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An investigation on the properties of injection-molded pure iron potentially for biodegradable stent application

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ABSTRACT

Metal injection molding (MIM) is a near-net-shape manufacturing process suitable for the production of small-size and complex-shape components. As a cost-effective and flexible manufacturing method, it may have distinct advantages over other methods when it comes to the manufacturing of implantable medical devices. However, up till now, the potential for MIM to be employed in the commercial-scale manufacturing of implantable medical devices has been insufficiently exploited. In the present research, an attempt was made to produce porous pure iron, as a metallic degradable biomaterial potentially for stent application, via the MIM route. The effects of iron powder loading and sintering temperature on the porosity, microstructure, mechanical properties, surface properties and in vitro degradation behavior of MIM iron were investigated. The results obtained were compared to those of cast iron. It was found that the amount of porosity retained in the as-sintered specimens had a major effect on their surface and mechanical properties. MIM iron exhibited strengths between those of magnesium alloys and 316 L stainless steel and very high ductility — a specially required property of stent materials. Its degradation rates in Hank's solution were superior to the degradation rate of cast iron. Interestingly, the material made from the feedstock containing 66% of iron powder, above the critical powder loading, showed the highest elongation and a good in vitro degradation rate. In conclusion, MIM is a promising method to be developed as a new route to produce thin-wall tubes for biodegradable stents.

1. Introduction

In 1991, Mullins et al. [1] and O'Laughlin et al. [2] introduced the principle of angioplasty in combination with the implantation of a stent into stenotic and hypoplastic artery of the patient with a congenital heart defect. Since then, the use of stents, made of stainless steel 316 L, shape-memory alloy Nitinol or cobalt–chromium alloys and typically having an outside diameter of 2.5–4.0 mm, a length of 8–38 mm and a wall thickness of 0.1–0.2 mm [3], has become widespread in treating numerous vascular diseases [4]. The growing interest in stenting is mainly due to the unprecedented success in enlarging the vessel lumen, reducing restenosis rates, being able to cover dissections, and reducing early ischemic complications, as compared with angioplasty alone [5,6]. Although coronary stents have remarkably improved the treatment of vascular diseases, there are still some disadvantages of stent implantation, such as chronic inflammation, restenosis and late-stage thrombosis, partly because of the permanent residence of stents in the body [4,5]. Release of metal ions, i.e., the corrosion products at the implantation site, may cause histological changes of the local tissue either by direct toxicants or through local hypersensitivity reactions, since the elements in stents, such as nickel, cobalt and chromium as well as their compounds are the known allergens [7]. Drug-eluting stents have been designed to reduce restenosis rates of bare-metal stents through localized release of anti-proliferative drugs, such as sirolimus and paclitaxel. The risk of late-stage thrombosis associated with drug-eluting bare-metal stents [5] is now dealt with by developing new thromboxane inhibitors as well as sophisticated stent surface structures that allow the loading and controlled release of the drugs [6].

In recent ten years, the development of biodegradable cardiovascular implants based on bare-metal corrosion has been considered as an alternative solution to avoiding the disadvantages of permanent stents [8,9]. The concept has been applied to magnesium-based coronary and peripheral stents [10]. It has however been found that too high corrosion rates of magnesium-based alloys result in dissatisfaction of the clinical requirements of stents to provide structural support over a period of 6–12 months when arterial remodeling and healing take place [10–12]. In vivo implantation of magnesium-based stents (made of the AE21 alloy) in the coronary artery of pigs, for example, revealed that due to a high corrosion rate of the magnesium alloy the implanted stents lost their mechanical integrity between 35 and 56 days [13].

Abbreviations: (MRI), Magnetic Resonance Imaging; (SFE), Surface Free Energy.

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Iron is another biodegradable metal with mechanical properties similar to 316 L stainless steel. It is an essential co-factor for a multitude of enzymes involved in diverse physiological processes, such as oxygen binding, DNA synthesis and redox enzyme activity. As such, it presents itself as an interesting candidate material for biodegradable stent applications. In vivo tests of iron stents have shown that pure iron exhibits a degradation rate slower than that estimated from in vitro testing results and thus faster degradation is desired [9,10], which may be achieved by modifying the chemical composition of iron, controlling its microstructure (grain structure and phase constituents) or introducing micro porosity. Fe–Mn alloys with magnetic resonance imaging (MRI) compatibility have been developed [14]. Powder metallurgy (P/M) and rolling-sintering steps have been taken to achieve desired microstructure and mechanical properties. Indeed, the degradation rates of Fe–Mn alloys can be increased by more than two times in comparison with pure iron [15]. The control of the distribution of porosity in the materials throughout processing via the P/M route has been found to be of critical importance, as the mechanical properties of the materials are also influenced by the porosity. To understand the mechanical behavior of stents, thin-wall tubes were made from rectangular bars by using wire electro-discharge machining and turning, followed by laser cutting, annealing and descaling [16]. The multi-step processing involved in stent fabrication led to surface irregularities such as pores, high roughness and even cracks. It became obvious that the adoption of suitable stent fabrication technologies was of critical importance in achieving desired physical, mechanical and chemical properties of biodegradable stents.

