Acta Biomaterialia 10 (2014) 1475–1483

Contents lists available at ScienceDirect

Acta Biomaterialia

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

Magnesium in the murine artery: Probing the products of corrosion

Patrick K. Bowen [a,*], Jaroslaw Drelich [a,*], Jeremy Goldman [b]

[a] Department of Materials Science and Engineering, Michigan Technological University, Houghton, MI 49931, USA
[b] Department of Biomedical Engineering, Michigan Technological University, Houghton, MI 49931, USA

ARTICLE INFO

Article history:
Received 2 September 2013
Received in revised form 4 November 2013
Accepted 22 November 2013
Available online 1 December 2013

Keywords:
Magnesium stent
Bioabsorbable
Infrared spectroscopy
Corrosion mechanism

ABSTRACT

Many publications are available on the physiological and pseudophysiological corrosion of magnesium and its alloys for bioabsorbable implant application, yet few focus on the characterization of explanted materials. In this work, commercially pure magnesium wires were corroded in the arteries of rats for up to 1 month, removed, and both bulk and surface products characterized. Surface characterization using infrared spectroscopy revealed a duplex structure comprising heavily magnesium-substituted hydroxyapatite that later transformed into an A-type (carbonate-substituted) hydroxyapatite. To explain this transformation, an ion-exchange mechanism is suggested. Elemental mapping of the bulk products of biocorrosion revealed the elemental distribution of Ca, P, Mg and O in the outer and Mg, O and P in the inner layers. Carbon was not observed in any significant quantity from the inner corrosion layer, suggesting that carbonates are not a prevalent product of corrosion. Backscatter electron imaging of cross-sections showed that thinning or absence of the hydroxyapatite in the later stages of degradation is related to local thickening of the inner corrosion layer. Based on these experimental observations, mechanisms describing corrosion in the quasi-steady state and during terminal breakdown of the magnesium specimens are proposed.

1. Introduction

Magnesium and its alloys have been heavily researched in recent years due to interest in their application as bioabsorbable vascular scaffolding [1]. Prior to widespread clinical adoption, extensive in vitro and in vivo corrosion testing is required. While there is a plethora of corrosion data from in vitro experiments [2], it appears that in vivo study is a major deficiency of the absorbable stent literature. Most contributions thus far have relied on porcine arterial implants [3–6] or are based on clinical (human) experience [7–10]. Very few contain appropriate descriptions of material degradation, and, of these, none completely disclose their corrosion analyses. A lack of disclosure is likely related to intellectual property concerns. Even so, some mechanisms and products of magnesium corrosion have become common knowledge, such as the general tendency for magnesium to form an oxygen-bearing product: MgO, $Mg(OH)_2$, a Mg carbonate or a mixture thereof [6,11]. Several references are made to the gradual replacement of magnesium by calcium and phosphorus in vivo [5,6,8,9].

Characterization of the explanted stent materials and identification of the products thereby generated are critical to the maturation of this class of absorbable implants. For this reason, among others, two recent reviews of in vitro corrosion methodology called for detailed in vivo studies [2,12]. Wittchow et al. [6] recently reported useful cross-sectional data from an explanted stent corroded in a porcine model using energy dispersive X-ray spectroscopy. They noted two corrosion layers: an inner layer that they concluded could be either $MgCO_3$ or $Mg(OH)_2$, and an outer layer comprising an amorphous calcium phosphate. Elemental maps related to secondary components of the corrosion layer (e.g. rare-earth-bearing oxides, aluminum, zinc) are not disclosed, nor are the X-ray diffraction patterns referenced in the report. Nevertheless, this seems to represent the most complete published material characterization of an explanted magnesium cardiovascular device to date.

The conventional method of stent fabrication and animal testing involves laser cutting and electropolishing a stent that is then implanted into a porcine model. This approach is generally inaccessible to academic researchers due to the expense of stent tube production and laser cutting, restrictions on the large animal subjects and relatively high institutional and marginal costs of housing. As an alternative, an inexpensive in vivo method of biocorrosion simulation using wires [13,14] or strip-shaped [15] samples implanted in the arterial walls of rats was recently developed by the authors. The wire geometry simulates the dimensions of a stent strut and lends itself to many analyses, including mechanical evaluation [16] and formulating quantitative relationships between in vivo and in vitro tests [17].

* Corresponding authors.
E-mail addresses: pkbowen@mtu.edu (P.K. Bowen), jwdrelic@mtu.edu (J. Drelich).

1742-7061/$ - see front matter © 2013 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.actbio.2013.11.021

An improved understanding of the corrosion mechanism at later stages of degradation has the potential to expose new routes for improving the corrosion resistance of magnesium stent materials through surface modification and/or alloying. Additionally, understanding the stages of degradation directly preceding fragmentation has great engineering value, as it would allow designers to anticipate the loss of scaffolding function in an absorbable stent. Here, the corrosion products on magnesium in the murine aortic wall are examined at times varying from 5 days to functional degradation (failure) of the implant at 32 days. Optical microscopy, microscopic Fourier transform infrared spectroscopy (μFTIR), cross-sectioning, electron imaging and elemental mapping have been used to characterize the explants. Identification of corrosion products with relevance to the long-term degradation mechanism of magnesium is thus pursued.

