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Useful Corrosion - Potential of Magnesium Alloys as Implants

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Degradable implants have been in use for bone surgery for decades. However, degradable metal implants are one of the new research areas of biomaterials science. Magnesium has good biocompatibility due to its low toxicity, and it is a corroding, i.e. dissolvable, metal. Furthermore, magnesium is needed in human body, and naturally found in bone tissue. There have been some published reports also asserting the potential bone cell activation or bone healing effect of high magnesium ion concentrations. The classic method for achieving intertransverse process fusion involves autogenous iliac crest bone graft. Several investigations have been performed to enhance this type of autograft fusion. However, there is no research which has been undertaken to investigate the efficiency of pure magnesium particles in posterolateral spinal fusion. In this study, corrosion behavior of magnesium metal at the bone interface, the possibility of new bone cell formation and the degree of effectiveness in producing intertransverse process lumbar fusion in a sheep model have been investigated. Cortical bone screws were machined from magnesium alloy AZ31 extruded rod and implanted to hip-bones of sheep via surgery. Three months after surgery, the bone segments carrying these screws were removed from the sacrificed animals. Samples were sectioned to reveal Mg/bone interfaces and investigated using optical microscope, SEM-EDS and radiography. Optical and SEM images showed that there was a significant amount of corrosion on the magnesium screw. The elemental mapping results indicate, due to the presence of calcium and phosphorus elements, that there exists new bone formation at the interface. Furthermore, sixteen sheep were subjected to intertransverse process spinal fusions with pedicle screw fixation at various locations along their spines. Each animal was treated with 5cc autograft bone at one fusion level and 1cc magnesium+5cc autograft bone at the other. Six months after surgery, bone formation was evaluated by gross inspection and palpation, and radiological, histological, scanning electron microscopic and x-ray diffraction analyses. It may be stated that the potential for using useful corrosion of magnesium alloys in medical applications is expected to be significant.

Keywords *: magnesium; AZ31; biomaterial; bone implants.*

1. Introduction

Magnesium, as a biocompatible and biodegradable implant metal, has recently become a material of interest in biomaterials science. In addition to the good biocompatibility due to the low toxicity the main chemical characteristic of magnesium, which has an electrochemical standard potential of E_o = -2,375 V, is the low corrosion resistance.[1)-3)] Therefore, magnesium is attacked expressively in the environment of the human organism and this property creates an opportunity for magnesium to be used as an absorbable implant material, although this is an undesirable characteristic for structural applications.[4)] Mechanical properties of magnesium alloys are dimensionally comparable to the cortical bone substance and better than alternative degradable material, poly-lactides.[4)] Magnesium alloy implants were tried in orthopedic and trauma surgeries of animals.[1),2)] There have also been attempts towards application of magnesium as a degradable stent.[5),6)]

There have been some published reports also asserting the potential bone cell activation or bone healing effect of high magnesium ion concentrations.[1)] However, there is no research that has been undertaken to investigate the efficiency of pure magnesium particles in posterolateral spinal fusion, a procedure commonly performed for spinal stabilization. Increasing the incidence and speed of stable spinal fusion is a primary goal in spinal surgery. Autogenous bone is considered the most effective bone graft material for posterolateral lumbar arthrodesis, yet nonunions occur in up to 30% of patients. In addition, donor site complications may occur in 25-30% of patients. This has

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prompted investigation of bone graft extenders, enhancers, and substitutes to enhance the autogenous iliac crest bone graft fusion. There exist numerous clinical and experimental studies in the literature investigating these materials such as bone marrow, demineralized bone matrix, collagen, ceramics, bone morphogenic proteins etc..[7)-21)]

In this study, we used a sheep model to evaluate the effectiveness of Mg metal particles when used in conjunction with the autogenous bone to facilitate posterior intertransverse process lumbar spinal fusion. The fusion formation and the quality of fusion results of Mg and autogenous bone mixture at one level were compared with another level fused with autogenous bone alone in sixteen sheep. Furthermore, as a part of the same research project, corrosion behavior of magnesium metal was investigated at the magnesium/bone interface by employing cortical bone screws made of a magnesium alloy.

Admittedly, however, before magnesium becomes commonly accepted as an implant material further research is needed. Firstly, corrosion behavior of magnesium metal should be investigated at the bone interface to understand magnesium-bone interactions. In addition, the possibility of new bone cell formation at the interface should be studied.