Metal injection molding (MIM) is a well-established P/M technology and a viable alternative to machining and investment casting. It has distinct advantages in producing small, complex shapes in large quantities and has been applied in the manufacturing of components in cars, aerospace vehicles, medical instruments and telecommunication equipment. Micro MIM technology that has been intensively developed in recent years is capable of achieving thin walls down to 20 μm and surface roughness values less than 0.05 μm [17], which demonstrates the MIM technology readiness to produce thin-wall tubes as the precursors of stents. As a matter of fact, MIM has been successfully utilized to produce tubes with longitudinal and circumferential channels for drug-eluting stents [18]. Thin-wall stainless steel tubes with outside diameters of 1.524 to 2.413 mm and wall thicknesses of 0.05 to 0.25 mm were realized as an embodiment of the MIM technology developed and patented [18]. Clearly, from a geometrical point of view, the MIM technology is able to satisfy the requirements of thin-wall tubes for stents. However, no research has ever been performed on the MIM process for biodegradable iron stent precursors. From a microstructural point of view, the MIM technology is of great interest, because it offers a porous microstructure, allowing accelerated degradation of iron in physiological environments and providing drug reservoir capabilities. The key lies in the control of micro porosity to reach an optimum balance between degradation rate and mechanical properties. Micro pores on the surface affect surface roughness and in turn have a direct impact on cellular responses [4]. Many studies have in recent years been conducted to determine the influence of surface chemistry and topography on cellular responses [6].

The present study was the first attempt to develop the MIM technology for pure iron as a biodegradable metal potentially for stents. Particular attention was paid to the interplay between MIM material and process parameters (i.e., powder loading in MIM feedstock and sintering temperature), porosity, mechanical properties, surface roughness, surface energy and degradation behavior of MIM iron. The main objective was to assess the potential of applying the MIM technology to produce iron products for biodegradable stents in the near future.

2. Materials and methods

2.1. MIM feedstock and specimen preparation

In this research, an iron powder with a carbon concentration of 0.02%, spherical particle shape and a median particle size of 3.61 μm was used to prepare MIM feedstock. A multi-component binder system consisting of paraffin wax, polypropylene and stearic acid was employed in feedstock preparation. The volumetric compositions of the feedstock are given in Table 1. The powder and binder were blended in a glove box under a protective atmosphere with oxygen content <0.5 ppm to minimize oxidation. The feedstock was prepared at 175 °C with the binder melted first and then the iron powder added incrementally. Powder loadings in the feedstock were 54, 58, 62 and 66%. These iron powder loadings were chosen based on the value (56%) used in earlier research on MIM of pure iron [19] and on the consideration of a range around the critical iron powder loading (63% by volume) so as to illustrate the effect of powder loading in the present MIM feedstock — a material variable on the resultant porosity, mechanical properties and degradable behavior of the materials after sintering.

The critical powder loading was determined in accordance with the method described in [20]. A Haake Rheomix 3000p rheometer with blade-type rotors coupled with a Haake Rheocord 252p module was used. At a temperature of 175 °C and a rotor speed of 40 rpm, torque changes with time were monitored. The iron powder was added at a step of 1 vol% from 60% in the feedstock. The experiment was stopped when the mixing torque increased significantly and became erratic, indicating the attainment of the critical loading. The effect of iron powder loading on the mixing torque is shown in Fig. 1.

The feedstock was afterwards pelletized. Injection molding was performed by using a 12.5 MPa injection molding machine to produce dog-bone-shaped tensile specimens with a nominal length of 95 mm and a square gauge area of 15.6 mm^2. Debinding was realized in a two-step solvent/thermal operation. Green parts were solvent debound in heptane at 60 °C for 4 h, followed by thermal debinding during heating at a slow rate. Weight losses during solvent debinding are given in Table 2. Sintering of all specimens was performed in a furnace with a reducing atmosphere composed of H_2 and Ar. The sintering cycle was as follows: heating at a rate of 0.5 °C/min to 450 °C for thermal debinding and pre-sintering. This heating hate was considerably lower than the values found in the literature for the thermal debinding of titanium [21,22] and 316 L stainless steel [23] in order to minimize the retention of the binder in sintered specimens. A heating rate of 5 °C/min to the sintering temperature was employed, followed by cooling to room temperature at 10 °C/min in a hydrogen atmosphere. Three different sintering temperatures, i.e., 1040, 1080 and 1120 °C in the typical range for the sintering of iron, were used to reach different porosity levels.

As the process involves the use of the binder and the debinding step, concerns may be raised about the remaining binder in the sintered product. The biocompatibility of MIM samples was determined and the results were reported in the literature for stainless steel (316 L) [5] and titanium [21,22]. The biocompatibility of porosity-free pure iron was also investigated [9,24–26]. Furthermore, in vivo tests were performed in the case of pure iron and no particular toxicity issues were raised.

Table 1
Volumetric compositions of the feedstock for MIM.

Component	Volume (%)			
Pure iron	54	58	62	66
Polypropylene	19.7	18.7	17.7	16.9
Paraffin wax	19.3	18.5	18.0	17.5
Stearic acid	3.0	2.8	2.3	1.9