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In vivo degradation of magnesium plate/screw osteosynthesis implant systems: Soft and hard tissue response in a calvarial model in miniature pigs

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ABSTRACT

Biodegradable magnesium plate/screw osteosynthesis systems were implanted on the frontal bone of adult miniature pigs. The chosen implant geometries were based on existing titanium systems used for the treatment of facial fractures. The aim of this study was to evaluate the in vivo degradation and tissue response of the magnesium alloy WE43 with and without a plasma electrolytic surface coating. Of 14 animals, 6 received magnesium implants with surface modification (coated), 6 without surface modification (uncoated), and 2 titanium implants. Radiological examination of the skull was performed at 1, 4, and 8 weeks post-implantation. After euthanasia at 12 and 24 weeks, X-ray, computed tomography, and microfocus computed tomography analyses and histological and histomorphological examinations of the bone/implant blocks were performed. The results showed a good tolerance of the plate/screw system without wound healing disturbance. In the radiological examination, gas pocket formation was found mainly around the uncoated plates 4 weeks after surgery. The micro-CT and histological analyses showed significantly lower corrosion rates and increased bone density and bone implant contact area around the coated screws compared to the uncoated screws at both endpoints. This study shows promising results for the further development of coated magnesium implants for the osteosynthesis of the facial skeleton.

1. Introduction

Over the last two decades, biodegradable materials have increasingly been used for bone fixation in orthopaedic surgery. The cranio-maxillofacial (CMF) region is an area that is generally considered suitable for osteosynthesis using biodegradable materials because the midfacial and cranial bones require only a low load-sharing fixation, and subsequent removal of the plates and screws is often not desirable (Thorén et al., 2008). The first resorbable polymers for CMF surgery were introduced in the 1980s (Suuronen et al., 2004). Today, most of the biodegradable fixation devices in clinical use consist of polylactide (PLA)–based co-polymers. Several such polymer-based osteosynthesis devices of various configurations and mechanical properties are available on the market. Modern, amorphous second-generation PLA-based systems are well established and accepted in cranio-facial paediatric indications, e.g., for craniosynostosis (Guzman et al., 2011; Hayden Gephart et al., 2013). However, their limited strength restricts their use for higher load-bearing indications. Stronger and less co-polymerized PLA materials, on the other hand, show considerably longer degradation times (Bergsma et al., 1995a). Moreover, the degradation intermediates of these typically crystalline PLA implants—stable crystal-like particles—may cause adverse tissue reactions such as subcutaneous swelling and inflammation (Bergsma et al., 1995b). Last, but not least, from a

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technical point of view, the relatively soft consistency of PLA devices in general complicates handling during surgery compared to titanium implants, and usually requires the use of a water bath for the shaping of plates prior to implantation. Hence, there is a need to develop alternative bioresorbable materials with improved strength and biocompatibility for bone fixation applications (Schumann et al., 2013).

Since the first use of magnesium implants for osteosynthesis (Lambotte, 1932; Verbrugge, 1934), an important advance in research on this metallic resorbable material was the development of new alloys with lower impurities, higher biocompatibility, and higher corrosion resistance. Magnesium was therefore rediscovered as an implant material approximately 10 years ago, and the first magnesium cardiac stents and orthopaedic screws have been tested in clinical trials (Zartner et al., 2005; Windhagen et al., 2013). Implants of magnesium provide potential advantages over PLA due to its non-acidic degradation products, superior mechanical strength, and visibility on radiographs (Witte et al., 2005). The corrosion characteristics of magnesium may be altered by alloying, developing optimized manufacturing methods, or making modifications to the implant surface (Witte et al., 2006; Hort et al., 2010; Gunde et al., 2010; Cui et al., 2013). The addition of rare earth elements seems promising for producing a suitable biomaterial with good degradation and strength properties (Castellani et al., 2010; Al-Samman and Li, 2011; Birbilis et al., 2011; Keim et al., 2011; Marukawa et al., 2015).

However, the exact magnesium corrosion mechanism under physiological conditions is still poorly understood. When in contact with body fluids, magnesium and magnesium alloys degrade, due to their limited corrosion resistance, into hydrogen gas and magnesium hydroxide, with concomitant alkalization of the surrounding tissue and formation of calcium phosphate (Rettig and Virtanen, 2008; Han et al., 2015). This corrosion is influenced by various conditions such as the surrounding tissue ion composition, osmolality, temperature, and pH (Witte et al., 2006; Kraus et al., 2012; Sanchez et al., 2015; Rössig et al., 2015). Furthermore, although the importance of the cellular response of the surrounding tissue has been described (Feyerabend et al., 2015), the mechanism of action of the cellular active regulation of the corrosion mechanism is still poorly understood. Jung et al. demonstrated that the corrosion rate as well as the implant surface properties influences the cytocompatibility (Jung et al., 2015). Interestingly, magnesium hydroxide has been shown to increase bone formation and to temporarily inhibit osteoclastic activity (Janning et al., 2010), but the release of hydrogen gas can lead to emphysema if the rate surpasses the absorption and transportation capacity of the involved tissue (Witte et al., 2005; Kuhlmann et al., 2013). As such, relatively slow corrosion rates when used on hard tissue or implant surfaces with high cytocompatibility are needed so as not to compromise the properties of the surrounding bone (Staiger et al., 2006; Jung et al., 2015). Although previous studies have investigated the in vivo degradation profiles (Thomann et al., 2010; Waizy et al., 2013) and have shown the successful use of magnesium implants for fracture healing (Chaya et al., 2015a, 2015b; Han et al., 2015), these studies were conducted mainly in smaller animals such as rabbits. As there is no known direct correlation between the implant size and in vivo corrosion profile, the results from these studies may not be directly predictive and representative of the actual degradation profiles in humans (Sanchez et al., 2015). For subsequent clinical applications, a device must be developed that can also be used in real operations in human beings. As far as we are aware, there has been no study on magnesium osteosynthesis systems with standard sized plate/screw constructs in a large-animal model.

