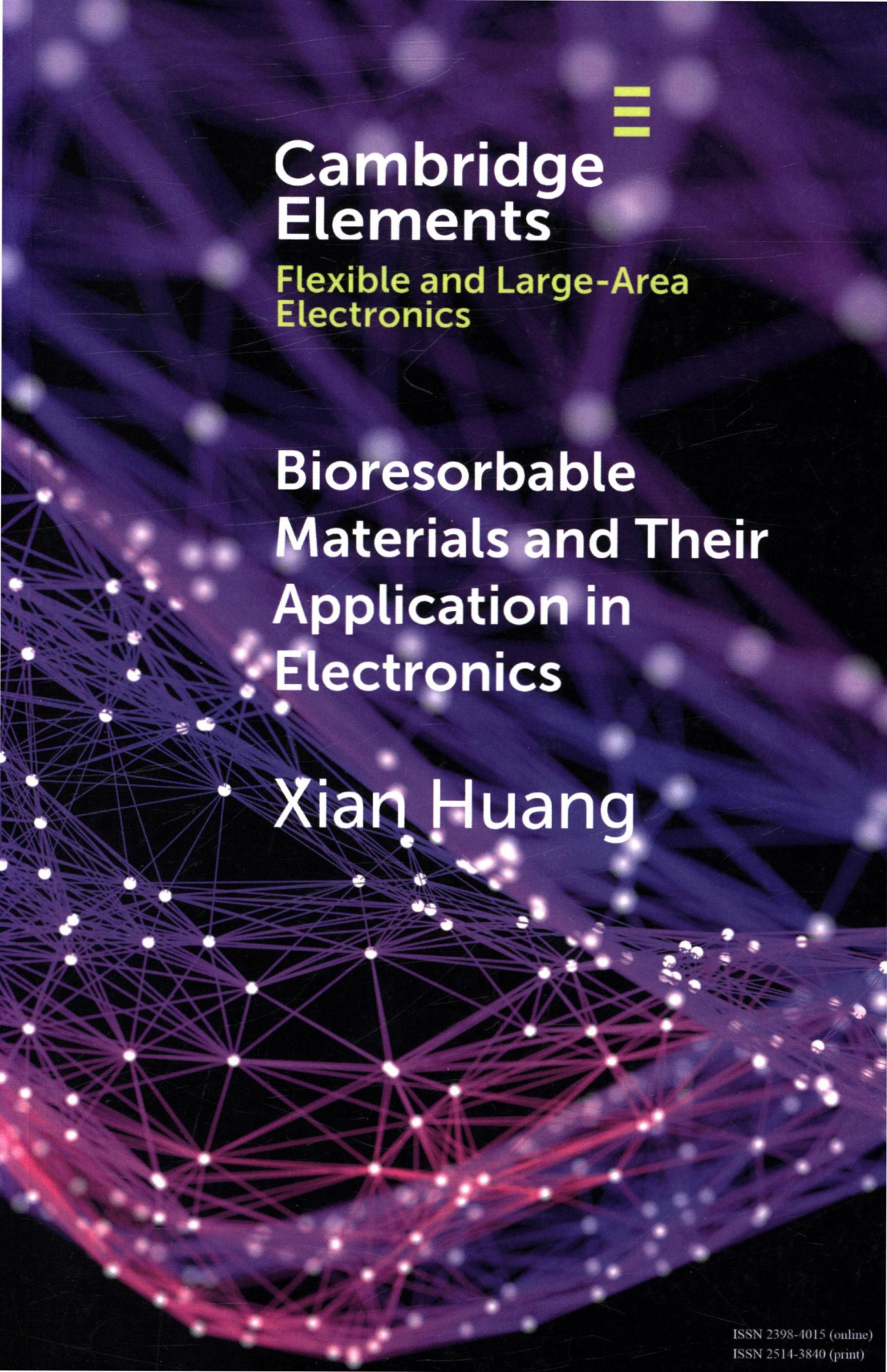

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Flexible and Large-Area Electronics

Bioresorbable Materials and Their Application in Electronics

Xian Huang

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Bioresorbable electronics that can dissolve away in aqueous environments and generate biologically safe products offer a revolutionary solution to replace the built-to-last electronics predominantly used in implanted devices and electronic gadgets. Their use can reduce the risk of surgical complications by minimizing the number of necessary surgeries, and prevent production of electronic waste by allowing rapid device recycling. This Element presents bioresorbable materials such as metals, polymers, inorganic compounds, and semiconductors that have been used to construct electronic devices, and analyzes their unique dissolution behaviors and biological effects. These materials are combined to yield representative devices including passive and active components and functional systems.

