Scientists develop 'safe' bone grafts from cow bones to heal bone fractures and injuries

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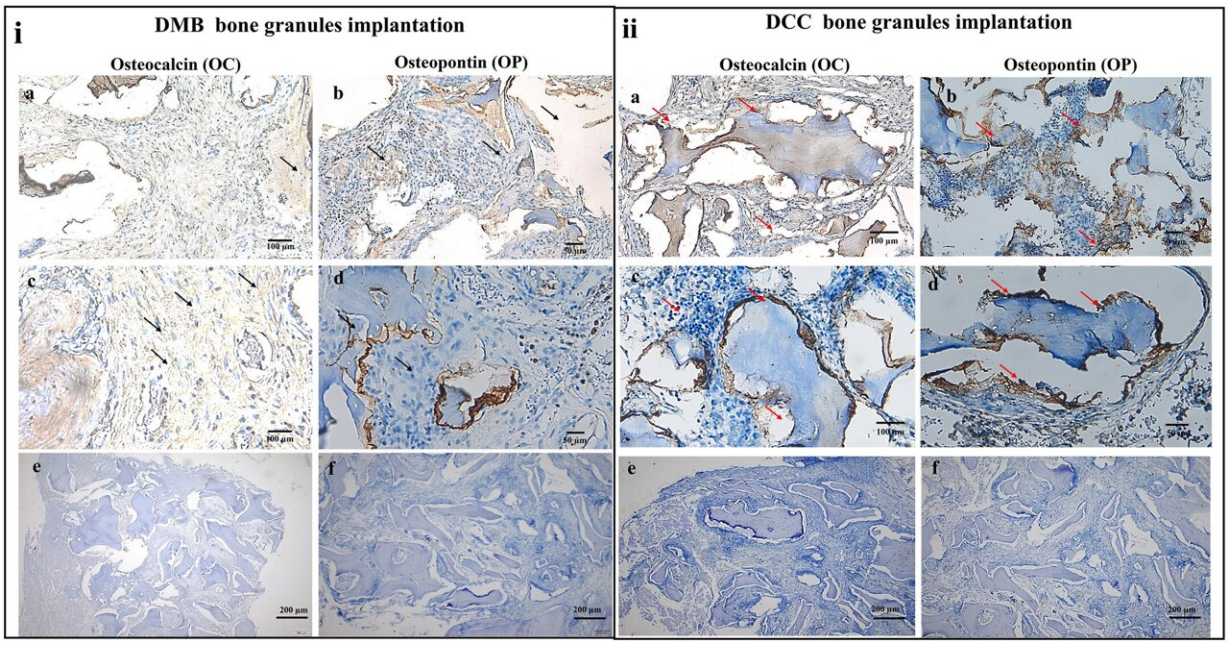

Representative images of immunohistochemical staining of DMB and DCC implantation sites to visualize the intensity distribution of osteogenic factors. Credit: *PLOS ONE* (2023). DOI: 10.1371/journal.pone.0294291

Using bovine bones obtained from cows, a group of scientists say they have developed novel bone graft material that can help fractured and injured bones to grow with minimum adverse body reactions.

The scientists, whose procedure is detailed in *PLOS ONE*, tried their

improved bone grafts on rats and mice and found them to have promoted rapid healing for injured and fractured bones.

More interestingly, the scientists noted that their mice model showed their newly developed bone grafts were well incorporated and did not cause much of adverse complications to the animal immune system.

Dr. Ali Al Qabbani of the Department of Oral and Craniofacial Health Sciences at the University of Sharjah, who led the team said, "The result was achieved because of our novel bone treatment procedure which helped in removing cells, DNA, and substances that can cause unwanted/adverse reactions in hosts.

"We have checked biological parameters such as the number of white blood cells, spleen size, and liver and kidney changes in the animals. We found that our bone grafts did not cause any harm to the internal organs when tested on animals."

Fractures due to bone diseases afflict millions of people and their treatment constitutes a heavy financial burden on government's health budgets.

About 1.5 million individuals are reported to suffer from bone fractures every year. The problem of bone diseases exacerbates with age and hits women the hardest. In the United states, roughly 4 in 10 women aged 50 or older suffer from hip, spine, or wrist fractures.

The art of treating bone defects is at least 3,000 years old when humans began using sticks or metals, among other things, to fill-in bone defects with variable degrees of success. Currently, surgeons rely mostly on synthetic bone grafts, which are artificially produced for treatment.

