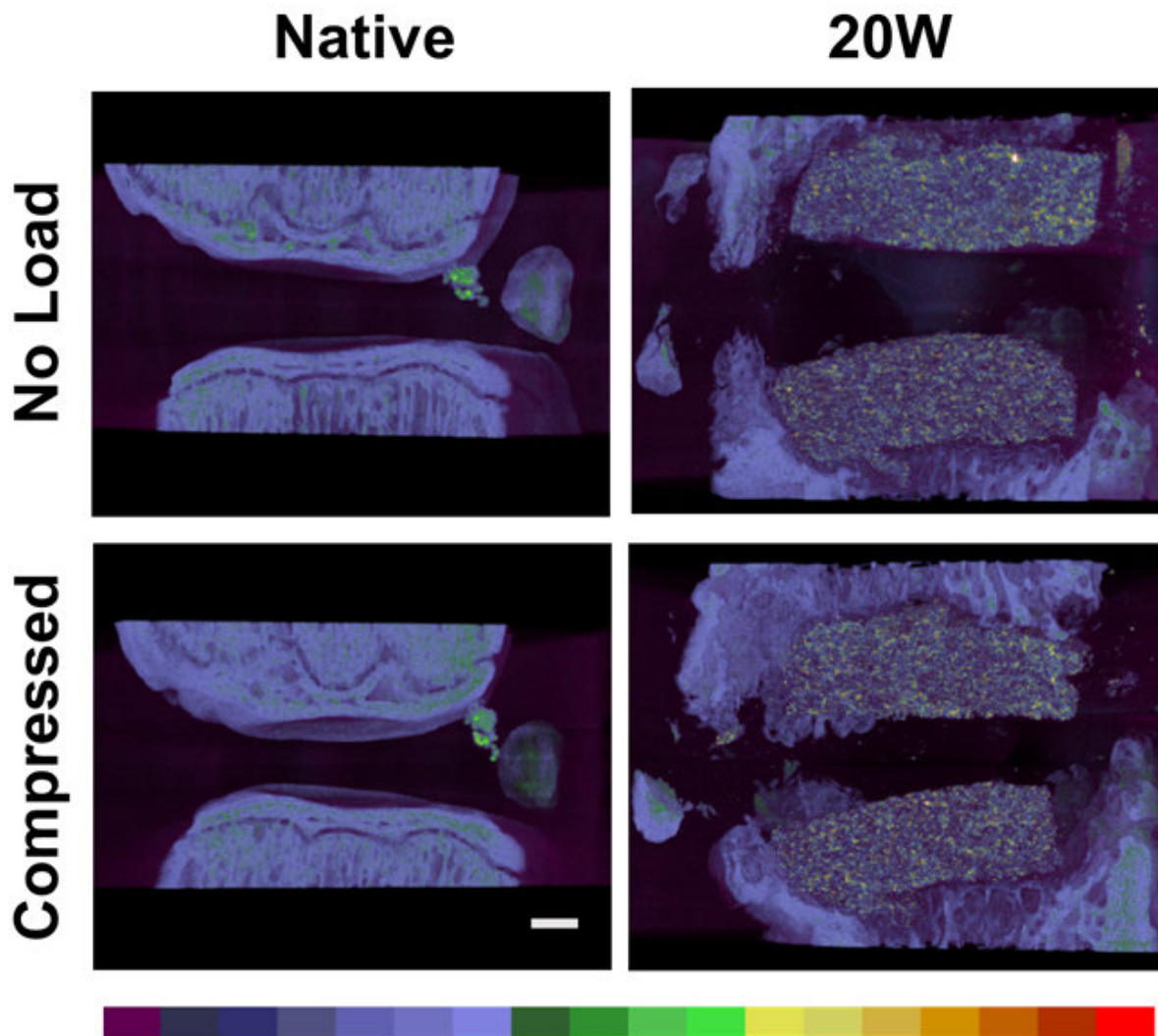


# Treating spinal pain with replacement discs made of 'engineered living tissue' moves closer to reality

November 21 2018



CT scans of the tissue-engineered disc 20 weeks after being implanted into the tails of rats. The scan compares the implant (right column) to native discs (left column) under no load and when compressed. Credit: S.E. Gullbrand et al., *Science Translational Medicine* (2018)

For the first time, bioengineered spinal discs were successfully implanted and provided long-term function in the largest animal model ever evaluated for tissue-engineered disc replacement. A new Penn Medicine study published in *Science Translational Medicine* provides compelling translational evidence that the cells of patients suffering from neck and back pain could be used to build a new spinal disc in the lab to replace a deteriorated one. The study, which was performed using goats, was conducted by a multidisciplinary team in the University of Pennsylvania's Perelman School of Medicine, School of Engineering and Applied Science, and School of Veterinary Medicine.