2. Methods and materials

2.1. Corrosion protocol

Magnesium wire of 99.9% purity and 250 ± 25 μm diameter was purchased from Goodfellow (Coraopolis, Pennsylvania). Per specification, typical impurities included <1 ppm Ag, 10 ppm Ca, 5 ppm Cu, 100 ppm Fe, 300 ppm Mn, <1 ppm Na and 100 ppm Si. The iron content is above the typical tolerance limits [18,19], and so some degree of microgalvanic action is expected. The wire was divided into 10 and 20 mm segments and the ends smoothed with 800-grit sandpaper to remove any burrs that may hinder implantation. The wires were then cleaned with ethyl alcohol to remove dust and other surface contaminants.

Adult male Sprague–Dawley rats were anesthetized with isoflurane in oxygen. The 10 mm wire segments were used to puncture the arterial adventitia of the abdominal aorta, and the wire was led in for the full length, thus firmly embedding it in the arterial medium. Next, 20 mm segments were implanted proximally to the first wire, within the abdominal aorta, and, after explantation, were used for mechanical analysis, as reported elsewhere [17]. It is noted that the arterial wall implantation method lacks some features of a fully expanded magnesium stent of the same material, including: (i) a lack of direct blood contact meant to simulate a post-encapsulation environment; (ii) an absence of local cold work that would modify the corrosion kinetics; and (iii) freedom from the cyclic stresses generally experienced by stents. This procedure was reviewed and approved by Michigan Technological University's Institutional Animal Care and Use Committee (IACUC).

Rats were housed until their euthanization in accordance with the Panel on Euthanasia of the American Veterinary Medical Association, and extrication of the wires at ten time points ranged from 5 to 32 days. During the removal procedure, it was confirmed by visual examination that the implants had not shifted to a position outside the arterial medium or adventitia. The 32 days sample was observed to be fragmented in situ, constituting "functional degradation", defined elsewhere [17]. The explants were cleared of biological fluids by wicking away surface moisture with a soft cloth and stored in a desiccated environment prior to analysis with optical microscopy, scanning electron microscopy (SEM), μFTIR and cross-sectioning.

2.2. Explant analyses

Examination of the wires was carried out in a specific order to avoid chemically modifying the corrosion layers. Techniques that do not subject the sample to vacuum or impact of high-energy particles are unlikely to affect the chemical profile of the surface, particularly waters of hydration. For this reason, optical examination and μFTIR were performed first. SEM imaging of the surface, cross-sectioning and examination of the cross-sections were conducted afterwards.

2.2.1. Optical imaging of the surface

Optical imaging of the corroded wire samples was performed with a Wild Heerbrugg M5a stereomicroscope and a Leica EC3 microscope camera (Leica Microsystems, Buffalo Grove, Illinois) at 50× nominal magnification. White-light illumination and exposure settings were the same from sample-to-sample to produce comparable images.

2.2.2. Microscopic Fourier transform infrared spectroscopy

μFTIR was conducted in diffuse reflectance mode with a Jasco FTIR-4200 spectrophotometer equipped with an IRT-3000 microscope attachment. The IR microscope was used to limit the infrared light exposure to a $\sim 250 \times 500$ μm representative area on each sample. A series of 1024 scans were performed at 1 cm^{-1} resolution from 600 to 4000 cm^{-1}. Background correction and a center-weighted boxcar smoothing algorithm were used to correct the data. Peak modeling was performed using peak-o-mat [20], an open source, Python-based software package.

2.2.3. Electron imaging of the surface

Scanning electron microscopy performed on the surface was done using a JEOL JSM-6400 (Peabody, Massachusetts) research-grade thermionic emission scanning electron microscope. An accelerating voltage of 5 kV and reduced beam current was used for all samples. Only secondary electron imaging was used to characterize the wire surfaces. A thermionic emission scanning electron microscope (vacuum level of $\sim 10^{-6}$ torr) was preferred to a field emission one ($\sim 10^{-8}$ torr) because dehydration of the sample degrades the high vacuum and poses a contamination risk to the emission tip.

2.2.4. Cross-sectional analysis

Following the above analyses, the wires were placed in plastic sample clips and mounted in two-part epoxy inside a silicone tube (~8 mm inner diameter). After curing, the mounted wires were removed from the silicone tubes. The ends of the corroded wires, deformed by cutting, were avoided for this analysis; sectioning began at a minimum distance of 0.5 mm from the end of the wire. Cross-sections were prepared by grinding the exposed wire in a metallographic fashion with 600- and 800-grit SiC paper and polishing with a 1 μm Al_2O_3 slurry on microfiber. The polished end was then cut to create a section of 0.8–1 mm thickness. The newly exposed surface was ground, polished and sectioned as before to produce multiple sections. A representative section of good quality from four time points (7, 14, 21 and 32 days) was selected for detailed analysis.

The embedded sections of wire were carbon-coated to improve conductivity and then imaged with the JEOL JSM-6400 scanning electron microscope, this time using its backscattered electron detector to provide phase contrast. Elemental mapping via energy dispersive spectroscopy (EDS) was performed using a 4pi Analysis system (Hillsborough, North Carolina) with a Si(Li) detector. Elemental maps for magnesium, oxygen, carbon, phosphorus, calcium, chlorine and sodium based on K_α radiation were captured at a 512 × 512 pixel resolution at 1500× nominal magnification. A detector dead time of $\geqslant$40% and pixel dwell time of 30 ms ensured a sufficient number of X-rays detected for each pixel.