Bone Regeneration with Calcium Sulfate/ Poly (l lactic acid) Composites

S. Mamidwar[1], M. Weiner[2], A. Yampolsky[2], J. L. Ricci[2], H. Alexander[1]
[1]Orthogen Corporation, Springfield, NJ, [2]Dept. of Biomaterials and Biomimetics, NYU College of Dentistry, New York, NY

Introduction: Calcium sulfate (CS) has been used as a bone graft material since 1892. It is completely biodegradable, biocompatible, osteoconductive and nontoxic. It also possesses certain properties that no other bone graft materials possess: It is angiogenic [1] and works as a hemostat and a guided tissue regeneration membrane. However, it undergoes rapid dissolution, and in some cases, especially in large defects, it is completely degraded before bone has grown into the defect area. Hence, we developed composites of CS and poly l (lactic acid) (PLLA) with time tailored degradation rates. PLLA is also used in bone grafting applications on its own and as part of composites and is biocompatible and biodegradable. In vitro studies have shown that CS/PLLA composites undergo slower degradation than pure CS, with the rate of degradation decreasing as the ratio of PLLA: CS in composite increases [2]. Calcium phosphate forms as this composite degrades. Different forms of CS/PLLA composite, called Time Release Calcium Sulfate (CSTR) were manufactured. In vivo bone response to these composites is presented in this work.

Materials and Methods: Three CSTR materials were studied. CSTR1: PLLA solution (PLLA dissolved in methylene chloride) was sprayed on calcium sulfate powder in a rotating drum to form 425-600 micron CSTR particles. PLLA mixed with the CS powder as well as coated the pellets in this process. (ratio of CS: PLLA = 96:4). CSTR2 and CSTR3: Pure CS pellets (500 micron) were coated with PLLA solution to form CSTR2 (ratio of CS: PLLA = 93:7) and CSTR3 (ratio of CS: PLLA = 87:13). Twenty-six New Zealand white rabbits were used in this study. Defects were created in the tibial intramedullary canals of New Zealand White rabbit and were packed with the CSTR materials. Animals were sacrificed at 4, 8, and 16 weeks. Sections of the bone where composite was implanted were removed and studied by Faxitron x-ray analysis, microCT and histology. The resulting sections were further characterized by scanning electron microscopy and X-ray microprobe analysis.

Results: CSTR materials underwent slower degradation in vivo than pure CS pellets. At 4 weeks, most of the CSTR materials showed minimal to no degradation on x-ray and microCT. MicroCT showed, and histological sections confirmed, formation of calcium phosphate towards the periphery of CSTR pellets at 4 weeks. Histological sections also confirmed mostly intact CSTR pellets at 4 weeks. By 16 weeks, CSTR1 underwent major degradation. Bone formed in the area (which is seen on the x-ray and microCT) that was filled with the CSTR1 composites. MicroCT showed up to 22% bone formation in these defects. CSTR2 also underwent major degradation by 16 weeks, however not much bone or calcium phosphate was observed in the defects. However, CSTR3 pellets hardly underwent any degradation even after 16 weeks. Intact pellets were seen on x-ray. No adverse reaction to any of the composite was observed. Pure CS pellets were completely degraded only at 4 weeks with minimal calcium phosphate formation in the defects.

Discussion: CSTR composites underwent slower degradation as compared to pure CS pellets in vivo. Calcium sulfate and PLLA were mixed together in CSTR1 while PLLA was coated onto CS pellets in the CSTR2 and CSTR3 groups. CSTR1 underwent slower degradation, allowed bone formation and elicited no adverse reaction. CSTR2 underwent slower degradation, but did not result in bone formation. CSTR3 did not undergo any degradation even after 16 weeks.

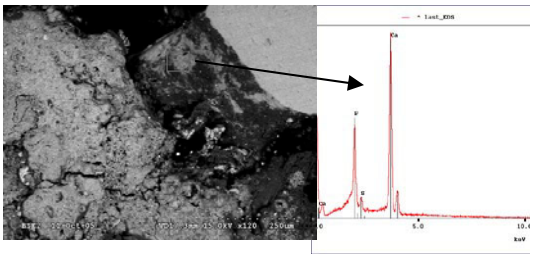

Fig 1: SEM of CSTR1 at 4 weeks. Corresponding spectrum of interface shows presence of calcium phosphate.

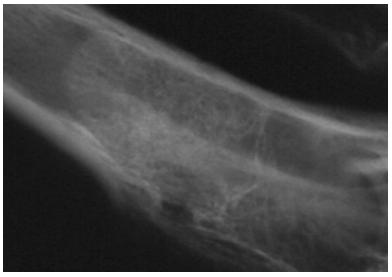

Fig 2: Faxitron X-ray of CSTR1 at 16 weeks. Trabecular bone formation is observed.

Conclusions: 1. CSTR composites undergo slower degradation in vivo as compared to pure CS. 2. No adverse reaction to CSTR composites in vivo is observed. 3. "Mixed" composite (CSTR1) elicit better and more efficient bone response as compared to "coated" composites (CSTR2 and CSTR3).

References:

1. Strocchi, J Oral Impl, 2002, 28, (6), 273-8.
2. Mamidwar, SFB Transactions, 2002, 34.