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Vergleichende Untersuchung zur Biokompatibilität von MgCa0.8 und chirurgischem Stahl 316L: Eine in vivo Studie am Kaninchen
Comparative Characterisation of the Soft Tissue Biocompatibility of MgCa0.8 and Stainless Steel 316L: An in vivo Study in Rabbits

Introduction
Magnesium alloys are promising candidates for an application as biodegradable implants [1]. Information concerning the biocompatibility of an implant material is obtained by studying the reactions at its interface to adjacent tissue. MgCa0.8 generally showed good biocompatibility [2], however little is known about its interaction with muscle tissue. Therefore, aim of the present study was to compare MgCa0.8 and commonly used surgical steel concerning their reactions at the interface to skeletal muscle in vivo.

Materials and Methods
Magnesium calcium alloy (MgCa0.8) and stainless steel (S316L) screws of identical geometries were implanted into the tibiae of adult rabbits slightly proximal of the tibial insertion. Daily clinical and weekly radiographical examinations were performed. After a follow up of 2, 4, 6 and 8 weeks the animals were sacrificed. The tibialis cranialis muscle was embedded in paraffin as it was adjacent to the screw head. Sections of 2-3 μm were stained for histology (H.E.) and immunohistochemically. Macrophages, giant cells and heterophils were differentiated on H.E. sections according to their morphology as well as fibrosis and necrosis. Mouse anti-CD79a (HM 47/ A9, Acris) and rat anti-CD3 (CD3-12, Serotec) monoclonal primary antibodies were used for B- and T-lymphocyte detection. Evaluation of all sections was performed applying a semi quantitative score.

Results
Clinically, both implant materials were tolerated well. Neither infections nor other adverse reactions occurred during the postoperative follow up. Regarding MgCa0.8 low to moderate subcutaneous emphysema was clinically and radiographically detected at the implantation site of all animals from the first week after surgery. Evaluation of H.E. sections revealed that a layer of fibrous tissue had formed between implant and overlying muscle in MgCa0.8 and S316L, which contained cellular infiltrations of macrophages, giant cells and heterophils as well as areas of necrosis. The fibrous tissue was demarcated by an epithelium consisting of synoviocyte-like cells at its point of contact to the implant. In case of MgCa0.8 also cavities were found within the connective tissue, which were surrounded by the same kind of epithelium. Throughout the follow up the thickness of the fibrous layer as well as the amount of necrosis and cellular infiltrations continuously decreased in S316L. In contrast, a decrease could only be noted in the first weeks of implantation in MgCa0.8, whereas parameters were increasing again at the end of the observation period. B- and T-lymphocyte detection revealed that both cell types only occurred in low numbers. B-lymphocytes were found more often in MgCa0.8 showing the same tendency as described above: decreasing in number in the first weeks of implantation and increasing again after eight weeks. In S316L B-lymphocytes barely occurred, thus no B-cell could be detected after eight weeks. In contrast, S316L showed a higher quantity of T-lymphocytes than MgCa0.8, which was continuously decreasing with increasing implantation time.

Discussion
Moderate chronic inflammation was present in both groups 2 weeks after surgery. The main difference between MgCa0.8 and S316L revealed to be the involvement of the immune system. In S316L cell-mediated immunity was predominant as mainly T-lymphocytes were found and B-lymphocytes barely occurred. In contrast, a higher quantity of B-lymphocytes was detected in MgCa0.8 indicating humoral immunity and the presence of soluble antigens. No difference could be observed concerning the grade of inflammation indicating comparable biocompatibility for MgCa0.8 and S316L. Wound healing lead to a gradual decrease of inflammation in S316L throughout the follow up. The same tendency was shown for MgCa0.8, however, only in the first weeks of implantation. At the end of the observation period inflammation was increasing again, which might be caused by intensified degradation of MgCa0.8. To observe the development of inflammation it would be of particular interest to investigate MgCa0.8 over a longer implantation period additionally to the present study.

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