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Osteosynthesis of a cranio-osteoplasty with a biodegradable magnesium plate system in miniature pigs

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ABSTRACT

Biodegradable magnesium alloys are a new class of implant material suitable for bone surgery. The aim of this study was to investigate plates and screws made of magnesium for osteosynthesis in comparison to titanium in a cranial fracture model. Implants were used for internal fixation of a cranio-osteoplasty in nine minipigs. Computed tomography was conducted repeatedly after surgery. The implants and the adjacent tissues were harvested 10, 20 and 30 weeks after surgery and investigated by micro-computed tomography and histological analysis. The surgical procedure and the inserted osteosynthesis material were well tolerated by the animals, and the bone healing of the osteoplasty was undisturbed at all times. The adjacent bone showed formation of lacunas in the magnesium group, resulting in a lower bone-to-implant contact ratio than that of titanium (72 vs. 94% at week 30), but this did not lead to clinical side effects. Radiological measurements showed no reduction in osteosynthesis material volume, but indicated signs of degradation: distinct volumes within the magnesium osteosynthesis group had lower density in micro-computed tomography, and these volumes increased up to 9% at week 30. The histological preparations showed areas of translucency and porosity inside the magnesium, but the outer shape of the osteosynthesis material remained unchanged. No fracture or loosening of the osteosynthesis devices appeared. Soft tissue probes confirmed sufficient biocompatibility. Given their biodegradable capacity, biocompatibility, mechanical strength and visibility on radiographs, osteosynthesis plates made of magnesium alloys are suitable for internal fixation procedures.

Statement of Significance

To the best of our knowledge this is the first study that used biodegradable magnesium implants for osteosynthesis in a cranial fracture model. The cranio-osteoplasty in miniature pigs allowed *in vivo* application of plate and screw osteosynthesis of standard-sized implants and the implementation of surgical procedures similar to those conducted on human beings. The osteosynthesis configuration, size, and mechanical properties of the magnesium implants within this study were comparable to those of titanium-based osteosynthesis materials. The results clearly show that bone healing was undisturbed in all cases and that the biocompatibility to hard- and soft tissue was sufficient. Magnesium implants might help to avoid long-term complications and secondary removal procedures due to their biodegradable properties.

1. Introduction

Today, open reduction and internal fixation is the gold standard for the treatment of most cases of cranio-maxillofacial trauma surgery [1]. Current plate osteosynthesis systems, consisting of plates and screws, are available in a multitude of sizes and configurations for the fixation of a variety of indications [2] and are often made of high-purity titanium or titanium alloy Ti6Al4V [3]. Plate and screw systems are also used in orthognathic surgery and augmentation procedures. In the implant field, titanium is considered to be a non-degrading metal that provides excellent biocompatibility

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due to its bioinert properties, among others. In general, the mechanical properties of titanium allow designing minimal dimensions to the corresponding osteosynthesis implants. However, there is a controversial discussion of whether the removal of Ti-based implants is required once bone healing is completed [4–6]. Reported complications are exposure, infection, loosening of the implants and foreign body sensations [7]. The complication rate for Ti-based implants ranges from 3% to 25% and is dependent on the location and the amount of inserted osteosynthesis material [4,8]. Another adverse effect that has been reported in permanent implants is stress shielding, which leads to osteopenia of the affected bone. However, most of the removal procedures have been conducted due to the wishes of patients to live without residual osteosynthesis material. To avoid long-term complications and secondary removal procedures, the use of biodegradable osteosynthesis implants is required [9].

In the past, degradable polymers, such as polylactic acid (PLA) and polyglycolic acid (PGA), were used for internal fixation procedures. The composition of the copolymer influences the stability and degradation kinetics [10], but in general, these copolymers are much weaker than the metals currently used for osteosynthesis [11]. Thus, the size (surface area) of polymer-based implants must be larger to withstand the same loads as common metal implants [12,13]. Degradation of the polymers is mainly characterized by an acidic hydrolysis [14], which has been proven not only to negatively affect bone healing but also to lead to wound healing disorders [15] and foreign body reactions [16,17]. In a clinical trial investigating plates of a biodegradable polymer blend in maxillofacial trauma and orthognathic surgery, the rates of complications and removal procedures were significantly higher than those in the group that received titanium osteosynthesis [18]. Due to these disadvantages, polymers have not been used in maxillofacial surgery on a routine basis yet. These days, the use of biodegradable polymers is limited to certain non-load bearing applications and in the growing skeleton [19,20].

