A BIOHYBRID APPROACH TO REBUILDING THE BODY

At VA's Center for Restorative and Regenerative Medicine, leading-edge scientists are working on innovative ways to help injured Veterans regain their independence

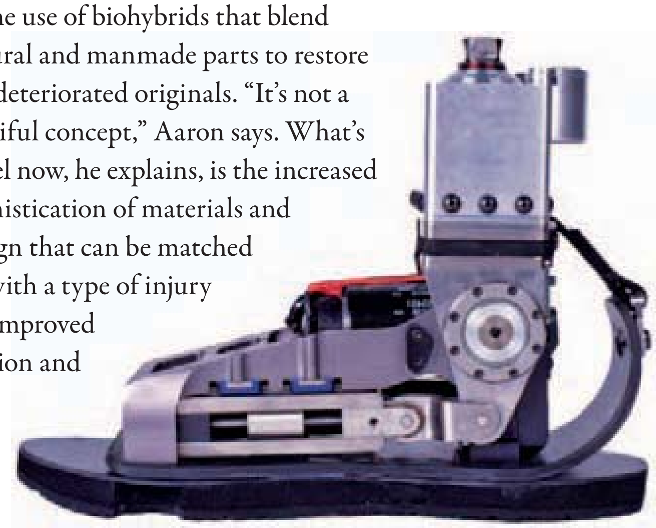
Researchers with the Center for Restorative and Regenerative Medicine (CRRM) are content to leave Superman's bounds over tall buildings and the Six Million Dollar Man's bulldozer-strength bionic arm in the realm of implausible fiction. It's the natural body's real-life feats of movement and function that CRRM researchers are bent on mimicking. The center's investigators, representing the Providence (R.I.) VA Medical Center, Brown University and the Massachusetts Institute of Technology, are studying new-millennium methods for restoring quality of life to those hurt by disease or injury. A primary focus is the marrying of human tissue and mechanical elements into lifelike "biohybrid" limbs that handily outperform currently available prostheses.

The center—which was founded in 2004 and will be rededicated this year with a new 24,000-square-foot, state-of-the-art research space—specifically targets problems experienced by Veterans, notes the director of CRRM, Brown University professor of orthopedic surgery Roy Aaron, MD. "People in civilian life are affected by the conditions we study," he says, "but mostly we're focused on conditions such as devastating limb injury, burns, traumatic brain injury, and posttraumatic stress disorder, which are much more prevalent in Veterans."

The CRRM collaboration addresses these needs through a team approach. Its researchers boast expertise in tissue engineering, orthopedics, neurotechnology, prosthetic design and rehabilitation. "At the end of the day, the science and medicine of limb restoration and advanced rehabilitation are creative processes that benefit from all sorts of disciplines," says Al Lo, MD, PhD, a neurorehabilitation expert and CRRM's associate director.

Bionic ankle embodies 'biohybrid' concept

Today's hip and knee replacements are examples of the use of biohybrids that blend natural and manmade parts to restore the deteriorated originals. "It's not a fanciful concept," Aaron says. What's novel now, he explains, is the increased sophistication of materials and design that can be matched up with a type of injury for improved motion and



PowerFoot, a bionic ankle developed by Dr. Hugh Herr of the Massachusetts Institute of Technology and VA's Center for Restorative and Regenerative Medicine.

function. Every battlefield injury is different, for example—sometimes it's better to rely on biological reconstruction to salvage a limb, and in other cases it's preferable to do an amputation and prosthetic fitting. "The biohybrid concept allows the unification of metals and other disparate materials that influence biological tissue differently depending on their shape, texture and other characteristics," Aaron explains.

The first powered ankle-foot prosthesis, constructed by MIT prosthetics engineer Hugh Herr, PhD, is an example of a biology-mimicking ("biomimetic") component developed through the center. The computerized below-the-knee prosthesis, called PowerFoot, propels a user forward with tendon-like springs and an electric motor. "This design releases three times the power of a conventional prosthesis to propel you forward, and for the first time, provides amputees with a truly humanlike gait," says Herr, who many years ago lost both of his own legs below the knee from frostbite suffered during a mountain-climbing expedition.

Garth Stewart, a 24-year-old Army Veteran who lost his left leg below the knee from an injury in Iraq, demonstrated the new prosthesis at its unveiling at the Providence VA Medical Center. "One of the first things I noticed was a huge relief in back pressure," said Stewart of the prosthetic, which was designed to reduce fatigue and improve balance better than previously available alternatives.

Joel Kupersmith, MD, VA's chief research and development officer, points out that "up to now, prosthetic devices have not been able to duplicate the complex functions of our feet and ankles as we walk and run. The ingenious computerized design of this new prosthesis changes all of this. It constantly 'thinks' and responds, allowing the person to walk or run in a more natural and comfortable way."

