Silicon-Substituted Calcium Phosphate Biomaterials—The Effect of Strut Porosity on Osteoinduction

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Statement of Purpose: Autologous bone grafts are considered gold standard in the repair of bone defects. However, their supply is limited and they are associated with donor site morbidity. Allografts and xenografts are alternatives but are subjected to processing techniques prior to use and as a result are not as effective. This has led to the development of synthetic bone graft substitute materials and hydroxyapatite has been used successfully in many clinical applications and is reported to be osteoinductive. The chemical composition of the substitute material is important as is the structure, and smaller pores, termed ‘strut porosity’ may also be important for osteoinduction. It has recently been reported that levels of material derived osteoinduction can be predictive of the levels of orthotopic bone formation and therefore our hypothesis was that silicate-substituted calcium phosphate (SiCaP) with increased strut porosity would have greater osteoinductive ability.

Methods: This study investigated the osteoinductivity of two materials: SiCaP granules of 22.5% strut porosity (AF+) and SiCaP granules of 47% strut porosity (AF++). These materials investigated had an identical morphological structure with a macroporosity of 80% but with different levels of strut porosity. The SiCaP scaffolds (wt 0.8%) were phase-pure 80% porous calcium phosphate with a trabecular structure similar to cancellous bone and high levels of interconnectivity between macro pores within the strut porosity. Micropores < 50µm were present in the struts surrounding the macropores in both groups. In each animal, eight implants were inserted into distinct regions along the left and right paraspinals muscles in skeletally mature female commercially cross-bred sheep weighing between 65 and 80kg and aged between 2 and 5 years. All procedures were carried out in compliance with UK’s Home Office regulations (Animal Scientific Procedures Act (1986). Twelve implants were investigated in each experimental group and samples were implanted into the paraspinal muscle mass at the level of L1/L2 or L2/L3. Implants remained in vivo for 8 and 12 weeks and on retrieval, specimens were prepared for undecalcified histology and longitudinal thin sections were prepared through the middle of each implant. Sections were stained with Toluidine Blue and Paragon and examined using light microscopy. Bone formation within the scaffold in the two groups was measured by selection of seven random regions of interest along the length of the implant. Specimens were also analysed using Backscattered Scanning Electron Microscopy (bSEM). The Mann-Whitney U test was used for statistical analysis where p values < 0.05 were considered significant.

Results: Results showed that the mean bone area was greater in the higher strut porosity group (AF++) at 8 weeks (AF+0.2%+/-0.15; AF++0.44%+/-0.12) and significantly higher at 12 weeks (AF+1.33%+/-0.84; AF++6.17%+/-1.51) (p<0.035). The results also showed that the % of graft measured was less in the higher strut porosity group at 8 (AF=39.06%+/-1.26; AF++=33.09%+/-2.14) and 12 weeks (AF=36.05%+/-3.55; AF++=30.60%+/-2.29) and increased %bone/implant contact area was also observed in this group at 8 weeks (AF+1.21%+/-0.99; AF++2.71%+/-0.75) and at 12 weeks (AF=6.99%+/-3.47; AF++=16.72%+/-4.79). Histological examination revealed that i) Bone formation was observed preferentially within the bone graft substitute material rather than at the implant/muscle interface ii) Bone formation appeared to begin concentrically within the macropores in both groups and was preceded by soft tissue concentrations which stained heavily for Toluidine Blue. (iii) Both endochondral and intramembranous ossification were observed in both groups. (iv) Tissue which stained in a similar manner to bone was observed within the implant strut porosity. bSEM showed bone formation within the struts and in pores <15µm in size.

Conclusions: Scaffolds at both strut porosities were osteoinductive and results indicate that a higher strut porosity promotes the apposition of significantly greater amounts of new bone at an earlier time point. This could be attributed to the micropores providing a greater surface area for the action of angiogenic proteins and osteoblasts leading to the formation of blood vessels and bone at an earlier time point. Both endochondral and intramembranous ossification were observed. Endochondral ossification is an unusual finding associated with osteoinductive biomaterials as this is usually associated with bone formation secondary to Bone Morphogenetic proteins (BMPs). This suggests that the osteoinductive mechanisms by silicon-substituted graft materials may involve cytokines such as BMPs. Results indicate SiCaP to be an important bone substitute option available to the surgeon when the successful repair and augmentation of bony tissue is required. This work was funded by Apatech Ltd, Elstree, UK.

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