

Novel Composite 3D Scaffold for Bone Tissue Engineering.

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Introduction.

Scaffolds for bone tissue engineering (*t.e.*) should ensure both mechanical stability and adequate strength and show a completely interconnected porous network for cell migration and proliferation, while also providing specific signals for bone regeneration [1]. These issues are very well known ever since early maxillo-facial surgery in the 80's [2]. Moreover, connective tissue adhesion should be promoted. Biopolymers [3], bioglass and bioceramics [4] are often considered to satisfy these requirements at least in part [5]. Here, Industrie Biomediche Insubri S/A developed and produced a new composite 3D scaffold thought for bone *t.e.*, particularly for maxillo-facial surgery, using a novel concept based on biomaterial assembly [6], thus avoiding drawbacks of interfacial bonding.

Materials and methods.

This novel matrix has a composite structure based on a bone graft specifically reinforced with biodegradable polymers and bioactive agents. The bone grafts allow to maintain the adequate 3D-structure and porosity, the biopolymers permit to achieve good mechanical properties while bioactive agents promote cell adhesion and proliferation. All used components are approved for human use and scaffolds are produced according to GMP standards at the Micro-Sphere S/A facility. Both process and product are proprietary [6].

Microstructure was evaluated by SEM imaging (Evo 50EP, Zeiss-Cambridge Instruments, Germany). Handling tests were performed by surgeons to assess applicability in oral surgery. Preliminary *in vitro* tests with bovine chondrocytes were performed to evaluate the ability to support and promote cells proliferation within the matrix.

Results.

This novel composite 3D scaffold resulted feasible for oral surgery, being both easy to shape and resistant to screws and fixation manoeuvres (as depicted in Fig 1). Moreover, SEM imaging confirmed that its microscopic structure resembles that of human cortical bone (as evident from Fig 2). Cell proliferation, assessed by Alamar Blue™ test, and viability resulted both positive and fully comparable in terms of values referred to controls. Further confirmations came from morphological analysis performed via SEM imaging.

Conclusions.

Data collected represent a positive proof of concept for the developed process and the application of this new type of matrix as scaffold for bone tissue regeneration. Morphological analysis of structure confirmed the

presence of a well diffused cortical bone human-like porosity. Preliminary mechanical investigation showed easy shaping by common surgical instruments in order to replicate and thus replace bone defects. Furthermore, preliminary biological investigations showed scaffolds to be promising substrates for cell adhesion and growth.



Figure 1: the matrix (about 1c.c.) shows both rigidity and elasticity and appears easy to be handled and shaped by surgeons to be adapted to local defects and needs.

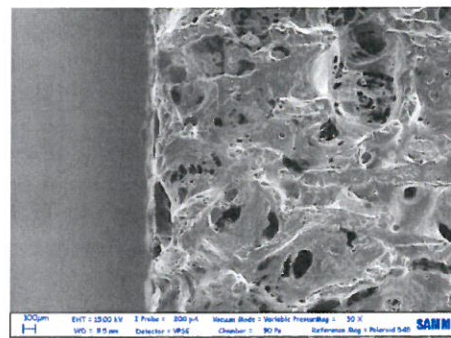


Figure 2: Microscopic structure evidences strong affinities with human cortical bone, particularly related to porosity which appears completely comparable in terms of size and cells seeding spaces to human cortical bone.

References.

- [1] Mistry A.S., Mikos A.G. *Adv Biochem Engin/Biotechnol* 94:1-22, **2005**.
- [2] Mulliken J.B. *et al. Proc Ann Meet Am Surg Ass* 194(3):366-372, **1981**.
- [3] Kretlow J.D., Mikos A.G. *Tissue Eng* 13(5):927-938, **2007**.
- [4] Barrère F., van Blitterswijk C.A., de Groot K. *Int J Nanomed* 1(3) 317-332, **2006**.
- [5] Christenson E.M. *et al. J Orth Res* 25:11-22, **2007**.
- [6] Pat. Pr. Appl. CH.01997/08.