Available online at www.sciencedirect.com
ScienceDirect
Acta Biomaterialia 4 (2008) 370–377
Acta BIOMATERIALIA
www.elsevier.com/locate/actabiomat

Bone ingrowth in macroporous Bonelike® for orthopaedic applications

M. Gutierres [a], M.A. Lopes [b,c], N. Sooraj Hussain [b,c], A.F. Lemos [d], J.M.F. Ferreira [d], A. Afonso [e], A.T. Cabral [a], L. Almeida [a], J.D. Santos [b,c,*]

[a] *FMUP – Faculdade de Medicina da Universidade do Porto, Hospital de São João, Largo Hernâni Monteiro, 4200 Porto, Portugal*
[b] *FEUP – Faculdade de Engenharia da Universidade do Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal*
[c] *Instituto de Engenharia Biomédica (INEB), Laboratório de Biomateriais, Rua do Campo Alegre 823, 4150-180 Porto, Portugal*
[d] *Dep. De Eng. Cerâmica e do Vidro, UIMC, Universidade de Aveiro, Aveiro, Portugal*
[e] *FMDUP, Faculdade de Medicina Dentária da Universidade do Porto, Rua Dr. Manuel Pereira da Silva, 4200-393 Porto, Portugal*

Received 30 November 2006; received in revised form 30 April 2007; accepted 21 June 2007
Available online 18 July 2007

Abstract

The aim of this study was to evaluate the biological behaviour of porous scaffold structures of Bonelike® which is suitable for either direct clinical use or tissue engineering applications. Porous cylindrical specimens 8×10 mm were implanted in the lateral aspect of the tibia of 13 patients (mean age 54 years), during osteotomy surgery for the treatment of medial compartment osteoarthritis of the knee. Implanted cylinders were retrieved at the same time as the removal of the blade plates at 3, 6, 9 and 12 months. Scanning electron microscopy and histological evaluations were performed to observe the biological responses of human bone tissue to porous Bonelike®. The penetration depth was determined for all implantation periods, and after 6 months it was already possible to see new bone in the centre of the implanted cylinders, which gives 100% of penetration depth for all implantations periods except for 3 months when bone could only be seen in the peripherical region. Regarding the percentage of the area covered by new bone calculated from two-dimensional histological sections, values of 53 ± 15, 76 ± 12 and $88 \pm 9\%$ were achieved for 6, 9 and 12 months, respectively. Due to its structural features porous Bonelike® permitted effective vascularization and bone ingrowth, and therefore was fully osteointegrated as shown in the histological surveys. A slow biomaterial degradation with implantation time is envisaged since the material has displayed surface degradation. Bonelike® scaffolds show potential for complete ingrowth of osseous tissue and restoration of vascularization throughout the defected site.

Keywords: Bonelike®; Porous materials; Bone graft; Orthopaedic

1. Introduction

In the treatment of monocompartmental osteoarthritis of varus knees, high tibial osteotomy (HTO) is considered as to be an effective procedure to reduce pain and control the progression of the disease, delaying more aggressive surgeries as total knee arthroplasties. This effect is based in the reduction of the stress and weight over the affected compartment that is produced when the mechanical axis is transferred from the medial compartment to the junction of the lateral third with the two medial thirds. This corresponds to an alignment of 9–10° valgus. Some authors have demonstrated that one year after a HTO, it is possible to detect radiologically a reduction in the bone density in the medial compartment, thus reflecting a slower progression of the ostheoarthritis [1]. Others have described some degree of histological cartilage regeneration after the joint surface has been unloaded [2].

The closing wedge osteotomy that was used in this study is the most common technique, but recently open wedge procedures have been described with autografts [3], allografts, cement [4] and hydroxyapatite [5]. This second

* Corresponding author. Tel./fax: +351 22 5081419.
E-mail address: jdsantos@fe.up.pt (J.D. Santos).

1742-7061/$ - see front matter © 2007 Published by Elsevier Ltd. on behalf of Acta Materialia Inc.
doi:10.1016/j.actbio.2007.06.009

technique provides a more accurate correction of varus deformity when compared with the conventional lateral closing-wedge HTO, but in a time of great developments in knee arthroplasties, autologous chondrocyte implantation and growth factors, there is still a place for both approaches.

