Materials Letters 262 (2020) 127130

Contents lists available at ScienceDirect

Materials Letters

journal homepage: www.elsevier.com/locate/mlblue

In vivo studies on Mg-1Sc alloy for orthopedic application: A 5-months evaluation in rabbits

Yulin Lin [a,1], Jianing Liu [b,1], Dong Bian [c], Zhiqiang Huang [d], Zefeng Lin [e], Ming Wang [f], Xiao Chu [g], Mei Li [g], Yu Zhang [g,*], Yufeng Zheng [b,c,*]

[a] Department of Orthopedics, The Fifth Affiliated Hospital of Guangzhou Medical University, Guangdong 510700, China
[b] Academy for Advanced Interdisciplinary Studies, Peking University, Beijing 100871, China
[c] Department of Materials Science and Engineering, College of Engineering, Peking University, Beijing 100871, China
[d] Department of Orthopedics, Foshan Hospital of TCM, Foshan 528000, Guangdong Province, China
[e] Guangdong Key Lab of Orthopedic Technology and Implant Materials Key Laboratory of Trauma & Tissue Repair of Tropical Area of PLA Department of Orthopedics, Guangzhou School of Clinical Medicine, Southern Medical University (Guangzhou General Hospital of Guangzhou Military Command of PLA), Guangdong 510010, China
[f] The First School of Clinical Medicine, Southern Medical University, Guangdong 510010, China
[g] Department of Orthopedics, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510080, China

ARTICLE INFO

Article history:
Received 22 July 2019
Received in revised form 25 November 2019
Accepted 5 December 2019
Available online 9 December 2019

Keywords:
Mg-Sc alloy
In vivo
Biocompatibility
Surfaces
Metals and alloys

ABSTRACT

The feasibility of Mg-1Sc alloy as orthopedic implant was studied by in vivo implantation into femur shaft of rabbit. The in vivo corrosion rate of Mg-1Sc alloy was 0.60 ± 0.06 mm·y^{-1}. Mg-1Sc alloy could maintain its structural and mechanical integrity for more than 5 months. Compared with Ti_6Al_4V alloy, Mg-1Sc showed better osteogenesis. The corrosion products were mainly composed of $Mg(OH)_2$, $MgCO_3{\cdot}3H_2O$ and calcium phosphate, which would not induce toxic effect. In general, the decent degradation rate in vivo and superior osteogenesis of Mg-1Sc alloy indicate that it may be a promising candidate for biodegradable orthopedic implants.

1. Introduction

By addition of rare earth elements (REEs), the corrosion resistance and mechanical properties of magnesium alloy could be effectively improved, which make it more suitable for biomedical application [1]. According to the phase diagrams, scandium (Sc) is the only one REE which could transform the matrix phase of magnesium into body-centered cubic (bcc) structure. From the biological perspective, Sc is reported to possess inhibitive effect on mouse carcinoma and antithrombic effect [2]. In our previous study, the feasibility of bcc-structured Mg-30Sc alloy as orthopedic implant has been investigated [3]. Although the Mg-30Sc alloy showed superior corrosion resistance in vivo, the impurities should be strictly controlled during melting process. Besides, the expensive price of scandium also hinders the application of Mg-30Sc alloy. In this study, the content of scandium is reduced to 1 wt% and the in vivo implantation of Mg-1Sc alloy was carried out to explore its feasibility for orthopedics. The traditional titanium alloy (Ti_6Al_4V) was adopted for comparison.

2. Materials and methods

Binary Mg-1Sc alloy was melted with pure Mg (99.9 wt%) and pure scandium (greater than 99.5 wt%, industrial grade), cut into cylinders with a diameter of 39.6 mm and extruded to rods with a diameter of 12 mm. Commercial Ti_6Al_4V (TC4) alloy and as-extruded Mg-1Sc alloy were machined, polished and sterilized under Co60 γ radiation. Twenty-four male New-Zealand rabbits (2.2–2.7 kg) were equally divided into two groups for implantation. After shaving and disinfecting, a circular hole with a diameter of 3 mm was made around the bilateral femoral shaft nearby the knee section and the Mg-1Sc as well as TC4 alloys with a dimension of Φ 3 × 12 mm were inserted. By overdosage anesthesia, the rabbits were respectively sacrificed at 1, 3 and 5 months' post operation. All the surgical procedures met the requirements of the animal ethic committee in General Hospital of Guangdong Military

* Corresponding authors at: Department of Materials Science and Engineering, College of Engineering, Peking University, Beijing 100871, China (Y. Zheng).
E-mail addresses: luck_2001@126.com (Y. Zhang), yfzheng@pku.edu.cn (Y. Zheng).
[1] These two authors contributed equally to this study.

https://doi.org/10.1016/j.matlet.2019.127130
0167-577X/

Command. The rabbit femurs were retrieved for micro-CT (Aloka LaTheta LCT-200) and histological analysis. The Mg-1Sc alloy implants were retrieved and the volume and weight loss were calculated by Micro-CT and weighing after corrosion product removal, respectively. The corrosion rate of Mg-1Sc alloy was calculated by the following equation [4]:

$$C = \Delta V / At$$

where ΔV, A and t respectively represent the reduction in volume, surface area and implantation time. The corrosion behavior of Mg-1Sc alloy was evaluated by SEM coupled with EDS (Hitachi, S-4800), XPS (Axis Ultra, Kratos Analytical Ltd.), FTIR (Nicolet iS 50, Thermo Scientific) and XRD (DMAX 2400, RIGAKU).

