Magnesium-based biodegradable metal materials: past, present and future

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Metallic materials represent the most important implantable biomaterials for a variety of clinical applications. Traditional metallic implants require metals to be inert under physiological conditions to minimise the immune response and reduce corrosion. As a result, stainless steels, titanium alloys and cobalt-chrome-based alloys represent the most common metallic materials in the development of medical devices and implants due to their excellent corrosion resistance and adequate mechanical properties relative to local biological tissues.

Over the past two decades, many new concepts in biomaterials development have been popularised in translational medical research, such as additive manufacturing, smart materials, tissue-inducting materials, bioactive materials, and biodegradable implant materials. Among them, the discovery and development of novel biodegradable metallic implants and devices have drawn great attention from biomaterials scientists and clinicians. In particular, magnesium (Mg)-based biodegradable materials have been extensively studied and new products have been approved for clinical applications in many countries.[1] For example, the first commercial Mg-based screw, called MAGNEZIX, which was first approved in 2013 for use in surgery to treat hallux valgus, has so far been successfully registered in 58 countries or regions. In 2015, the K-MET screw, composed of a Mg-Ca-Zn alloy, was approved by the Korean Food and Drug Administration to fix distal radius fractures. In 2019, high-purity Mg screws received approval from the National Medical Products Administration in China for a multicentre clinical trial for the treatment of patients with femoral head vascular necrosis. More recently, a new type of Mg alloy screw, named JDBM with the composition of Mg-Nd-Zn-Zr, was approved for clinical trial in China for the treatment of medial malleolus fractures.[1]

Compared with other metal implants, Mg-based metal implants have the following advantages:

- ***Biodegradability:*** Mg-based implants can be completely degraded in the body, slowly releasing bio-benign Mg ions.
- ***High biocompatibility:*** Mg is one of the essential trace elements in the human body. Excess Mg absorbed by the body can be excreted through the urinary system without causing significant changes in serum Mg level or severe adverse effects.
- ***Multiple bioactivities:*** Mg exhibits a variety of important regulatory effects *in vivo*. The appropriate supply of Mg ions plays an active role in promoting the regeneration and repair of nerves, blood vessels, bones and other tissues, regulating metabolism and modulating the microenvironment.
- ***Good biomechanical compatibility:*** Mg-based metal alloys show biomechanical properties comparable to human bones. They have densities and elastic moduli similar to bones, therefore effectively alleviating the stress shielding effect.

Although Mg-based metal implants have the aforementioned advantages, the fast degradation rate, the drastic changes in mechanical properties upon corrosion, and the burst release of degradation products are still obstacles preventing their large-scale clinical application. Researchers have developed methods including alloying and surface coating to control the degradation rate of Mg-based metal implants and have achieved impressive progresses.

To promote this important research direction, ***Biomaterials Translational*** organised a special forum entitled "*Update of R&D of Mg-based Biodegradable Implants and Its Clinical Translation in Orthopaedics*" in February 2021. A group of leading scientists in the field participated in this forum, serving as speakers and panelists, and more than two hundred researchers attended the discussion. The forum was well received. Following suggestions by the panellists and participants, we gratefully present here a themed

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issue to highlight the current research progress in Mg-based implants and to discuss the perceptions of future research directions, with contributions from the front runners in the field of biodegradable metals research.

The first paper of this issue is by Zheng's group,[2] which gives an overview of recent developments in the use of biodegradable metals in translational applications. Qin's group[1] reviewed the research advances related to Mg-based biodegradable implants and their clinical translation, and their review is followed by review papers by Chiu's and Yuan's groups,[3, 4] highlighting the application of biodegradable Mg alloys for orthopaedic and vascular stents applications, respectively. Yang's group[5] further discuss the application of Mg as a coating material for the development of implant materials.

The toxicity and corrosion behaviour of Mg-based biomaterials are two major concerns associated with their clinical usage. Staiger's group[6] contributed an article which discusses the use of *in silico* modelling methods to investigate the corrosion behaviour of Mg-based materials, and the design of appropriate experiments to validate the modelling results. A research paper from Lai's group[7] reports the evaluation of acute systemic toxicity of Mg-polymer composite materials, which serves as a guide for further translational medical development of such materials.

Finally, we continue the tradition of this journal by including an animal model review[8]–Guo's group present a comprehensive overview of animal models used for Mg-based materials research.[9] This review summarises the characteristics, advantages and disadvantages of magnesium-based bone implants, the safety and osteogenic effects of magnesium-based materials used in animal models, and provides guidance for the selection of appropriate animal models in related translational research works.

With this special issue, we hope to highlight the future directions of the use of Mg and related metal-based biodegradable materials in clinical translational research, and to promote a collaborative research endeavour between biomaterials scientists and clinicians to contribute to this very exciting research field.

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