2. Experimental procedure

In order to investigate the effectiveness of magnesium metal particles in producing intertransverse process lumbar fusion was investigated in a sheep model, sixteen skeletally mature, female sheep were subjected to intertransverse process spinal fusions with pedicle screw fixation at L2-L3 and L5-L6. Each animal was treated with 5cc autograft bone at one fusion level and 1cc magnesium+5cc autograft bone at the other. Six months after surgery, bone formation was evaluated by gross inspection and palpation, and radiologic, histologic, scanning electron microscopic and x-ray diffraction analyses. Radiologic results were evaluated by using computerized tomography (CT) scans. The quality of the fusion was graded by assigning a histological score of 0 to 7 in which a score of 0 represented an empty cleft, and a score of 7 complete bridging of bone between the transverse processes. The trabecular bone formation in each fusion level and calcium hydroxyapatite crystalline structure in core biopsies were also evaluated by histological analysis as well as scanning electron microscopy and x-ray diffraction examinations.

Second aspect of the study was *in vivo* evaluation of magnesium as a degradable implant. Cortical bone screws were machined from magnesium alloy AZ31 (3 wt% Al-1 wt% Zn) extrusion rod to serve as implant material. Other than magnesium, some traditional screws were used for comparison such as titanium, hydroxyapatite coated titanium and bioabsorbable polymer. Cortical bone screws were machined according to ASTM standard.[7)] These screws were implanted to hip bones of sheep via surgery. Three and six months after surgery, these hip bones were removed from the sacrificed animals. Radiography is applied on these hip bones.

Some of the implants-bonecouples were cut from the hip bones, fixed in formaldehyde, and then cut and mounted in epoxy. Mounted samples were ground and polished carefully on fresh medium at any particular instant and in single direction so as to keep the bone side in compression to minimize contamination due to debris from magnesium.

Synchrotron-radiation based micro-computed tomography (SRμCT) allows the 3D reconstruction of a specimen from a set of 2D projections using the backprojection of filtered projection algorithm. Thus, magnesium screw specimens were also imaged by microtomography utilizing synchrotron radiation in absorption mode. Due to the size of the bone-screw explants they were scanned in three different hight levels and the reconstructed tomographs were stacked to an entire data-set allowing to characterize the interphase of the screw and the bone at the entry of the screw into the bone and the bone-screw interphase in the cancellous bone.The SRμCT were performed at beamline HARWI II using 30 keV photon energy at Hamburger Synchrotronstrahlungslabor HASYLAB at Deutsches Elektronen Synchrotron DESY (Hamburg, Germany). Exposed to the parallel synchrotron X-ray beam, the sample was precisely rotated 0.25° stepwise to 180°, and after every fourth step the reference image (projection) was recorded to eliminate intensity inhomogeneities and variations of the X-ray beam.

Optical metallography was performed on the epoxy-impregnated samples, which were removed from sheep after implantation to have a general view. For further study of the implant-bone interface JEOL-JSM-6335 FEG-SEM, operated at 20 kV and equipped with an Oxford EDS system and Inca software, was used. Moreover, samples stored in 10% Formalin and cylinders of implant screws in bones are drilled. These cylinders will be investigated by synchrotron-radiation-based microtomography.

3. Experimental results

The microstructure of the magnesium AZ31 screw and the particulate magnesium material are shown in Fig. 1. No complications due to surgeries were observed. However, since it was pointed out by previous studies dealing with magnesium, we were anticipating a wound complication in the form of subcutaneous hydrogen gas bubbles accumulation due to rapid corrosion rate of magnesium in the electrolytic physiological environment.[1),22)] We observed various amount of gas production in each animal at wound subcutaneous area. Subcutaneous gas accumulation appeared within one week after surgery and disappeared after 2-3 weeks. Gas bubbles were punctured in sterile conditions in case of causing subcutaneous tension when needed. No adverse effects due to the gas bubbles were observed in none of the sheep.

Although gross inspection and manual palpation showed better fusion in the spine segments where magnesium was used, the statistical difference was not significant between these locations and the control segments where only autograft bone was used. Computer tomography (CT) scans showed good solid fusion in the areas of metallic magnesium application in particulate form (Fig. 2). No metallic magnesium particles were observed in histological analysis or in SEM examinations indicating complete degradation of particulate metallic magnesium through corrosion.

