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In vitro and in vivo evaluation of biodegradable, open-porous scaffolds made of sintered magnesium W4 short fibres ☆

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ABSTRACT

A cytocompatible and biocompatible, degradable, open-porous, mechanically adaptable metal scaffold made of magnesium alloy W4 melt-extracted short fibres was fabricated by liquid phase sintering. Cylindrical samples (3 × 5 mm) of sintered W4 short fibres were evaluated under in vitro (L929, HOB, eudiometer, weight loss) and in vivo conditions (rabbits: 6 and 12 weeks). The in vitro corrosion environment (e.g., temperature, flow, composition of corrosion solution, exposure time) significantly influenced the corrosion rates of W4 scaffolds compared with corrosion in vivo. Corrosion rates under cell culture conditions for 72 h varied from 1.05 to 3.43 mm y^{-1} depending on the media composition. Corrosion rates measured in eudiometric systems for 24 h were ~24–27 times higher (3.88–4.43 mm y^{-1}) than corrosion in vivo after 6 weeks (0.16 mm y^{-1}). Moreover, it was found that the cell culture media composition significantly influences the ionic composition of the extract by selectively dissolving ions from W4 samples or their corrosion products. A pilot in vivo study for 6 and 12 weeks demonstrated active bone remodelling, no foreign body reaction and no clinical observation of gas formation during W4 scaffold implantation. Long-term in vivo studies need to be conducted to prove complete degradation of the W4 scaffold and total replacement by the host tissue.

1. Introduction

Since the late 1960s, the devolvement of porous metals has been setting the stage for the concept of osteointegration of metallic implants [1]. In a recent review [1], Galante et al. [2] were identified as pioneers in developing open-porous fibre metals and leading them to successful clinical use as porous coatings in hip and knee arthroplasty. Today, open-porous metallic implants are made of various alloys and are widely accepted in musculoskeletal surgery [1]. However, in some clinical applications, permanent metal implants are not necessary, and a temporary implant concept could lead to complete regeneration of the injured tissue. This concept demands biodegradable implant materials. The requirements for such implant materials are complex, but they all include three main prerequisites: (i) they should provide a controlled degradation profile; (ii) they should allow appropriate mechanical stability at any time; and, finally, (iii) the biodegradable material should be completely replaced by the host tissue.

In contrast to conventional permanent metal implants, biodegradable metals such as magnesium and its alloys corrode in vivo and do not require additional surgery for implant removal, eliminating surgery-related costs and health risks for patients [3,4]. Further advantages and challenges of this rediscovered class of biomaterials are reviewed elsewhere [3–8].

Open-porous implants made of biodegradable magnesium alloys as temporary bone replacements have been investigated in vivo [9,10]. They have demonstrated enhanced bone remodelling and an appropriate host response, but they corroded too rapidly in vivo, and concomitant subcutaneous gas cavities were observed [9,10]. However, successful biodegradable magnesium implants corrode in vivo without the occurrence of clinically observable gas cavities. Since open-porous implants provide a large surface area, only very slow-corroding magnesium alloys should be investigated. In this project, the magnesium alloy was composed of 96 wt.% magnesium and 4 wt.% yttrium (W4). The element yttrium has the benefit that it promotes the grain refinement of the material [11]. Some studies also suggest that yttrium decreases

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the corrosion rate of magnesium alloys and provides sufficient cytocompatibility [12–14].

In previous studies on open-porous magnesium scaffolds, a negative salt-pattern moulding process has been found not to be suitable for implant production [9]. Remaining salt inclusions were found inside closed pores, and the initial degradation behaviour of the implants was too rapid in vivo [9,15]. Several alternative techniques for production of open-porous magnesium scaffolds have been discussed in the literature, such as the powder metallurgical route [16–18], unidirectional solidification of the melt in a pressurized hydrogen atmosphere [19] and melt infiltration after creating ordered polymer templates by three-dimensional (3D) printing [20]. However, these production routes cannot yet provide implants with sufficient strength and ductility needed for cancellous bone replacement [21]. Production routes such as the mechanical and laser perforation technique [22] showed adequate mechanical properties. However, these open-porous implants have not yet been investigated in vivo.

