

Microporosity affects Bioactivity of Macroporous HA Bone Graft Substitutes

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Introduction

The combined affects of an ageing population and greater expectations in quality of life have resulted in an increasing global demand for orthopaedic implants for the replacement or augmentation of damaged bones & joints. In bone grafting current 'gold standards' include the use of autograft (living bone from the patient) or allograft (dead, sterilised bone from bone banks) but these methods are increasingly recognised as non-ideal due to limitations in supply & consistency. Porous ceramics have been considered for use as bone graft substitutes in the treatment of bone defects for over 30 years. In particular, calcium phosphates such as hydroxyapatite (HA) have been promoted as a result of their osteoconductive properties. However, while it is well recognised that both the rate of integration & the final volume of regenerated bone may be primarily dependent on various features of the macroporosity, such as volume fraction, pore size and pore connectivity, recent in vitro studies have demonstrated bone cell sensitivity to the level of microporosity within the ceramic struts. The aim of this study was to investigate the influence of microporosity on early osseointegration within porous HA (PHA) scaffolds.

Materials & Methods

Two batches of phase pure PHA were produced using a novel slip foaming technique, both had total porosities of approximately 80%, but varied in the volume fraction of porosity distributed between their macropore (>50 μ m) & micropore (<20 μ m) populations (Fig. 1a). Morphological characterisation of both the macro- & microporosity was performed through a combination of immersion densitometry & image analysis of serial sections using a Zeiss Axioskop optical microscope linked to a KS300 image analyser. Macropore size, interconnection size & connectivity index (CI), a measure of inter-pore connectivity, were all measured. Both the open & closed % of microporosity within the struts was quantified. Cylindrical specimens 4.5mm in diameter were implanted in the distal femur of 6 month New Zealand White rabbits & retrieved for histological & histomorphometric analysis at 1 & 3 weeks. The volume of new bone ingrowth was calculated using a Weibel grid & the mineral apposition rate (MAR) was determined through the administration of fluorochrome labels at 1 and 2 weeks.

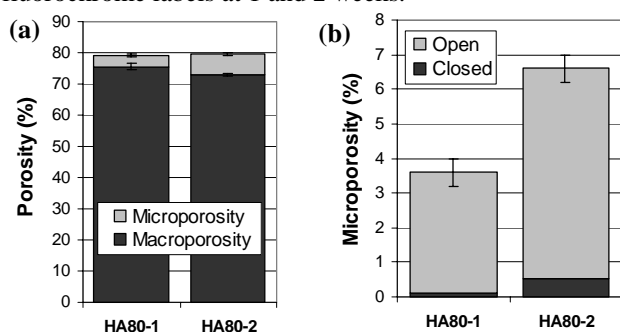


Figure 1 – Porosity distribution of batches HA80-1 & HA80-2

Results

There was no significant difference in the mean pore size, pore interconnection size or connectivity index of the two batches. Modal values of pore size were 150 and 175 μ m for batch HA80-1 & HA80-2 respectively, while 93 & 88% of the total microporosity within the struts of the two batches was confirmed as being interconnected with the macroporosity (Fig 1b) and significantly different in volume between the two batches ($P < 0.05$).

At one week osseointegration of the PHA scaffolds was well progressed, bone apposition was evident within peripheral porosity and neovascularisation was evident throughout HA80-2 and within the deep porosity of HA80-1. However, at 3 weeks there was a distinct variation in the morphology of bone ingrowth within the two scaffolds, with both 'free standing' trabeculae and regions of direct bone apposition on the scaffold struts appearing thicker within HA80-2. These observations were confirmed by histomorphometric evaluation of bone ingrowth within the two batches (Fig. 2). Despite having statistically similar levels of porosity there was a significant difference in the amount of bone ingrowth within the two batches of PHA ($P < 0.05$), & in the MAR of bone deposited between weeks 1 & 2 ($P < 0.01$).

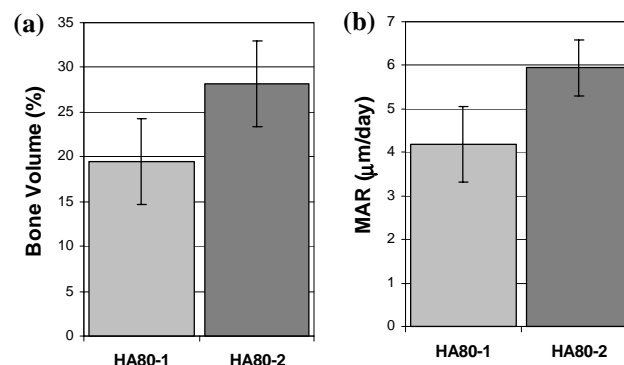


Figure 2 – Variation in the (a) volume & (b) rate of bone ingrowth within the two batches of PHA scaffolds.

Discussion & Conclusions

The results of this study indicate that the bioactivity of PHA scaffolds may be improved by increasing the level of microporosity within the ceramic struts. Possible explanations for this behaviour include variation in the mechanical environment within the scaffolds acting via mechano-transduction on local bone cell activity and/or increased permeability within the more microporous scaffolds acting to up-regulate the process of osseointegration through enhanced nutrient transfer and induction of angiogenesis. Revascularisation is known to be a prerequisite to bone formation in fracture repair. The disparity in capillary penetration within the scaffolds at 1 week suggest that the relative rate of development of the vascular network within the PHA scaffolds may have contributed to the observed variation in bone apposition at these early time points.