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Flow-induced corrosion behavior of absorbable magnesium-based stents

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ABSTRACT

The aim of this work was to study corrosion behavior of magnesium (Mg) alloys (MgZnCa plates and AZ31 stents) under varied fluid flow conditions representative of the vascular environment. Experiments revealed that fluid hydrodynamics, fluid flow velocity and shear stress play essential roles in the corrosion behavior of absorbable magnesium-based stent devices. Flow-induced shear stress (FISS) accelerates the overall corrosion (including localized, uniform, pitting and erosion corrosions) due to the increased mass transfer and mechanical force. FISS increased the average uniform corrosion rate, the localized corrosion coverage ratios and depths and the removal rate of corrosion products inside the corrosion pits. For MgZnCa plates, an increase of FISS results in an increased pitting factor but saturates at an FISS of ~0.15 Pa. For AZ31 stents, the volume loss ratio (31%) at 0.056 Pa was nearly twice that (17%) at 0 Pa before and after corrosion. Flow direction has a significant impact on corrosion behavior as more severe pitting and erosion corrosion was observed on the back ends of the MgZnCa plates, and the corrosion product layer facing the flow direction peeled off from the AZ31 stent struts. This study demonstrates that flow-induced corrosion needs be understood so that Mg-based stents in vascular environments can be effectively designed.

1. Introduction

Absorbable magnesium-based stents implanted into stenotic vessels to restore the lumen have attracted a great deal of attention, as they have several advantages over the existing conventional bare metal and drug-eluting stents [1,2]. Absorbable Mg-based stents can provide temporary scaffolding to diseased vessels, dissolve gradually when no longer purposeful and be completely metabolized by the human body [3–5]. To effectively study, model and optimize Mg stent degradation, Mg corrosion needs to be performed and characterized in hydrodynamic conditions found within vessel walls. Wentzel et al. found that the presence of a deployed stent in an artery increases the shear stress by 30% [6]. The fluid drag force acting on the vessel wall is mechanotransduced into biochemical and biophysical signals that result in changes in degradation behavior [7], particularly when the stent has direct contact with the blood in the initial stage. Various vessels have different values of mean wall shear stress, as shown in Table 1. Thus, it is important to analyze the effects of flow conditions in a biologically relevant range of flow conditions for the successful application of Mg to vascular stents [8] and other clinical applications for stents such as trachea and ureter stenosis [9,10].

Local hydrodynamics plays a crucial role in the biodegradation of Mg [14]. Studies demonstrate that the corrosion rate is increased, compared to the static condition, during the flowing [15], circulating [16], rotating [17] and local peri-implant perfusion in vivo [18] conditions. Furthermore, corrosion types are affected by shear stress. Levesque et al. reported that the Mg alloy (AM60B-F) surface was protected from localized corrosion at low shear stress (0.88 Pa), while more uniform corrosion and some localized corrosion occurred at high shear stress (8.8 Pa) [14]. In addition, it has been shown that flow prevents the accumulation of corrosion products for pure Mg [19]. However, the biodegradation of Mg-based stents in a vascular environment is a complex process [20] and little information is available about the systematic understanding of flow–magnesium interaction, including corrosion type, corrosion rate, corrosion products, hydrogen evolution and local pH change.

In vitro testing methods that accurately mimic the in vivo environment are required to improve the standardization process

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Table 1
Mean wall shear stress of typical vascular sites in healthy subjects.

Implantation position	Mean wall shear stress (Pa)
Coronary artery	0.68 ± 0.03 [11]
Femoral artery	0.36 ± 0.16 [12]
Supraceliac aorta	0.35 ± 0.08 [13]
Infrarenal aorta	0.13 ± 0.06 [13]

by which a material is deemed appropriate for more costly in vivo testing, which further involves the welfare of animals. A key step is to identify and test relevant local environmental parameters that affect degradation behavior significantly in a complex biological system [20]. Relevant studies towards the understanding of Mg bio-corrosion have focused on the composition of the solution [14,21,22], dynamic whole blood in vitro [23] and CO_2 concentration [20]. These factors can affect large variations in the corrosion rate and the corrosion products of Mg. Simulating an environment similar to in vivo/clinical conditions is necessary to study Mg alloys and stents interacting with fluid flow.

In an effort to understand the impact of vascular conditions on Mg alloy corrosion we measured corrosion types, corrosion rate, corrosion morphologies, composition and thickness of corrosion products, and hydrogen evolution of Mg alloys and stents as a function of flow-induced shear stress in a vascular bioreactor.

