Something Lost, Something Gained: High-Tech Prosthetics Build on New Understandings of the Human Body

In the spring of 2012, Brandon Prestwood lost his lower left arm in an industrial accident. "The next 3 years were a struggle, physically and mentally," Prestwood recalls. His injury meant he had to quit his career as a machinery technician. And without one of his hands, not only did daily tasks become more difficult, but he also suffered psychologically from the loss, feeling awkward in his social interactions.

Four years later, Prestwood had a meeting that changed his life. A group of researchers led by Dustin Tyler, a biomedical engineer at Case Western Reserve University and the Veterans Affairs Medical Center, was working on a new prosthetic device that would connect directly with the remaining nerves of an amputated limb. Prestwood agreed to be a test subject.

A few months later, Prestwood received an implant into his residual limb. When he was linked to a prosthetic after the procedure, he felt something he had not experienced in years: sensory feedback from his missing arm. Feeling his wife's hand with his left arm for the first time since the accident generated "an abundance of joy," Prestwood says. "It means so much to me to be able to feel that connection. To have that piece I'm missing replaced to the point where I get to interact again is amazing."

Humans have been creating artificial limbs for thousands of years: One of the oldest replacement body parts identified—an artificial wooden toe from the foot of an ancient Egyptian mummy—may date as far back as 950 B.C.[1] Throughout their long history, prosthetics have evolved from simple replicas to multi-functional devices. The past few decades in particular have seen rapid advances, as scientists, clinicians, and engineers combine technological advances with increasing knowledge about the mechanisms of human movement to make prosthetics more functional and versatile than ever before.

Johnny Matheny, a resident of Port Richard, Florida, who lost his left arm to cancer in 2007, has dedicated his life to testing new prosthetic technologies. In early 2018, he became the first person to take home the Modular Prosthetic Limb (MPL), one of the world's most advanced upper-limb prosthetics, for a year-long trial.

The MPL is the product of a decade-long, Defense Advanced Research Projects Agency (DARPA)-funded research project led by scientists and engineers at Johns Hopkins University's Applied Physics Laboratory (APL). The bionic arm has more than 100 sensors that receive information that is crucial for movement—such as force, vibration, torque, and temperature—as well as 17 separate motors controlling 26 joints in the fingers, hand, and

[1] BBC News. 2007. Cairo toe earliest fake body bit. http://news.bbc.co.uk/2/hi/health/6918687.stm (accessed June 10, 2019).

upper and lower arm. This design makes the prosthetic highly dexterous and capable of producing complex movements in a manner remarkably similar to an intact limb.[2]

With this device, Matheny says he can do everything from cooking to working in his woodshed with much more ease. During the past year, he has even started learning how to play the piano.[3]

Developing a device that possesses some of the capabilities of a human upper limb was a difficult task that took many years. A key challenge, according to Michael McLoughlin, the engineer who led the project while at APL, was figuring out how to pack all of the motors and electronics into an artificial arm that was approximately the same size and weight as the arm of an average male.

To create the prosthesis, researchers started with detailed analyses of hand and arm motions in able-bodied individuals, identifying the motions most critical for carrying out daily activities, says McLoughlin, who is now the vice president of Zeteo Tech, a biodefense and medical device company. "If you think about all the ways you can move your fingers, the hand is really remarkable—nature's been able to engineer something much better than we've ever been able to make," McLoughlin says. "So DARPA wanted us to make something as close to that as possible." The goal, he adds, was not necessarily to recreate a biological arm, but to design a prosthetic that could reliably emulate human movements.

Even more impressive, perhaps, is that the MPL is controlled by the user's mind. Electrodes on the prosthetic pick up movement-related electrical signals—sent from the brain to nerves in targeted muscles—and convert them into commands for the motors within the artificial arm.

To effectively control the MPL with his mind, Matheny had to first undergo targeted muscle reinnervation (TMR),[4] a surgical procedure in which the severed nerves remaining in a person's limb after an amputation are rewired onto nearby muscles. This procedure, developed by Todd Kuiken, a physician and engineer at the Rehabilitation Institute of Chicago (now the Shirley Ryan AbilityLab), and his colleagues in the early 2000s, has provided hundreds of amputees with the potential ability to control motorized arms with their mind. Prior to the invention of TMR, individuals with amputations had only limited control over motorized prostheses. To move them, they had to think about moving a specific muscle on the remaining limb, which would operate a function on their artificial arm.

