

# Bone Development is Sensitive to Silicon Level in Substituted Apatites

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**Introduction** Porous bioceramic alternatives to bone autograft have been under investigation for over 30 years. One group that has received considerable attention are the calcium phosphates, particularly hydroxyapatite (HA), which exhibits similarities to natural bone mineral and is osteoconductive. Another group, the bioglasses are reported to be both osteoconductive & osteoinductive. However, bioglasses are rarely used for large defect filling as a result of their low mechanical properties and rapid rates of dissolution due to the high level of Silica present (45 wt%). Carlisle has identified the presence of Silicon at trace levels in growing bone [1], but not in mature bone, and has suggested that it plays a metabolic role in new bone formation. As a logical extension of these concepts, the metabolic effect of substituting silicate ions into the more stable HA lattice has been studied with the hypothesis that the inclusion of trace levels of silicon via site-specific substitution in a phase-pure hydroxyapatite will enhance the bioactivity of a bone graft substitute.

**Materials & Methods** Four batches of phase pure PSA substituted with 0.2, 0.4, 0.8 & 1.5wt% Silicon were manufactured using novel synthesis[2] and slip foaming techniques[3], with total (TP) & strut (SP) porosities of 74±5% & 26±5%, respectively. Stoichiometric porous HA (PHA) with a TP & SP of 73±1% & 22±2%, respectively, was used as a control. 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 & 6 weeks. The % bone ingrowth was calculated using a Weibel grid & the mineral apposition rate (MAR) was determined by administration of fluorochrome labels at 1 & 2 weeks. Sections were stained with Toluidine Blue & Goldner's Trichrome for histological evaluation.

**Results** At one week bone ingrowth within the 1.5 & 0.8% PSA was more dense in appearance (numerous thick trabeculae) as compared to that within the PSA substituted with 0.4 and 0.2% Si, (numerous thin trabeculae), & PHA (few thick trabeculae). Furthermore, vascular penetration of the PSA scaffolds appeared more advanced, particularly in 1.5 & 0.8% PSA where capillaries were observed through out the scaffolds. After 3 weeks a dense trabecular network had formed within the 1.5 & 0.8% PSA, to the extent that in 2D section some pores within the 0.8% PSA appeared completely filled with bone. Ingrowth within 0.4% PSA was generally sparser, & that within 0.2% PSA was sporadic. A high proportion of the trabecular surfaces of the bone within 0.4 & 0.2% PSA had a scalloped/pitted appearance indicative of osteoclastic/phagocytic activity. Fluorochrome labelling demonstrated that there was little 1 week labelled woven bone within 1.5% PSA as compared to the other scaffolds, while the amount of 2 week labelled lamellar bone was reduced in 0.4 and 0.2% PSA scaffolds. These observations were reflected by the MAR of bone deposited between weeks 1 & 2 (Fig. 1a), where the low

MAR within the 1.5% PSA was a consequence of minimal bone apposition after the first week. At 3 weeks, despite having similar levels of porosity, there was a significant difference in the % bone ingrowth between 0.8% PSA vs PHA, 0.4 & 0.2% PSA ( $P < 0.02$ , Fig 1b). At 6 weeks the % ingrowth within 0.8% PSA was significantly greater than in all other PSA scaffolds ( $P < 0.05$ , Fig 1b). However, ingrowth surfaces in both 0.8 & 1.5% PSA were often occupied by plump osteoblasts or were scalloped indicating regions of both active bone deposition and resorption whereas that within the 0.4% PSA was dominated by scalloped surfaces & ingrowth within the 0.2% PSA was still sporadic. Furthermore, bone within the 1.5 & 0.8% PSA had a more organised, appearance.

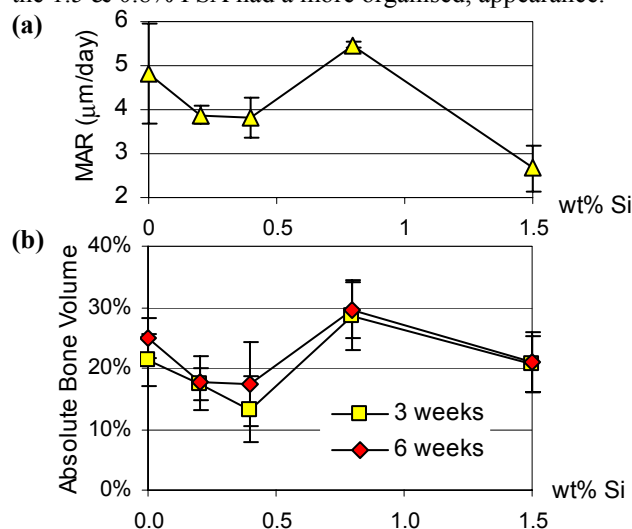


Figure 1 – Variation in the (a) MAR & (b) absolute volume of bone ingrowth within PSA & PHA scaffolds.

**Discussion & Conclusions** The substitution of silicon into the apatite lattice had a significant affect on bone development within the PSA scaffolds. Small additions promoted the rapid apposition of immature woven bone, which subsequently underwent extensive remodelling. Increasing the amount of silicon to ≥0.8wt% appeared to accelerate mature bone formation within the defect site. It was noteworthy that despite the active appearance of bone surfaces at 6 weeks there was no significant difference in the % ingrowth within PSA from 3-6 weeks, suggesting that 'equilibria' bone volumes had been attained at 3 weeks and subsequent activity was devoted to remodelling of the trabecular network, whereas, there was an increase in % ingrowth within the PHA over this period. The significantly higher level of ingrowth in 0.8% PSA as compared to PHA would suggest that where superior bone formation & a rapid assimilation of the scaffold is required the optimum level lies around 0.8 wt%.

## References

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