

MOLDABLE PUTTY-LIKE RESORBABLE CALCIUM ALKALI PHOSPHATE BONE SUBSTITUTE CEMENTS FACILITATE RESTORING CONTOURS IN CRANIOFACIAL SURGERY *IN VIVO*

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ABSTRACT

This study evaluates the effect of four novel putty-like calcium alkali orthophosphate (CAOP)-based bone substitute cements on bone regeneration and expression of osteogenic markers after implantation in contour defects in the sheep mandible for 1, 3, 6, and 12 months. This was in addition to examining the biodegradability. These materials were developed in order to create putty-like moldable biodegradable bone substitute cements for restoring outer contours in craniofacial surgery that degrade, but still stimulate osteogenesis at the same time, thereby resulting in bone repair and regeneration with fully functional bone tissue. A tricalcium phosphate (TCP) putty material served as reference material and empty defects as controls. With the 401545-Z and 401545(70)-Z cements, based on the main crystalline phase $\text{Ca}_{10}[\text{KNa}](\text{PO}_4)_7$, shrinkage during setting and implant loosening or loss occurred in 50% of the cases. Of the four CAOP cements studied, GB9-Z and GB14-Z, which had the crystalline phase $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$ and a small amorphous portion containing magnesium potassium phosphate or silica phosphate, displayed excellent surgical handling and setting properties. They also had the greatest stimulatory effect on bone formation, expression of osteogenic markers, and best bone bonding behavior, while exhibiting the highest biodegradability among the tested cements. It was lower than that of the TCP putty, which was a non-setting material with higher porosity containing TCP granules. The TCP-putty, however, did not fulfill its space maintaining function, and therefore did not facilitate restoration of the outer bony contour of the mandible. GB9-Z and GB14-Z, in contrast, facilitated excellent tissue integration and excellent restoration of the outer bony contour without and resorption after 1 year. As a result, GB9-Z and GB14-Z are promising bone grafting materials for reconstructing contour defects in craniofacial surgery.

Keywords: bone substitutes, calcium alkali orthophosphates, resorbable, bone substitute cements, bioactive, bone regeneration, osteogenesis, contour defects, craniofacial, mandible

INTRODUCTION

Although autogenous bone grafts are currently the standard of care for bone reconstruction, bone substitute materials are extensively studied in order to avoid harvesting autogenous bone. To fill bone defects, calcium phosphates are mainly applied as granules. For restoring outer contours in craniofacial surgery, however, putty-like moldable bone substitutes with improved surgical handling properties are needed, which can be molded into the desired shape intraoperatively, then subsequently set in situ and also maintain the augmented bone volume over time. Over the past decade various bioactive calcium phosphate cements have been developed. In most cases hydroxyapatite is formed during setting, which limits their biodegradability [1]. More recent developments include cements, which form calcium alkali phosphates (CAOP) during setting, which have been shown to have a stimulatory effect on osteogenesis *in vitro* [1,2], and *in vivo* [1,3]. These cements are designed for higher biodegradability. This study evaluates the effect of four novel putty-like CAOP-based bone substitute cements on bone regeneration