Scanning electron microscopy examinations on a large number of samples and areas showed that the trabecular bone formation in the fusion segments of the magnesium treated segments was greater as compared to control segments not containing metallic magnesium. The details of the SEM examinations and the histological evaluations are given elsewhere.[23)]

The magnesium screws machined from an extrusion rod has an equiaxed grain structure with a grain size of approximately 20 µm (Fig. 1). Screw implantation during surgery can be seen in Fig. 3(a). From the radiologic view of implanted screws, (from left to right: magnesium, titanium, hydroxyapatite coated titanium and bioabsorbable poly-

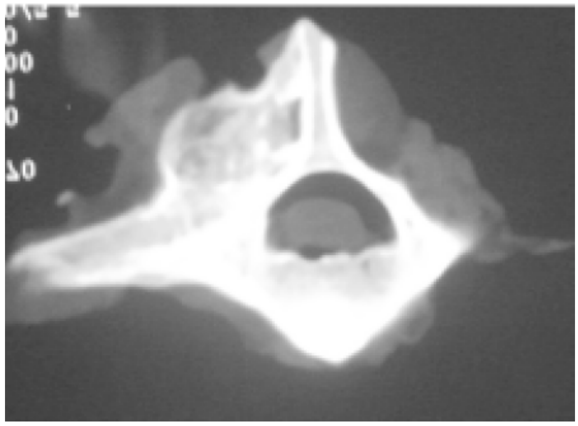

Fig. 2. A CT scan showing sufficient solid fusion in the L2-3 spinal segment where particulate magnesium metal was employed.[23)]

mer) removed six months after surgery, it is observed that other than the bioabsorbable polymer screw, other screws look like keeping their original shapes (Fig. 3b). In Fig. 3(c) one of the screws used in the experiments is seen before the surgery.

The three-dimensional visualization of the corrosion layer on cortical bone magnesium screws applied in a sheep model was possible using synchrotron-raditaion based microtomography (SRµCT). The results of the synchrotron-radiation microtomography (SRµCT) showing the 3D orientation of the magnesium screw inside the sheep bone is given in Fig. 4. While the screw head exhibited severe surface corrosion on the convex areas of the screw head at 3 months post-operatively (deep grey areas, Fig. 4a; front head area, Fig. 4b), just minor corrosion attack was observed on the screw head area of the machined hexagonal screw drive (Fig. 4). The threads of

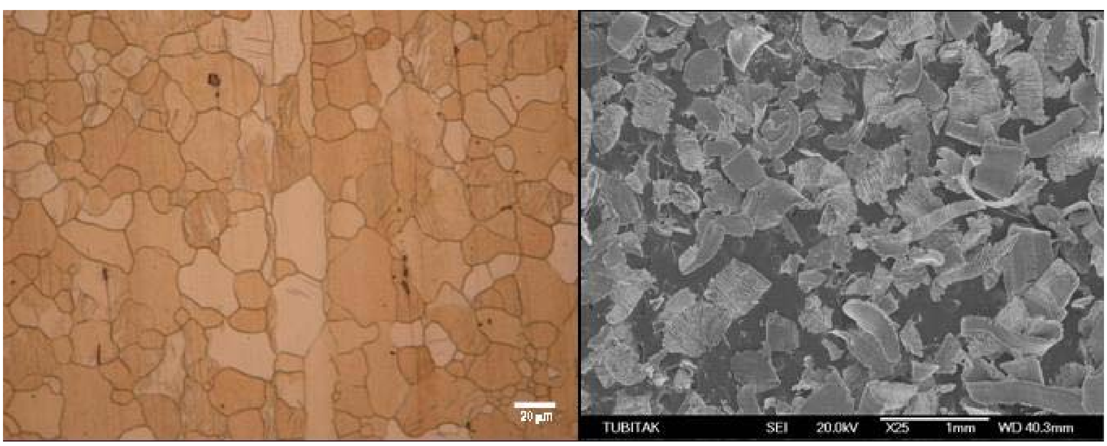

Fig. 1. Optical micrograph showing the microstructure of the magnesium alloy AZ31 bone screw, and the particulate magnesium material employed in this study.

