O8.9

In vivo resorption of biomimetic hydroxyapatite/collagen composites: injectable cements versus pre-set microspheres.

Erika Silva[2], Roman A. Perez[1], Jordi Franch[2], Cristina Manzanares[3], Maria-Pau Ginebra[1]

[1]Biomaterials, Biomechanics and Tissue Engineering Group, Department of Materials Science and Metallurgy, Technical University of Catalonia, Barcelona, Spain, [2]Department of Animal Medicine and Surgery, Autonomous University of Barcelona, Barcelona, Spain, [3]Department of Pathology and Experimental Therapy, Bellvitge Health Sciences Campus, University of Barcelona, Barcelona, Spain

Background: Calcium phosphate cements (CPC) are low-temperature self-setting materials that have become widely used as synthetic bone grafts due to their excellent osteoconductive properties and similarity to the bone mineral phase (1). Nevertheless, their slow degradation *in vivo* (e.g. months up to years) delays the appearance of new bone (2).

Aim: To investigate new routes for accelerating the resorption of these materials through their combination with collagen, and their processing as pre-set microspheres (MS).

Material and Methods: The MS were prepared by water in oil emulsion. The CPC powder phase consisted of α-TCP which hydrolyses into hydroxyapatite. Water or a collagen solution was used as the liquid phase. Femoral condyles of female New Zealand white rabbits were used as animal model. Five 5 mm critical size defects were created and the MS were mixed with 1 ml of the animal's blood to make a clot, implanting if afterwards in the defect. As a control, dense formulations of the same CPC compositions were prepared by mixing the liquid and the powder phase *in situ* to form a paste, injecting it afterwards in the defect. The animals were sacrificed at 1 and 3 months post-operative to analyse material resorption and bone formation by histology and scanning electron microscopy.

Results: A significant increase of material resorption was found for the MS as compared to the dense CPC already after 1 month, although these became more evident at 3 months (Fig 1 A, B). The amount of remaining biomaterial in the site of defect was around 75% and 69% for the dense CPC and collagen-CPC respectively, but was reduced to 35% and 20% for their respective MS formulations after 3 months. Furthermore, new tissue was able to grow within the implanted biomaterials, with ten times higher values for the MS compared to the dense CPC. Dense CPC allowed bone formation in the external perimeter of the material, and cell infiltration within the cracks (Fig 1 C), whereas the MS allowed higher cell infiltration throughout the whole defect site, showing perfect integration with the new bone formed without disrupting the trabecular structure (Fig 1D).

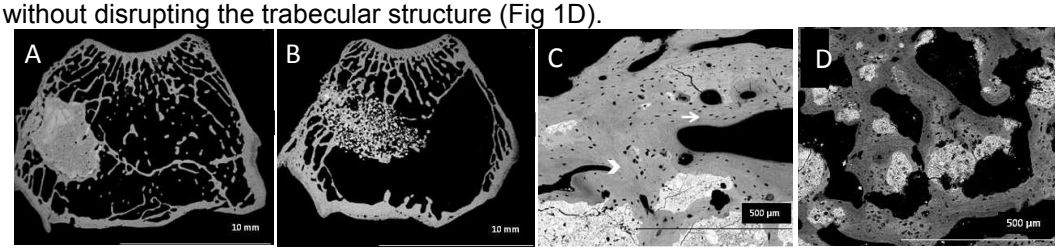

Figure 1. Backscattered electron images of the dense collagen-CPC (A and C) and the collagen-CPC MS (B and D) after 3 months implantation.

Conclusions: The results showed an enhanced MS resorption and accelerated bone formation that was even higher in the presence of collagen. The use of these MS as carriers

for other biologically active molecules, enabled by their high microporosity and low-temperature processing is under investigation.

References: (1) Acta Biomaterialia 6 (2010), 2863–2873; (2) J Biomed Mater Res A, 61 (2002), 9–18

Acknowledgments: Spanish Government, Project MAT2012-38438-C03.