomes Dan Ma as an assistant professor. Ma's research focuses on the development of novel MR acquisition, reconstruction and visualization technologies for the improvement of scan efficiency, sensitivity and specificity, patient comfort and clinical outcome.

CHECKING IN WITH ALUMNI



Shoshana Ginsburg (PhD '15)

Shoshana Ginsburg, who earned her PhD in biomedical engineering from Case Western Reserve University in 2015, is chief technology officer at Quanterra Software LLC. Through its CattleQuants™ service, the company collects aerial images via drone, runs the images through its AI-powered counting software and provides detailed inventory reports to feedlots and banks. Quanterra recently received a Phase I Small Business Innovation Research (SBIR) grant from the National Science Foundation for its project entitled, "Automated Cattle Counting and Bovine Temperature Screening from Aerial Feedlot Images."

As a graduate student, Ginsburg worked in the Center for Computational Imaging and Personalized Diagnostics (CCIPD) directed by Anant Madabhushi, the F. Alex Nason Professor II of biomedical engineering. "Shoshanna is developing and applying novel artificial intelligence and computer vision tools for interrogating aerial imagery to provide automated analysis of crop areas and livestock quantification – important questions for the agricultural community to address," says Madabhushi.



Thomas Bulea (PhD '12)

Thomas Bulea is a staff scientist at the National Institutes of Health in the Functional and Applied Biomechanics Section of the Rehabilitation Medicine organization. Bulea received his PhD in biomedical engineering from Case Western Reserve University in 2012 and received the 2012 Doctoral Excellence Awards in Biomedical Sciences from the Case Western Reserve University School of Medicine. He completed a post-doctoral fellowship at the National Institutes of Health and a visiting post-doctoral fellowship at the University of Houston.

Ronald Triolo, executive director of the Advanced Platform Technology Center and professor of biomedical engineering at Case Western Reserve University, served as Bulea's primary research advisor for his doctoral dissertation. "Dr. Bulea did some ground-breaking work on the role of knee joint damping on walking and stair climbing with a novel assistive exoskeleton for persons with paralysis resulting from spinal cord injury at the Louis Stokes Cleveland

VA Medical Center," says Triolo. "His work advanced our understanding of the interactions between joint mechanics and muscle activation."

Bulea's current research integrates neural interfacing with rehabilitation robotics to develop new therapeutic tools and interventions for treatment of movement disorders and paralysis. Since joining the Intramural Research Program at the NIH Clinical Center in 2014, one major focus of his research has been developing novel exoskeletons to improve walking in children with cerebral palsy (CP). Results from the first clinical study of his group's pediatric exoskeleton to treat crouch gait from CP were published in Science Translational Medicine and featured in national news outlets including CNN. His work at the NIH has also been recognized by receipt of an NIH Clinical Center Director's Award in 2016 and an NIH Director's Award for Scientific/Medical Research in 2018.



Sahana Kukke (MS '01)

Sahana Kukke is a program director in neural engineering at the National Institute of Neurological Disorders and Strokes (NINDS), where she oversees a portfolio of research awards, training awards and cooperative agreements in

the field of neural engineering in NINDS and the BRAIN Initiative, a public-private collaborative research effort to develop innovative technologies to understand the brain. Kukke earned her master's degree in biomedical engineering from Case Western Reserve University in 2001, then a PhD in bioengineering from Stanford University. Prior to joining NINDS, she was assistant professor of biomedical engineering at the Catholic University of America.

Ronald Triolo, executive director of the Advanced Platform Technology Center and professor of biomedical engineering at Case Western Reserve University, served as Kukke's research advisor for her master's thesis. "Dr. Kukke was the first to quantify how stiffening the spine and hips of persons paralyzed by spinal cord injuries with electrical stimulation can improve seated posture and reachable workspace," says Triolo. "Her foundational study set the stage for continuing exploration of more sophisticated controllers for maintaining seated postures and affording wheelchair uses an enhanced ability to reach and manipulate objects without fear of falling or using restrictive chest straps for seat belts."

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