

MICROPOROSITY AN IMPORTANT MEDIATOR OF BIOACTIVITY IN BONE GRAFT SUBSTITUTES

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INTRODUCTION

The combined affects of an ageing population & greater expectations in the 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 & allograft 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 to replace or extend traditional bone grafts 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 macro-porosity, such as volume fraction, pore size & 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

Four batches of phase pure PHA were produced using a novel slip foaming technique, two had a total porosity (TP) of 70% & two had a TP of 80%. However, the TP paired batches varied in the volume fraction of porosity distributed between their macropore (>50µm) & micropore (<20µm) populations such that the total strut porosity (SP) was either 10 or 20% (Fig. 1). 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, & both the open & closed % of microporosity within the struts was quantified. Cylindrical specimens 4.5mm in diameter & 7mm long 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 bone ingrowth was calculated using a Weibel grid & the mineral apposition rate (MAR) was determined through administration of fluorochrome labels at 1 & 2 weeks.

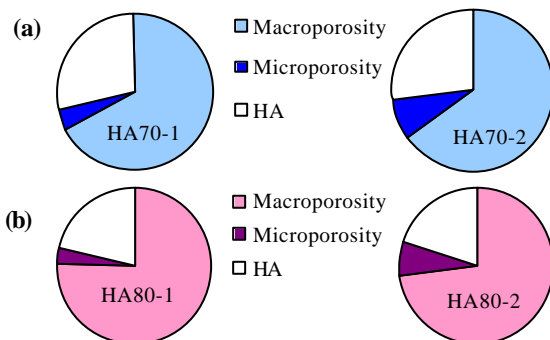


Figure 1 – Porosity distribution of (a) 70% & (b) 80% TP PHA.

RESULTS

There was no significant difference in the mean pore size, pore interconnection size or connectivity index of the paired 70 & 80% TP batches. Modal values of pore size were 150 & 175 µm for batch HA80-1 & HA80-2 respectively, as compared with modal values of 175 and 200µm for HA70-1 & HA70-2 respectively. Over 85% of the total microporosity present within the struts of all four batches was confirmed as interconnected with the macroporosity, while the TP was found to be significantly different between the two sets of paired batches ($P < 0.05$). At one week osseointegration of the PHA scaffolds was well progressed, bone apposition was evident within peripheral porosity & neovascularisation was evident throughout HA80-2, within the deep porosity of HA70-2, HA80-1 & to a lesser extent HA70-1. However, at

3 weeks there was a distinct variation in the morphology of bone ingrowth within the various scaffolds, with regions of direct bone apposition on the scaffold struts appearing thicker within the scaffolds possessing 20% SP. Furthermore, trabeculae of ingrowth observed to have no contact with the scaffold struts within the plane of sample section were common only in the 80% scaffolds, particularly in HA80-2. These observations were confirmed by histomorphometric evaluation of bone ingrowth within the four batches (Fig. 2). Despite having statistically similar levels of porosity there was a significant difference in the amount of bone ingrowth within both the 70 & 80% TP paired batches of PHA ($P < 0.05$), & in the MAR of bone deposited between weeks 1 & 2 ($P < 0.01$) (Fig 2a&b). Furthermore, at a level of 10% SP increasing the level of macroporosity did not significantly affect the MAR or the volume of ingrowth when normalised for the available pore space (Fig 2 b&c), whereas at 20% SP there was a significant improvement in both values with an increase in TP ($P < 0.05$).

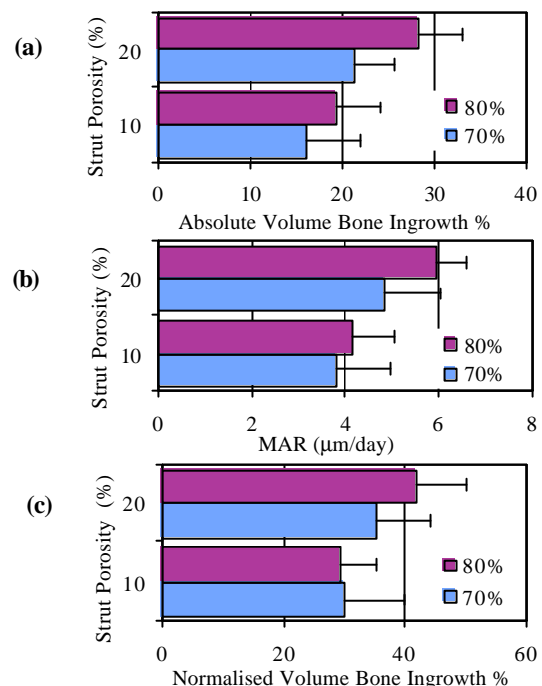


Figure 2 – Variation in the (a) absolute volume %, (b) MAR & (c) normalised volume % of bone ingrowth within 70% & 80% TP PHA.

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 &/or increased permeability within the more microporous scaffolds acting to up-regulate the process of osseointegration through enhanced nutrient transfer & 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 suggests 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. Furthermore, the disparity between the affects of altering TP between scaffolds with 10 and 20% SP suggests that increasing the microporosity had an additive affect on the biological response.

ACKNOWLEDGMENTS

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