A careful selection of the candidates is essential not only for the success of the surgery but also for the success of a clinical trial aiming to assess a new bone graft substitute. Because bone is a porous tissue material, there is a physiological rationale for the use of porous materials in its replacement. Moreover, porous bone grafts are advantageous for the early incorporation of the graft into or apposed to the bone tissue surrounding it [6–8]. Several key aspects should be considered when designing porous materials for bone grafting [6,9,10]: (i) the size of pores at the surface of the graft, to actually allow for bone to ''flow into'' the graft and fill all of its structure; (ii) the size of porous network connecting the surface pores to allow areas of bony ingrowth to ''meet up'' within the porous graft; (iii) the extent (percentage) of the porosity; (iv) the ability for blood vessels and canaliculi to form within the porosities.

Regardless of the use of porous materials, bone engineering is an area of considerable ongoing scientific exploration, and it seems that the ultimate porous ceramic has yet to be designed. A variety of fabrication methods have been proposed [6,9–19] to produce porous scaffolds with interconnected pore networks, such as the polymeric sponge method or foaming processes, but a general problem is how to control the processing and the ultimate material properties. There is also a new family of forming techniques, known as direct consolidation techniques, which allow generation of complex shapes, but require a good knowledge of the rheological behaviour of concentrated biomaterial suspensions [20–23].

The balance between porosity and initial mechanical strength must be precisely controlled in order to allow the optimal scaffold for each surgical application to be engineered while maintaining the structural parameters necessary for host bone ingrowth. Some controversial issues have arisen regarding the importance of specific structural parameters, such as pore morphology, percentage of porosity, pore connectivity and the strut microstructure, to the biocompatibility of the bone graft [24–31]. For instance, a number of works have suggested [32–35] that the degree of interconnectivity is more critical than the pore size since the vascular network needed for new bone formation or repair is strongly influenced by the degree of structural interconnectivity among pores, whereas other works seem to give the same importance to both parameters.

Despite the fact that nature can be hardly ever reproduced, it is well established that improved mechanical properties of hydroxyapatite (HA) and better chemical similarity between HA grafts and bone can be obtained through liquid phase sintering route using $CaO–P_2O_5$ glasses as a sintering aid; this has been confirmed by extensive published data regarding the development of Bonelike® novel bone graft [36–41]. During the sintering process $CaO–P_2O_5$ glass reacts with HA, forming β-tricalcium phosphate (β-TCP), which then can transform into α-TCP at higher temperatures. The relative proportions of the β- and α-TCP phases in the final microstructure depend upon several experimental factors, including the glass content and composition. Bonelike® has been reported to be osteoconductive and bioactive, supporting the formation of mechanically and chemically bonded bone directly on its surface [42–47]. The bioactivity of Bonelike® is determined by an optimal balance of the least soluble phase of HA and most soluble phase of TCP.

This study aimed at evaluating the biological responses of human bone tissue to porous Bonelike® by implanting cylindrical specimens in the lateral aspect of the tibia of patients with medial compartment osteoarthritis of the knee during osteotomy surgeries.

2. Materials and methods

2.1. Material preparation

Commercial, synthetic, medical-grade HA powder (Plasma Biotal Limited, UK) underwent calcining and milling procedures to yield an average particle size of about 1.5 μm. Well-dispersed aqueous suspensions were prepared with solid loadings as high as 60 vol.% following a deagglomeration procedure, in the presence of a ammonium polycarbonate, as previously described [20,21]. These suspensions were then used to consolidate macroporous cylinders by suitably combining the microstructural capabilities of the foaming method with the shaping capabilities of starch consolidation method, as reported elsewhere [21,22]. Briefly, starch was added to the stock suspension prior the incorporation of the foaming agents, in a proportion of 10 vol.% relative to HA. The amount of foaming agents added was 4 wt.%, relative to the mass of water present in the suspension, and the mass proportion between foam-bath concentrate and sodium lauryl sulphate was 80/20. The final mixtures were poured into a closed mould and consolidated at 80 °C for 1 h to obtain cylindrical samples of 8×10 mm. The samples were demoulded, dried and pre-sintered at 1100 °C for 1 h. These pre-sintered ceramic bodies were impregnated with a glass solution, in optimized conditions as previously described [23], in order to incorporate about 4 wt.% of glass (glass composition used: $65P_2O_5–15CaO–10CaF_2–10Na_2O$ in mol.%), and then sintered at 1300 °C at 4 °C min^{-1} for 1 h.

2.2. Material characterization

The apparent density was evaluated from the weight and dimensions of the samples. Scanning electron microscopy analysis (S-4100, Hitachi, Tokyo) performed on fracture surfaces of the samples was used to characterize the microstructure and qualitatively assess pore size and pore morphology.

ID	Title	Pages
1847	Bone ingrowth in macroporous Bonelike® for orthopaedic applications	8