Under these considerations, we have constructed a plate/screw bone fixation device made of a magnesium alloy. In the present study, an improved WE43 alloy was used, which showed no gas pockets or a significant increase in push-out forces compared to PLA and titanium in a growing rat model (Tschegg et al., 2011). A plasma electrolytic coating was also applied to the WE43 alloy to delay the initial release of hydrogen gas, reduce the risk of stress corrosion cracking, increase the hardness of the surface, and improve bone adhesion. Taking into account that the craniomaxillofacial (CMF) region is a suitable area for osteosynthesis using biodegradable materials, an in vivo experimental model on the calvarial bone of miniature pigs was chosen. The miniature pig is known as a useful large-animal model for dental and orofacial research (Wang et al., 2007). The advantages of this model are that plates/screws with dimensions comparable to those used in humans can be used, and the soft tissue properties in the midface and the skull bone of miniature pigs are similar to those in humans. The aims of this study were to evaluate the in vivo degradation behaviour of standard-sized plate/screw constructs, to determine their effects on the surrounding tissues in a miniature pig calvarial model, to investigate the differences in the degradation process between the coated and uncoated implants, and to examine the effect of the coating in preventing gas pocket formation.

2. Material and methods

2.1. Implants

All magnesium implants used in the study were made of a modified WE43 alloy based on the ASTM B80 standard for WE43 (chemical composition: Mg–Y–Nd-heavy rare earths). The modified alloy version, with a lower impurity level, was developed and manufactured by Magnesium Elektron (Swinton, UK). Half of the magnesium implants received a 10-μm-thick plasma electrolytic coating from AHC (Kerpen, Germany) using a proprietary Magoxid electrolyte (400 V DC, 1.4 A/dm^2) with a grain size number according to the standard ASTM E112 of G = 8. The other half was used without a coating. The surface roughnesses were measured optically according to the standard EN ISO25178 using a confocal microscope. The arithmetical mean height of the surface was Sa = 0.2 μm for the noncoated magnesium and Sa = 1.2 μm for the coated magnesium. The increase in surface roughness is related to

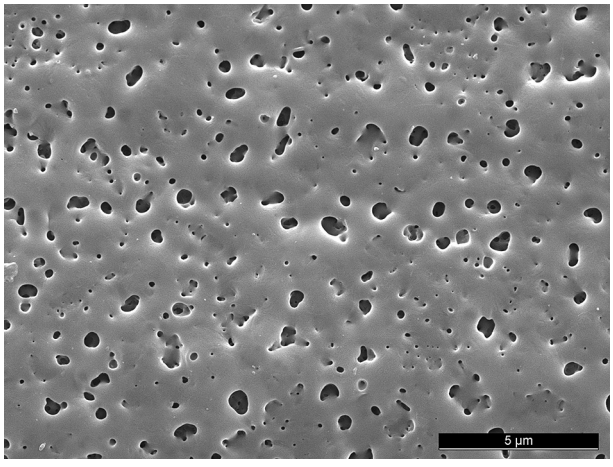

Fig. 1. Representative electron microscopy image of the porous surface of a coated magnesium implant.

the porous nature of the coating (Fig. 1). The EDX analysis showed mainly magnesium phosphate on the coated surface. The design of the used plate/screw systems was based on the titanium version of commercially available implants. A thin plate with 8 holes (40 × 5 × 0.9 mm) and a mandible plate with 6 holes (60 × 6 × 1.5 mm) were used, along with cortex screws with a 2.0-mm-thread diameter and 6-mm length. The magnesium implants were machined dry using hard metal tools, cleaned with ultrasound assistance in 90–100% ethanol, dried in air, packaged in vacuum pouches, and gamma-sterilized with a dose of 25–30 kGy. For the control group, the same-sized titanium (DePuy Synthes GmbH, Switzerland) plates/screws were used.

2.2. Experimental animals and treatment groups

All animal experiments were conducted according to the Swiss federal animal welfare legislation and in accordance with the Swiss Animal Protection law. The study protocol was approved by the Committee for Animal Research, Canton of Bern, Switzerland (Approval No. 50/09). This study included 14 skeletally mature minipigs with an age between 30 and 36 months and an average weight of 53 ± 7 kg. The minipigs were identified by ear markers and randomly assigned to one of the two treatment groups to compare the degradation processes of coated and uncoated magnesium implants.