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This innovative series provides authoritative coverage of the state-of-the art in bendable and large-area electronics. Specific Elements provide in-depth coverage of key technologies, materials and techniques for the design and manufacturing of flexible electronic circuits and systems, as well as cutting-edge insights into emerging real-world applications. This series is a dynamic reference resource for graduate students, researchers, and practitioners in electrical engineering, physics, chemistry and materials science.

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ELEMENTS OF FLEXIBLE AND LARGE-AREA ELECTRONICS

Ravinder Dahiya
and
Luigi Occhipinti

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Bioresorbable electronics that can dissolve away in aqueous environment and generate biological safe products offers revolutionary solutions to replace current built-to-last electronics predominantly used in implanted devices and electronic gadgets. Its contribution involves reducing risk of surgical complications by minimizing number of surgery and preventing production of electronic waste by allowing rapid device recycling. This Element presents bioresorbable materials (e.g. metals, polymers, inorganic compounds, and semiconductors) that have been used to construct electronic devices and analyzes their unique dissolution behaviors and biological effects. These materials are combined to yield representative devices including passive and active components and functional systems.

Bioresorbable Materials and Their Application in Electronics

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Abstract: *Bioresorbable electronics that can dissolve away in aqueous environments and generate biologically safe products offers revolutionary solutions for replacing current built-to-last electronics predominantly used in implanted devices and electronic gadgets. Its contribution involves reducing the risk of surgical complications by minimizing the number of surgeries required and preventing the production of electronic waste by allowing rapid device recycling. This text presents bioresorbable materials (e.g. metals, polymers, inorganic compounds, and semiconductors) that have been used to construct electronic devices and analyzes their unique dissolution behaviors and biological effects. These materials are combined to yield representative devices including passive and active components and functional systems.*

Key words: *Bioresorbable materials, bioresorbable electronics, transient electronics, biomedical implants, dissolution.*

1 Introduction to Bioresorbable Devices

The dissolution of materials in aqueous media is a common phenomenon that has inspired numerous applications in daily life and scientific research. Some materials can dissolve in biofluids and generate products that are biologically safe, and, thus, are termed as bioresorbable materials. Modern applications of bioresorbable materials include biomedical implants (e.g. stent[1, 2], fixation[3, 4], scaffold[5, 6], bone graft[7, 8], and suture[9–11]) (Figure 1), food/medicine

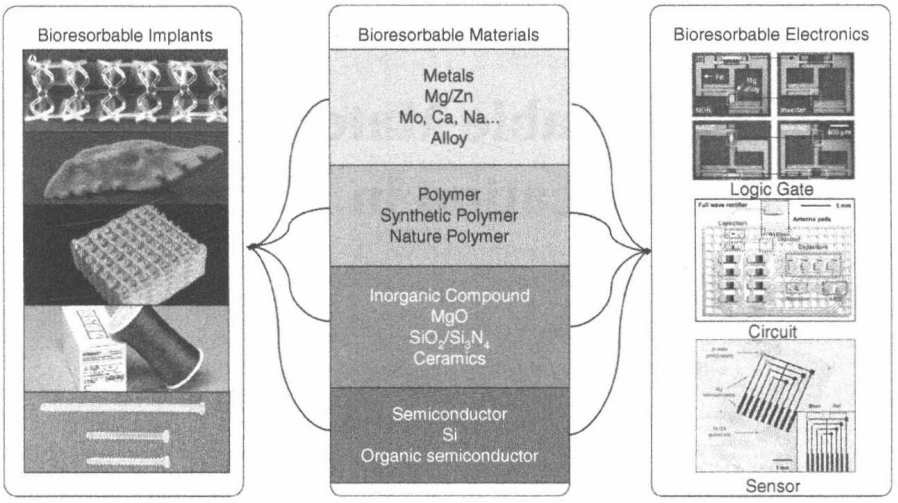

Figure 1. Lists of bioresorbable materials that have been used for biomedical implants and bioresorbable electronics.

