Osseointegration of a Novel Strontium-substituted Bioactive Glass Implant Coating compared with Hydroxyapatite

INTRODUCTION

Rapid and reliable osseomechanical integration of devices is a highly desirable element of skeletal reconstructive surgery. Surface coating with hydroxyapatite is effective but it is also time consuming and expensive to apply. A more bioactive coating, which induces rapid bone formation and is cheap and simple to apply would have significant attraction, particularly in those areas of the skeleton where the bone-implant interface may be subjected to tension or shear stresses.

Bioactive glasses are ceramics typically with a silica content of 40-45 mol.%. When exposed to physiological fluids, the glasses leach silicon and other cations which help lead to the formation of a silica gel layer onto which hydroxyapatite precipitates. The dissolution products of the glasses have osteoinductive properties, promoting the growth, maturation and activity of osteoblasts [1]. Strontium, taken orally in the form of Strontium Ranelate (Protelos), upregulates osteoblasts and downregulates osteoclasts [2] resulting in increased bone mass as we have demonstrated in a murine model [3]. We have shown similar cellular effects in vitro with Strontium-substituted bioactive glasses [4].

The aim of this study was to investigate the degree of osseointegration and new bone formation associated with a new Strontium-substituted bioactive glass implant coating compared to a commercially available hydroxyapatite coating.

MATERIALS AND METHODS

Implant Preparation: Bioactive glass in the system: SiO₂·MgO·Na₂O·K₂O·ZnO·P₂O₅·CaO, with 50% of the Ca being replaced by Sr, was prepared through a melt-queench technique. TiAlV cylinders 3.6mm diameter and 6mm length were grit blasted with alumina, ultrasonically washed, plasma-sprayed with either hydroxyapatite (Catalyst 30, Plasma Biotal, UK) or Strontium-substituted bioactive glass. Implants were sterilized by gamma-irradiation.

In Vivo Study: Animal experiments were performed under the approval of the UK Home Office. 27 3.5-3.8kg six month old male New Zealand White rabbits underwent bilateral press-fit implantation of cylinders into both the medial femoral condyle and the proximal tibia. A pre-selected randomized limb of each rabbit contained bioactive glass implants, the other hydroxyapatite. Animals were sacrificed at 6, 12 and 24 weeks.

Mechanical Testing: Tibial samples were dissected to completely expose both ends of the implant. Push-out testing was performed using a screw driven Instron machine with a crosshead speed of 1mm/min. Maximal pushout force was measured and a value for maximal shear strength calculated for each sample.

Histology: Femoral samples were fixed in 10% neutral buffered formalin before dehydration in ethanol and embedding in PMMA resin. 15µm undecalcified sections stained with acid fuchsin and methylene blue, were prepared using a diamond saw. Bone-implant contact and bone to total volume for the 6 week post-implantation samples were quantified using Osteomeasure software (Osteometrics, Decatur, GA).

Statistical analysis: Wilcoxon Sign Rank Test was used to compare hydroxyapatite and bioactive glass groups at each time point. Variation between time points was analyzed with the Mann-Whitney U Test.

RESULTS

Implant Preparation and In Vivo Study: Strontium-substituted bioactive glass was produced successfully and milled to produce a powder of similar particle size distribution to the commercially available hydroxyapatite. Bioactive glass and hydroxyapatite implants were successfully produced and sterilized as described previously. Two rabbits were found to have joint effusions at sacrifice (one hydroxyapatite and one bioactive glass) and were excluded, leaving n=8, 9 and 8 rabbits respectively in the 6, 12 and 24 week groups.

Mechanical Testing: Despite the small size of the study, there was a trend for increasing maximal shear strength in push-out tests with the bioactive glass samples between weeks 6 and 24 (p=0.059) which was not replicated in the hydroxyapatite group. No statistically significant difference was found in maximal shear strength between the two groups at any time point (Figure 1). Visual inspection of the implants following push-out showed adherent bone at 6, 12 and 24 weeks in the hydroxyapatite group and 12 and 24 weeks in the bioactive glass group.

DISCUSSION

Hydroxyapatite has been proven to be an effective implant coating for use in total hip arthroplasty. However, it has no significant osteoinductive effect which would be a desirable attribute in patients with reduced bone mineral density. These results show that a Strontium-substituted bioactive glass coating increases peri-implant bone volume in the early stages following surgery. This process aids the osseomechanical fixation of the implant.

Osteointegration is defined as the formation of a direct and functional connection between ordered, living bone and the surface of a load-carrying implant [5]. Measurement of bone-implant contact and pushout testing are established methods for assessing the extent of osseointegration. The results show, on the basis of these parameters, that Strontium-substituted bioactive glass achieves parity with hydroxyapatite in terms of osseointegration. The presence of adherent bone on the hydroxyapatite implants, but not bioactive glass implants, following push-out testing at 6 weeks is noted. This may indicate faster initial osseointegration with hydroxyapatite. However, the similarity in mean push-out test values suggests the superior osseomechanical integration of the bioactive glass implants compensates for this.

These results suggest that in the future Strontium-substituted bioactive glass implant coatings could provide a viable alternative to hydroxyapatite. Further work will quantify the osteoinductivity of this promising new coating in different biomechanical environments.