Based on clinical relevance in humans and preliminary studies, 12 and 24 weeks were chosen as the most appropriate time points for the evaluation of the degradation of the implants. The second time point was also needed to more accurately track the degradation status. To achieve a meaningful statistical comparison, at least 3 animals were required per treatment group. For the control group, one animal at each time point was needed. With two treatment groups and two time points, 14 minipigs were needed.

2.3. Surgical procedure

The same surgical team performed all operations on the animals in a standardized manner. Animals were anaesthetized via intramuscular administration of atropin 0.05 mg/kg, xylazin 2 mg/kg, and ketamine 20 mg/kg. General anaesthesia was induced with the aid of intravenous thiopental 10–15 mg/kg. After endotracheal intubation, anaesthesia was maintained with isoflurane (1–1.5%), and fentanyl was used for analgesia. The pain level was determined by the observation of vital parameters (pulse, blood pressure) and movement after pain stimulation, and the fentanyl was adjusted accordingly from 5 μg/kg per hour up to 30 μg/kg per hour. The body temperature was monitored with a rectal thermometer and kept constant between 37 °C and 38 °C with an active warming system to ensure normothermia.

The minipigs were placed in a supine position and prepared for an aseptic operation of the face. The midface was approached through a 10-cm median skin incision beginning at the dorsal nose and ending at the frontal bone. No osteotomy was inflicted on the skull. The plates were fixed to the forehead using the plates as a template for the drilling of the 1.5 mm holes. Screws that broke during insertion were overdrilled and replaced by an identical screw. The plates were placed in parallel, as shown in Fig. 1. The orientation of the plates could be tracked at all times by placing 3 screws cranially and 2 screws caudally. A two-layer skin closure was performed. The implant position was directly radiologically controlled for every animal as the baseline for the comparison of the implant positions at various time points post-operation. The animals were thereafter extubated and brought back to the farm.

2.4. Examination methods

The 14 animals were examined for wound healing and gas pocket formation daily. Radiographs of the head (antero-posterior and lateral views) were performed after 1, 4, and 8 weeks, and just prior to sacrifice, with a C-arm machine (Philipps BV Pulsera) and with the animals under short general anaesthesia. The radiographs were examined for implant positioning, integrity, and degradation.

2.5. Sacrifice and computed tomography

Euthanasia was performed with a lethal dose of potassium chloride. A computed tomography scan (spiral cone beam, General Electric) of the head was then performed and evaluated for implant position, degradation, and gas pockets around the implant. Subsequently, the implant sites were reopened, the complex of face bone and plates was removed, and the local tissue response and implants were examined macroscopically. The pH of the implant bed was determined using a pH-sensitive strip (pH range 6.4–8.0, Merck).

2.6. Microfocus computed tomography and histological analysis

The plate/screw implants on the frontal bone were explanted with the surrounding bone. The harvested bone blocks and plates were fixed in 70% ethanol. The proximal and distal parts (a1, a8, b1, b6) of the plate/screw system were used for the analysis (Fig. 2). High-resolution computed tomography was carried out on these two plate/screw areas with 15 μm resolution (Scanco MicroCT40, Brüttisellen, Switzerland).

Using microfocus CT (micro-CT) analysis, the anatomical location within the bone structure, the integrity of implant, the residual volume of two screws per animal, and the density of the bone (defined as Bone Volume/Total Volume (BV/TV)) at 50–500 μm surrounding the screws were determined. Due to scattering from the metal alloys, the bone could not be quantified very close to the surface of the implant. In fact, the conversion layer to calcium phosphate on the surface of the implant is difficult to determine using micro-CT analysis. Therefore, the volume from 0 to 50 μm was excluded, and only the bone density at the distance of 50 μm–500 μm from the implant was quantified.

After the micro-CT analysis, the bone blocks were prepared for histological processing. The samples were cut to size and dehydrated in an ascending alcohol series and then placed in xylene for several days prior to embedding in methyl methacrylate (MMA). A transverse cut in the central plane of the screw was performed with a Leica SP1600 diamond saw (Leica, Heerbrugg, Switzerland) and sectioned to a thickness of approximately 200 μm. Staining was applied using a Mc Neal procedure. The bone implant contact area (BIC) was determined using a cycloid grid placed on the top of the histological section (Fig. 3) for each screw (proximal and distal).

2.7. Statistical analysis

The values determined for the present study were collected using Microsoft Excel (Microsoft Office XP, Microsoft Corporation, Redmond, WA, USA). Values of four samples per animal were collected and analysed using the statistical software package IBM SPSS version 22. All data were determined to be normally distributed using the Shapiro–Wilk test. A two-sample independent *t*-test was used to compare the outcomes of the residual volumes of the coated magnesium screws (n = 12 per time point) versus uncoated magnesium screws (n = 12 per time point). The comparison of the values of the surrounding bone density and the values for the bone implant contact area around the titanium screws (n = 4 per time

