Researchers develop more reliable, less expensive synthetic graft material

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With a failure rate as high as 50 percent, bone tissue grafts pose a significant obstacle to orthopedic surgeons attempting to repair complex fractures or large areas of bone loss, such as those often caused by trauma and cancer. Current synthetic substitutes rarely possess the bone-like properties needed for successful grafting and are often difficult for surgeons to manipulate in the operating room. In response to these challenges, researchers at UMass Medical School have developed an easy-to-produce, inexpensive, synthetic bone material called FlexBone.

Building upon previous development of a material that combines a key mineral found in bone (nanocrystalline hydroxyapatite) with a hydrogel similar to that used in contact lenses, Jie Song, PhD, assistant professor of orthopedics & physical rehabilitation and cell biology, and a team of graduate students and orthopedic surgeons, along with their collaborators at the University of Michigan, have created a bone substitute that can be press-fit into a bony lesion.

"Functionally sophisticated synthetic materials don't have to be complicated to manufacture or difficult to reproduce," said Dr. Song. "Our idea was to create an inexpensive, off-the-shelf product that can be easily manipulated in the operating room to fill large bone voids and facilitate the tissue repair." Research published online ahead of print in *Tissue Engineering Part A* describes the efficacy of the FlexBone as a synthetic bone substitute in repairing large bone defects in animal models.

In large, complex bone voids caused by trauma or tumor removal, stabilization with traditional metal plates and other internal and external fixation devices often isn't enough to facilitate healing. In many cases, surgeons turn to bone tissue grafts to bridge the gap left by the break, transplanting bone from another donor. Complications from infection, immune response or incomplete union between the transplanted and host tissue, however, result in almost 50 percent of these procedures failing. Synthetic substitutes, meanwhile, do not have the necessary bone-like properties to make them an ideal alternative.

David Ayers, MD, the Arthur M. Pappas, MD, Chair in Orthopedics and chair and professor of orthopedics & physical rehabilitation said, "FlexBone has a bone mineral content approaching that of human bone, enabling the elastic FlexBone material to be cut and shaped prior to surgery or intraoperatively and then pressed into a bone gap. When used in conjunction with traditional fixation techniques, the FlexBone material provides ideal scaffolding for new bone growth."

The density of the FlexBone material also allows surgeons to pre-drill channels in it, allowing for bone marrow from adjacent bone to migrate and penetrate. This helps to attract progenitor cells that are critical to new bone formation.

Beyond the benefits of its physical properties, FlexBone has also proved to be an ideal material for speeding recovery. "What makes FlexBone so ideal for healing large bone gaps is that it absorbs and retains the proteins associated with the natural healing process from the surrounding tissue once implanted," said Song. "This helps accelerate healing." Conversely, it can also be loaded with therapeutic agents, such as protein factors and antibiotics that can facilitate faster healing and fight infection through localized and controlled delivery over a sustained period of time.

"Because of this combination of factors, our study shows that FlexBone, combined with a protein growth factor in a dose 100 times less than what currently needed, was able to heal a large, long bone defect that would not heal on its own in a short period of time," said Song. "This material has enormous potential to solve a major problem that orthopedic surgeons face when reconstructing large bone deficits in the skeleton."

"Its ability to deliver growth factors and antibiotics to the patient and the handling characteristics simplifying the surgical procedure combine to make this material very exciting," said Dr. Ayers.

Song and Ayers would like to next test the safety and efficacy of the material in large animals, which they hope will pave the way for future clinical trials.

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