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Editorial

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Editorial

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Conventional metallic biomaterials for medical applications are made of corrosion-resistant materials and are designed to remain intact in a human body for a long time. They are characterized by excellent corrosion resistance. In contrast, biodegradable materials could adapt to the human body and eventually dissolve when their presence is no longer required. Why would a clinician want an implant to dissolve in the human body? There are a variety of reasons, but the most fundamental begins with the desire to deploy a device that does not require a second removal surgical intervention. Alongside the elimination of the need for secondary surgery, in the case of the orthopedic devices, the dissolution of the implant in the human body offers other advantages. For example, a fractured bone that has been fixated with a rigid, permanent 316 stainless steel- or titanium-based device has a tendency to refracture upon removal of the implant. Moreover, due to the stress shielding arising from the presence of a tough implant, the bone might not be able to carry sufficient load during the healing process. However, an implant made of absorbable biomaterial can be designed to degrade at a rate that will slowly transfer load to the healing bone. Another example is a stent used to treat blockages in coronary arteries. This small implant can cause an immune response leading to the formation of blood clots or restenosis. The use of bioabsorbable stents drastically reduces, if not eliminates, some potentially long-term clinical problems related to permanent stents including chronic inflammation, late stent thrombosis, in-stent restenosis and stent strut fracture, which can damage the local vasculature. The concept of an absorbable stent is to keep the occluded arteries open during the remodeling period and degrade harmlessly afterward, when its mechanical scaffolding effect is no longer needed. The stent material and its corrosion products must be non-toxic and compatible with the vascular environment. Resorbable stents, as well as bone fixation implants, have other advantages in pediatric applications, showing the ability to adjust to the tissue growth. Other exciting uses in which biodegradable materials offer huge potential are drug delivery systems and regenerative medicine.

Biodegradable implant degradation rates and resulting mechanical integrity should vary depending on specific circumstances after implantation and during tissue healing period. For stenting applications, a gradual corrosion rate is initially required to preserve the optimal mechanical integrity of the implant until the arterial vessel remodeling and healing process is completed. Afterward, the stent should disappear and leave behind a naturally functioning artery. An ideal period of 6–12 months is foreseen for artery tissue

remodeling. In the case of bone fractures, healing occurs in three stages: inflammation, repair and remodeling phases. The time to reach the hard bone merger depends on the fracture type and its location, the state of the surrounding soft tissues as well as patient characteristics (age, health and other injuries/diseases).

Polymeric and metallic materials have been rigorously studied for use in degradable implants. Polymers prepared from glycolic and lactic acids have found several applications in the medical industry, beginning with biodegradable sutures first approved in the 1960s. Ever since, diverse products mainly based on lactic and glycolic acids have been accepted for use as medical devices. In addition to these approved devices, extensive research has focused on polyanhydrides, polyphosphazenes, polyorthoesters and other biodegradable polymers. Polymeric biomaterials are widely used in wound management, orthopedic devices, dental applications, cardiovascular applications and tissue engineering, as depicted in Figure 1. Degradable polymers have shown promise in applications in drug delivery and, therefore, they are widely investigated to develop drug carriers such as nanoparticles, microparticles, microspheres and matrix devices that could be used for local or targeted and controlled, sustained drug or gene delivery.

Over the last two decades, in the field of degradable metals, numerous studies on iron (Fe), magnesium (Mg) and zinc (Zn)-based alloys have been reported with efforts on tailoring mechanical and corrosion behavior to address the requirements of degradable load and non-load-bearing bone implants, cardiovascular stents and other implantable medical devices such as biodegradable sutures and clips (Figure 2). At the industrial and clinical levels, the following companies already have a CE-approved metallic degradable implant on the market: Syntellix AG (Mg-based screw), Biotronik AG (drug-eluting coronary Mg-based stent) and Transluminal Technologies (vascular closure device). Other degradable implants are in the regulatory approval process including Mg-based implants for oral surgery applications (by Botiss Biomaterials GmbH, Germany), Mg implants for orthopedic applications (by EONTEC and Magnesium Innovation in China) and iron-based cardiovascular stents (by LifeTech Scientific, China). A large number of clinical translations is foreseen in the future for metallic implants leveraging this innovative, degradable technology.

