Evaluation of four biodegradable, injectable bone cements in an experimental study in sheep

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Introduction: Injectable calcium phosphate bone cements have been proven to be valuable bone substitutes in long bones[1]. As any other transplant in bone they are replaced by "creeping substitution"[2] and the speed of resorption is dependent on their composition. Cements based on carbonated apatite (CA) resorb much slower compared to others based on a final composition of brushite [dicalcium phosphate dihydrate (DCPD)]. Both types showed excellent results, the latter especially if used as biphasic cements combined with TCP-granules[1,3]. The goal of this study was to test CA cement enriched with synthetic fibers and a cement of DCPD combined with TCP fragments of the same composition but different shape compared to chronOS™Inject spheres. In addition, cement resulting in DCPD alone and a calcium sulfate cement were used for comparison. Apart from biocompatibility issues, the study was based on the hypothesis that the *i)* synthetic fibers would improve the mechanical properties of the CA cement, *ii)* the shape of the TCP granules would alter the resorption behavior of the DCPD, *iii)* resorption properties of the four types could be utilized according to medical indications and local properties of the implantation site.

Materials & methods: Four groups of cements were made: 1) DCPD matrix alone, 2) DCPD incorporating TCP fragments, 3) HA cement enriched with synthetic fibers, and 4) calcium sulfate cement (Plaster of Paris). All cements were implanted in epiphyseal and metaphyseal, cylindrical bone defects of 9 experimental sheep[4]. Animals were followed for 2, 4 and 6 months. Qualitative, semi-qualitative and quantitative evaluation of the cement samples was performed for macroscopic and radiographic appearance, cellular reaction, cement resorption, new bone formation and remodeling. Non-decalcified bone samples containing the original defects were embedded in plastic sections (PMMA). Ground sections were surface stained with toluidine blue, thin (5µm) sections with TB and von Kossa /McNeal to document calcification.

Results: All four cement types showed good biocompatibility and differed mainly in their resorption time. Calcium sulfate was the fastest to be resorbed almost completely at 2 months, and showed variable amounts of new bone formation over all time periods. The two DCPD cements in contrast were slowly degraded to a large extent over 6 months, whereas the apatite cement was almost unchanged over time. Macrophages were responsible for cement resorption with the DCPD and calcium sulfate and osteoclasts for the CA cement.

Conclusion: The fast resorption time of some calcium phosphates cements may render them suitable as drug delivery system in specific applications, the DCPD cements showed similar behavior, but no real advantage to the already available chronOS™Inject cement, and the addition of synthetic fibers to the CA cement improved the quality for long term applications in cases, where mechanical stability may be an issue.

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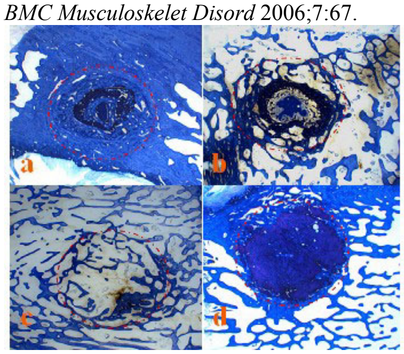

Cements shown at 6 months: a) DCPD, b) DCPD/TCP, c) calcium sulfate, d) CA enriched with synthetic fibers. The red circle indicates the original defect.