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Synthesis and Properties of Ceramic Foams for Hard Tissue Repair

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ABSTRACT

Development of materials for bone repair has stimulated a wide field for research in the recent decades. This work describes manufacturing methods of porous ceramics which can provide suitable porous structures for tissue regeneration. Emphasis is given to foaming of ceramics suspensions and gelcasting setting with organic monomers, which yields materials of a wide range of porosity and enhanced mechanical strength. The interconnected network of macropores in foams provides the means of access for tissue in-growth while the intricate framework enables cell attachment and supports the organisation of the growing tissue.

Key-words: porous hydroxyapatite; gelcasting of foams; biocompatibility; rabbit tibia; bone grafts.

INTRODUCTION

Despite the processing complexity and inherent brittleness of ceramics, they have been widely investigated for skeletal repair applications due to a high biocompatibility. Whereas some are interesting because of their high wear resistance and good chemical stability in contact with body fluids, others are more reactive and can resorb to be replaced by the new tissue at controlled rates, depending on the composition. A class of ceramics that has received much attention in the field of bone repair involves materials containing calcium and phosphate, widely used in cements for prosthesis fixation and bone-defect filling materials.[1] The success of Ca-P compositions can been attributed to the essential roles of calcium and phosphate in the natural process of bone regeneration and proliferation.[2] Calcium-phosphate based compounds are osteoconductive and can establish a physico-chemical bond to bone during the bone regenerative process. Their degree of reactivity with the living tissues, which relates to the healing ability, has shown to depend on the chemistry, as well as on the physical structural features, such as mineralogical composition, degree of crystallinity, and porosity.

Porosity in materials used for bone repair gives the potential for penetration of osseous tissue and restoration of vascularity throughout the repair site, improving fixation and healing rates. Although introduction of porosity in ceramics implies substantial loss of mechanical properties, *in vivo* studies and clinical evidence of

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fast healing in the presence of grafts have been favourable towards the continuous development of new technologies to produce porous materials.

Depending on the processing technique used to manufacture ceramics, porosity size can lie within the nanometer range (sol-gel materials, xerogels), sub-micron range (bisque firing) or in the range of hundreds micrometers (volatile phases, replication of foams, foaming).[3] Large interconnected pores are seen as necessary in bone graft applications because of the need for tissue ingrowth and vascularisation, with a minimum limiting size of approx. 100 µm.[1] Smaller pores in the sub-micrometer range enhance cell adhesion and proliferation in the implant site and have the potential to absorb substances that work in the regenerative process, such a proteins and growth factors.[4] Combining pores in the sub-micron range within the framework of a macroporous network ideally provides hierarchical structures similar to that of bone. Bisque firing macroporous polycrystalline ceramics or creating macroporous structures with intrinsically mesoporous materials, such as foaming of sol-gels,[5] are some possible routes to produce large and small pores within the same structure. However, there are limitations associated to these routes because of the intrinsic compromise between mechanical strength and porosity fraction and size. Optimisation of processing procedures and parameters is of prime importance to obtain a fully homogeneous and optimum strength material.

Recently, the method of gelcasting foams has shown suitability to manufacture strong and reliable macro-porous ceramics that have great potential to replace bone tissue. The ability of a foamed structure in providing a network for tissue regeneration is shown herein through the results of *in vivo* evaluation of hydroxyapatite foams.

MATERIAL AND METHODS

Macroporous bodies of biomedical-grade hydroxyapatite (Plasma Biotal Ltd., U.K.) were produced by the gelcasting of foams method.[6] The procedure involves dispersion of the ceramic powder in aqueous medium, foaming by agitation in the presence of surfactants and setting by the *in situ* polymerisation of acrylic monomers. The gelled bodies were dried and then sintered at 1350°C for 2 hours for matrix consolidation. Scanning electron microscopy (SEM) and mercury porosimetry were carried out for evaluation of the porous structure produced.

Cylinders of 3 mm diameter of sintered HA foams containing 85 vol% porosity were sterilised and implanted in the tibia of albino New Zealand rabbits under general anaesthetic conditions and antibiotic protection.[7] The implants were removed after a period of 8 weeks to observe the bone regenerative potential of the foams. The area of implantation was fixed, dehydrated and embedded in resin. Slices were cut perpendicularly to the tibial axis, ground and polished for observation on scanning electron microscopy.

RESULTS AND DISCUSSION

The process of gelcasting foams is known to yield non-cytotoxic materials with optimised strength and open spherical pores, and can be applied to many raw-materials as shown in previous works.[6,8] A representative specimen of the hydroxyapatite foams tested in this work containing approximately 85% porosity is shown in Figure 1. The structure is highly porous and thoroughly interconnected. The framework is composed of large spherical pores of 100-500 µm and interconnecting windows of 30 and 120 µm enclosed by a compact framework of polycrystalline hydroxyapatite. The size of pores and volume porosity can be varied and controlled by the amount of foam produced or by expansion of the liquid foam using vacuum prior to gelation.

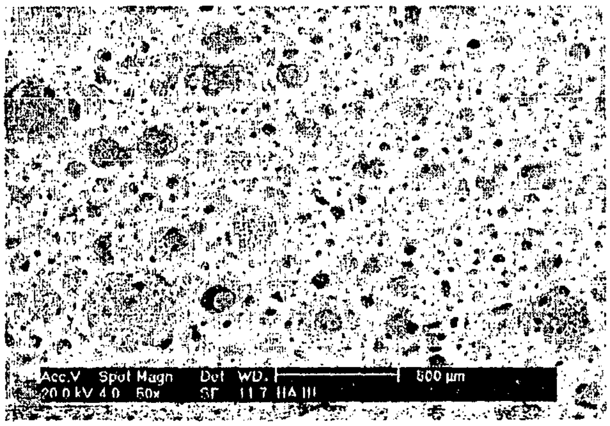

Figure 1. SEM micrograph of macro-porous hydroxyapatite manufactured by the gelcasting of foams method.