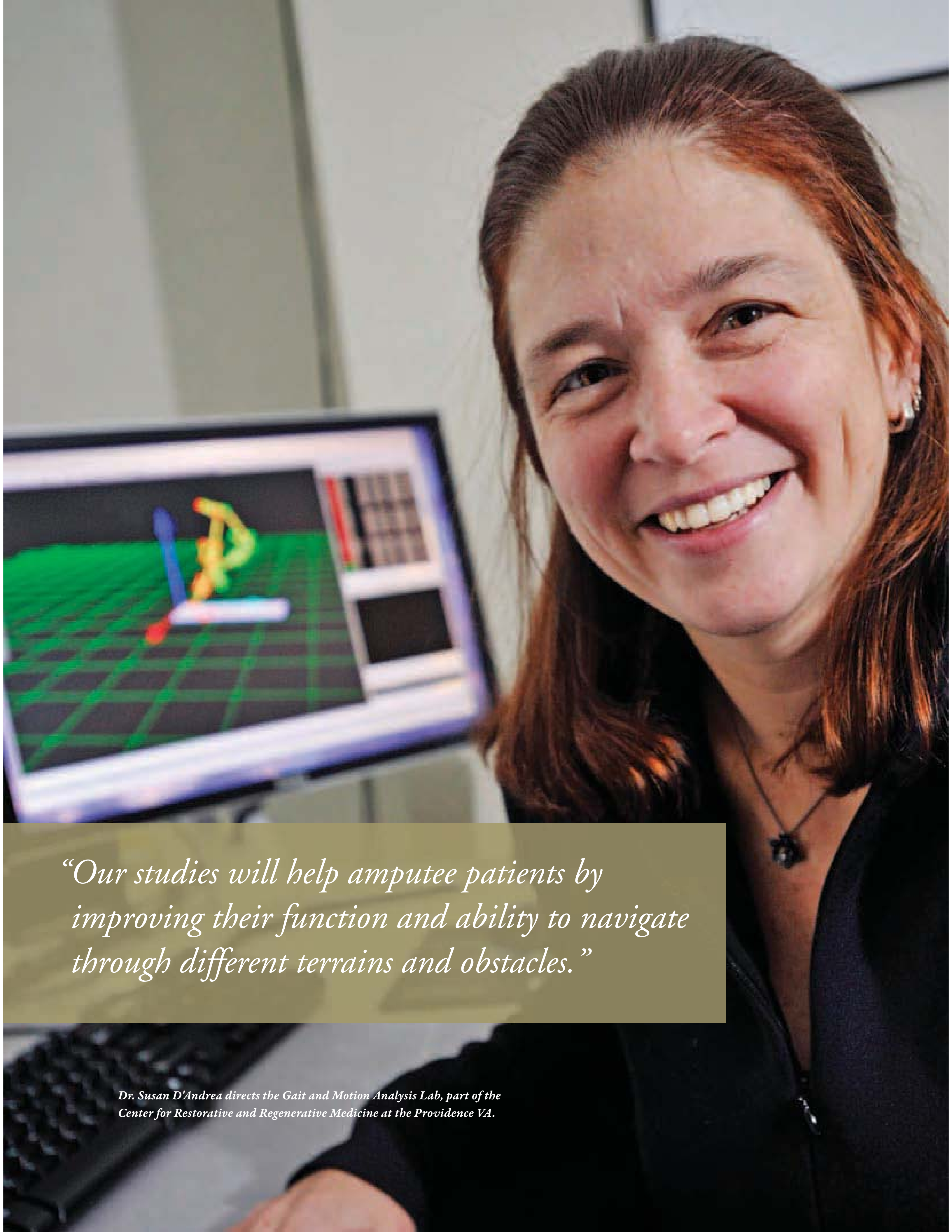
Optimizing a space-age artificial arm

For those who have lost an arm from a battlefield injury or other cause, a CRRM-led VA study will help put the polish on the design of a sophisticated prosthetic arm that supports tasks as intricate and diverse as picking

Iraq Veteran Garth Stewart helped Dr. Hugh Herr's lab test PowerFoot, which propels users forward with tendon-like springs and an electric motor.

up a key, holding a pencil, and using a power drill. The artificial arm, developed by the DEKA Research and Development Corporation through funding from the Defense Advanced Research Projects Agency, is being tested at four VA sites before being commercialized. Frederick Downs Jr., director of VA's Prosthetic and Sensory Aids Service, who lost his left arm during combat in Vietnam, says he was "brought to tears" recently when the device allowed him to smoothly bring a water bottle to his mouth and drink—a task that may sound simple but that requires fine control to accurately maneuver the bottle without crushing it.

"The device has six different grips, including a fine pinch for picking up paper clips, a spherical grip to pick up a round ball, and a lateral pinch to cut with scissors," explains study leader Linda Resnik, PhD, a VA research scientist and Brown University associate professor. The other extraordinary feature of the arm under



"Our studies will help amputee patients by improving their function and ability to navigate through different terrains and obstacles."

Dr. Susan D'Andrea directs the Gait and Motion Analysis Lab, part of the Center for Restorative and Regenerative Medicine at the Providence VA.