Kuiken started testing the rewiring procedure on rodents during his doctoral studies in the 1980s after reading an academic article that proposed moving nerves left over after a limb amputation to muscles in another part of the body as a method of enhancing the electrical

[2] Johannes, M. S., J. D. Bigelow, J. M. Burck, S. D. Harshbarger, M. V. Kozlowski, and T. Van Doren. 2011. An overview of the developmental process for the Modular Prosthetic Limb. Johns Hopkins APL Technical Digest 30(3):207–216.

[3] See https://www.youtube.com/watch?time_continue=313&v=DP677lA_DEA (accessed June 10, 2019).

[4] Kuiken, T. A., L. A. Miller, R. D. Lipschutz, B. A. Lock, K. Stubblefied, P. D. Marasco, P. Zhou, and G. A. Dumanian. 2007. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: A case study. *The Lancet* 369(9559):371–380.

signals from the severed fibers.[5] In the paper, the authors suggested that each time an amputee thought about moving his or her prosthetic, signals sent from the brain to the severed nerves would be amplified by the new muscles that housed them, allowing them to be detected by electrodes placed on the skin.

Almost two decades after Kuiken began his work, Jesse Sullivan, a lineman from Tennessee who lost both of his arms to an electrical injury, became the first human to undergo the procedure.[6] Subsequent studies by Kuiken and his colleagues showed that TMR consistently improved amputees' ability to control their prosthetic arms.[7] Surgeons have now performed the procedure on hundreds of amputees around the world.

TMR had two other, unexpected outcomes. First, in many patients, the procedure significantly reduced post-amputation pain caused both by neuromas (tangled balls of nerve fibers that grow out of the severed nerve) and phantom limb sensations (ongoing feelings in the missing body part).[8] Glen Lehman, a former member of the U.S. Army who lost his arm in a grenade explosion and one of the earliest recipients of TMR, says that his phantom limb pain was "excruciating" before the procedure. "After the surgery, that sensation went away," he says.

Another unanticipated consequence of TMR was that some patients began to experience induced sensations from their missing limbs. In a follow-up session after surgery, one subject reported feeling coldness in his missing hand immediately after an experimenter dabbed an alcohol swab on the part of his chest where his severed nerves had been rerouted. Further assessments revealed that the person could also feel other sensations in his amputated hand, such as temperature and light touch, via the reinnervated nerves in his chest.

Intrigued, one of Kuiken's former students, neuroscientist Paul Marasco, began examining this phenomenon in his own lab at the Cleveland Clinic in Ohio. Along with several colleagues, Marasco has been working on restoring touch sensation for people with artificial limbs. In recent years, the team has also developed a method of restoring proprioception—the ability to sense the position of one's body parts—that involves vibrating reinnervated muscles while they move.[9] This technique is based on a phenomenon first reported by scientists in the 1980s: the so-called kinesthetic illusion, which is a false sense of movement caused by muscle vibrations.

---

[5] Hoffer, J. A., and G. E. Loeb. 1980. Implantable electrical and mechanical interfaces with nerve and muscle. Annals of Biomedical Engineering 8(4–6):351–360.

[6] Belluck, P. 2009. In New Procedure, Artificial Arm Listens to Brain. *The* New York Times, February 10, p. A1.

[7] Kuiken, T. A., G. Li, B. A. Lock, R. D. Lipschutz, L. A. Miller, K. A. Stubblefield, and K. B. Englehart. 2009. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA 301(6):619–628.

[8] Dumanian, G. A., B. K. Potter, L. M. Mioton, J. H. Ko, J. E Cheesborough, J. M Souza, W. J. Ertl, S. M. Tintle, G. P. Nanos, I. L. Valerio, T. A. Kuiken, A. V. Apkarian, K. Porter, and S. W. Jordan. 2018. Targeted muscle reinnervation treats neuroma and phantom pain in major limb amputees: A randomized clinical trial. Annals of Surgery. doi: 10.1097/SLA.0000000000003088. E-pub ahead of print.

[9] Marasco, P. D., J. S. Hebert, J. W. Sensinger, C. E. Shell, J. S. Schofield, Z. C. Thumser, R. Nataraj, D. T. Beckler, M. R. Dawson, D. H. Blustein, S. Gill, B. D. Mensh, R. Granja-Vazquez, M. D. Newcomb, J. P. Carey, and B. M. Orzell. 2018. Illusory movement perception improves motor control for prosthetic hands. Science Translational Medicine 10(432):eaao6990.

