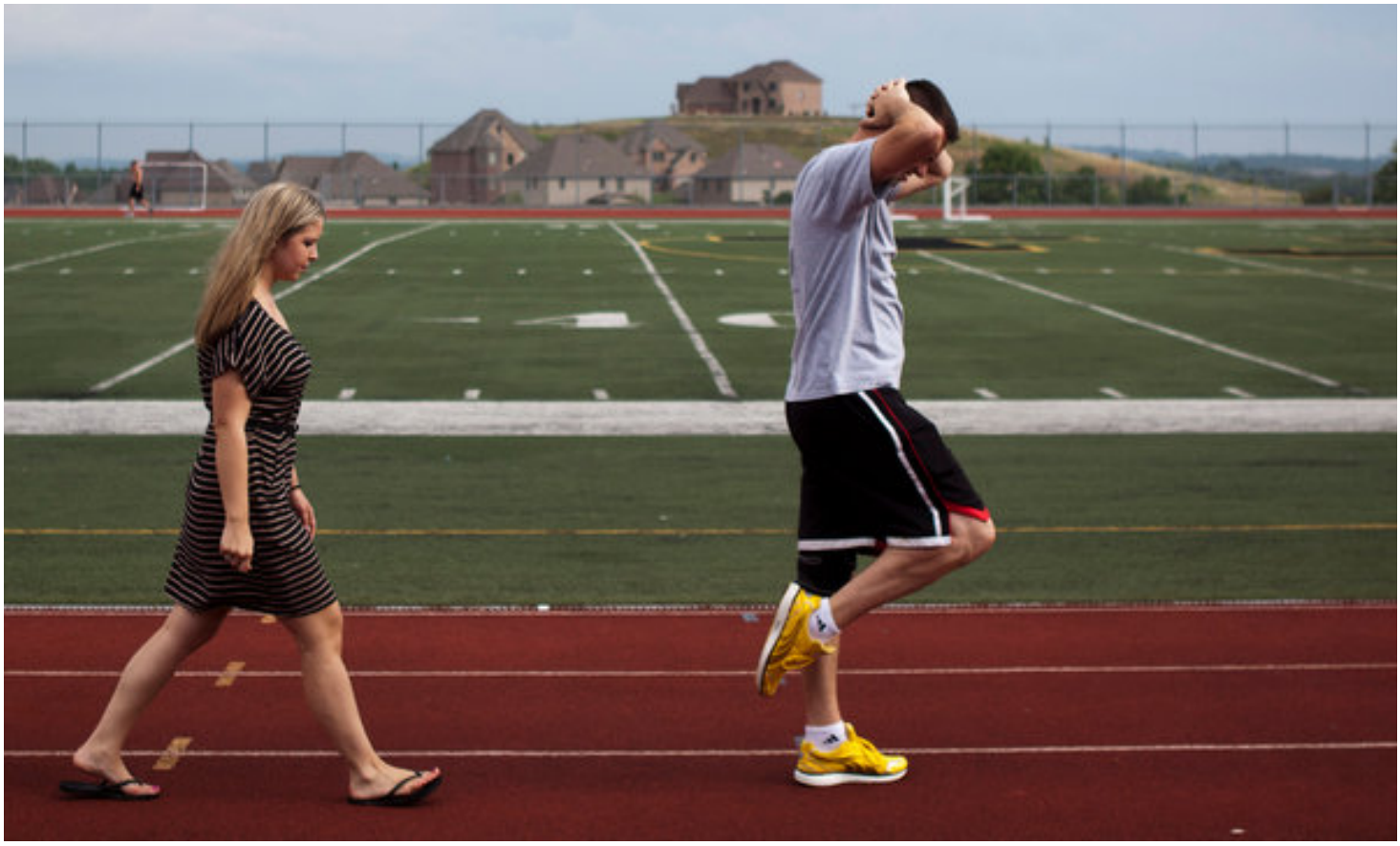
Human Muscle, Regrown on Animal Scaffolding



PITTSBURGH — In the months after a roadside bomb in Afghanistan blew off part of his left thigh, Sgt. Ron Strang wondered if he would ever be able to walk normally again.

The explosion and subsequent rounds of surgery left Sergeant Strang, 28, a Marine, with a huge divot in his upper thigh where the quadriceps muscle had been. He could move the leg backward, but with so much of the muscle gone he could not kick it forward. He could walk, but only awkwardly.

“I got really good at falling,” he said of his efforts. And Sergeant Strang, a tall, athletic man, had to give up running.

But that was two years ago. Now he walks easily, can run on a treadmill and is thinking of a post-military career as a police officer. “If you know me, or know to look for it, you can see a slight limp,” he said. “But everybody else, they go, ‘I would never have guessed.’ ”

There is something else they would never have guessed: Sergeant Strang has grown

new muscle thanks to a thin sheet of material from a pig.

The material, called extracellular matrix, is the natural scaffolding that underlies all tissues and organs, in people as well as animals. It is produced by cells, and for years scientists thought that its main role was to hold them in their proper position.

But researchers now know that this scaffolding also signals the body to grow and repair those tissues and organs. Armed with that knowledge, the new body builders are using this material from pigs and other animals to engineer the growth of replacement tissue in humans.

The technique used on Sergeant Strang, though still in development, holds particular promise for some of the thousands of veterans of the Iraq and Afghanistan wars who have been maimed by explosives and have lost so much muscle from an arm or a leg that amputation is sometimes the best alternative.