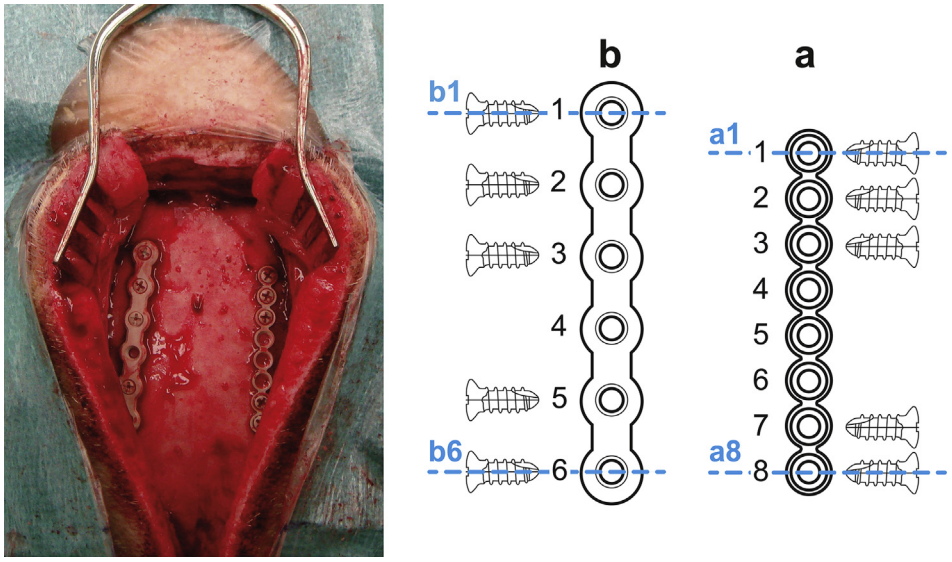

Fig. 2. Surgical access of the frontal bone with plate/screw system (left) and evaluation area (right). The orientation of the plates was tracked by placing three screws cranially and two screws caudally. After sacrifice, microfocus computed tomography and histological analysis were performed on the proximal and distal parts (a1, a8, b1, and b6), as indicated by the dotted lines in the figure.

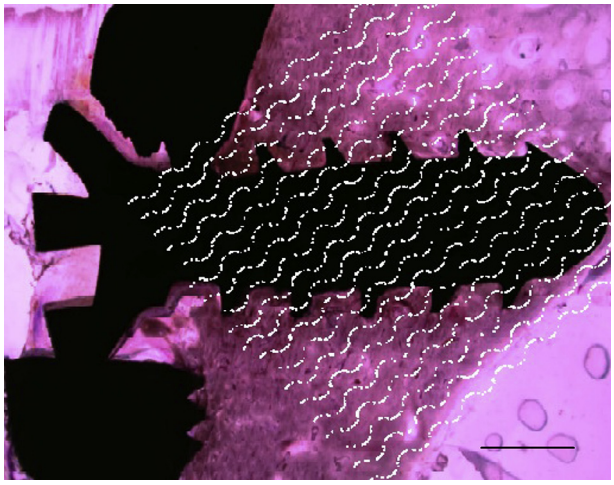

Fig. 3. Cycloid grid placed on the top of the section. In this figure, the grid has been magnified for clearer representation (scale bar: 1.0 mm).

point), uncoated magnesium (n = 12 per time point), and coated magnesium screws (n = 12 per time point) was performed using the one-way analysis of variance followed by a Tukey post hoc analysis. P values of less than 0.05 were deemed to indicate statistical significance and P values of less than 0.001 high significance. Values are presented as the mean (%) ± standard deviation.

3. Results

3.1. Macroscopic and radiological examination

All 14 minipigs survived until the end of the study and showed no complications during wound healing. No plate exposure was encountered. The animals did not exhibit any signs of disturbance from the implants or morbidity. No major secondary effects such as allergic reactions or changes in the behaviour of the animals were observed after implantation of the plates. The degradation phase of the plates is characterized by the release of gas. The production of gas was detected as a crepitus on clinical examination in 4 of the 6 cases in the uncoated group and 1 of the 6 cases in the coated group. This finding was subsequently confirmed by the observation of soft tissue cavities around the implants after sacrifice and implant site reopening. Subcutaneous gas pocket formation of the uncoated implant group was radiologically detectable or at least suspected 1 week after surgery (Fig. 4). In all cases, a decrease of cavity occurrence was observed with time. For the coated implant group, cavity formation was suspected in only one case 8 weeks after surgery. On macroscopic examination after euthanasia, there were no plate fractures seen, but all plates showed a change in appearance, with white corrosion products on the surface and new bone formation at the borders of the plates. The surrounding soft tissue around the implants showed no major change in consistency, and no sign of soft tissue calcification was seen in computed tomography. No disturbances in wound healing or signs of foreign body reaction were observed at the end of the study. The pH measurement of the local environment showed physiological values.

3.2. Computed tomography

Using computed tomography after euthanasia, no intraosseous cavity formation around the titanium plate/screws was observed. Small subcutaneous and intraosseous cavity formation was observed around the coated (Fig. 5) and uncoated implants at 12 and 24 weeks after surgery. No complete corrosion of any implant was observed.

3.3. Microfocus computed tomography analysis

For one uncoated screw, a measure 24 weeks after surgery was not available due to a technical failure. Twelve weeks after implantation, a significant difference in the residual volume ($p = 0.004$) was detected between the coated screws (80 ± 6.3) and uncoated screws (70 ± 8.2) screws. At 24 weeks post-implantation, the residual volumes were significantly lower ($p = 0.001$) for the uncoated screws (43.0 ± 20.9) compared to the coated screws (76.3 ± 19.2) (Fig. 6).