"It's one thing to be able to touch and feel something, but it's another thing to understand how you're controlling your joint movement and where you are in space," says Jacqueline Hebert, a professor of rehabilitation medicine at the University of Alberta in Canada and one of Marasco's collaborators. For amputees, proprioception is an important missing feature, because it is key to conducting smooth, effortless movements—such as grabbing a salt shaker from the dinner table—without the need to constantly keep an eye on the moving limb.

Several other research teams are also working on methods of restoring sensation and proprioception. Some methods, such as the implanted device designed by Tyler's group at Case Western Reserve University, are designed to connect directly with the nerves in the remaining limb.

Through these direct attachments, electrical pulses—generated by stimulation to sensors on the prosthetic device—can activate nerves in an individual's amputated limb to mimic real sensations. Tyler and his colleagues have shown that this system can reliably reproduce both touch sensations and proprioception, allowing amputees to more easily engage in everyday tasks—for example, buttoning a shirt and cracking open an egg—and even doing some tasks that were previously impossible, such as feeling a loved one's hand, as Prestwood experienced.[10]

According to Tyler, the eventual goal of this work is to create a prosthetic that integrates so seamlessly with the user that it becomes a part of who they are. "If they forget they're wearing a prosthesis—that would be ideal."

Other researchers are taking yet another approach: interfacing directly with the brain. Although this may not be the first choice for amputees because it requires implanting a device into the brain, the technique has potentially wide-reaching benefits for many patient groups, including people who have lost the ability to control their limbs due to spinal cord injuries, stroke, or neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS). Researchers have already shown that such devices can be used to control robotic arms and, more recently, paralyzed limbs.[11] In 2017, a consortium of researchers called BrainGate reported successfully implanting a device to allow a man with quadriplegia—paralysis in all four limbs—to feed himself for the first time since his injury.[12]

Currently, a big limitation of this approach is that it requires users to be tethered with wires to an external machine. But researchers are developing smaller, wireless interfaces that are safer and more practical for everyday use. Rikky Muller, an engineer at the University of California, Berkeley, is creating devices capable of simultaneously receiving signals from the

[10] Graczyk, E. L., L. Resnik, M. A. Schiefer, M. S. Schmitt, and D. J. Tyler. 2018. Home use of a neural-connected sensory prosthesis provides the functional and psychosocial experience of having a hand again. Scientific Reports 8:9866.

[11] Collinger J. L., B. Wodlinger, J. E. Downey, W. Wang, E. C. Tyler-Kabara, D. J. Weber, A. J. McMorland, M. Velliste, M. L. Boninger, and A. B. Schwartz. 2013. High-performance neuroprosthetic control by an individual with tetraplegia. The Lancet 381(9866):557–564.

[12] Ajiboye A. B., F. R. Willett, D. R. Young, W. D. Memberg, B. A. Murphy, J. P. Miller, B. L. Walter, J. A. Sweet, H. A. Hoven, M. W. Keith, P. H. Peckham, J. D. Simeral, J. P. Donoghue, L. R. Hochberg, and R. F. Kirsch. 2017. Restoration of reaching and grasping movements through brain-controlled muscle stimulation in a person with tetraplegia: A proof-of-concept demonstration. The Lancet 389(10081):1821–1830.

brain and delivering electrical stimulation. Modern pacemakers work in a similar way, by both detecting abnormal heart activity and treating it on demand. In addition to aiding individuals who have lost limbs due to spinal cord injury or disease, these so-called closed-loop devices could also be beneficial to people with conditions such as Parkinson's or epilepsy, where direct electrical stimulation to the brain can alleviate symptoms.

With highly dexterous limbs, brain-controlled prosthetics, and the restoration of sensation, prosthetics research has come a long way from the ancient wooden toe and other simple replacement limbs made from basic materials such as wood and metal. As the science continues to advance, more developments are on the horizon. "I'm excited for how transformative the technology [could be] for patients," Muller says. "For their quality of life but also for what we can learn about the brain, and how we can use that to understand how to treat diseases in completely new ways."

This article was written by Diana Kwon for *From Research to Reward*, a series produced by the National Academy of Sciences. This and other articles in the series can be found at www.nasonline.org/r2r. The Academy, located in Washington, DC, is a society of distinguished scholars dedicated to the use of science and technology for the public welfare. For more than 150 years, it has provided independent, objective scientific advice to the nation.