Biocompatibility and degradation behavior of Mg-Sr alloy as temporary cardiovascular implants

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Statement of Purpose: Magnesium (Mg) is a potential material to use in biodegradable implants due to low density, non-toxicity and mechanical properties similar to that of human bone. Its specific properties make it appropriate for a wide range of applications ranging from bone implants to cardiovascular stents[1,2]. The main shortcoming of Mg alloys as biodegradable materials is the high corrosion rate in physiological conditions and the large volume of hydrogen gas released during degradation. Adding a proper amount of non-toxic elements slows down the corrosion rate of pure Mg without compromising biocompatibility. Strontium (Sr) is an attractive element to use in medical applications[3]. It was found that the addition of small amounts of Sr to Mg (~ 0.5 wt%) improves the mechanical properties and increases the corrosion resistance of Mg[3]. However, the corrosion mechanism of Mg-Sr alloys has not been well understood so far. In this work we investigate the in-vitro and in-vivo biocompatibility of Mg-0.5Sr alloy as a temporary vascular stent, and we study its degradation behavior and corrosion mechanism in physiological conditions.

Methods: A thin plate of Mg-0.5Sr alloy was prepared by melting down pure Mg (99.9wt%,) and pure Sr (99.99wt%), both supplied by Applied Magnesium (Formerly Timminco), in a Lindberg/Blue M Crucible Furnace. Mg-0.5Sr was immersed in simulated body fluid (SBF) to study its degradation behavior. X-ray diffraction (XRD) was performed on the corroded surface and scanning electron microscopy (SEM) equipped with energy-disperse spectrometry (EDS) was used to study the degradation mechanism of the alloy. The surface composition of the corroded samples was characterized by X-ray photoelectron spectroscopy (XPS). The samples were etched with Ar ions in-situ to obtain compositional depth profiles. Cytotoxicity of the alloy was evaluated by indirect cell viability assay. Samples were incubated in 10 ml of F-12K medium for 72 hrs to obtain the extraction medium. HuVEC cells were exposed to the Mg-0.5Sr extraction medium in a humidified atmosphere with 5% CO_2 at 37°C for 1, 4 and 7 days. Also, a tubular Mg-0.5Sr stent sample was implanted into the right femoral artery of a dog to investigate the in-vivo biocompatibility of Mg-0.5Sr. The sample was retrieved after three weeks for further analysis.

Results: XRD characterization revealed the formation of hydroxyapatite (HA) and $Mg(OH)_2$ as corrosion products on the surface of Mg-0.5Sr after 3 days of immersion in SBF. SEM analysis showed that the morphology of the surface scale varies from globular in Mg-0.5Sr to needle-like in pure Mg. EDS analysis on both surfaces

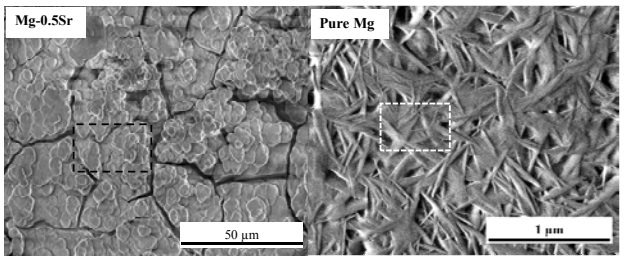

Figure1. Secondary electron image from the surface of Mg-0.5Sr and pure Mg after immersion in SBF.

indicated the presence of Ca and P, and a Ca/P ratio ~1.6, corresponding to the formation of HA. XPS showed the formation of a Sr-substituted HA layer on the alloy surface, which is probably responsible for the observed stabilization and lower degradation rate of the alloy. Cytotoxicity assays showed that the viability of HuVEC cells cultured in Mg-0.5Sr extraction medium is close to the control after 24h of exposure and the viability increases with longer exposure to the alloy extract. This indicates that the extracted cations can promote healthy growth of the cells. Mg-0.5Sr alloy stent implanted in femoral artery did not trombose after 3 weeks. The retrieved sample was degraded to almost half of its initial volume. The degradation rate of this sample indicated that the daily Sr intake from a typical stent would be 0.01-0.02 mg/day which is well below the maximum daily Sr intake levels of 4 mg/day[4].

Conclusions:
In vitro and in vivo tests show that Mg-0.5Sr has the potential to be used as temporary vascular implant: its released ions were not toxic to HuVEC cells and a stent made with this alloy did not lead to thrombosis during three weeks of animal implantation.
A crucial finding of this study is the formation of a Sr-substituted HA layer on Mg-0.5Sr during bio-corrosion in SBF. The formation of this modified layer stabilizes the surface and reduces the degradation rate of this alloy in physiological conditions.

References:
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