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Editorial

Biodegradable Metals

Eli Aghion

Department of Materials Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel; egyon@bgu.ac.il

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1. Introduction and Scope

Over the last two decades, significant scientific efforts have been devoted to developing biodegradable metal implants for orthopedic and cardiovascular applications, mainly due to their improved mechanical properties compared to those of biodegradable polymers. Naturally, the main focus of such efforts was directed at structural metals with the best biocompatibility characteristics, namely magnesium, iron, and zinc, as well as their alloys. However, it soon became evident that the use of such metal systems in vivo resulted in major problems, limiting their capabilities to act as acceptable structural materials for biodegradable implants in practical applications. These hurdles are exemplified by the accelerated corrosion rate of Mg, accompanied by hydrogen gas evolution that can lead to premature loss of mechanical integrity of the implant, separation of tissues, and, in extreme situations, gas embolism [1,2]. In the case of iron-based implants, although iron corrodes at a reasonable rate, it accumulates a voluminous corrosion product that repels neighboring cells and biological matrices and does not appear to be either metabolized or excreted at an appreciable rate [3]. As for zinc-based implants, they possess relatively low mechanical properties in vivo, as well as reduced corrosion rates, which can provoke fibrous encapsulation processes, which limit their prospects as practical biodegradable implants [4,5]. As such, efforts have been directed at overcoming these hurdles.

This Special Issue introduces the latest scientific advances in developing innovative biodegradable metal implants for various applications and examines the safety of such materials. The collection of high-quality papers comprising this Special Issue is divided into three parts according to the major metal matrix component involved, namely Mg-, Fe-, and Zn-based implants.

2. Contributions

The first part of this Special Issue addresses scientific progress made with magnesium-based implants. The paper by Lumei Liu et al. [6] evaluates the safety of biodegradable Mg-based implants by assessing their impacts at the cellular/molecular level, including in terms of cell adhesion, signaling, immune response, and tissue growth, during the degradation process. In addition, they also evaluate the effect of Mg-based implants on gene expression/protein biosynthesis at the site of implantation, as well as throughout the body. The outcomes of their study serve as the basis for an innovative prediction method to assess the safety of magnesium-based implants. Muhammad Imran Rahim et al. [7] concentrated their efforts on bacterial biofilm infections, as well as bone growth stimulation, given the mechanical forces imposed by magnesium corrosion products. Their novel model for examining implant-derived infections suggests that host cell adhesion to implants is important to prevent bacterial invasion of the exposed host tissue surface, and not, as previously thought, to prevent bacterial adhesion to the implant. According to their model, they predict that passive antibacterial implant-coating strategies would not be efficacious in vivo. Jakub Tkacz et al. [8] examined the effects of solution composition and material surface finish on the corrosion degradation behavior of AZ31 and AZ61 alloys by analyzing the corrosion products created at the implant surface. Their results reveal differences in the response of the Mg alloys to the commonly used cell culture medium Hank's balanced salt solution (HBSS), lacking Mg and Ca ions, and enriched HBSS (HBSS+), containing these ions. Although both alloys exhibited better corrosion resistance in the enriched HBSS+ solution, AZ61 presented higher values of polarization resistance than did AZ31 in both corrosion solutions. As for surface finish (i.e., ground vs. polished), no significant effects were observed during EIS measurements of AZ31 alloy in both HBSS solutions. By contrast, ground samples of AZ61 in HBSS+ solution displayed R_p values which are higher than those obtained with polished samples. The effect of processing parameters on mechanical properties and corrosion degradation of pure Mg in terms of powder metallurgy technology was evaluated by Matej Brezina et al. [9]. They found that cold-compacted samples were quite brittle, with reduced strength (up to 50 MPa) and accelerated corrosion degradation, as compared to hot-pressed samples that yielded much higher strength (up to 250 MPa) and significantly improved corrosion resistance. Overall, applying temperatures treatments of 300 and 400 °C and high pressures of 300–500 MPa had a significantly positive influence on material bonding, and mechanical and electrochemical corrosion properties. A higher compaction temperature of 500 °C had a detrimental effect on material consolidation processes at compacting pressures above 200 MPa. Apart from using Mg-based implants as a supporting device for orthopedic and cardiovascular applications, Da-Jun Lin et al. [10] evaluated the possibility of using Mg-5Zn-0.5Zr alloy for dental-guided bone regeneration. They managed to develop and integrate an optimized solution of heat-treatment and surface fluoride coating to produce an Mg-based regeneration membrane. Their heat-treated Mg regeneration membrane ARRm-H380 was able to provide a proper concentration of Mg ions to accelerate early stage bone growth, encouraging the formation of more than 80% of the new bone.

