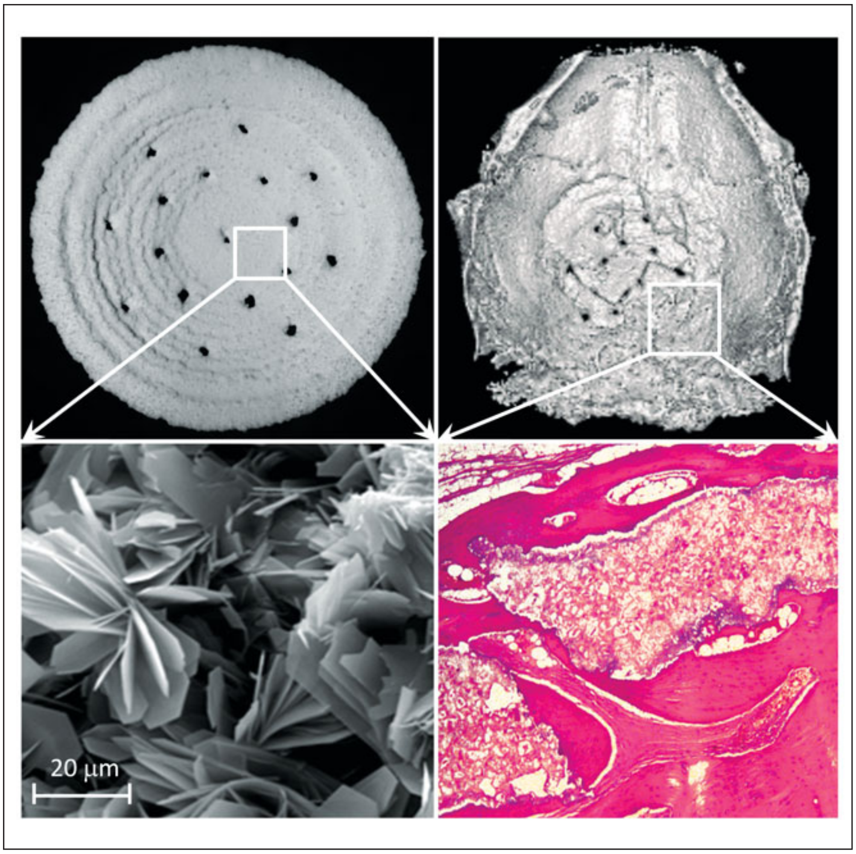
Bio Focus

3D-printed octacalcium phosphate bone substitutes reduce defect region

A significant challenge facing the fabrication of effective bone implants is the manipulation of synthetic materials to construct structures that mimic the complex form of native bone. As a technique attracting considerable attention for multiple applications, three-dimensional (3D) printing is being explored to generate synthetic biocompatible materials for guided bone regeneration and bone substitutes. However, the two principal existing techniques require an annealing step that can lead to mineral decomposition and the introduction of impurities. Now, a research group at the Russian Academy of Sciences has developed a method involving 3D printing of octacalcium phosphate (OCP) that does not require a heating step. The printed OCP block was implanted into a bone defect of size (20 mm) larger than mouse cranial bone defects that can be restored by native osteogenesis. The defect size was reduced 2.5 times in diameter over 6.5 months. The research is reported in the June 8 issue of *Frontiers in Bioengineering and Biotechnology* (DOI: 10.3389/fbioe.2015.00081).



General views of printed implant before (left top) and after implantation (right top). Scanning electron micrograph (left bottom) shows a flower-like morphology of dicalcium phosphate dihydrate crystals. Histotopogram (at 100× magnification) (right bottom) indicates the margin of the regenerated bone tissue that retains the implant. Credit: Vladimir S. Komlev.

"Vladimir S. Komlev et al.'s work is really exciting, innovative, and timely. The current paper is going to give a new direction to the current biomaterials processing research," says Chandra Sekhar Tiwary, a researcher from Rice University and the Indian Institute of Science. "The use of simple and easily scalable 3D printing technology for shaping ceramic biomaterials into a complicated shape will definitely attract many biomaterials researchers. Printing ceramic using 3D printing with the current method is not just useful for biomaterials, but also for ceramic processing industries. Also, shaping the structure from a bottom-up approach opens a new direction of engineering materials," Tiwary says.

Previous studies revealed that OCP ceramics facilitate bone marrow cell differentiation and spur osteogenesis after *in vivo* implantation. Komlev and colleagues thus brought ideas from this technology to the 3D printing of ceramics. The OCP implant was formed by a two-step process. The desired 3D ceramic model was first uploaded to a custom-designed 3D printer; dicalcium phosphate dihydrate (DCPD) was then formed during the printing process thanks to the interaction between tricalcium phosphate powder and diluted phosphoric acid, which serves as a binder liquid and ink. Subsequent chemical treatment of the printed DCPD materials transformed them into a needle-like OCP phase. The resultant OCP materials exhibited a threefold increase in compressive strength compared to 3D-printed DCPD samples due to the formation of OCP crystals and enhanced bonding between particles.

Evaluation of the new materials *in vivo* as bone graft materials demonstrated that fibrous tissues filled whole defect areas, including the pores of the printed implant. The printed materials supported bone growth at the defect edges—which are peripheral sites containing bone cell producing osteoinductive factors—and developed thickness of the growing fibrous tissue. The 2.5 times reduction in diameter in a defect region where very little spontaneous bone repair took place demonstrates success in bone tissue regeneration. However, the center of the defect showed no sign of osteogenesis. Komlev believes that for such a large bone defect, the OCP 3D-printed graft should also comprise osteoinductive components such as cells, growth factors, and gene constructions to increase the activity of bone tissue formation.

