A COMPARATIVE STUDY OF THE BIODEGRADABILITY OF CALCIUM-ALKALI-ORTHOPHOSPHATE CERAMICS IN VITRO AND IN VIVO

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Introduction

This study compares an in vitro method for evaluating the biodegradability of novel calcium-alkali-orthophosphate ceramic particulates - by using solubility measurements - to histomorphometric evaluation of the biodegradability of these materials by determining the decrease of particle size in histological sections which were obtained subsequent to implantation in vivo using a sheep model.

Material and Methods

The solubility of the test materials: GB14, GB9 and GB9/25 particulates (grain size 355-400 µm), which were fabricated using reagent grade $CaHPO_4$, Na_2CO_3, K_2CO_3, $MgCO_3$, SiO_2 and H_3PO_4, was determined by immersion in TRIS buffer solution 0.1M (pH7.4, 37°C) according to DIN ISO EN10993-14 for periods up to 15 weeks in order to extend the in vitro study over a time period which would be comparable to the implantation period in vivo.

Furthermore, an *in vivo* study was performed, in which the same bone substitute materials were implanted in the sheep mandible to regenerate membrane protected critical size defects as described by von Arx et al. After 4, 12 and 24 weeks of implantation the mandibles were harvested and the augmented sites were processed for histological evaluation.

Results and Discussion

The findings of the in vitro immersion studies suggest that the biodegradation or resorption process of these calcium-alkali-orthophosphate materials is diffusion controlled. This is in contrast to the degradation process encountered with TCP particulates which exhibit a more uniform solubility. However, the grain size of the particulates did hardly change over the 15 week immersion period. This was in contrast to the in vivo findings, in which a considerable decrease of particle size was noted.

However, the morphological appearance of the residual granules observed after 12 weeks of implantation in the sheep mandible was similar to that of the leached particles which were obtained after 15 weeks of immersion in TRIS buffer solution, indicating that extensive leaching as well as dissolution and reprecipitation phenomena had occurred in the centre of the particles. The differences, which were observed with respect to particle size between the in vitro and in vivo setting, might be related to the presence of an array of proteins which are present in the in vivo settings. Immersion experiments, in which immersion of bioactive ceramics in protein-free solutions was compared to that in solutions which contained serum-proteins, demonstrated that the surface structure morphology of the surface reaction layer that forms due to dissolution and reprecipitation phenomena was significantly different when serum-proteins were present. Furthermore, the reaction kinetics were significantly influenced by the presence of serum proteins. Consequently, studies to elucidate the surface transformations of these novel bioactive calcium-alkali-orthophosphate ceramics and the protein adsorption events associated with immersion in biological fluids are currently underway.