Sergeant Strang's is one of the first cases in what will eventually be an 80-patient trial to grow limb muscle. It is financed by the Defense Department's Office of Technology Transition, but it will include civilians as well.

Dr. Peter Rubin, a plastic surgeon at the University of Pittsburgh Medical Center who is a leader of the study, said that early results with Sergeant Strang and a handful of other patients showed that the animal scaffolding was spurring muscle growth. "We are seeing evidence of remodeling of tissues," he said.

Last fall, Dr. Rubin cut out the scar tissue from Sergeant Strang's leg and stitched a sheet resembling a thick piece of parchment paper — extracellular matrix from a pig urinary bladder, which had shown excellent results in lab studies — into the remaining healthy thigh muscle.

His body immediately started breaking down the matrix, which consists largely of collagen and other proteins. But the doctors expected, and wanted, that to happen — by degrading into smaller compounds, the matrix started the signaling process, recruiting stem cells to come to the site where they could become muscle cells.

"We're trying to work with nature rather than fight nature," said another leader of the study, Dr. Stephen Badylak, deputy director of the McGowan Institute for Regenerative Medicine at the university.

Dr. Badylak is a pioneer in the use of extracellular matrix, having discovered many of its properties more than two decades ago while performing biomedical engineering research at Purdue University. As part of his work on a mechanical heart device, he was looking for a way to move blood from one part of the body to another but wanted to avoid synthetic materials, which can cause blood clots.

"I thought, what looks like a tube?" he recalled. "A piece of intestine." So using a research dog named Rocky, he replaced its main artery near its heart with a section of its small intestine. ("I'd have a tough time getting that experiment approved today," Dr. Badylak said.)

When he arrived at work the next morning, he was expecting all sorts of problems. "But Rocky is standing up in his cage, wanting breakfast and wagging his tail," Dr. Badylak said. "I thought, well, this is pretty cool."

Later experiments showed that over time the tube had lost the internal cells that are specific to intestines and gained cells specific to blood vessels. "It had morphed into a blood-vessel-like structure, which we thought was incredible," he said. "Eventually we figured out that it was not the whole intestine but just the extracellular matrix that was responsible."

Extracellular matrix from pigs, sheep and other animals has been used in the past decade as a reinforcing layer to help repair rotator cuff damage, hernias and other injuries. "Surgeons think of them as meshes that hold things together," Dr. Badylak said. Most of them do not understand the matrix's role in signaling and repair. "They don't get it," he said. "We didn't either at first."

The scaffolding is isolated by stripping out all of the living cells from a tissue or organ, leaving an intricate three-dimensional web of proteins and other compounds. Removing the cells eliminates the possibility that the material, of animal origin, will be rejected outright by the body when it is implanted. But the matrix does provoke a less intense immune response, Dr. Badylak said, which is necessary for it to work. "You actually need the immune system to recognize the material."

"The body can say, 'This is not me,' but the signals that are there are actually telling me that I need to rebuild that tissue," he added.

The matrix has to be in contact with healthy tissue, which is why scar tissue must be

removed first. “If it’s put in the middle of a scar, it doesn’t remodel because it’s not exposed to the bloodstream and sources of cells,” Dr. Badylak said.

Stitching it directly to the muscle also ensures that it will be stretched when the muscle is activated, beginning the day after surgery, when patients start an intensive program of physical therapy. Putting a mechanical load on the matrix tells the body, in effect, that this should become muscle and not some other kind of tissue.

Sergeant Strang was skeptical when he first signed up for the trial and cleared all the physical hurdles to qualify for it — among other things, patients must have some muscle remaining and enough undamaged nerves so the muscle can work. But at that point he was willing to try anything to be able to walk normally again.

Ten soldiers, American and Afghan, were wounded on the road in Helmand Province that Easter Sunday, Sergeant Strang the most severely. He was given 42 units of blood, airlifted to Germany and then treated for a month at Walter Reed Army Medical Center in Bethesda, Md.

Sergeant Strang returned to his home outside Pittsburgh, where he underwent outpatient physical therapy for months. When he walked he favored his right leg, which caused pain in his knees, back, hip and neck. “Everything was torqued to the side,” he said.

When the doctors told him what they planned to do, “I kind of didn’t believe it at first,” Sergeant Strang said. “It strikes you as science fiction stuff when they explain it to you.”

Dr. Badylak said it was important not to set unrealistic expectations.

“We tell them, this isn’t magic. It’s not a miracle,” he said. “We’re not going to restore your 100 percent normal anatomy. But we think we’re going to be able to make a difference for you. You’ll be able to do things you can’t do now.”

There is still a big divot in Sergeant Strang’s leg, graphically illustrating how just a little new muscle tissue can make a difference.

“It was amazing,” he said. “Right off the bat I could do a full stride, I could bend my knee, kick it out a little bit, just enough to get that initial spring where gravity would take it the rest of the way.” Two weeks later he was out in the woods hunting with

friends.

Some of the initial improvement may be from the mechanical connection between the matrix and the existing muscle, the doctors said. But as the matrix has degraded, Sergeant Strang has continued to improve, although there are signs that his progress is slowing down.

The improvement had a psychological effect, too, Sergeant Strang said. Before, if he went to a busy restaurant or other crowded place, he would spend time planning where to sit, because he knew he would not be able to move quickly in the event of danger. “It was always in the back of my mind,” he said.

But now, he said, “I don’t have to sit by the door.”

Tuesday: Growing a Spare Part Inside the Body.