Granules of a bone substitute biomaterial have a 3D arrangement mimicking bone microarchitecture

Bone is a naturally rigid and porous tissue of the body. The pores allow the circulation of blood vessels and the creeping of bone-forming cells at the surface of the tissue. Bone loss can occur systemically, for example during aging (osteoporosis). However, a localized bone loss can also occur, as in some defects, such as bone cysts or acquired bone defects (as observed after tooth extraction). Bone substitutes are often used to fill these defects, especially in non-bearing bones. The final goal is to obtain a reconstitution of the volume of bone that has been lost. This is especially important in dental surgery to prepare to the placement of bone implants. For filling these defects which have frequently non-regular contourss, the use of granules of biomaterials is the preferred form.

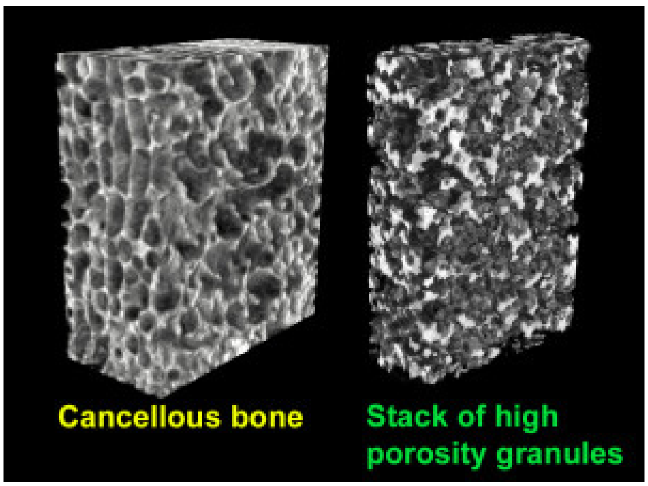

Fig. 1. 3D microtomographic analysis of cancellous bone (left) and a stack of ?-TCP granules with a high porosity

The granules can be prepared by splitting bone harvested in the patient itself (autograft) of from bone from a donor (allograft) or an animal bone (xenograft). However, autograft requires another surgical site and exposes to complications. Granules from bone banks or animal bone exposes to the risk of infection by unconventional agents (prions). Synthetic calcium-phosphate ceramics can be produced in large quantity by industry and are absolutely safe. Among them beta-tricalcium phosphate (?-TCP) appears the most suitable, particularly in maxillo-facial and dental surgery. Granules of 1000-2000µm diameter represent the most commonly used size for filling dental sockets or increasing volume in bone cysts or grafts. However, when the surgeons place these rather brittle granules within a bone defect, classical recommendation by biomaterial manufacturers is to gently pack the granules in the grafted area, without crushing them in order to preserve the 3D structure produced. The voids between the granules represent the space available for vascular sprouts and bone cells to invade the grafted area and condition the success of the graft. The geometry of a grafted material is known to be a critical parameter favoring bone formation but the 3D arrangement of a grafted stack of granules is largely unknown and depends on the shape of the granules.

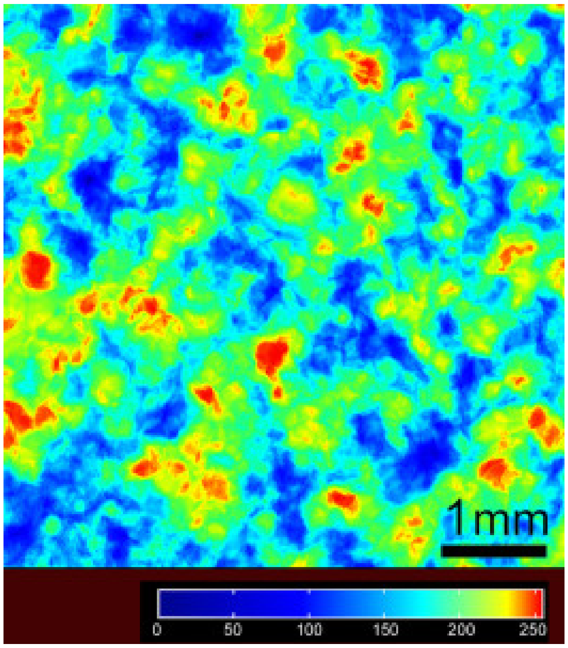

Fig. 2. Vector analysis of a stack of high porosity granules. The pseudo-color illustrate the amount of porosity and material across the stack: blue indicates a high amount of material; green to red: the pores inside the stack.

The 3D arrangement of two types of commercially available ?-TCP granules was compared with the microarchitecture of real cancellous bone. Granules were prepared by the same technique but the shape of the granules markedly differed, although their size was similar (1000-2000µm): the dense granules contained more biomaterial; the high porosity granules had thinner walls and exhibited a larger interface. Stacks of granules were prepared in similar test tubes and analyzed by microcomputed tomography (microCT). The method is a miniaturized version of the computerized axial tomographs commonly used by radiologists but has a resolution in the order of a few micrometers. MicroCT allows also direct measurement of the amount of the material and porosity of the stacks of granules in 3D. Image sections were also analyzed by a newly described algorithm to determine the projected porosity of the stacks by using vector analysis and fractal geometry. In parallel, two types of cancellous bone cylinders were harvested from young and old controls and analyzed similarly. Stacks of high porosity granules had porosity and fractal values intermediate between that of young and old bones but exhibited a greater interface (available for bone cells) than the dense granules. 3D arrangements of the dense granules created large pores coexisting with dense areas of material. Vector analysis evidenced a more regular arrangement of ?-TCP granules than bone trabeculae and denser granules. ?-TCP granules prepared differently did not produce the same interconnected porosity. Stacks of high porosity granules create scaffolds resembling cancellous bone in its porous microarchitecture although the granules are physically independent.

Publication

3D porous architecture of stacks of ?-TCP granules compared with that of trabecular bone: a microCT, vector analysis, and compression study
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