The soft tissues in the spinal column, the [intervertebral discs](#), are essential for the motions of daily life, such as turning your head to tying your shoes. At any given time, however, about half the adult population in the United States is suffering from back or neck pain, for which treatment and care place a significant economic burden on society—an estimated \$195 billion a year. While spinal disc degeneration is often associated with that pain, the underlying causes of disc degeneration remain less understood. Today's approaches, which include spinal fusion surgery and mechanical replacement devices, provide symptomatic relief, but they do not restore native disc structure, function, and range of motion, and they often have limited long-term efficacy. Thus, there is a need for new therapies.

Tissue engineering holds great promise. It involves combining the patients' or animals' own stem cells with biomaterial scaffolds in the lab

to generate a composite structure that is then implanted into the spine to act as a replacement disc. For the last 15 years, the Penn research team has been developing a tissue engineered replacement disc, moving from in vitro basic science endeavors to small animal models to larger animal models with an eye towards human trials.

"This is a major step: to grow such a large disc in the lab, to get it into the disc space, and then to have it to start integrating with the surrounding native tissue. That's very promising," said Robert L. Mauck, Ph.D., a professor for Education and Research in Orthopaedic Surgery in Penn's Perelman School of Medicine and a Research Health Scientist at the Corporal Michael Crescenz VA Medical Center (CMC VAMC) in Philadelphia, and co-senior author of the paper. "The current standard of care does not actually restore the disc, so our hope with this engineered device is to replace it in a biological, functional way and regain full range of motion."

Past studies from the team successfully demonstrated the integration of their engineered discs, known as disc-like angle ply structures (DAPS), in rat tails for five weeks. This latest research extended that time period in the rat model—up to 20 weeks—but with revamped engineered discs, known as endplate-modified DAPS, or eDAPS, to mimic the structure of the native spinal segment. The addition of the endplates helped to retain the composition of the engineered structure and promote its integration into the native tissue.

MRI, along with histological, mechanical, and biochemical analyses, showed that the eDAPS restored native disc structure, biology, and mechanical function in the rat model. Building off that success, the researchers then implanted the eDAPS into the cervical spine of goats. They chose the goat because its cervical spinal disc dimensions are similar to humans' and goats have the benefit of semi-upright stature.

Researchers demonstrated successful total [disc replacement](#) in the goat cervical spine. After four weeks, matrix distribution was either retained or improved within the large-scale eDAPS. MRI results also suggest that disc composition at eight weeks was maintained or improved, and that the mechanical properties either matched or exceeded those of the native goat cervical disc.

"I think it's really exciting that we have come this far, from the rat tail all the way up to human-sized implants," said Harvey E. Smith, MD, an associate professor of Orthopaedic Surgery and Neurosurgery at the Perelman School of Medicine and Staff Surgeon at the CMC VAMC, and co-senior author and clinical lead on the study. "When you look at the success in the literature from mechanical devices, I think there is a very good reason to be optimistic that we could reach that same success, if not exceed it with the engineered discs."

The research team credits the success of the work to the multidisciplinary and translational approach they've taken since it began at Penn, which is home to the many experts from the different departments and schools who were involved in this project.

"We've galvanized all of the different ventures that Penn has under its roof, from the basic research to the clinicians. We have an incredible network that can be leveraged for this, and other, research," said study author Thomas P. Schaer, VMD, director of Translational Orthopaedic Research & Preclinical Studies at the University of Pennsylvania School of Veterinary Medicine New Bolton Center. "Not every academic institution has that kind of collaborative ecosystem, which has been a tremendous advantage to us when getting this research started, and then sustaining it over time."

The team also includes first author Sarah E. Gullbrand, Ph.D., a research associate in the department of Orthopaedic Surgery at Penn Medicine

and the Translational Musculoskeletal Research Center of the Corporal Michael J. Crescenz VA Medical Center, Lachlan J. Smith, Ph.D., an assistant professor of Neurosurgery and Orthopaedic Surgery at Penn, and Dawn M. Elliott, Ph.D., a former Penn researcher who is now Chair of Biomedical Engineering at the University of Delaware.

The next step will be to conduct longer-term studies to further characterize the function of the eDAPS in the goat model, the authors said, as well as model the degeneration of spinal discs in humans and to test how their engineered discs perform in that context.

"There is a lot of desirability to implant a biological device that is made of your own cells," Smith said. "Using a true tissue-engineered motion preserving replacement device in arthroplasty of this nature is not something we have yet done in Orthopaedics. I think it would be a paradigm shift for how we really treat these spinal diseases and how we approach motion sparing reconstruction of joints."

**More information:** S.E. Gullbrand et al., "Long-term mechanical function and integration of an implanted tissue-engineered intervertebral disc," *Science Translational Medicine* (2018).

[stm.sciencemag.org/lookup/doi/.../scitranslmed.aau0670](http://stm.sciencemag.org/lookup/doi/.../scitranslmed.aau0670)

Provided by Perelman School of Medicine at the University of Pennsylvania

Citation: Treating spinal pain with replacement discs made of 'engineered living tissue' moves closer to reality (2018, November 21) retrieved 25 April 2024 from <https://medicalxpress.com/news/2018-11-spinal-pain-discs-tissue-closer.html>

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