2. Experimental

2.1. Magnesium alloy preparation

Magnesium alloy (MgZnCa) with 5 wt.% zinc (Zn) and 0.3 wt.% calcium (Ca) with a high corrosion rate and clearly visible grain boundaries was chosen for fast and efficient observation and analysis of degradation behavior. It was prepared by melting and casting to a low carbon steel mold with protection of ultra-high purity argon. Strip specimens 5 mm in length, 2.7 mm in width and 1.4 mm in thickness were cut from the as-cast alloy. The samples were mechanically polished with silicon carbide (SiC) paper progressively up to 1000 grit with water and then polished with 1200 grit SiC paper with isopropyl alcohol. Specimens were then ultrasonically cleaned with acetone and ethanol solutions, and dried using compressed air.

2.2. Preparation of photochemically etched Mg stent

The corrosion behavior of a novel photochemically etched stent made of AZ31 alloy with a diameter of 4.5 mm and a length of 33 mm was studied. Electrochemical etching for making Mg stents is explored in this work. In brief, the stent is fabricated by photochemical etching a 200 μm thick foil made of AZ31 alloy. This approach included photolithography to transfer a pattern on the foil, followed by chemical etching. The resulting etched foil has a desired pattern that is determined by the photolithographic mask. The etched foil is rolled to form a seamless cylinder and laser spot welding has been used to complete the stent manufacturing [24]. The major advantage of the described approach for manufacturing Mg stents is that expensive laser cutting is avoided. The formation of the fine surface texture of the photochemically etched stent is a process that takes place at room temperature, and therefore no post chemical etching or thermal annealing is needed. Also, the surface roughness of the photochemically etched stent depends on the surface roughness of the initial Mg foil used to make the stent. Photochemical etching prevents sputtering of Mg and re-deposition on the stent surface, which is seen in typical laser cutting processes. The employed photochemical etching is a scalable process, affordable in practice, and attractive for commercialization. A stent and a dimensioned repeating unit of the stent's geometry are shown in Fig. 1.

2.3. Vascular bioreactor

A vascular bioreactor was developed to simulate physiological conditions encountered in in vivo vessels. The vascular bioreactor consisted of a test channel, corrosion medium, variable-flow chemical transfer pump, reservoir and incubator. The test channels were made from silicone tubing with an inner diameter of 3.2 mm for the strip MgZnCa alloy specimen and a diameter of 6.3 mm for the AZ31 stents. Dulbeco's modified Eagle's medium (DMEM) with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin was chosen as a pseudo-physiological solution due to its stability and ion composition similar to that of human blood plasma. The pH value of the solution was adjusted to 7.40 ± 0.05 prior to the test. The volume of corrosion medium was kept at 300 ml. Each strip of MgZnCa sample was sealed with silicone glue with an uncovered working surface area of 0.135 cm^2, and put into a test channel/tubing. The sample was located in the middle of the outlet tubing; the distances from pump to sample and from sample to reservoir were both 1 m. The entire system was sterilized by 70% ethanol solution for 30 min. Then DMEM solution was introduced into the test channel and samples were incubated under cell culture conditions (37 °C, 5% CO_2, 95% RH) [22] for one day. For AZ31 stent samples, each was mounted onto an angioplasty balloon in the test channel and dilated from 4.5 mm to 6.3 mm in diameter by the balloon. The struts of the stent adhered to the inner wall of tubing after expansion. To minimize the effects of mechanical stress on degradation, the stents were not expended fully. The stents were incubated for 7 days.

2.4. Computational model

Computational fluid dynamics (CFD) simulation was used to predict flow-induced shear stress (FISS) distribution on the MgZnCa strip surface as a function of the flow rate using COMSOL Multiphysics®. FISS, as a terminal statement, is independent of the geometry of samples and reactor, and is currently being applied in clinical data. The mathematical model assumed an incompressible and isotropic Newtonian fluid. The FISS on a two-dimensional (2-D) surface was calculated by the following equation [25]:

$$\tau_{ij} = \eta\left(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i}\right) \quad (1)$$

where η is the shear viscosity of the fluid, x_j is the jth spatial coordinate, v_i is the fluid's velocity in the direction of axis i and τ_{ij} is the jth component of the stress acting on the faces of the fluid element perpendicular to axis i. The viscosity and density of DMEM with supplements at 37 °C are 0.78 mPa s and 0.99 g cm^{-3}, respectively [26]. The diameter (D) of the lumen of the tubing was 3.2 mm, as in the above-mentioned test channel. Different values of flow rate (i.e. 0, 5, 10, 20 and 40 ml min^{-1}) were used to simulate the experimental conditions. The inlet boundary condition has a laminar flow with a 1 m entrance length, and outlet boundary condition has a laminar outflow with zero pressure and a 1 m exit length. FISS distribution on the strip surface as a function of the flow rate was calculated.

FISS on the stent was calculated using Doriot's equation [11]:

$$\tau = 32\eta Q/(\pi D^3) \quad (2)$$

where τ and Q are the shear stress and laminar flow rate, respectively. The diameter of the lumen of the tubing was 6.35 mm. Wall

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