"The development of this approach opens new possibilities for creating modern bioengineered equivalents of hard tissues of humans," said Komlev. "Nevertheless, we consider the results

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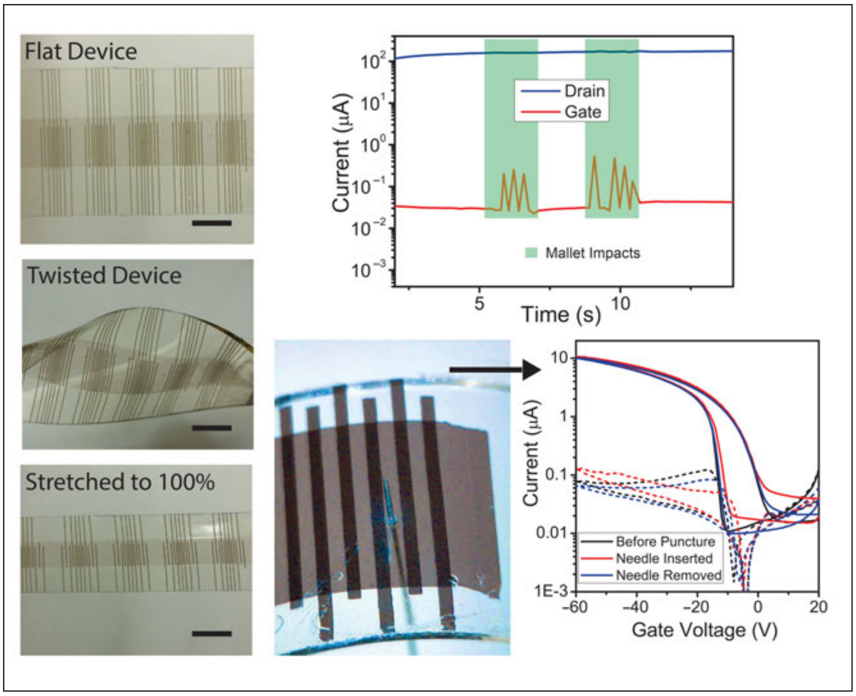
obtained so far in bone repair by the 3D printing approach to be very encouraging, but not optimal. To overcome the difficulties related to scientific, clinical, and commercial areas, innovative developments are further proposed. In particular, new types of 3D advanced ceramic scaffolds based on OCP and plasmid DNA with the gene encoding vascular endothelial growth factor have been developed by us. We hope that these novel methodologies will truly represent a new product—and possibly a new gold standard—in the tissue engineering field of bone repair."

Yung Chan

Nano Focus

Stretchable carbon nanotube transistors are put to the test



Photographs of the stretchable carbon nanotube transistor being twisted, stretched, and punctured. Accompanying graphs show electrical properties returning to normal after mallet impacts and needle punctures. Scale bars are 4 mm. Credit: Alex Chortos.

The advent of wearable devices has signaled a modern trend toward higher levels of integrated technology. The natural progression of this field is a move from wearable technologies such as smartwatches or glasses to more cohesive or even implantable technology. However, current electronic transistors are typically made of stiff, brittle materials that make them unfit for applications that require flexibility or durability, such as in biomedicine or biosensing. In order for this evolution in personal technology to continue, significant strides must be achieved toward more adaptable electronics.

Interest in stretchable electronics has been growing rapidly in recent years and while numerous studies have demonstrated feasibility, they have yet to address the mechanical resilience of these devices. Alex Chortos and colleagues from Zhenan Bao's group at Stanford University and Samsung Electronics are setting the bar for mechanical robustness with a new study published in the July 14 issue of *Advanced Materials* (DOI: 10.1002/adma.201501828) on stretchable yet durable electronic transistors that can be easily interfaced with soft moving objects. The researchers developed a new type of flexible transistor using carbon nanotubes (CNTs) embedded in a tough, but flexible, biocompatible thermoplastic polyurethane. This was formed using a solution-processable sequential coating/transfer process which has the potential for high-throughput device fabrication. This durable polymer can be stretched and flexed without damage and, once punctured or cut, will even resist the propagation of a tear. When combined with CNTs, which independently possess a large tensile modulus, these durable transistors can be flexed and stretched, while still retaining the bulk of their electrical properties.

After fabrication, the stretchable transistors were put through a gauntlet of physical testing. The transistors were stretched to strain values up to 100% in directions both parallel and perpendicular to current flow. Stretching to 100% strain resulted in a negative shift in threshold voltage and a drop of nearly 50% in both ON and OFF current values. However, after the initial decrease with the first stretching cycle, these values remained relatively constant over 1000 more stretching cycles.

The researchers also tested how these transistors resist sudden impacts from both a rubber mallet and a metal hammer. They found that the gate current and ON current both increased at the time of impact, but returned to approximately the original value afterward.

Even after the transistors were punctured or cut, they still remained functional while strained and unstrained. However, the researchers say that there are still further tests to be made. "Eventually we'd like to test chemical stability and … environmental stability to see how that changes the performance of the device," Chortos says. The toughness of these transistors as well as their consistent performance while sustaining impacts, tears, and extensive stretching supports their potential use in the unpredictable and extreme environments of everyday life.

Ian McDonald

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