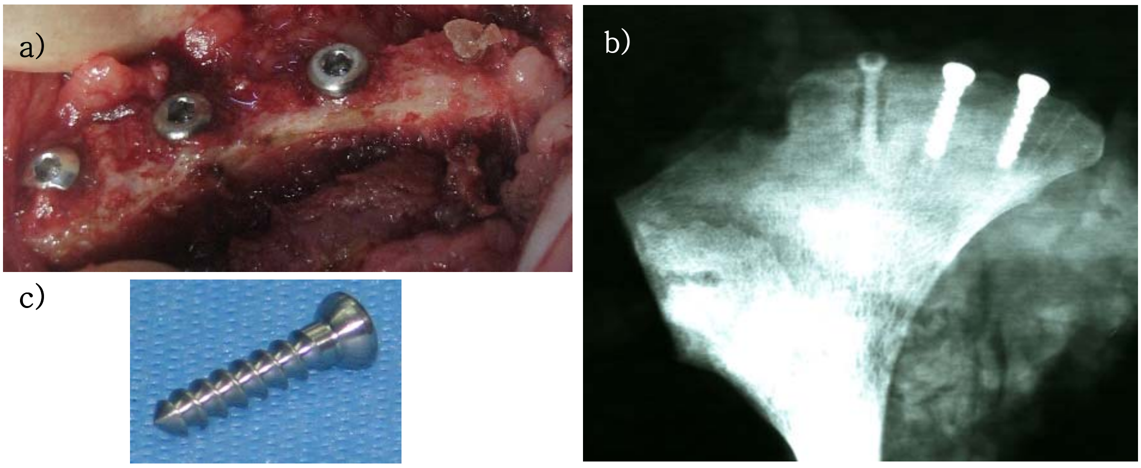

Fig. 3. (a) Screw implantation during surgery in one of sheep hip bone, (b) radiologic view of implanted screws, (from left to right: magnesium, titanium, hydroxyapatite coated titanium and bioabsorbable polymer) and c) picture of the screw used in the experiments.

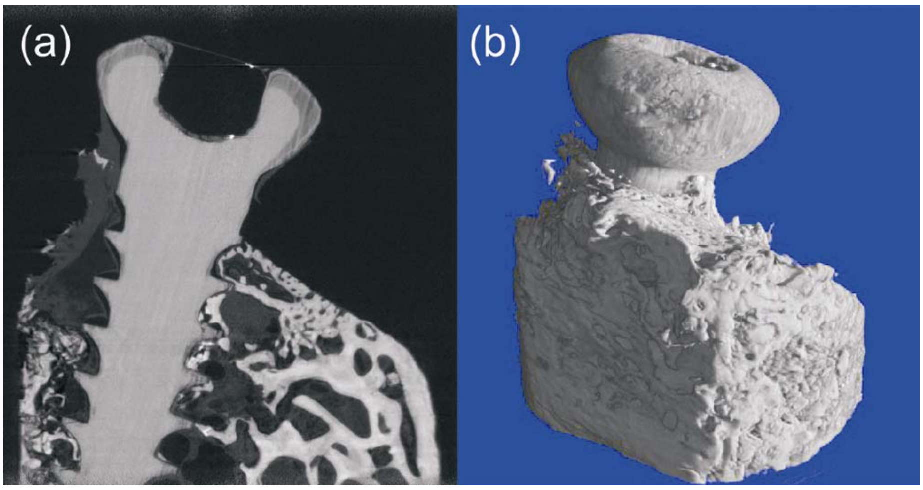

Fig. 4. Synchrotron-radiation microtomography (SRμCT) images showing the 3D orientation of the magnesium screw inside the sheep bone. Left image (a) shows a longitudinal section through the 3D reconstructed and stacked data-sets of a AZ31 magnesium screw that was implanted into sheep bone for 3 months. Rigth image (b) shows the external appearance of the same data-set as displayed in the left image (a).

the screw displayed a quite homogeneous corrosion layer (Fig. 4a) that was thicker at the tip of the threads. Partly direct contact of the screw to adjacent bone tissue was observed. Cancellous bone formation were observed inside the pitches assuming a good mechanical hold of the magnesium screw, even though the threads were partly corroded.

Both optical and SEM images also showed the presence of a significant amount of corrosion layer on the magnesium screw even after the one month implantation period. As can be seen in Fig. 5, the screw lost its original sharp contours. The corrosion layer can be easily seen in Fig. 5(c) due to its different contrast. The elemental mapping results indicate, due to the presence of calcium and phosphorus elements, that there is a new bone formation at the interface. Degraded magnesium alloy screw is replaced by this newly formed phase of Ca and P.