The properties of foams have shown to depend directly on their density and pore size.[8] Even though large pores are greatly desirable for bone repair applications, there is a maximum pore size limit which is determined by the minimum mechanical strength required to a particular use. Curves illustrating the trends of strength and elastic modulus decreasing as the density decreases are sown in Figure 2. This decrease is commonly associated with the intrinsic increase in pore size and the production of foams with thinner walls as density is lowered.

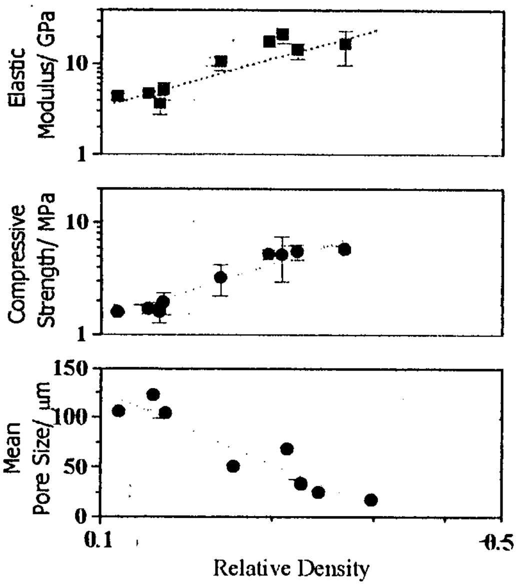

Figure 2. Mechanical properties and mean pore size of hydroxyapatite foams as a function of density.[8]

The suitability of the foam network produced with HA to promote tissue regeneration was verified by *in vivo* experiments. All animals survived the 8 weeks study period without evidence of inflammation or infection at the implantation site. The results revealed that the HA foam structure was filled almost entirely with newly formed trabecular bone within the implantation period. Figure 3 illustrates bone-implant integration, with new bone filling the foam structure progressively, from areas of neighbouring old bone towards the inner part of the implant. Newly formed bone tissue at various stages of maturation were detected, with osteoids mainly present within larger pores in the foams, indicating that vascularisation is improved when interconnecting windows are larger, as expected.

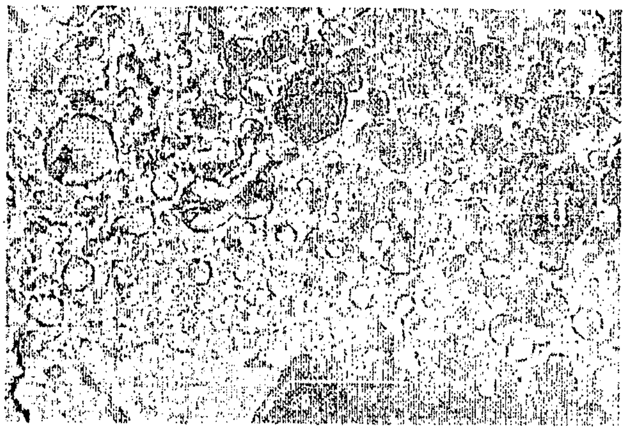

Figure 3. Cross-section showing original old bone (a) in contact with a HA foam (85% porosity) after 8 weeks of implantation. Healing is shown from the stage of pores filled with collagen (d) at the outermost zones of the implant towards pores completely filled with trabecular bone and osteoids (c).

CONCLUSIONS

The framework of foams provide the scaffold for extensive bone ingrowth allowing an adequate osteointegration, associated with the high osteoconductive potential and high biocompatibility of hydroxyapatite. The results demonstrate that the foams provide a potential structure for bone repair. Different raw materials with a similar porous structure to the one shown here can provide a variety of chemical, mechanical and bioactive properties in order to suit a wide variety of applications.

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REFERENCES

1. Ravaglioli, A., Krajewski, A. Bioceramics: materials, properties, applications. Chapman & Hall; 1992.
2. Xynos, I.D., Edgar, A.J., Buttery, L.D.K., Hench, L.L., Polak, J.M. Gene-expression profiling of human osteoblasts following treatment with the ionic products of Bioglass (R) 45S5 dissolution, J. Biomed. Mat. Res. 2001;55(2):151-157.
3. Sepulveda, P. Gelcasting foams for porous ceramics. Am. Ceram. Soc. Bull. 1997;76(10):61-65.
4. Hench, LL. Sol-gel materials for bioceramic applications. Curr. Opinion in Solid State & Mat. Science 1997;2:604-610
5. Sepulveda, P., Jones, J.R., Hench, L.L. Bioactive sol-gel foams for tissue repair, J. Biomed. Mater. Res., In Press.
6. Sepulveda, P., Binner, J.G.P., Rogero, S.O., Higa, O.Z., Bressiani, J.C. Production of porous hydroxyapatite by the gel-casting of foams and cytotoxic evaluation. J Biomed Mater Res 2000;50:27-34
7. König Jr, B., Beck, T.J., Kappert, H.F., Kappert, C.C., Masuko, T.S. A study of different calcification areas in newly formed bone 8 weeks after insertion of dental implants in rabbit tibias. Ann. Anat. 1998;180:471-475.
8. Sepulveda, P., Ortega, F.S., Innocentini, M.D.M., Pandolfelli, V.C. Properties of highly porous hydroxyapatite obtained by the gelcasting of foams. J. Ceram. Am. Soc. 2000;83(12):3021-3024.

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