An alternative method of producing open-porous scaffolds was investigated in this study using liquid phase sintering of magnesium short fibres. Previous publications have shown general suitability of this sintering technique for magnesium fibres [23]. The aim of the present study was to investigate whether mechanically adaptive, open-porous structures can be manufactured by the crucible melt extraction (CME) process and sintering of MgY4 fibres. Furthermore, the in vitro corrosion behaviour, the cytocompatibility and the feasibility of sintered MgY4 short fibres to serve as an open-porous implant material for cancellous bone replacement is addressed by this study.

2. Materials and methods

2.1. Manufacturing and characterization of open-porous magnesium samples

Open-porous structures were manufactured of the magnesium alloy W4 (MgY4). The CME process was used to produce single short fibres of the Mg alloy with a length of 4–8 mm and a diameter ranging from 100 up to 250 μm, using a high-purity argon-6.0 atmosphere (Fig. 1a). The fibres were continuously deposited onto a tantalum substrate with a MgO barrier and subsequently sintered

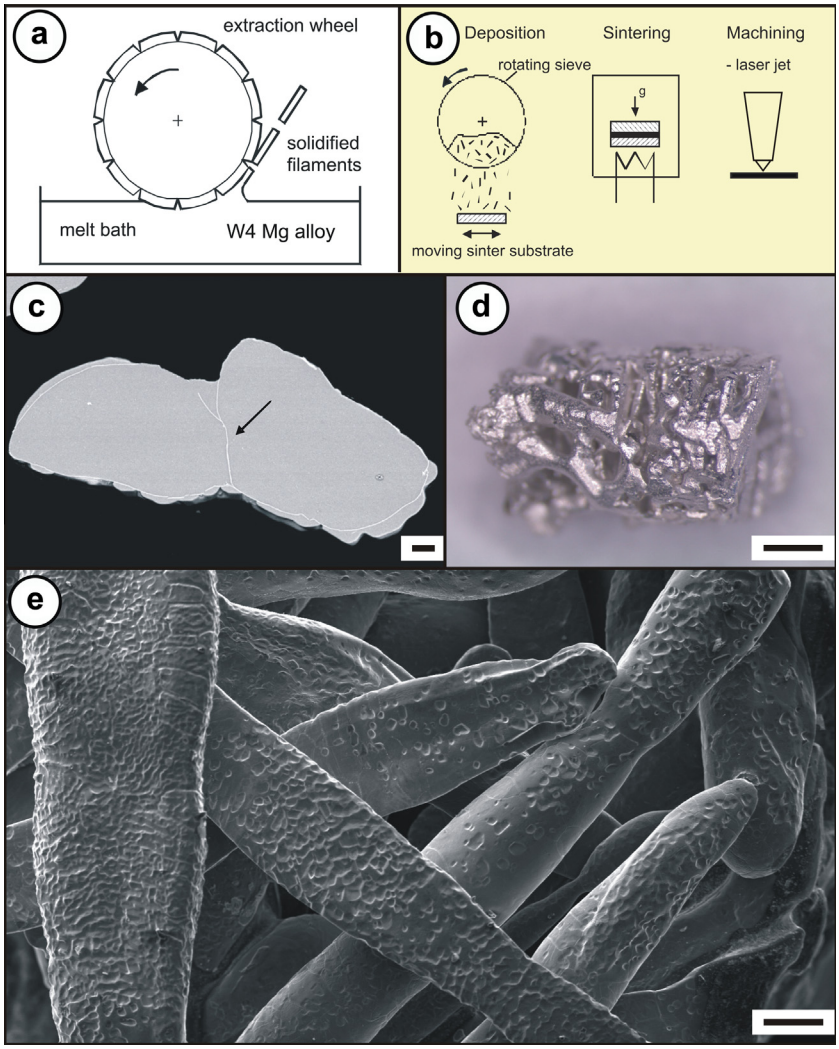

Fig. 1. (a) Schematic view of the melt extraction procedure to create MgY4 alloy short fibres. (b) The melt extraction procedure is performed in a crucible under high-purity argon atmosphere. The Mg short fibres are deposited onto a moving substrate through a sieve, then sintered and finally cut into 3 × 5 mm cylinders by laser jet cutting. (c) The sinter bonds (arrow) can be observed by SEM on cross sections and are composed of Mg and $Mg_{24}Y_5$ (bar = 20 μm). (d) The produced cylinders were cleaned and gamma sterilized before cell testing or implantation (bar = 1000 μm). (e) The cleaning process is a mild etching procedure, which creates a clean surface with visible grains on the fibres (bar = 200 μm).

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