The second part of the Special Issue is devoted to innovative efforts aimed at using iron as a structural material for biodegradable implants. These activities were carried out mainly due to the inherent limitation of iron, manifested by a reduced corrosion rate in vivo. Although different methods have been proposed for improving the corrosion rate of iron, including modification of alloying elements, poly (lactic-co-glycolic acid) infiltration, and coating, Reza Alavi et al. [11] examined the possibility of using iron-foams as an alternative. The objective of their study was to investigate the mechanical behavior of iron foams with different cell sizes in various compression tests under dry and wet conditions and after being subjected to degradation in HBSS. In general, they found that a wet environment did not significantly change the mechanical behavior of the iron foams, while degradation processes resulted in reductions of elastic modulus, yield strength, and energy absorption. Another attempt to overcome the reduced corrosion degradation of iron is introduced in the review from Mohammad Asgari et al. [12], which notes that sandblasting treatment can increase the degradation rate of pure Fe in simulated body fluid (SBF). The main reasons for the increased corrosion rate were changes in surface composition, and the high roughness and density of dislocations.

The third and final section of the Special Issue is dedicated to the prospects of zinc as a promising alternative to magnesium and iron to overcome the critical limitations of these metals in terms of their suitability for clinical applications. The review paper by Galit Levy Katarivas et al. [13] indicates that Zn^{2+}, the main byproduct of zinc metal corrosion, is highly regulated within physiological systems and plays a critical role in numerous fundamental cellular processes. However, the use of pure Zn as a biodegradable metal for most medical device applications is limited due to its insufficient strength, plasticity, and hardness, as well as its reduced corrosion rate. Although a number of zinc alloys with relatively improved mechanical properties have been developed, such as Zn–Mg and Zn–Al, they still do not present satisfactory properties for practical biodegradable implants. Innovative efforts to develop a new zinc-based alloy were carried out by Alon Kafri et al. [14]. Their research aimed at evaluating the possibility of using Fe as a relatively cathodic biocompatible alloying element in zinc that can tune the implant degradation rate via microgalvanic effects. The selected Zn–1.3wt %Fe alloy composition produced by gravity casting was examined both in vitro and in vivo. The absence of undesirable systemic effects in terms of gain, subject well-being, and hematological characteristics (i.e., red blood cell, hemoglobin, and white blood cell levels) of rats during 14 weeks of implantation, as well as adequate histology results in subcutaneous tissues close to the tested implants, suggests that the Zn–1.3%Fe alloy can be considered as a potential candidate for biodegradable implants. Another attempt carried out by Michaela Krystynova et al. [15] aimed at developing zinc implants via powder metallurgy technology. Their study focused on consolidating zinc powders with two different particle sizes, 7.5 µm and 150 µm, by cold-pressing, followed by sintering and hot-pressing. The obtained results showed that the mechanical properties of samples made from 150 µm particle size powder were better than those prepared with 7.5 µm particle size powder.

In summary, the articles comprising this Special Issue clearly demonstrate the potential of magnesium-, iron-, and zinc-based systems to be a suitable options as structural materials for biodegradable metals implants. However, looking ahead, there are still many challenges to be overcome before these options can be realized. These include: (i) Precisely controlling the degradation kinetics of biocompatible metals and their corrosion products according to in vivo absorption capabilities, while maintaining mechanical integrity prior to significant degradation processes; (ii) correlating the mechanical properties of metal implants according to the required properties of the designated medical device application; and (iii) conducting long-term clinical trials to obtain full biocompatibility responses. Considering the importance of realizing these goals, it is reasonable to expect solutions sooner, rather than later.