A study volunteer runs on a treadmill in the Gait and Motion Analysis Lab at the Center for Restorative and Regenerative Medicine, his legs taped with reflective markers that are tracked by motion-capture cameras. Meanwhile, researchers check the results from software that creates a 3D representation of the volunteer's leg movements.

study, according to Resnik, is a fully powered shoulder, which allows people who have lost an arm at that high a level to function far better than they could with any previously available artificial arm. "Many people who have lost their arm including their shoulder don't even use a prosthetic limb," Resnik points out, "because they can get so little function out of it."

Turning brain waves into action

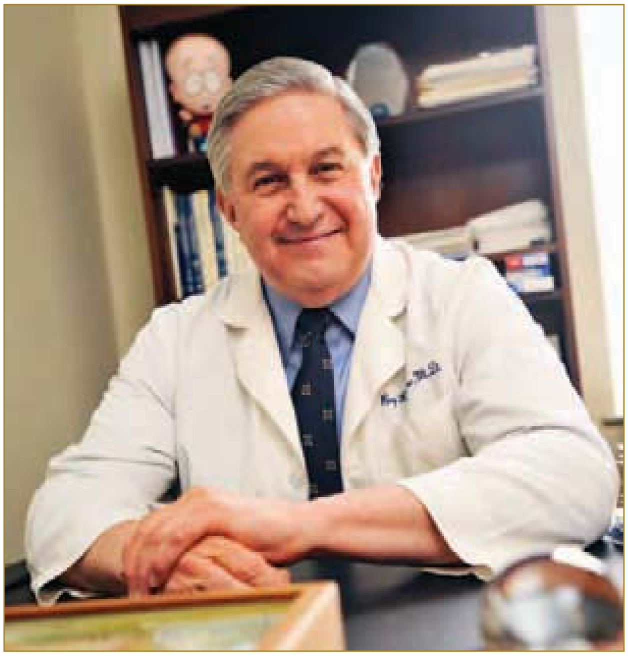
CRRM researchers are working on additional prostheses to respond more accurately to the user's intent. "You can have the most beautiful prostheses, but if people can't power them to perform as they intend," they're hardly useful, says CRRM director Aaron.

A system called BrainGate, developed by Brown-VA researcher John Donoghue, PhD, allows signals from the brain to be picked up by a sensor implanted in a part of the brain that controls voluntary movement. The signals are then decoded into commands that drive prosthetic or other robotic and electronic devices. In a pilot study, the BrainGate system enabled a 25-year-old man with quadriplegia to operate a computer cursor and perform other tasks solely through his thoughts. When the BrainGate study team, led by Leigh Hochberg, MD, PhD, published the results, the research earned headlines worldwide: A London newspaper, for example, referred to the trial participant as "the first bionic man" and a Canadian newspaper proclaimed, "Movement by Thought: Science Fiction to Fact."

The BrainGate research team is now focused on extracting the neural signals related to the intention to move one's limb, and in turn a computer cursor, to use applications such as e-mail and word processing. The researchers are also working on allowing people to use the system to control prosthetic limbs or even their own limbs that have lost function. The device has the potential to restore the fundamental ability to communicate and to increase independence for those with spinal cord injury, stroke, ALS (also known as Lou Gehrig's disease) and other disorders of the nervous system.

High-tech approaches to PTSD

Many other sophisticated tools are in early testing at CRRM to improve Veterans' physical, as well as mental, functioning. For example, a recently launched study



Dr. Roy Aaron is director of VA's Center for Restorative and Regenerative Medicine and a professor of orthopedic surgery at Brown University.

is evaluating whether a "Virtual Iraq" virtual reality program, used for years in exposure-based therapy to recreate distressing situations in controlled clinical settings, can identify someone at increased risk for posttraumatic stress disorder before major symptoms appear. "Experts believe that early intervention will make a difference," says William Unger, PhD, chief of the PTSD program at the Providence VA Medical Center and a Brown University assistant clinical professor. "What we're working on now is an objective way to identify those at higher risk who might benefit from such early treatment."

In another example of forward-looking research, Aaron and a team of CRRM researchers are developing a method to measure blood flow in bones noninvasively, just by an MRI, to distinguish live from dead tissue. "Surgeons have a tough time telling live from dead tissue in a fresh wound," Aaron explains. "This distinction is extremely important for wound management because we want to save all live tissue, but dead tissue can become dangerously infected."

Because Veterans wounded in the conflicts in Iraq and Afghanistan are returning with devastating injuries that would have been fatal in past wars, there is a heightened need for these types of progressive healing approaches. It's a prime example of scientific inquiry driven by real-world needs. Sums up Aaron, "We're cranking up our research base to catch up with the clinical need."

Terms in restorative and regenerative medicine

Biohybrid Limbs. Artificial arms and legs that incorporate human tissue with manmade elements to perform like natural limbs.

Tissue Engineering. Replacement, repair, or regrowth of tissues using synthetic materials and human cells.

Biomimetics. Creation of materials that imitate natural biology.

Neurotechnology. Application of science to elucidate and harness the brain's power to improve the body's ability to function.