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In vivo comparison of two hydraulic calciumphosphate cements in a drill hole model in sheep

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INTRODUCTION: Synthetic bone replacements are used to fill bone defects in orthopedic surgery as blocks, granules and recently also as injectable hydraulic cements.[1, 2] Especially the latter have an interesting potential due to the possibility to mold its form according to the clinical situation. These types of cements may be distinguished into hydroxyapatite (PHA) and dicalciumphosphate-dihydrate (DCPD) (also called brushite cements), which mainly differ in their resorption behavior. While PHA based cements resorb slowly over a period of many months, brushite cements are resorbed faster and thus, are supplemented with the addition of á-tricalcium phosphate granules. The granules provide a nidus or crystallization point for new bone deposition. In this study a commercially available injectable PHA-based cement (Biobon®) was compared to a newly developed brushite cement (chronOS inject™) placing emphasis on ease of application, biocompatibility and its resorption behavior over time.

MATERIAL AND METHODS: Biobon® and chronOS inject™ were applied into a drill hole defect (8mm in Ø, 13mm in length) in the proximal and distal femora and humeri of 10 female, skeletally mature sheep in a randomized fashion. Each sheep had 3 holes filled with Biobon®, 3 with chronOS inject™ and 2 holes were left empty as controls. The cements were filled into the defects and the tissue was closed after hardening of the cement (Biobon® 3min, chronOS inject™ 12 min). Animals were sacrificed at 2,4,8,16 and 24 weeks after surgery. Macroscopical assessment was followed by preparation of the bone specimens for histology where sections were embedded in plastic sections. Thick or ground sections stained with toluidine blue were used to calculate the percentage of new bone formation, fibrous tissue and remaining cement, while thin or 5µ sections stained with toluidine blue or von Kossa/McNeal served to study cellular reactions within the tissue.

RESULTS: chronOS inject™ was easier to apply than Biobon®, i.e. it bonded nicely to the adjacent bone matrix, did not mix with blood within the wound area but rather pushed it out of the drill hole. In addition, the application device of chronOS inject™ was better. At sacrifice inflammation of the adjacent soft tissue was observed in the early specimens at 2 weeks with the chronOS inject™ whereas in Biobon® this was noticed up to 4 months, similar to the controls. In the histological sections, significant differences were seen in cement resorption and new bone formation ($P<0.05$) such that Biobon® was almost unchanged 24 weeks after surgery with only minor new bone formation within the cement cracks. This was in contrast to chronOS inject™ where already 2 weeks after surgery a small seam of osteoblasts was noticed at the periphery and at 24 weeks almost the entire cement was replaced with new bone. On a cellular level also major differences were found between the two cements. chronOS inject™ was resorbed continuously over time by macrophages, whereas Biobon® was subjected to osteoclast activity. In addition, foreign body cells and active bone remodeling were noticed in the adjacent bone matrix in Biobon®, which was not the case in chronOS inject™.

CONCLUSION: chronOS inject™ proved to be suitable as bone cement for orthopedic surgery and was superior to Biobon® in regard of biocompatibility, speed of new bone formation and cement resorption.

1. **Bohner M, Theiss F, Apelt D, et al.** Compositional changes of a calcium phosphate dihydrate cement after implantation in sheep. *Biomaterials*. 2002;*in press*.
2. **Bohner M.** Calcium orthophosphates in medicine: from ceramics to calcium phosphate cements. *Injury*. 2000;31:S D37-47.