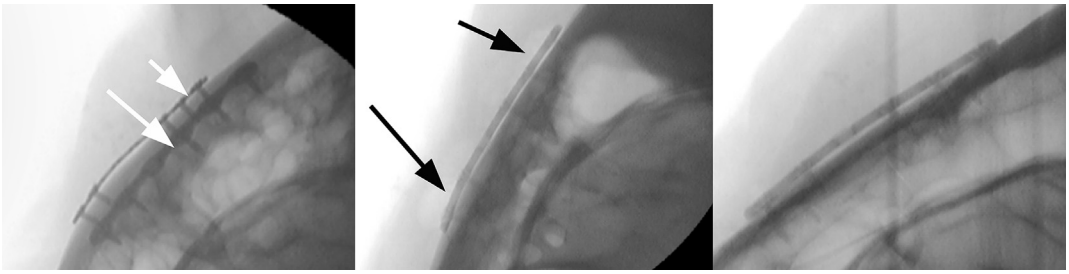

Fig. 4. Plate/screws on the frontal bone after 1 week of implantation. Minipig frontal bone with titanium plate/screws (left, short white arrow: thin plate, long white arrow: thick plate) and coated magnesium plate/screws (right) without subcutaneous gas bubble formation, minipig with uncoated magnesium (middle) plate/screws and subcutaneous gas bubble formation (black arrows).

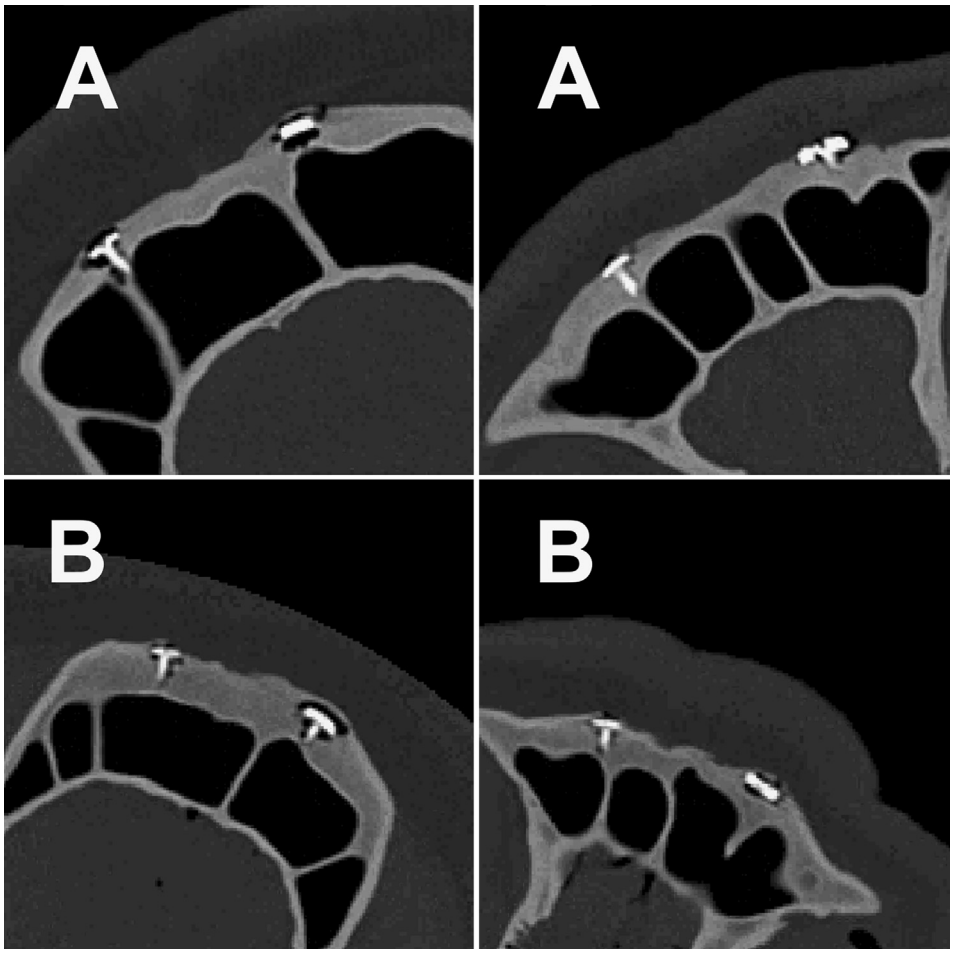

Fig. 5. Computed tomogram (CT) of minipig with magnesium-coated plate/screws after euthanasia at 12 weeks after surgery (A) and 24 weeks after surgery (B), through the topmost screw a1 (left) and the bottommost screw a8 (right).

The post hoc analysis showed a significant higher bone density (BV/TV) around the titanium screws (79.2 ± 10.6) compared to the coated (46.4 ± 12.4, $p < 0.001$) and uncoated (34.1 ± 9.5, $p < 0.001$) magnesium implants at 12 weeks. When compared with the uncoated implants, the bone density around the coated implants was significantly higher ($p = 0.035$). Similar results were found at 24 weeks, with a significantly higher bone density around the titanium implants (83 ± 5.5) compared to the coated implants (42.1 ± 15.0, $p < 0.001$) and uncoated implants (15.1 ± 9.5, $p < 0.001$). At 24 weeks, the bone density around the coated screws was significantly higher than around the uncoated ones ($p < 0.001$) (Fig. 7).

