Bioactive Materials 1 (2016) 122–126

Contents lists available at ScienceDirect

Bioactive Materials

journal homepage: http://www.keaipublishing.com/en/journals/bioactive-materials/

Research of a novel biodegradable surgical staple made of high purity magnesium

Hongliu Wu [a], Changli Zhao [a], Jiahua Ni [a], Shaoxiang Zhang [b], Jingyi Liu [b], Jun Yan [c], Yigang Chen [d], Xiaonong Zhang [a, b, *]

[a] State Key Laboratory of Metal Matrix Composites, School of Materials Science and Engineering, Shanghai Jiao Tong University, Shanghai, 200240, China
[b] Suzhou Origin Medical Technology Co. Ltd., Jiangsu 215513, China
[c] Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, 200233, China
[d] Department of General Surgery, Wuxi No. 2 People's Hospital, Nanjing Medical University, Wuxi, 214002, China

ARTICLE INFO

Article history:
Received 4 February 2016
Received in revised form
8 September 2016
Accepted 9 September 2016
Available online 5 October 2016

Keywords:
Biodegradable staple
High purity magnesium
Finite element analysis
Corrosion
In vivo

ABSTRACT

Surgical staples made of pure titanium and titanium alloys are widely used in gastrointestinal anastomosis. However the Ti staple cannot be absorbed in human body and produce artifacts on computed tomography (CT) and other imaging examination, and cause the risk of incorrect diagnosis. The bioabsorbable staple made from polymers that can degrade in human body environment, is an alternative. In the present study, biodegradable high purity magnesium staples were developed for gastric anastomosis. U-shape staples with two different interior angles, namely original 90° and modified 100°, were designed. Finite element analysis (FEA) showed that the residual stress concentrated on the arc part when the original staple was closed to B-shape, while it concentrated on the feet for the modified staple after closure. The in vitro tests indicated that the arc part of the original staple ruptured firstly after 7 days immersion, whereas the modified one kept intact, demonstrating residual stress greatly affected the corrosion behavior of the HP-Mg staples. The in vivo implantation showed good biocompatibility of the modified Mg staples, without inflammatory reaction 9 weeks post-operation. The Mg staples kept good closure to the Anastomosis, no leaking and bleeding were found, and the staples exhibited no fracture or severe corrosion cracks during the degradation.

1. Introduction

Titanium and titanium alloys surgical staples are widely used in the reconstruction of the intestinal tract and stomach [1]. The application of staples in gastrointestinal anastomosis shorten the operation time, reduce surgical complication and alleviate the patient's pain. But these served Ti staples cannot be absorbed and retain in human body for a long time. In addition, the Ti staples produce artifacts on Computed Tomography (CT) and other imaging examination which increase the risk of misdiagnosis. On the contrary, the bioabsorbable staple made from polymers that can degrade in human body environment, is an alternative. Currently, polylactic and polyglycolic acid subcuticular absorbable staples are available in skin closure [2]. However, the poor mechanical properties of polymers restrain their applications in gastrointestinal anastomosis which need high closure strength.

Due to the biodegradable property [3], good biocompatibility [4], and significantly higher mechanical stability and ductility than polymers [5], magnesium and its alloys are considered to be candidates as surgical staples. Yan et al. [6] implanted Mg-6Zn pins in Sprague–Dawley rats' cecum and found the Mg alloy exhibited promising applications in gastrointestinal reconstruction because of good biocompatibility and better performance in promoting healing process and reducing inflammation compared to Ti alloy. Chng et al. [7] used Mg based microclip, similar to surgical staple, for pig vocal fold microsurgery. The results showed that the Mg microclip could be absorbed and had good biocompatibility in pig vocal fold after 2 weeks and 3 weeks post-implantation. Another practical Mg based surgical staple was developed by Cao et al. [8]. They implanted Mg alloy surgical staples into beagle dogs by

* Corresponding author. State Key Laboratory of Metal Matrix Composites, School of Materials Science and Engineering, Shanghai Jiao Tong University, Shanghai, 200240, China.
E-mail address: xnzhang@sjtu.edu.cn (X. Zhang).
Peer review under responsibility of KeAi Communications Co., Ltd.

http://dx.doi.org/10.1016/j.bioactmat.2016.09.005

performing gastrojejunal and colonic anastomosis. 90 days post-operation, the anastomosis healed well and Mg based staple degraded completely. Histological examination showed that the degradation of Mg based staple didn't harm the important organs. It concluded that Mg based staple was safe and feasible for gastrointestinal anastomosis in beagle dogs.

The closure of staple often induce residual stress on the surface, which will influence the corrosion behavior of Mg in physiological environment. However, few studies considered residual stress in the implantation of the staple. In present study, we aimed to develop a novel biodegradable staple made of high purity Mg (HP-Mg) for gastric anastomosis to reduce the effect of residual stress on the corrosion of Mg. In vitro corrosion behavior of the original right angle and modified 100° staples were investigated. Then the modified staple was implanted in pigs' stomach to assess in vivo corrosion performance.

