ABSTRACT SUBMISSION

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In vivo evaluation of 3D printed BCP scaffolds for maxillofacial bone reconstruction in a critical-size bone defect model of rabbit

Matthias Schlund[1,2], Arnaud Depeyre[1,3], Vincent Hornez[4], Jean-Christophe Hornez[5], Thomas Wojcik[1,6], Pierre Machandise[7], Guillaume Penel[7], Pierre Gosset[8], Baptiste Delaire[8], Nicolas Blanchemain[1], Joel Ferri[1,2], Feng Chai[1]

1. Université de Lille, Inserm U1008, CHU Lille, Pôle de Recherche, Faculté de Médecine, 1 Place de Verdun - 59045 Lille
2. Centre Hospitalier Universitaire de Lille, Service de Chirurgie Maxillo-Faciale, 2 Avenue Oscar Lambret, 59000 Lille
3. Centre Hospitalier Universitaire de Clermont-Ferrand, Service de Chirurgie Maxillo-Faciale, Stomatologie et Chirurgie Plastique de la Face, 1 Place Lucie Aubrac, 63003 Clermont-Ferrand, France
4. CryoCeram-Startup, Serre Numérique de Valenciennes, 2 rue Péclet, Parc des Rives Créatives, BP 80577 - 59308 Valenciennes Cedex
5. LMCPA-Université de Valenciennes, Campus Mont Houy - 59313 Valenciennes Cedex 9
6. Centre Oscar Lambret, 3 Rue Frédéric Combemale, 59000 Lille
7. Université de Lille, EA4490 PMOI Physiopathologie des Maladies Osseuses Inflammatoires, Faculté de Chirurgie Dentaire, Place de Verdun - 59000 Lille
8. Immunohistochimie et Recherche, Laboratoire d'Anatomie et Cytologie Pathologiques, Pôle hospitalo-universitaire de biopathologie, Hôpital Saint Vincent de Paul, Boulevard de Belfort – BP 387, 59020 Lille Cedex

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ABSTRACT. Biphasic calcium phosphate (BCP) bioceramics have great potential for applications as a bone substitute because of their excellent chemical bone-bonding ability and higher bioresorption property. On the other hand, 3D printing methodology is an excellent approach to support effective and fast patient-specific fabrication of individual complex bone substitutes. Here, we aimed to elaborate a 3D printed BCP scaffold (3D-BCP), and *in vitro / in vivo* evaluate its biocompatibility.

The implantable disk samples were fabricated by a custom-designed CryoCeram 3D printer from synthetized BCP powder (60 wt% HA / β-40 wt% TCP). *In vitro* biological assessment of 3D-BCP was carried out with pre-osteoblast cell lines (MC3T3-E1). *In vivo* evaluation of 3D-BCP scaffold was further conducted by the implantation in a developed critical-size bone defect model in the rabbit skull (Ø 10 mm) and mandible (11×6 mm) followed by X ray micro-CT imaging and histological evaluation at 4 and 12 weeks after surgery.

The obtained results confirmed the 3D-BCP scaffold promotes well the adhesion and the proliferation *in vitro* of pre-osteoblast cells. *In vivo*, acquired micro-CT images, in agreement with histological analysis, showed that the bone defects in the sham group, in which no scaffold was implanted, still had a lack of newly formed bone at 12 weeks. The defects filled with the 3D-BCP scaffolds formed new bone and better-repaired bone defect (higher BV/TV value) than the sham. While difference of response was also found between mandible and skull defect site.

This study indicates that our 3D printed BCP scaffolds with desired shapes and internal structures exhibited a good bioactivity and biocompatibility *in vitro* and *in vivo*, and promoted appropriate new bone formation *in vivo*. Future study will focus on incorporating bioactive factors (platelet-rich fibrin) and osteoprogenitor cells to enhance the osteoconductive and osteoinductive stimuli for better repair of bone defects.

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