Doped calcium phosphate based bone cements for biomedical applications

M. Fosca [a], V. Graziani [a,b], M. Ortenzi [a], V. Komlev [c], R. Caminiti [d], J.V. Rau[a]

[a] Istituto di Struttura della Materia (ISM-CNR), Via del Fosso del Cavaliere 100, 00133 Rome, Italy
[b] Dipartimento di Scienze di Base e Applicate per l'Ingegneria, Università di Roma "La Sapienza", Via A. Scarpa 14-00161 Roma, Italy
[c] A.A. Baikov Institute of Metallurgy and Materials Science, Russian Academy of Sciences, Leninsky prospect 49, 119991 Moscow, Russia
[d] Dipartimento di Chimica, Universita di Roma "La Sapienza" , Piazzale Aldo Moro, 5-00185 Rome, Italy
e-mail: marco.fosca@ism.cnr.it

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Calcium phosphate based cement (CPC) materials are currently among the most promising synthetic substitutes for bone defects and teeth reconstruction, due to their chemical similarity to the mineral component of the natural bone tissue. However, the proposed up to now new cement compositions lack for the required mechanical properties, which should be as close as possible to the native bone. Among these, the compressive strength must be significantly improved.
Nowadays, considerable efforts have been focused on the CPC mechanically reinforced compositions, developed to restore the damaged human calcified tissues, like vertebras and osteoporotic bone. Recent literature [1] reports the results indicating that calcium phosphate cements with MWCNT (multiwall carbon nanotube) additions possess the increased compressive strength and are non toxic, thus promoting the osteogenic differentiation of osteoblast cells and being, therefore, a promising bone graft material. Furthermore, we plan to endow cements with antimicrobial properties doping them with Argentum and Zinc ions, i.e. introducing Ag^{2+} and Zn^{2+} substitutions into calcium phosphate molecule.
The mentioned above tasks could be reached by an in-depth investigation of the CPC hardening mechanism. Usually, for cement preparation, a powder and a hardening liquid are mixed in certain proportion, forming a creamy paste, which hardens upon time. Our previous studies demonstrated that hardening mechanism is a complex process, and that a suitable tool for its investigation is the Energy Dispersive X- Ray Diffraction (EDXRD) technique [2-6]. Correlation between macroscopic mechanical properties and microscopic structural behaviour are well known and were proved in our previous work [7]
By means of this technique, a real time *in situ* monitoring of the CPC's hardening process can be performed. A 3D map containing a sequence of diffraction patterns, collected as a function of the scattering parameter and of time, can be obtained. Phase transformations (new phases and possible intermediate phases), amorphous-into-crystalline conversion (primary and secondary crystallization processes) can be followed. Long-time *in situ* EDXRD measurements demonstrated that hardening process of the CPCs is much more complex than expected and revealed by the conventional laboratory Angular Dispersive X-Ray Diffraction. In Fig.s 3 and 4, the 3D diffraction maps of OCP (octacalcium phosphate) and DCPD (dicalcium phosphate dehydrate) based cements are shown, supported by the SEM images. The OCP cements systems were chosen, since OCP is supposed to be a possible precursor phase during the HA crystallization upon the biomineralisation 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 ostoinductive 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.

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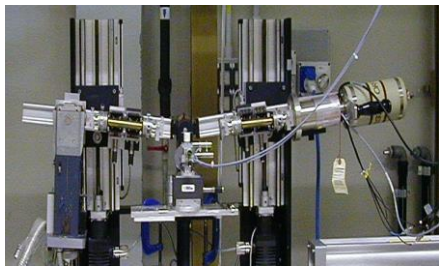

Figure 1. Energy Dispersive X-Ray Diffraction Experimental Setup.

Figure 2. Schematic collage of possible applications

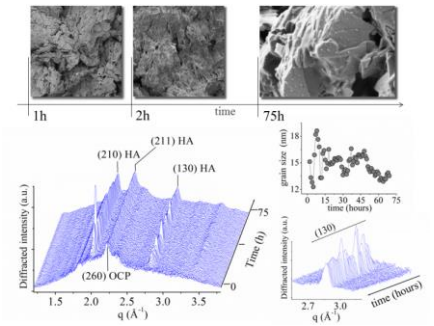

Figure 3. Sequence of EDXD patterns collected upon the OCP – chitosan cement [2]. SEM images (75x) correspond to certain time intervals.

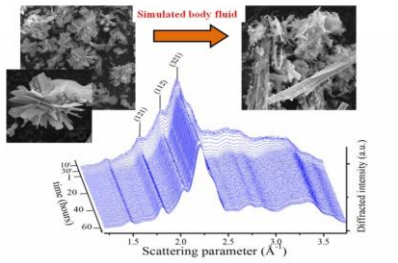

Figure 4. Sequence of EDXD patterns collected upon the OCP – DCPD cement. SEM images (5x) correspond to certain time intervals [3].