3.4. Histological analysis

The histological analysis showed no sign for inflammatory response or encapsulation of the implants. Neither the presence of inflammatory cells such as neutrophils, monocytes, macrophages, or multinucleated giant cells nor an increase in the number of osteoclasts was observed. Representative histological preparations of a coated and uncoated screw are shown in Fig. 8.

The analysis of the bone contact area around the screw using the grid technique showed that at 12 weeks after implantation, the BIC was significantly higher for the titanium implants (85.5 ± 11.8)

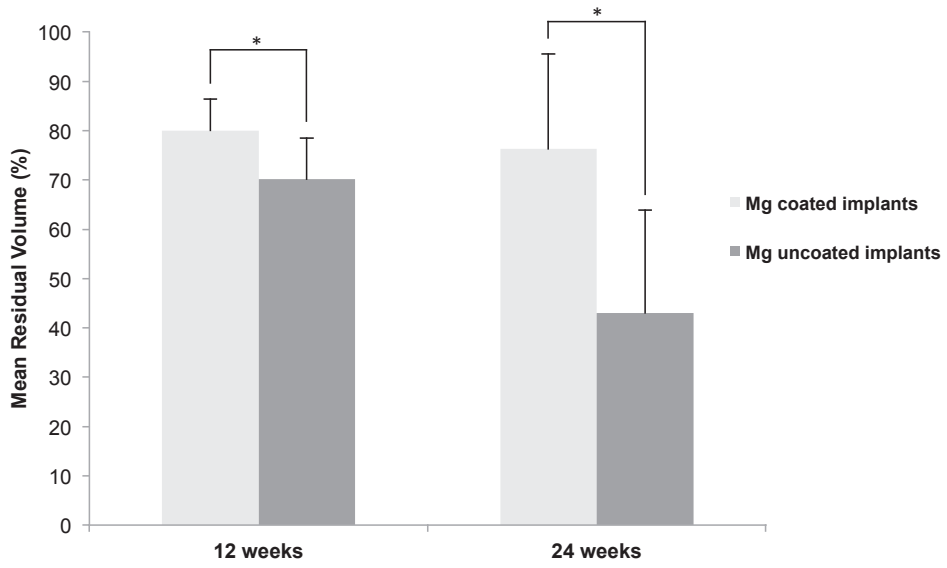

Fig. 6. Mean (±SD, %) residual volume of coated and uncoated screws (n = 12 per time point) measured with micro-CT analysis at 12 weeks and 24 weeks post-implantation (*significant difference in magnesium-coated compared to uncoated implants).

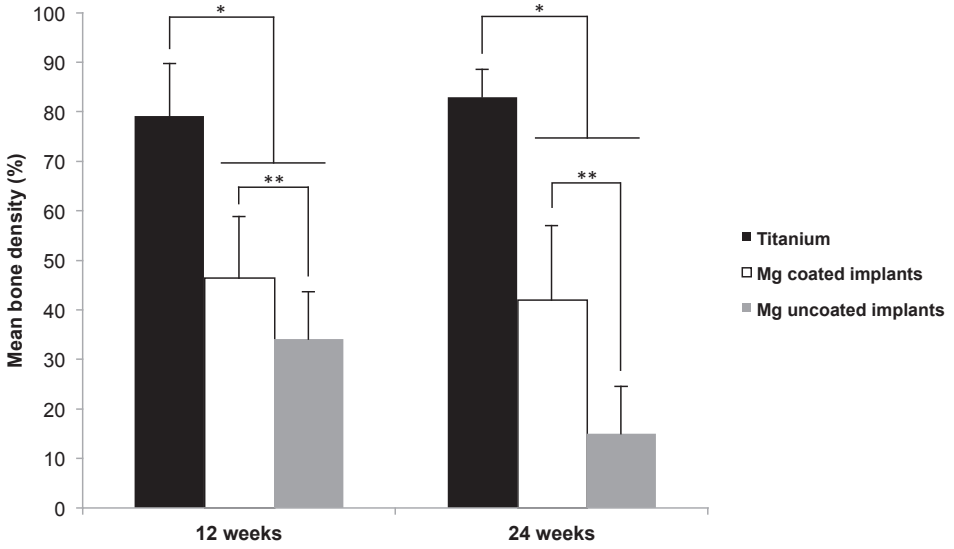

Fig. 7. Mean (±SD, %) bone density 50–500 μm around titanium (n = 4 per time point), and coated and uncoated screws (n = 12 per time point), measured with micro-CT analysis at 12 weeks and 24 weeks post-implantation (*significant difference in titanium compared to both magnesium implants; **significant difference in magnesium-uncoated compared to coated implants).

compared to the coated (62.7 ± 5.5, $p < 0.001$) and uncoated (54.4 ± 7.7, $p < 0.001$) magnesium implants. At 12 weeks post-implantation, there were statistically significant differences between the coated and uncoated magnesium implants ($p = 0.036$). At 24 weeks post-implantation, the titanium implants (90.5 ± 2.9) had a significantly higher BIC compared to the coated magnesium (73.2 ± 5.9, $p = 0.006$) and uncoated magnesium (46.1 ± 11.4, $p < 0.001$) implants (Fig. 9).