Recently, different types of magnesium alloys have been developed for use in biodegradable and temporary implants. Magnesium is considered being an excellent base material for biodegradable metallic implants, as humans generally show a high daily demand for magnesium before exceeding the element's toxicity limit [11,21]. As pure magnesium does not possess adequate strength properties for most clinical applications, various alloys have been developed, including calcium, zinc, zirconium and rare earth elements as suitable strength-increasing alloying elements [22,23]. The overall composition of Mg alloys significantly influences their strength and degradation properties [24,25]. The strength properties of magnesium alloys are considered superior to those of polymers [11] but remain lower than those of titanium and its alloys while being similar to those of human cancellous bone [26]. Current magnesium alloys possess tensile strengths (ts) ranging from 140 MPa to 550 MPa, pure titanium possess tensile strengths ranging from 240 MPa to 550 MPa, depending on its grade, the titanium alloy Ti6Al4V shows a ts of approx. 860 MPa and biodegradable polymers of up to 150 MPa in bulk condition respectively [11,27,28]. Since Mg and its alloys possess lower strength properties compared to some of the currently applied Ti-based materials one would expect that osteosynthesis-plates, designed for cranio-maxillofacial trauma-surgeries, will be slightly thicker in order to stand the same loads. However, this implies that currently available implants are specifically designed for use in cranio-facial-surgeries. A multitude of *in vitro* studies report on degradation kinetics suitable for osteosynthesis applications and excellent biocompatibility properties in a physiological environment [29,30]. *In vivo* studies using pins made of the alloy AX30 or ZEK100 have reported favorable degradation characteristics, but they induce adverse host reactions, namely, an osteoclast-driven resorption of bone and a subsequent periosteal formation of new bone [31]. Investigations with screws inserted in the mandible of rabbits showed Mg alloy screws degraded at varying rates depending on their location within the bone, whether the screw was in the cortical bone, the marrow space or the muscle [24]. Implanting rods made of Mg-Y-Nd-RE into the femoral bone of rats led to higher bone-implant contact and increased the bone-implant interface strength more than the titanium controls [32]. The degradation of magnesium and its alloys follows a surface-corrosion type resulting in magnesium hydroxide and hydrogen gas byproducts according to the reaction equation $Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2$ in the first stage [33,34]. The byproducts further react with physiological compounds in the vicinity and favor an environment that promotes the growth of new bone [35,36]. Due to the products resulting from its degradation, magnesium's degradation is considered alkaline [34], in contrast to the acidic degradation of polymers [37,38]. The release of hydrogen gas in general has to be adequately compensated, as an excess release has been reported to interfere with tissue healing, finally forming emphysema at the implant site [35,39,40]. Thus, current approaches in the development of magnesium-based biomaterials have focused on the modification of the alloys or their processing to further reduce gas release, among other modifications [41,42].

At present, osteosynthesis materials made of magnesium alloys are already used in orthopedic surgery. In several countries, compression screws and pins successfully passed approval and are now used for intraosseous fixations, such as in hallux valgus surgery and the fixation of scaphoid fractures [43,44]. Generally, these devices are fully anchored in bone and thus are mostly surrounded by hard tissue.

In maxillofacial surgery, implants are usually applied in the form of plate and screw systems, resulting in an altered tissue-to-implant contact situation. In such a case, the material remains not only inside the bone tissue but also on the cortical bone, staying in contact with the periosteum and further surrounding soft tissue. Plate osteosynthesis systems are multi-component devices that create further challenges in terms of new degradation parameters. As an alloy-to-alloy contact arises between the plates and screws, additional corrosion types, such as contact corrosion or crevice corrosion, must be expected [33].

In 2015, Chaya et al. reported on a fracture fixation using a pure magnesium plate/screw system in a small-animal ulna fracture model. The device degradation did not inhibit fracture healing and enhanced bone formation around the devices [45,46]. In the field of craniofacial surgery, only one published animal study exists that reports on the use of magnesium-based plate osteosynthesis in pigs, indicating a general lack of studies in this field. Within this study, plates and cortex screws manufactured from the alloy WE43 were inserted in the frontal bone without any osteotomy for 12 and 24 weeks, respectively. The authors did not detect major complications, but gas pockets to the soft tissue occurred, and the bone-to-implant contact was lower than in the titanium control. Based on their results, the authors predict that the further development of magnesium-based plate osteosynthesis systems are promising and are indeed of great clinical interest [47].

In the present study, we aimed to investigate the performance of plates and screws manufactured from a biodegradable magnesium alloy in a cranio-osteoplasty model in miniature pigs. The underlying hypothesis is that magnesium-osteosynthesis is equal to titanium in terms of bone healing and biocompatibility to the adjacent tissues, while the degradable property is an advantage in clinical application to avoid removal procedures.