Biodegradable Metal Technologies for Cardiovascular Stent Application

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Introduction

Current stents on market are wire mesh tube structures serving as scaffolds to keep occluded vessels open. Permanent stent implants can sometimes have long-term complications such as in-stent restenosis. Drug eluting stents have coatings that release pharmaceuticals intended to prevent restenosis, but these implants have the risks of late-stent thrombosis requiring on-going anti-platelet therapy. The concept of temporary, self-removing stents, which can be converted into bioabsorbable degradation products, is being explored as an alternative to permanent stent implants. However, how such stents function acutely relative to existing permanent stents and how biocompatibility and lumen patency are maintained throughout degradation are subjects in research. We will review interesting trends from materials selection work published over the past decade including both metals and polymers, and present our own work on methodology to study material degradation behavior.

Historical Perspective

Iron and magnesium are two pure metals or alloy systems that have been the subject of experimentation. Iron has mechanical properties similar to current permanent stent alloys. Magnesium degrades within a timeframe in the biological environment that may be compatible with desired luminal scaffolding duration. Both pure iron[1] and magnesium alloy[2] materials were first reported to have been implanted in animals in *Heart* in 2001 and 2003, respectively. Furthermore, an eight center clinical trial of 71 magnesium alloy stents for treating coronary arteries in 63 adults was conducted and the results were published in *The Lancet* in 2007[3].

Methods

The corrosive environment of body fluids can be simulated in a first approximation by saline (0.9% NaCl), phosphate buffered saline (PBS), simulated body fluid (SBF), or swine fluids held at a temperature of 37 ^{o}C. SBF is a commonly used aqueous solution for *in vitro* testing that mimics the ionic composition and pH of human blood, but does not contain protein, lipids or blood cells. In order to more closely simulate *in vivo* conditions, swine albumin can be added to the test solution.

Three types of *in-vitro* corrosion analyses were applied in biodegradable metal stent testing. Simple incubation testing allows periodic observations of material deterioration. It can also produce quantitative data such as mass loss rate per unit area. Potentiodynamic polarization measurement provides insight about corrosion behavior, and predicts initial corrosion rate. Electrochemical impedance spectroscopy can be used to measure corrosion resistance of a solid-liquid interface.

Results

Simple incubation tests were performed as a first screen of candidate materials. The objective is to compare observations of deterioration rate and formation of degradation products. Before and after images of simple incubation specimens are shown in Figure 1 with iron rod (GoodFellow, 98%) and magnesium alloy rod (GoodFellow, Mg:Al:Zn = 96:3:1) in PBS solution. To supplement the incubation observation, potentiodynamic polarization measurements revealed rest potentials of -790 and -1650 mV vs SCE, and corrosion current densities of 6 and 165 $\mu A/cm^2$ for Fe and Mg alloy, respectively. It appears that a faster degradation rate for iron and a slower rate for magnesium alloy are desired in order to meet optimal proposed clinical six months duration.

Both *in vitro* and *in vivo* stents made of Fe and Mg alloy materials showed same corrosion rate trends. Even though there was evidence of disintegration of the stent struts from *in vitro* testing, *in vivo* swine animal study found large portions of the stent remained intact for a period of time. Stent performance will be compared between biodegradable metals and polymers.

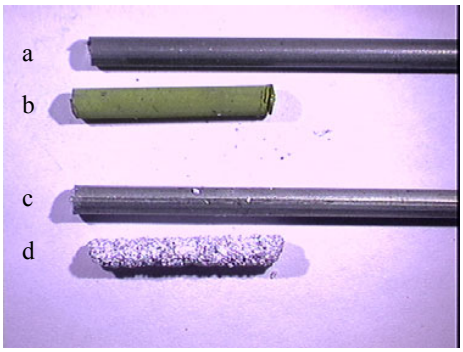

Figure 1. a. Fe rod; b. Fe in PBS for 1-week at 37 ^{o}C; c. Mg alloy rod; d. Mg alloy in PBS for 1-week at 37 ^{o}C.

Conclusions

Analytical laboratory methods can be utilized to develop biodegradable stent materials. *In vitro* test techniques should be used as a first approximation of *in vivo* environment to minimize live model testing for cost and ethical reasons. The historical research was beneficial in identifying promising aspects of the device concept and the challenges that lie ahead. Our technical development is intended to eventually provide the tools used to address these challenges.

[1] Peuster M, et. al., *Heart* 2001;86:563-569.
[2] Heublein B, et. al., *Heart* 2003;89:651-656.
[3] Erbel R, et. al., *The Lancet* 2007;369:1869-1875.