4. Discussion

No significant inflammatory response was observed due to application of metallic magnesium, and no magnesium particles were observed in any of the specimens, indicating that all Mg particles had degraded and been resorbed. In addition, no ectopic bone formation, neurological deficits, pathological abnormalities, or evidence of osteosarcoma was observed in association with the segments in the Mg

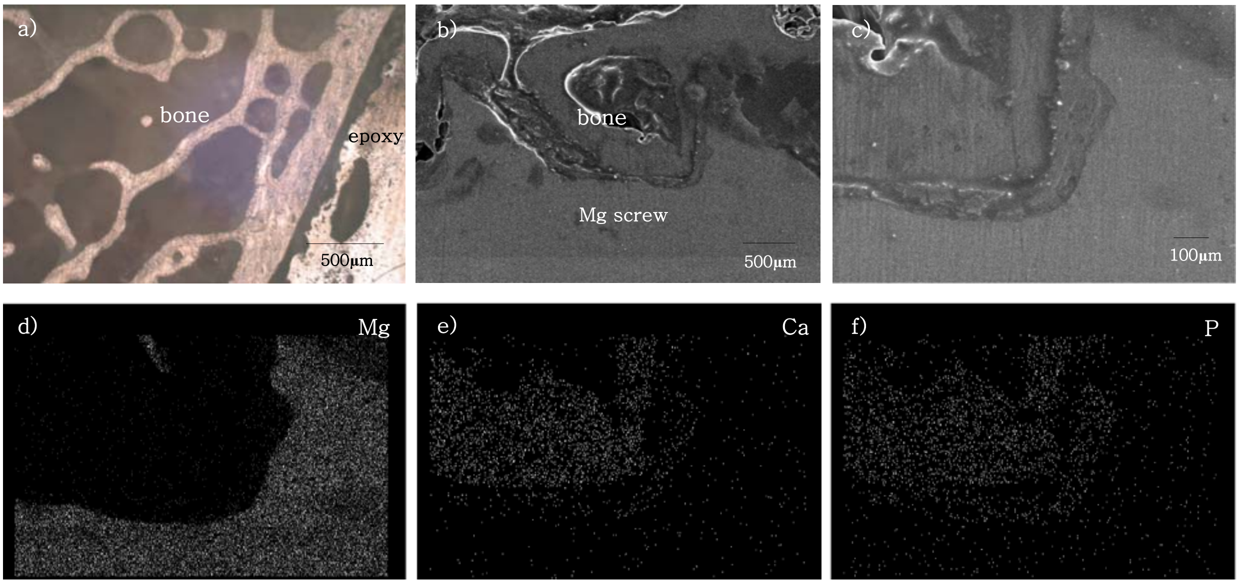

Fig. 5. (a) Optical microscope image of the bone mounted in epoxy, and scanning electron microscope images of magnesium alloy AZ31 screw implant-bone interface, (b) at low magnification, (c) at high magnification; and elemental mapping analyses of the interface showing elements: (d) magnesium, (e) calcium, and (f) phosphorus.

treated group.

From the results of this study, it can be observed that magnesium alloys readily degrade *in vivo* without causing medical complications. It can also be stated that magnesium can lead to new bone cell formation at the bone/implant interface. Therefore, the potential for using magnesium alloys as a bone implant material is expected to be significant.

The findings of this investigation are all supported by the existing literature. Several published studies have noted the potential bone-cell activating or bone-healing effect of a high Mg ion concentration.[24)-28)] A careful review of the use of Mg as a biomaterial indicates that these studies have been conducted since the first half of the twentieth century.[29)] Nevertheless, the first attempts to use Mg to promote bone healing and growth failed because of the rapid corrosion of Mg and a large amount of gas accumulation beneath the skin.[22)] Since then, alloying elements have been added to inhibit the rapid corrosion of Mg, and thus Mg alloys have been used in experimental studies. When Mg was used, a hard callous formation was reported at the fracture sites, which was interpreted as the osteoconductive effect of Mg at such sites.[1),30)-32)] Hydrogen gas accumulation due to the corrosion of Mg was observed without exception, but was easily treated by puncturing the bubbles with a subcutaneous needle, as we have also performed.[1)] These early results indicated that Mg-based materials are nontoxic and may actually stimulate bone tissue healing.

Useful corrosion in the case of magnesium has been a known concept as it has been in use for many decades for the protection of other metallic structures. In such applications, magnesium is kept in contact with another metal, thus forming a galvanic couple, and acting as the sacrificial anode that degrades by corrosion. On the other hand, the useful corrosion of magnesium in biomedical applications is yet to assume its full potential. In order to achieve this potential further studies must be undertaken to tailor the corrosion rate of magnesium either by controlling the alloy chemistry and/or microstructure.

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