However, scientific evidence has shown that no synthetic material can

replace the intricate structure of the human bone tissue, according to co-author Prof. A. R. Samsudin of the Oral and Craniofacial Health Sciences Department, at the University of Sharjah.

"We are left with only animal bone tissues that seem to have close similarity with that of human bones. This opportunity created the challenge for us to investigate and process bones from cows and to make bone grafting procedures as safe as possible for use to replace human bones."

Dr. Qabbani said, "The study was conducted in multiple phases. As a first step, bovine bones were obtained from cows. The bones were cut into smaller sizes and treated with various chemicals to remove certain components that can cause problems/complications in humans. This step was important as it ensured the bones would be safe and suitable for medical use.

"The bone samples were then dried using a freeze dryer to remove their water contents completely and sterilized by using gamma radiation by sending them to the Atomic Research Agency of Jordon. Sterilization of bone samples is very important to remove all the microbial presence. This will help to ward off infections when these bones are tested in humans."

Next the bone grafts were subjected to various physical tests to prove they were durable enough to withstand the stress after being implanted at bone injury sites and ensure they could effectively support and facilitate the healing process without breaking or weakening under pressure.

To establish the processed bone grafts would be accepted by human body, the authors checked how cells similar to human body reacted towards them.

Dr. Qabbani remarked, "Our bone grafts were found favorable for cell growth due to their being highly porous and possessing a rough surface. The cells preferred this kind of environment because it provided them ample space to communicate and grow well.

"We found that cells liked to form colonies in our bone grafts and grow happily. This is an important finding because an ideal bone graft material should be well suited for cell growth and cell performance which is an important feature that contribute to bone healing."

The main aim of the study, the authors write, was "to compare the ability of demineralized (DMB) and decellularized (DCC) bovine bone granules to support bone regeneration in rat calvaria critical-size defects. DMB and DCC were prepared using a previously published method."

One important step in the study involved testing the bone grafts by inserting them into an animal body before they could be used in humans, for which the authors employed mice and rats.

In rats, the scientists found their bone grafts were well incorporated and promoted rapid wound healing. While in mice, they found the bone grafts not to cause much adverse reactions on animals' immune system.

"This was achieved because our novel bone treatment procedure helped in removing cells, DNA, and substances that could cause unwanted/adverse reactions in hosts," Dr. Qabbani said.

Asked about the study's significance and its practical implications, co-author and Oral Biology Professor Sausan Al Kawas of the University of Sharjah said, "The main idea was creating a novel bone material that can be used as bone substitute in the management of bone loss due to injuries which can help in rapid bone healing and fast recovery.

"Our novel bone graft is safe for human use, and different from the commercially available material in the world. After testing this novel biomaterial, we have applied for patent in U.S. by the name of University of Sharjah.

"Our study explains a method to remove cells from bone material while keeping its important structure intact. We compared two ways of doing this. One method, called demineralized (DMB), removed some cells but left some genetic material behind.

"The other method, called decellularized (DCC), removed more cells and genetic material but kept some of the important parts of the bone intact. This DCC method seemed safer for future use in transplants because it caused fewer reactions in the body."

Prof. Samsudin was upbeat about the result of the study and the commercialization of the findings which he said illustrated that "our novel bone graft material helped new bone grow and caused fewer adverse reactions in the body when tested in mice and rats.

"Our biomaterial bone graft helped more new bone grow in rats with big bone injuries. More importantly, we discovered that our special granule, called decellularized (DCC), has a remarkable ability to help bones heal better, especially when they have big injuries."

Dr. Aghila Rani, a co-author and member of the University of Sharjah's Wound Healing and Oral Diagnosis Research Group, said the results of the study confirmed that "our bone grafts are not only safe but also incredibly resilient. Our findings highlight the importance of meticulous processing techniques in developing effective bone grafts.

"By eliminating potential complications and optimizing processing methods, we are paving the way for a successful and reliable bone

regeneration therapy that can withstand the demands of everyday life."

Sharjah University's Research Institute for Medical and Health Sciences is currently looking for a partner in the pharmaceutical industry to work out a plan on how to produce the bone graft technique the authors have developed on a large scale.

More information: Ali Al Qabbani et al, Evaluation of the osteogenic potential of demineralized and decellularized bovine bone granules following implantation in rat calvaria critical-size defect model, *PLOS ONE* (2023). DOI: 10.1371/journal.pone.0294291

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