Researchers and representatives from academia, industry and clinical institutions meet bi-annually during the Minerals, Metals and

Figure 1. Overview on the applications of biodegradable polymers: (a) use of the polymers for local or targeted and controlled/sustained drug/gene delivery; (b) degradable polymers as bone and dental regeneration scaffolds; (c) degradable anterior cervical plate – polymeric spine implant; (d) degradable polymeric stents available in clinical use: 1, DESolve (Elixir, CA, USA); 2, IDEAL II (Xenogenics Corporation, MA, USA); (e) degradable polymers as scaffold for skin and vascular tissue regeneration. Part (a) reproduced with permission from Prajapati *et al.*¹ (Elsevier); parts (b) and (e) reproduced with permission from Anju *et al.*² (Elsevier); part (c) reproduced with permission from Vaccaro *et al.*³ (Elsevier); part (d) reproduced with permission from Park *et al.*⁴ (Elsevier)

Materials Society (TMS) meetings, aiming at fostering networking and scientific exchange in all aspects of development, testing, characterization and commercialization of degradable biomaterials. The *Second International Symposium on Biodegradable Materials for Medical Applications* was held during the 2020 TMS Meeting in San Diego (CA, USA). The symposium had four oral sessions with four keynote presentations, seven invited talks and eighteen regular presentations, and a poster session with eleven posters. This year, special issues have been published in peer-reviewed journals, including this issue of *Surface Innovations*, *Journal of The Minerals, Metals & Materials Society* (vol. 72, no.5), *Metallurgical and Materials Transactions A* (vol. 51, no. TBD), providing insights into the latest research and encouraging other researchers to join the field. Accepted manuscripts cover a broad range of topics related to materials selection, development, processing/characterization, material surface treatments/modifications, in-vitro/in-vivo performance assessment and evaluation for biodegradable-based implants including vascular, orthopedic, tissue engineering and other applications.

Four symposium papers were selected to be published in *Surface Innovations* and all of them are included in this issue. In the Invited Feature Article entitled ‘Plasma surface modifications of orthopedic biomaterials by the adoption of bioinorganic cations’,⁶ Wang and Yeung discuss the challenges in using bioinorganic ions in bone healing. A variety of ions have been reported to alter different cellular functions, while also modulating signal transduction, energy metabolism and cell proliferation due to the electro-potential change of the cell membrane. The presence of Mg, strontium (Sr), Zn and lithium (Li) in the bone system plays a key role in bone remodeling and skeletal development. However, excess amounts of these ions are detrimental for mammalian cells. The authors highlighted the importance of the delivery devices’ development that could enable the release of such ions in a controlled manner. The plasma surface treatments that have been widely applied to orthopedic biomaterials have a strong potential in controllable delivery of therapeutic ions for bone regeneration.

Figure 2. Overview of applications of biodegradable metals in medical field. Reproduced with permission from Han *et al.*⁵ (Elsevier)

Biodegradable polymers are generally divided into two groups – natural and synthetic – based on their origin. Natural polymers offer advantages over synthetic ones due to their excellent biocompatibility and stronger biodegradability, and thus they are often considered as promising hydrogel candidates. In the paper entitled ‘Hydrogels from silk fibroin and multiarmed hydrolyzed elastin peptide’,⁷ Long *et al.* present hybrid hydrogels, which are intended to mimic certain properties of native tissues. Their materials made from silk proteins combined with elastin peptide have shown a potential in overcoming limitations of hydrogels prepared from conventional polymers. In their work, the rheological behavior and mechanical properties of the hybrid solutions/hydrogels for tissue engineering purposes, including biocoatings for biomaterials or bioceramics, were also assessed.

The next two papers deal with one of the major challenges in developing biodegradable metallic implants, which is representative of in-vitro degradation testing strategies. Typically, the corrosion rates determined in vivo do not correlate with those predicted by the previously accepted in vitro models. The development of a predictive in-vitro testing strategy is a formidable challenge given that the corrosion rate is also influenced significantly by the implantation site. Specifically, evidence has shown the relative rates of corrosion to be dependent on factors including tissue fluid flow rates and the presence of organic molecules such as proteins in the physiological solution. In the paper entitled ‘Proteins and medium-flow conditions: how

they influence the degradation of magnesium’,⁸ Willumeit-Römer *et al.* focus on the combined effects of proteins and medium-flow conditions on Mg degradation. Their results demonstrate that the medium turbulence decreases the inhibitive effect of proteins, implying their flow-dependent influence on the dissolution of Mg-based materials. The authors recommend DMEM+FBS as the most representative electrolyte for the corrosion assessment of Mg-based implant materials.

In the final paper of this collection, ‘Albumins inhibit the corrosion of absorbable Zn alloys at initial stages of degradation’, Sikora-Jasinska *et al.*⁹ examine how the presence of proteins impacts corrosion development on Zn-based materials. Their results revealed the inhibitive effect of albumins on the dissolution of Zn. The enhanced formation of phosphate-based corrosion products by organic components indicates the interaction between proteins and tissue regeneration or biomineralization. As a conclusion, the addition of proteins to the electrolyte for Zn-based biomaterials corrosion assessment is recommended to obtain corrosion patterns better correlating to an in vivo situation.

We hope that this small collection of quality papers on biodegradable medical materials will attract the attention of medical, bioengineering, materials science and engineering scholars.

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