

# Team IDs new way to grow, repair bone

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An international team of biomedical engineers, including several from MIT, has demonstrated for the first time that it is possible to grow healthy new bone reliably in one part of the body and use it to repair damaged bone at a different location.

The research, which represents a dramatic departure from the current practice in tissue engineering, is described in a paper titled "In Vivo Engineering of Organs: The Bone Bioreactor" published online the week of July 25 in the Proceedings of the National Academy of Sciences.

"This research has important implications not only for engineering bone but for engineering tissues of any kind," said Institute Professor Robert S. Langer, a co-author of the paper and a pioneer in the field of tissue engineering. "It has the potential for changing the way that tissue engineering is done in the future."

"We have shown that we can grow predictable volumes of bone on demand," said V. Prasad Shastri, assistant professor of biomedical engineering at Vanderbilt University, who led the effort. "And we did so by persuading the body to do what it already knows how to do."

The approach currently used by orthopedic surgeons to repair serious bone breaks is to remove small pieces of bone from a patient's rib or hip and fuse them to the broken bone. They use the same method to fuse spinal vertebrae to treat serious spinal injuries and back pain. Although this works well at the repair site, the removal operation is extremely painful and can lead to serious complications.

Living bone is continually growing and reshaping, but the numerous attempts to coax bones to grow outside of the body-in vitro-have all failed. Previous attempts to stimulate bone growth within the body-in vivo-had limited success but were extremely complex, expensive and unreliable.

Shastri and colleagues took a new approach that has proven much simpler. They decided to take advantage of the body's natural wound-healing response and create a special zone on the surface of a healthy bone in hopes that the body would respond by filling the space with new bone.

The new approach lived up to their highest expectations.

Working with mature rabbits, a species with bones very similar to those of humans, the researchers were delighted to find that this zone, which they have dubbed the "in vivo bioreactor," filled in with healthy bone in about six weeks. And it did so without the growth factors used to coax the bone to grow in previous in vivo efforts. Furthermore, the researchers found that the new bone can be detached easily before it fuses with the old bone, leaving the old bone scarred but intact.

"The new bone actually has comparable strength and mechanical properties to native bone," said Molly Stevens, currently a reader at Imperial College in London, England, who did most of the research as a post-doctoral fellow at MIT. "And, since the harvested bone is fresh, it integrates really well at a recipient site."

Long bones in the body are covered by a thin outer layer called the periosteum. The outside is tough and fibrous but the inside is covered with a layer of special cells that are capable of transforming into different types of skeletal tissue. So the researchers decided to create the bioreactor space just under this outer layer.

They created the space by making a tiny hole in the periosteum and injecting saline water underneath. This loosened the layer from the underlying bone and inflated it slightly. When they had created a cavity the size and shape that they wanted, the researchers removed the water and replaced it with a gel that is commercially available and approved by the FDA for delivery of cells within the human body. They chose the material because it contained calcium, a known trigger for bone growth. Their major concern was that the bioreactor would fill with scar tissue instead of bone, but that didn't happen. Instead, it filled with new bone indistinguishable from the original.

The scientists intend to proceed with the large animal studies and clinical trials necessary to determine if the procedure will work in humans and, if it does, to get it approved for human treatment. At the same time, they hope to test the approach with the liver and pancreas, which have outer layers similar to the periosteum.

If the new method is confirmed in clinical studies, it will be possible to grow new bone for all types of repairs instead of removing it from existing bones. For people with serious bone disease, it may even be possible to grow replacement bone at an early stage and freeze it so it can be used when needed, said Shastri.

Other contributors to the study include the late Dirk Schaefer, who was an orthopedic surgeon at Kantonsspital-Basel in Switzerland; Robert P. Marini, chief of clinical surgical facilities at MIT's Division of Comparative Medicine; and Joshua Aronson, a graduate student in the Harvard-MIT Division of Health Sciences and Technology.

Source: MIT

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