4. Discussion

Our results showed a very high tolerance to the combination of the plate/screw magnesium implant system on the minipig face. None of the animals in this study showed any sign of disturbance, and no surgical complication was observed. The slight protuberance in a few cases under the skin and mainly around the uncoated magnesium implants at the beginning was probably due to the build-up of gas after the first rapid corrosion following the surgery. Despite the resorption process of this plate/screw system, it did not affect the wound healing. Upon radiological examination, the resorbed and reformed bone around the implants presented a normal radiological signal, and no sign of implant displacement was observed at any time point. These findings demonstrate that the magnesium alloy derived plate/screw system was well accepted by the animals in vivo. The effect of the plasma electrolytic coating of the magnesium implant of the modified WE43 alloy on the facial skeleton was demonstrated clinically as well as radiologically by a significantly slower corrosion process and delayed onset of gas release. The significantly lower residual volume of the uncoated magnesium implants compared to the coated ones at both 12 and

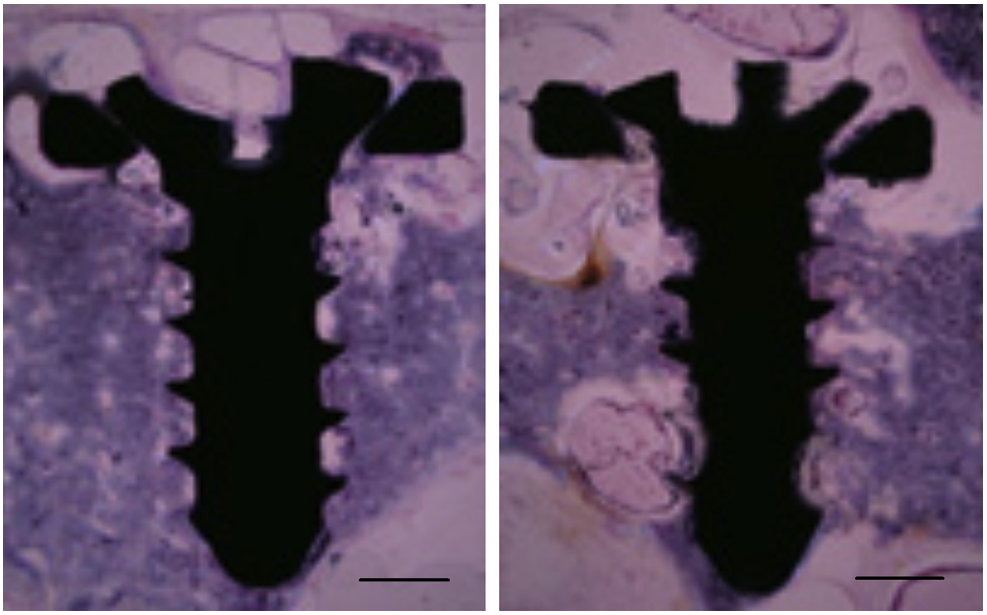

Fig. 8. Representative histological preparations of a coated (left) and uncoated screw (right) 12 weeks after surgery (scale bar: 1.0 mm).

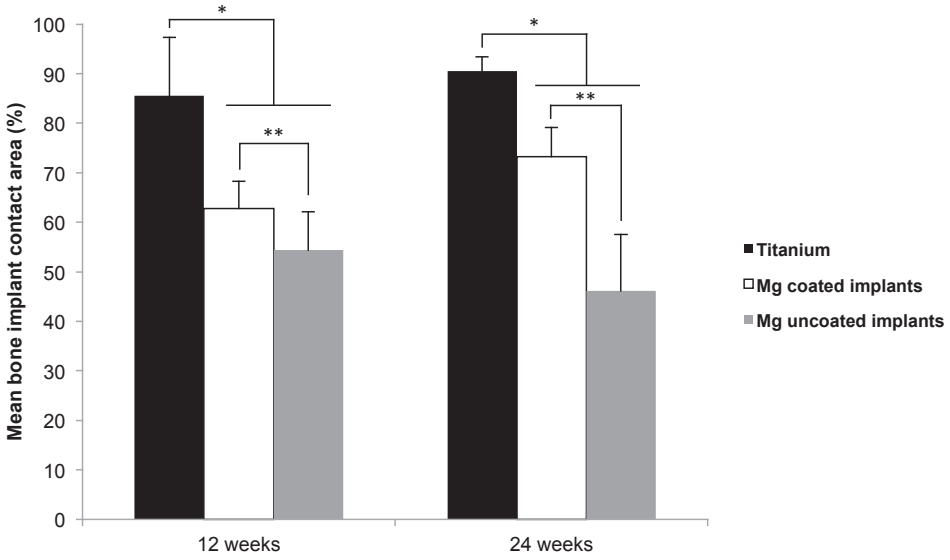

Fig. 9. Mean (±SD, %) bone implant contact area of titanium (n = 4 per time point), uncoated and coated screws (n = 12 per time point) at 12 weeks and 24 weeks post-implantation (*significant difference in titanium compared to both magnesium implants; **significant difference in magnesium-uncoated compared to coated implants).

