Explorations and revelations taking place in the medical school

Above: Spinal leads exit the back to connect to an external stimulator. Pitt researchers showed that spinal stimulation can be used to create tactile sensations in a prosthetic limb. Next up: designing fully implantable devices.
Imagine tying your shoes or taking a sip of coffee or cracking an egg but without any feeling in your hand. That’s life for users of even the most advanced prosthetic arms.

According to a new study from the University of Pittsburgh’s Rehab Neural Engineering Labs, spinal cord stimulators commonly used to relieve chronic pain could provide a straightforward and universal method for adding sensory feedback to a prosthetic arm.

For this study, published in July in eLife, four amputees received spinal stimulators, which, when turned on, create the illusion of sensations in the missing arm. The study was funded by the U.S. Army Research Office and the Defense Advanced Research Projects Agency.

“What’s unique about this work is that we’re using devices that are already implanted in 50,000 people a year for pain—physicians in every major medical center across the country know how to do these surgical procedures—and we get similar results to highly specialized devices and procedures,” says study senior author Lee Fisher, a PhD assistant professor of physical medicine and rehabilitation at Pitt. The strings of implanted spinal electrodes, which Fisher describes as about the size and shape of “fat spaghetti noodles,” run along the spinal cord, where they sit slightly to one side, atop the same nerve roots that would normally transmit sensations from the body, and to demonstrate that the sensory feedback can help to improve the control of a prosthetic arm. The researchers would like to see patients able to do everyday tasks like tie shoes or hold an egg without accidentally crushing it. Shrinking the size of the contacts—the parts of the electrode where current comes out—is another priority. That might allow users to experience even more localized sensations.

“When asked to describe not just where but how the stimulation felt, all four participants reported feeling natural sensations, such as touch and pressure, though these feelings often were mixed with decidedly artificial sensations, such as tingling, buzzing or prickling,” Fisher says. “Mostly we wanted to demonstrate the possibility that something like this could work.”

“Stability of these devices is really critical,” Fisher says. “If the electrodes are moving around, that’s going to change what a person feels when we stimulate.”

The next big challenges are to design spinal stimulators that can be fully implanted, rather than connected to a stimulator outside the electrodes, and the sensations they generated, mostly stayed put across the monthlong duration of the experiment. That’s important for the ultimate goal of creating a prosthetic arm that provides sensory feedback to the user.

“Physicians in every major medical center across the country know how to do these surgical procedures.”
University of Pittsburgh researchers have demonstrated the highest accuracy to date in recognizing and characterizing prostate cancer using an artificial intelligence (AI) program. The Lancet Digital Health published their study results in August.

“Humans are good at recognizing anomalies, but they have their own biases or past experience,” says senior author Rajiv Dhir, MD chief pathologist and vice chair of pathology at UPMC Shadyside and professor of biomedical informatics at Pitt. “Machines are detached from the whole story. There’s definitely an element of standardizing care.”

To train the AI to recognize prostate cancer, Dhir and his colleagues provided images from more than a million parts of stained-tissue slides taken from patient biopsies. Each image was labeled by expert pathologists to teach the system how to discriminate between healthy and abnormal tissue. The algorithm was then tested on a separate set of 1,600 slides taken from 100 patients seen at UPMC for suspected prostate cancer.

During testing, the AI demonstrated 98% sensitivity and 97% specificity at detecting prostate cancer—significantly higher than previously reported for algorithms working from tissue slides.

Also, this is the first algorithm to extend beyond cancer detection. It also performed well at grading and sizing tumors (assessing how likely they are to grow and spread) and determining whether they’d invaded surrounding nerves. All of these features are clinically important and required as part of the pathology report.

AI also flagged six slides that were not noted by the expert pathologists.

But Dhir, who also is affiliated with UPMC Hillman Cancer Center, explained that this doesn’t necessarily mean that the machine is superior to humans. Yet for less experienced pathologists, the algorithm could act as a fail-safe to catch cases that might otherwise be missed.

“Algorithms like this are especially useful in lesions that are atypical,” Dhir says. “A nonspecialized person may not be able to make the correct assessment. That’s a major advantage of this kind of system.”

Although these results are promising, Dhir cautions that new algorithms will have to be trained to detect different types of cancer. The pathology markers aren’t universal across all tissue types. But he doesn’t see why that couldn’t be done to adapt this technology to work with breast cancer, for example.

What does this study mean for patients? Technology like this will help further fine-tune cancer detection and standardize diagnosis.
John Mellors kept hearing the same story from perplexed physicians: a patient with HIV insists they’re taking daily medication to keep the virus in check. But testing says otherwise.

Late last year, Mellors—chief of the Division of Infectious Diseases at Pitt and UPMC who holds the Endowed Chair for Global Elimination of HIV and AIDS—and a team of researchers solved this mystery in a study published in the Journal of Clinical Investigation.

These patients, they showed, are hosting large clones of HIV-infected cells, “repliclones,” that produce infectious virus particles so plentiful that it could “appear that antiretroviral therapy isn’t working even when it is,” says Mellors.

HIV typically replicates by taking over a cell’s machinery and using it to produce more virus, which can infect other cells.

When taken daily, antiretroviral therapy prevents HIV from infecting new cells so that even though the virus can’t yet be cured, it can be controlled to the point that it isn’t detectable in blood tests.

Mellors and Elias Halvas, an assistant professor in Pitt’s Division of Infectious Diseases, led a multidisciplinary team of HIV scientists in investigating the medical records and blood from eight patients with nonsuppressible HIV viremia—i.e., detectable virus in the blood—despite adherence to antiretroviral medications. Repeated samples of each patient’s blood revealed identical viral genetic sequences that did not change over time.

Halvas says, “This indicates that, in the individual patients, the virus in their blood was coming from identical cellular factories”—repliclones.

Thanks to the antiretroviral medications these patients are taking, new cells are not becoming infected by the virus that’s produced by repliclones. However, repliclone products could cause other problems, such as chronic inflammation, says Mellors, who is also Distinguished Professor of Medicine at Pitt.

“If the patient were to stop drug therapy, the virus could have a head-start on rebounding. And repliclones are a key barrier to developing a true cure for HIV,” Mellors says.

What else does this mean for patients and their doctors?

Because switching treatments may not suppress viremia, says Mellors, clinicians should continue to watch for changes. Viremia might decline if repliclones shrink, which they often do—though not always.

Two remaining challenges for scientists: figuring out how repliclones escape the immune system and how they can be efficiently killed.

The team speculates that smaller repliclones may linger undetected and might even be responsible for the rapid rebound of HIV in patients who stop their therapy.

Scientists around the globe are working hard to track down repliclones and destroy them, says Halvas.