2. Materials and methods

2.1. Biodegradable surgical staple design

The cold-drawn HP-Mg wire (99.99 wt% Mg; 0.002 wt% Si; 0.0015 wt% Fe; 0.0008 wt% Al; 0.0008 wt% Mn; 0.0002 wt% Ni; 0.0003 wt% Cu) with a diameter of 0.26 mm, supplied by Suzhou Origin Medical Technology Co. Ltd., China was used as raw material in this study. The yield tensile strength of the HP-Mg wire was 147 ± 8 MPa, the ultimate tensile strength was 196 ± 5 MPa and elongation was 14.6 ± 5%. The original HP-Mg staple was designed according to the clinical used U-shape titanium staple. Considering the high stress corrosion sensitivity of magnesium [9–11], the interior angles of the modified staple were designed to 100°. The closure of the staples were performed through the linear cutter stapler (MLC-60, Nanjing Maidixin Medical Device Co., Ltd. China). After closure, the U-shape staples changed to B-shape. The residual stress distribution of two different staples during the deformation was simulated via FEA analysis by using Abaqus software (Abaqus 6.11-PR3, Dassault Systèmes).

2.2. In vitro corrosion experiment

In order to evaluate the in vitro corrosion behavior of the HP-Mg staple, the closure formed staples with two different staples were immersed in modified simulated body fluid (m-SBF) for 7 days. The m-SBF was prepared according to Ref. [12]. 10 staples as a group were immersed together in 100 ml m-SBF. After 7 days immersion, the staples were taken out and immersed in 200 g/LCrO_3 and 2 g/L $AgNO_3$ solution for 30s [13] to remove the corrosion products, then rinsed in deionized water and dried in flow air. After sputtered with gold, the corrosion morphologies of the samples were observed using field emission scanning electron microscope (FE-SEM, Quanta 250 FEG, FEI).

2.3. In vivo corrosion experiment

The experimental protocol was approved by the Animal Care and Experiment Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital. Three pigs with a body weight of ~40 kg were used for gastric anastomosis. After general anaesthesia, the pigs were intubated using a 5 mm endotracheal tube and anaesthesia was maintained with isoflurane (up to 3%). A median incision was made to expose the stomach of pigs in the abdomen. In order to drag the stomach out, a suture line was bound with parts of the stomach, as shown in Fig. 1a. When the stomach was dragged out, parts of the stomach was cut and closed using the linear cutter stapler loaded with the modified HP-Mg staples, as shown in Fig. 1b. Hemostasis was assessed immediately after the closure and again 2 min later, and the integrity and quality of the staple line was evaluated visually. After implantation, all animals received a subcutaneous injection of penicillin.

The pigs were sacrificed after 9 weeks post-implantation. Histological analysis of the stomach tissue around the anastomotic part aimed at assessing the local lesions relating to the HP-Mg staples, such as inflammation and tissue necrosis. The gastric tissue samples surrounding the staples were fixed in 10% buffered formaldehyde. After that, the gastric tissue samples were embedded in methylmethacrylate, according to the manufacturer's instructions, and stained with hematoxylin and eosin (HE), then were observed via an optical microscope (Scope.A1, ZEISS). The remained staples were retrieved and examined by FE-SEM and EDS.

3. Results and discussion

3.1. HP-Mg staple design and in vitro corrosion behavior

The schematic of the original and modified HP-Mg staples were exhibited in Fig. 2. It could be seen a wider distance between the feet of the modified staple in Fig. 2b because of a bigger interior angle of 100° than the original one in Fig. 2a. Accordingly, the residual stress distribution changed greatly after the staple closed to B-shape. FEA analysis showed that the residual stress mainly concentrated on the arc part of the original staple, whereas it concentrated on the staple feet for the modified staple.

The immersion test indicated that the modified staples kept almost complete in shape and the original staples broke apart after 7 days immersion (Fig. 3a, b). The arc part of original staple, which was the residual stress concentration site analyzed by FEA ruptured firstly as shown in Fig. 3a. The corrosion behavior of biodegradable Mg is affected by many factors, including alloy elements [14], the nature of corrosive environment [15], surface characteristics of samples [16] and residual stress as well as applied stress [17], etc.

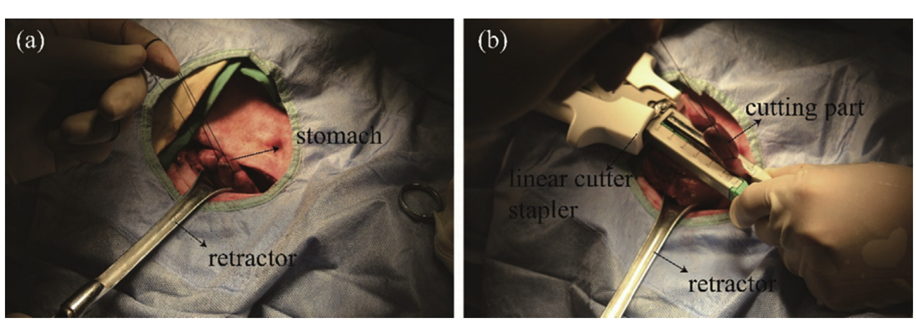

Fig. 1. The surgical procedure of gastric anastomosis. (a) The stomach was dragged out using a suture line, (b) Parts of the stomach was cut and closed using the linear cutter stapler loaded with HP-Mg staples.