Bio-resorption of Dicalcium Phosphate Cement Grafts: Brushite vs. Monetite

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Introduction:

Alloplastic biomaterials such as calcium phosphate cements are frequently utilised for a variety of orthopaedic and dental procedures and applications. Dicalcium phosphate dihydrate (brushite) and dicalcium phosphate anhydrous (monetite) are acidic calcium phosphates. Heating brushite (above 60°C) results in conversion to monetite by dehydration; hence brushite can be utilised as a precursor to monetite formation. Although both brushite and monetite are chemically very similar materials, post implantation results differ *in vivo*. Upon implantation, monetite does not to convert to hydroxyapatite (HA), unlike brushite. Monetite also demonstrates osteoconductive and osteoinductive potential. The conversion of brushite to HA after implantation limits the rate and extent of resorption and subsequently affects the replacement of the graft with new bone. As such the differences between bone grafts are attributed to material composition even though surface area and porosity invariably differ. In this study we have produced brushite and monetite grafts (by varying the processing conditions) to observe and evaluate the extent of graft resorption, changes in microstructure and physico-chemical properties upon implantation.

Materials and Methods:

Brushite and monetite ceramics were prepared with varying powder to liquid ratios. In order to produce comparative samples, materials were matched at high and low porosities and surface areas (SSA). Monetite formation conditions were varied (autoclaving and dry heat) to achieve the required physico-chemical parameters. This gave rise to several pairs of graft samples where only one parameter Ksp (solubility product constant), SSA or porosity was altered between brushite-monetite pairs. The grafts were characterised by employing BET surface area analysis, helium pycnometry and X-ray diffraction (XRD) techniques. The prepared bioceramic grafts were implanted subcutaneously (n=6) in rats for up to 8 and 12 weeks and then retrieved and characterised for changes in their microstructure and physico-chemical properties. Resorption of brushite and monetite grafts implanted subcutaneously was calculated and compared. Ethical approval was taken and animal protocol approved by the McGill University animal ethics review board. Statistical analysis was performed using the statistical software IBM®SPSS® (v.19, IBM SPSS Inc., Chicago, IL). Statistical significance ($p < 0.05$) between groups was determined by non-parametric analysis using *Wilcoxin sign rank test* ($\alpha = 0.05$).

Results:

As seen in Table 1. brushite and monetite grafts were produced with combinations of high or low porosity and with high and low SSA. Given the chemical similarity between brushite and monetite this enabled study of the effect of small changes in Ksp between brushite and monetite (2.77×10^{-7} and 1.26×10^{-7} mol^2/l^2 respectively), and within material comparisons of the effect of porosity and surface area. After subcutaneous implantation, all brushite and monetite cements demonstrated a significant increase in their percentage porosity. XRD analysis revealed that the brushite grafts demonstrated phase conversion at their surface to octacalcium phosphate (OCP) and HA after 12 weeks *in vivo* (but not 8 weeks). Analysis of the core of brushite grafts did not reveal any phase conversion. Phase conversion was not observed for any of the monetite grafts after 8 and 12 weeks of implantation (surface or core). The phase conversion of the surface layer limited the extent of resorption for both high and low porosity brushite grafts *in vivo*. All prepared monetite grafts resorbed to a greater extent and did not convert to OCP and HA when compared with brushite grafts for similar time periods *in vivo*. Interestingly, monetite grafts which were produced by autoclaving preset brushite showed greater resorption (30% and 48% for 3:1 and 1:1 P/L ratio grafts respectively) in comparison to the dry heat converted monetite grafts (24% and 39% for 3:1 and 1:1 P/L ratio grafts respectively) after 12 weeks of implantation. This can be attributed to the higher percentage porosity observed in the autoclaved monetite grafts.

Table 1. Summary of bioceramic properties with high porosity (55-75%), low porosity (30-50%) and high (18-22 m^2/g) and low (0.5-1 m^2/g) specific surface area (SSA).

Material	% Porosity	SSA
$CaHPO_4.2H_2O$	High	Low
	Low	Low
$CaHPO_4$	High	High
	High	Low
	Low	High

Discussion:

For the implanted bioceramics with high and low porosity neither solubility nor SSA played a significant role in the *in vivo* resorption. We conclude that resorption is dependent upon the initial porosity present. The results obtained from this study lays down the ground work for further investigation using further *in* orthotopic implantations to obtain a better understanding of the resorption processes and hence improving graft function *in vivo.*