REPORT

Visitor: Vladimir S. Komlev

From: A.A. Baikov Institute of Metallurgy and Materials Science, Russian Academy of Sciences

Degree: Dr. Sci., PhD

Host Institution: Institute of the Structure of Matter

Department: Italian National Research Council

Responsible person: Dr. J.V. Rau

Duration of stay: 09th October 2015 – 22rd October 2015

Title of the project: Calcium phosphate based bone cements for biomedical applications

Objective: The main goal of the project is to solve the fundamental problem in the multidisciplinary field, involving biotechnology of living systems and materials science, connected to the systematic investigation of kinetic features of phase formation upon hardening reaction in calcium phosphate bone cement systems. These materials are able to carry out complex functions, connected to the bone tissue engineering. Nowadays, fundamental science has not enough ground in order to propose suitable solutions to solve problems related to vertebroplasty applications of such hardening cement systems. The main objects of investigation are dispersed solutions of various calcium phosphates undergoing hardening process as a result of chemical reactions. During the realization of this project, two types of interactions will be studied: (1) acid-basic reaction with the formation of neutral compound and (2) hydrolysis reaction of metastable calcium phosphates. The investigation will be focused on the kinetic features of phase formation during the hardening process of these systems.

Results: Calcium phosphate based cement (CPC) materials are currently among the most promising synthetic substitutes for bone defects, due to their chemical similarity to the mineral component of the natural bone tissue. However, despite a number of manuscripts produced in the last decades on the development of CPCs for bone replacement and tissue engineering, there is still a need for their functionalization and the mechanical properties reinforcements.

Our goal was to develop CPC materials for implant use in bone tissue engineering, being the purpose twofold: (1) to provide the antibacterial properties to a CPC based on β-tricalcium phosphate by introducing Ag^{+} and Zn^{2+} ions, and (2) to enhance the mechanical characteristics of the cements.

For this latter task, MWCNT (multiwall carbon nanotube) additions are under investigation by us, since a very recent literature reports the results indicating much increased compressive strength of such systems, being able to promote the osteogenic differentiation of osteoblasts, and to serve as promising bone repairing graft material.

For the first task, we demonstrated the use of a relatively simple processing route based on preparation of silver and zinc-doped CPCs (CPCs-Ag and CPCs-Zn) through the preparation of silver and zinc-doped solid dispersed active phase (powders). The real-time monitoring of structural transformations and kinetics of several formulations were studied under physiological conditions. The formation of new phases was *in situ* monitored by the energy dispersive X-ray diffraction technique (EDXRD), allowing one to obtain a 3D map of diffraction patterns, collected as a function of the scattering parameter and of time. Different reagents-to-products rate of conversion, hardening times and crystallinity were registered for doped and non-doped cement samples, and a number of intermediate phases, evidencing the complex hardening mechanism were observed for the investigated systems.

Furthermore, long-time *in situ* EDXRD measurements were performed and demonstrated that hardening process of the CPCs is much more complex than expected and revealed by the conventional laboratory Angular Dispersive X-Ray Diffraction. We have been studied the 3D diffraction maps of OCP (octacalcium phosphate) and DCPD (dicalcium phosphate dehydrate). The OCP cements systems were chosen, since OCP is supposed to be a possible precursor phase during the HA (hydroxyapatite) crystallization upon the biomineralization process in vivo. In this work, special attention was paid to the in vitro behaviour of the nanograin size cements, and namely to the OCP-based bone cements, being of great interest for biomedical applications due to biocompatibility, osteoconductive and possibly osteoinductive properties. The obtained results demonstrate that formation of different types of calcium phosphates in synthetic and, all the more reason, in biologic systems, depends on the surrounding environment, pH and composition. It is expected that the investigated cements could be an ideal substrate for vascularization, cell attachment and proliferation due to the presence of a pores-reach network and nanocrystalline nature of the final HA phase. The investigated materials are currently under in vitro and in vivo study to prove their biocompatibility and osteoconductive properties. The obtained results are expected to contribute to the development of new biomedical technologies dedicated to the replacement and reconstruction of the damaged human bone tissue.

Publications:

Manuscripts:

1. V.S. Komlev, M. Fosca, A.A. Egorov, V. Graziani, Yu.V. Zobkov, M. Ortenzi, A.Yu. Fedotov, R. Caminiti, and J.V. Rau. Silver-doped calcium phosphate bone cement for biomedical application // 2015 in preparation. (to be submitted in Materials Letter).

2. V.S. Komlev, V. Graziani, A.A. Egorov, M. Fosca, Yu.V, Zobkov, M. Ortenzi, A.Yu. Fedotov, R. Caminiti, and J.V. Rau. Zink-doped calcium phosphate bone cement for biomedical application // 2015 in preparation.

3. V.S. Komlev, V. Graziani, M. Fosca, A. De Bonis, R. Teghil, A.Yu. Fedotov, and J.V. Rau. Calcium phosphate coatings grow *in vitro* on Titanium implants. // in preparation

Congress Presentations:

1. M. Fosca, V. Graziani, M. Ortenzi, V. Komlev, R. Caminiti, J.V. Rau. Doped calcium phosphate based bone cements for biomedical applications. /**Biophysics@Rome** National Conference, Rome, Italy, May 28-29, 2015.
2. V. Graziani, M. Fosca, M. Ortenzi, V.S. Komlev, R. Caminiti, J.V. Rau. Doped, mechanically reinforced calcium phosphate cements for bone tissue engineering applications. /**VI Workshop Nazionale AICIng,** Roma, 22-23 Giugno 2015.
3. V. Graziani, M. Fosca, V.S. Komlev, M. Ortenzi, J.V. Rau. Ag-, Zn-doped calcium phosphate bone cements for tissue engineering. /**School of Nanomedicine 2015, CNR-IC** (Institute of Crystallography) December 2-4, 2015. Bari, Italy.

(Komlev V.S.)

.... Firma

03.11.2015