References

1. Aghion, E.; Levy, G. The effect of Ca on the in vitro corrosion performance of biodegradable Mg-Nd-Y-Zr alloy. *J. Mater. Sci.* **2010**, *45*, 3096–3101. [CrossRef]
2. Aghion, E.; Levy, G.; Ovadia, S. In vivo behavior of biodegradable Mg-Nd-Y-Zr-Ca alloy. *J. Mater. Sci. Mater. Med.* **2012**, *23*, 805–812. [CrossRef] [PubMed]
3. Bowen, P.K.; Shearier, E.R.; Zhao, S.; Guillory, R.J., II; Zhao, F.; Goldman, J.; Drelich, J.W. Biodegradable Metals for Cardiovascular Stents: From Clinical Concerns to Recent Zn-Alloys. *Adv. Healthc. Mater.* **2016**, *5*, 1121–1140. [CrossRef] [PubMed]
4. Bakhsheshi-Rad, H.R.; Hamzah, E.; Low, H.T.; Kasiri-Asgarani, M.; Farahany, S.; Akbari, E.; Cho, M.H. Fabrication of biodegradable Zn-AlMg alloy: mechanical properties, corrosion behavior, cytotoxicity and antibacterial activities. *Mater Sci Eng C.* **2017**, *73*, 215. [CrossRef] [PubMed]
5. Guillory, R.J.; Bowen, P.K.; Hopkins, S.P.; Shearier, E.R.; Earley, E.J.; Gillette, A.A.; Aghion, E.; Bocks, M.; Drelich, J.W.; Goldman, J. Corrosion Characteristics Dictate the Long-Term Inflammatory Profile of Degradable Zinc Arterial Implants. *ACS Biomater. Sci. Eng.* **2016**, *2*, 2355–2364. [CrossRef]
6. Liu, L.; Wang, J.; Russell, T.; Sankar, J.; Yun, Y. The Biological Responses to Magnesium-Based Biodegradable Medical Devices. *Metals* **2017**, *7*, 514. [CrossRef]
7. Rahim, M.; Ullah, S.; Mueller, P. Advances and Challenges of Biodegradable Implant Materials with a Focus on Magnesium-Alloys and Bacterial Infections. *Metals* **2018**, *8*, 532. [CrossRef]
8. Tkacz, J.; Slouková, K.; Minda, J.; Drábiková, J.; Fintová, S.; Doležal, P.; Wasserbauer, J. Influence of the Composition of the Hank's Balanced Salt Solution on the Corrosion Behavior of AZ31 and AZ61 Magnesium Alloys. *Metals* **2017**, *7*, 465. [CrossRef]
9. Březina, M.; Minda, J.; Doležal, P.; Krystýnová, M.; Fintová, S.; Zapletal, J.; Wasserbauer, J.; Ptáček, P. Characterization of Powder Metallurgy Processed Pure Magnesium Materials for Biomedical Applications. *Metals* **2017**, *7*, 461. [CrossRef]
10. Lin, D.; Hung, F.; Lee, H.; Yeh, M. Development of a Novel Degradation-Controlled Magnesium-Based Regeneration Membrane for Future Guided Bone Regeneration (GBR) Therapy. *Metals* **2017**, *7*, 481. [CrossRef]
11. Alavi, R.; Trenggono, A.; Champagne, S.; Hermawan, H. Investigation on Mechanical Behavior of Biodegradable Iron Foams under Different Compression Test Conditions. *Metals* **2017**, *7*, 202. [CrossRef]
12. Asgari, M.; Hang, R.; Wang, C.; Yu, Z.; Li, Z.; Xiao, Y. Biodegradable Metallic Wires in Dental and Orthopedic Applications: A Review. *Metals* **2018**, *8*, 212. [CrossRef]
13. Katarivas Levy, G.; Goldman, J.; Aghion, E. The Prospects of Zinc as a Structural Material for Biodegradable Implants—A Review Paper. *Metals* **2017**, *7*, 402. [CrossRef]

14. Kafri, A.; Ovadia, S.; Goldman, J.; Drelich, J.; Aghion, E. The Suitability of Zn–1.3%Fe Alloy as a Biodegradable Implant Material. *Metals* **2018**, *8*, 153. [CrossRef]
15. Krystýnová, M.; Doležal, P.; Fintová, S.; Březina, M.; Zapletal, J.; Wasserbauer, J. Preparation and Characterization of Zinc Materials Prepared by Powder Metallurgy. *Metals* **2017**, *7*, 396. [CrossRef]

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