24 weeks post-implantation showed that the degradation process was significantly faster for the uncoated implants. This was especially so in the period between 12 and 24 weeks, when the mean residual volume of the uncoated implants dropped from approximately 70%–40% compared to the coated implants, which decreased only from 80% to 75% (Fig. 6). This was consistent with our hypothesis that the plasma electrolytic surface modification of the implants would improve the corrosion resistance and slow down the degradation profile, thereby preventing the undesirable rapid release and build-up of hydrogen gas as a by-product of the degradation process. The slower degradation profile corresponded to a significantly higher amount of bone formed around the coated implants compared to that of the uncoated implants at 12 and 24 weeks post-implantation (Fig. 7). The coated screws also had a significantly larger bone implant contact area than the uncoated screws (Fig. 9).

The analysis of our findings is in accordance with the studies of *Chaya* et al., showing successful fracture fixation using a magnesium plate/screw system in a small-animal fracture model (Chaya et al., 2015a, 2015b). They found similar surrounding bone properties with no adverse effect of the magnesium corrosion on the bone healing. Despite a longer observation time than that reported by Chaya et al., the plate/screw system showed no major change in shape in our human-sized model. Witte et al. first described the possible bone cell activation around magnesium implants in the femur of guinea pigs (Witte et al., 2005). These findings were consistent with our macroscopic and CT examinations of the plates with the formation of new bone at the borders of the plates. In accordance with skin test examinations on guinea pigs (Witte et al., 2008), no sign of inflammatory or allergic reaction was observed in our histological analysis. Another notable finding of our study was the confirmation of the

low in vivo degradation rate. Our previous study with the same material showed that the rates of mass loss and strength retention decrease were about four times lower in vivo than in vitro (Imwinkelried et al., 2013). This observation was also described in previous studies reviewed by Sanchez et al. (Sanchez et al., 2015). The difficulty in predicting the in vivo properties based on the in vitro results was mostly attributed to the lack of in vitro standardization, as the term "physiological corrosion" was only recently defined (Willumeit et al., 2013). Under in vitro conditions, Feyerabend et al. observed an influence in the blood cell activity on the corrosion mechanism (Feyerabend et al., 2015). In our study, similar mechanisms are supposed to explain the physiological wound healing and measures of normal pH values around the implants at 12 as well as 24 weeks after implantation.

However, due to the limited sample size, further experiments to confirm the results, as well as a longer follow-up until the complete resorption of the plate/screw system, are required. A further limitation was that continuous monitoring of the degradation using in vivo microfocus computed tomography, as described by Kraus et al., was not possible due to the large animal size (Kraus et al., 2012). Concerning the biocompatibility and toxicity of magnesium implants, we did not perform in vitro tests for cytocompatibility, as recommended by Jung et al., before our in vivo experiments (Jung et al., 2015), but no sign of inflammatory reaction was observed. On the other hand, due to the lack of predictability of the in vivo degradation process, the use of the adult minipig model has the important advantage of allowing the use of implants of similar size and the application of similar surgical procedures to those conducted on human beings. The plate/screw system configuration, size, and mechanical properties of the magnesium implants used in this study match those of titanium implants used in humans for bone fixation in the face. Furthermore, the skin and wound healing of the minipig is very similar to that of human skin.

Given its biodegradability capacity, biocompatibility, mechanical strength, and ability for visualization on radiographs, magnesium is a promising candidate for development and could be the first metallic biodegradable material for osteosynthesis (Witte et al., 2005; Chaya et al., 2015a, 2015b; Marukawa et al., 2015; Rössig et al., 2015; Han et al., 2015). The uniformity of degradation and reliable strength retention makes the investigated coated modified WE43 alloy a prime candidate for development as a metallic biodegradable material for osteosynthesis in craniomaxillofacial surgeries. This could be reinforced by the anatomical properties of the face, with the presence of air cavities that could permit a better diffusion of gas during the constant corrosion mechanism. This first model of a standard-size plate/screw system implanted on the face of a minipig model showed promising results, with no surgical complications or animal disturbance in the long-term (6 months) after surgery. The introduction of such biodegradable osteosynthesis plate/screw system devices in the future in the clinical practice would be of great interest and use for many surgical fields, in particular orthopaedic surgery, thoracic surgery, ENT, maxillofacial surgery, and neurosurgery, where currently titanium plates are mainly used.

5. Conclusions

Based on the interpretation of the study results, we can summarize as follows. First, the magnesium plate/screw combination was re-modelled from the outside to the inside with no change of shape. The plates and screws stayed in place, and no screw loosening was observed. The degradation was slower than expected from the in vitro tests, and the implants were still visible after 24 weeks. Second, the tissue response differed according to the surface coating. For the soft tissue, gas pockets were visible on X-rays within 1 week for uncoated implants. Less gas formation or a delayed occurrence was observed with coated implants. The hard tissue response showed that the bone contact was not as good as for titanium, presumably due to the onset of degradation, which counteracts the initial bone adhesion. The bone contact and bone volume decreased with time for the coated and uncoated implants. Finally, the effectiveness of the surface coating in preventing gas bubbles was seen on X-rays, with less gas formation visible. The coating was effective in diminishing the size of the voids in the surrounding bone. However, the coating did not fully prevent degradation, although it was effective in avoiding the undesired initial burst release of gas.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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