3. Results and discussion

Fig. 1 displays the in vivo degradation property of Mg-1Sc alloy. According to the micro-CT results shown in Fig. 1(a), the surface of Mg-1Sc alloy implant was smooth before operation. Afterwards, the implant gradually degraded and its surface became relatively rough. However, no severe local corrosion happened during the implantation period. The Mg-1Sc alloy could maintain its structural and mechanical integrity in vivo for more than 5 months. The volume loss and weight loss curves of Mg-1Sc alloy implants as well as the weight curves of corrosion products are shown in Fig. 1(b), (c) and (d), respectively. The curves for weight and volume loss showed similar variation tendency. According to the volume loss of 37.3 ± 4.2% after 5 months' implantation, the corrosion rate of Mg-1Sc alloy was 0.60 ± 0.06 $mm \cdot y^{-1}$, which was acceptable.

In order to analyze the corrosion products of Mg-1Sc implants, SEM coupled with EDS were adopted and the results are shown in Fig. 1(e) and (f). In correspondence with micro-CT analysis, no severe local corrosion regions were found, illustrating the decent corrosion rate of Mg-1Sc alloy. According to the XRD patterns shown in Fig. 1(g), $Mg(OH)_2$, $MgCO_3 \cdot 3H_2O$ and $Ca_5(PO_4)_3(OH)$ were detected. The formation of hydroxyapatite indicated the mineralization process of bone, which was relevant to the presence of osteoblasts.

The micro-CT images for 3D reconstruction and 2D slices after implantation are shown in Fig. 2. After one-month implantation, bone callus was formed around the interface between the implant and cortical bone, especially for Mg-1Sc alloy group. After implantation for 3 months, the newly formed bone tissue could directly attached to the Mg-1Sc alloy implant, which indicated that Mg-1Sc alloy possessed excellent osteoconductive properties. The newly formed bone grew into the medullary cavity, indicating the positive effect of magnesium on osteogenesis. As mentioned in the previous reports, Mg^{2+} could enter into periosteum and induce the sensory nerves to release neuropeptides, which is relevant to osteogenesis [5]. After implantation for 5 months, closer integration between newly formed bone and implants were observed. With the Mg-1Sc alloy degraded, hydrogen was released to the surrounding environment. Some gas cavities could be observed nearby the Mg-1Sc alloy implants and reduced with implantation time prolonged. Therefore, the gas cavities would not cause persistent negative effects on bone reconstruction.

The histological sections for decalcified bone tissue with H&E and ALP staining are displayed in Fig. 3. The original positions of implants were marked by black triangles. No tissue abnormalities or avascular necrosis could be found for both Mg-1Sc alloy and TC4 alloy groups. For both groups after 1-month implantation, bone callus was formed at which the relatively slight inflammatory response was observed. New bone was formed adjacent to the Mg-1Sc alloy implants. The TC4 alloy group, by contrast, was surrounded by a thin layer of fibrous tissue which became thinner and finally disappeared with the prolongation of implantation time. At a low magnification (40×), the bone tissue nearby Mg-1Sc alloy implant was relatively loose with some gas cavities, especially for 1 and 3 months' post-operation. According to ALP staining at a high magnification (200×), the osteoblasts were well arrayed along the bone tissue. Compared with the TC4 alloy group, more osteoblasts could be found in Mg-1Sc alloy group, indicating better osteogenesis of magnesium.

To confirm the corrosion products of Mg-1Sc alloy further, XPS and FTIR analysis were carried out, as shown in Fig. 4. The peaks of O 1 s at 532.8 eV and C 1 s at 289.2 eV suggested the presence of $MgCO_3$ or its hydrate [6]. Combined with the XRD results in Fig. 1, the corrosion products of Mg-1Sc alloy, that is, $MgCO_3$, $MgCO_3 \cdot 3H_2O$ and $Ca_5(PO_4)_3(OH)$, were unlikely to induce toxicity. Conversely, the presence of calcium phosphate was conducive to osteo-induction and osteo-conductivity [7].

4. Conclusions

In this study, the Mg-1Sc alloy was implanted into rabbits' femurs to investigate its potential usage within bone. The micro-CT results showed that the implants could maintain its integrity after 5 months' implantation. The corrosion rate of Mg-1Sc alloy was 0.60 ± 0.06 $mm \cdot y^{-1}$ in vivo. Mg-1Sc showed better osteogenesis than TC4 alloy. The corrosion products of Mg-1Sc alloy were mainly composed of $Mg(OH)_2$, $MgCO_3 \cdot 3H_2O$ and $Ca_5(PO_4)_3(OH)$. On this basis, Mg-1Sc alloy may be a promising candidate for orthopedic implant.

CRediT authorship contribution statement

Yulin Lin: Investigation. **Jianing Liu:** Writing - original draft. **Dong Bian:** Investigation. **Zhiqiang Huang:** Investigation. **Zefeng Lin:** Investigation. **Ming Wang:** Investigation. **Xiao Chu:** Software, Validation. **Mei Li:** Data curation. **Yu Zhang:** Supervision. **Yufeng Zheng:** Conceptualization, Methodology, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by National Natural Science Foundation of China (Grant No. 51871004 and 51431002) NSFC/RGC Joint Research Scheme (Grant No. 51661165014), and Peking University Medicine Seed Fund for Interdisciplinary Research (Grant No. BMU2018ME005).

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