ELSEVIER

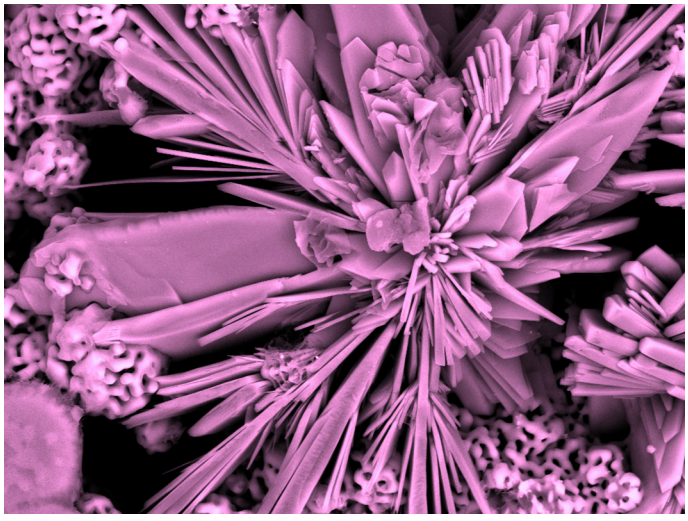
Uncovered

Calcium phosphate blossom for bone tissue engineering

3D printing scaffolds

Vladimir K. Popov[1,*], Vladimir S. Komlev[2] and Boris N. Chichkov[1,3]

[1] Institute of Laser and Information Technologies, Russian Academy of Sciences, Moscow, Russia
[2] A.A. Baikov Institute of Metallurgy and Materials Science, Russian Academy of Sciences, Moscow, Russia
[3] Laser Zentrum Hannover e.V., Hannover, Germany



The effective medical treatment of craniofacial and skeletal bone defects due to trauma, tumor removal or congenital abnormalities is a great challenge for reconstructive surgery. Biocompatible synthetic grafts and/or tissue engineering constructions based on cell-seeded scaffolds are the key elements required for success. For effective treatment, both the initial materials and the scaffold itself must meet the ''golden standard'' – autologous bone. This means that they must be biocompatible (possess low or preferably ''zero'' cytotoxicity), bioactive (initiate effective osteogenesis and neovascularization), bioresorbable (dissolve or degrade within the body with predetermined rate and by controllable manner) and have demanding mechanical characteristics. The particular requirement is that scaffolds must comprise interconnected porosity with specific surface functionalization of internal domains ensuring intensive osteoprogenitor cell attachment, proliferation and ingrowth, as well as nutrition and waste excretion.

There are a wide variety of materials (ceramics, bioglasses, polymers and their combinations) and methods (salt leaching, gas foaming, spray and freeze drying, etc.) that can be used to achieve this target. The application of different versions of Rapid Prototyping or Additive Manufacturing (layer-by-layer fabrication of solid replicas of three-dimensional computer modelling of the required objects) techniques for the effective production of bone tissue engineering scaffolds based on bioactive ceramics is currently considered one of the most advanced and attractive approaches. These techniques enable fast, reliable and reproducible fabrication of custom-designed matrixes of almost any demanded shape and internal structure using CAD/CAM (Computer-Aided Design/Computer-Aided Manufacturing) data. 3D-printing, where a liquid ''ink'' is binds together contours and layers of powder according to a sliced virtual model, unambiguously presents the most promising and cost-effective technology for R&D of new biomedical devices.

Over the last few decades, various calcium phosphates (hydroxyapatite, β-tricalcium phosphate, etc.) are widely used as bone substitute materials. Representing mineral content of natural bone, these components provide the intrinsic strength to the implants and functional scaffolding devices that are needed to sustain physiologically applied loads. The biodegradation rate of calcium phosphates (CP) can be adjusted, corresponding to the bone regeneration process, by the alteration of their chemical composition, crystallinity, and surface morphology.

The complexity of natural bone properties limits the creation of optimal materials and fabrication techniques for ideal custom-designed scaffolds required for guided bone tissue engineering. However, we believe that this problem can be solved via a 3D-printing methodology platform, using a combination of different CP powders, which could be selectively solidified with various binders.

*Corresponding author: Popov, V.K. (popov@laser.ru)

1369-7021/06/$ - see front matter http://dx.doi.org/10.1016/j.mattod.2014.01.015

The main concept of our work is based on the chemical interaction between initial calcium phosphate powders, e.g. tricalcium phosphate (TCP) and printing fluid (''ink''). It is known that TCP can react with phosphoric acid as bone cement, forming dicalcium hydrogen phosphate and dicalcium pyrophosphate, which are also bioresorbable calcium phosphates. Thus, the setting and solidification processes during 3D-printing rely on two types of interaction: acid–base reactions with the formation of a neutral compound or the hydrolysis reaction of the metastable phosphate resulting in an adhesive effect between particles. The main final phases of the 3D product are apatite or dicalcium phosphate and dicalcium phosphate dihydrate. To this end, the chemical and phase composition of the 3D printed scaffold can be adjusted to control its biodegradation rate and the specific ion release/absorption process into the surrounding tissue. It can be done by soaking the scaffold in solution (Simulation Body Fluid, Dulbecco's Modified Eagle Medium, etc.) with a controlled pH and temperature for a predetermined time. Moreover, this final procedure can also improve both mechanical integrity and the osteointegration properties of the structure.

This issue's cover image shows the ''blossom-like'' microstructure of bioceramic scaffolds, 3D-printed from fine (ca. 40–60 μm) tricalcium phosphate powder using phosphoric acid-based adhesive ''ink'' and soaked afterwards in aqueous sodium acetate solution for 24 h at 80 °C (intermediate phase – dicalcium phosphate dihydrate). In this study, various 3D-printed scaffolds based on octacalcium phosphate were provided for biological tests *in vivo*. We expected that a significant improvement in material performance will provide better implant integration with the host tissue during the initial post-operative period and its complete substitution with newly formed bone in the long run.

Finally, we believe that further development of this methodology should lead to the production of new, advanced biomedical devices ensuring high quality, reliability, sustainability and cost-effective level of medical assistance in therapy and surgery associated with bone fractures and diseases.

Acknowledgments

This work was supported by the Russian Foundation for Basic Research (grant nos. 13-02-12041 and 13-03-12021) and Government of the Russian Federation (contract no. 14.B25.31.0019).