packages[12, 13], and additives to cosmetic and pharmaceutical products[14]. These applications have inspired the use of bioresorbable materials in the recent development of bioresorbable electronics (or transient electronics)[15] (Figure 1) that can disappear into the surrounding environment via controlled physical or chemical changes with defined rates (from minutes to weeks) (Figure 2).

Emerging bioresorbable electronics undergoes several stages, and benefits from the development of bioresorbable materials that were originally used in biomedical implants. Traditional biomedical implants are realized by nonabsorbable materials, including metals and polymers such as stainless steel[16–18], cobalt alloys[19–21], titanium and its alloys[22–24], and carbon fiber composites[25–27]. These materials offer high corrosion resistance in the implantation environment, but may release toxic chemicals[28] such as Fe(III), Ti(IV), Cr(VI), and Co(II) during degradation processes[29], causing local inflammation[30], osteolysis[31], hypersensitivity[32], and neuropathy[33]. As a result, bioresorbable metals, polymers, and inorganic compounds are introduced as alternative materials for biomedical implants. The addition of bioresorbable semiconductors further enriches

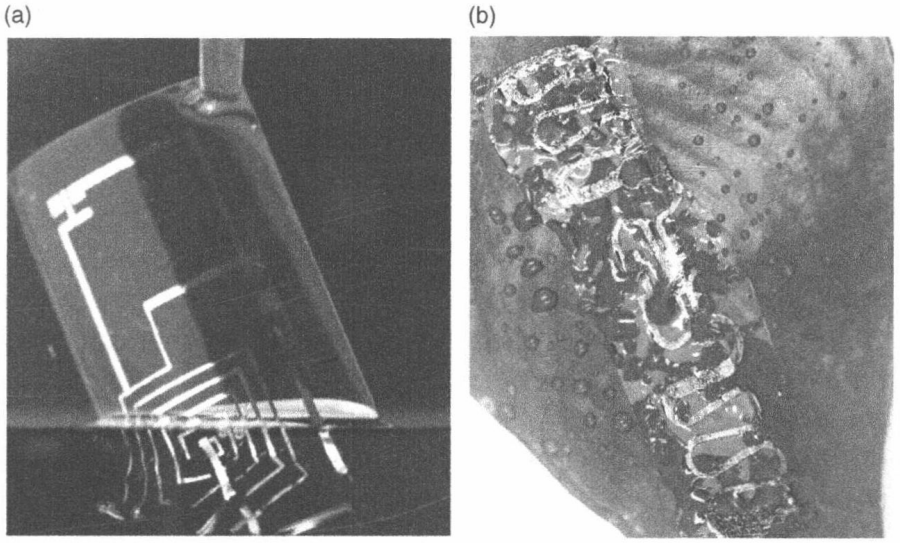

Figure 2. Examples of bioresorbable (transient) electronics devices. (a) A transient rectification circuit on a silk substrate that is dissolving in water (photo: John A. Rogers). (b) A screen-printed bioresorbable antenna based on zinc microparticles on sodium carboxymethyl cellulose. The antenna can be dissolved away by rinsing with water (photo: Xian Huang).

material selection, allowing the appearance of bioresorbable electronics that contains both passive and active electronic components. Currently, more materials are being added to the list of materials that can be used to make bioresorbable electronic devices.

Some pioneering work in developing bioresorbable electronics involves the development of partly resorbable electronic devices[34–36] and the investigation of various types of bioresorbable materials that are suitable for constructing transient electronic devices[37–40]. The collective effort of the research mentioned above has yielded the development of fully bioresorbable electronic devices, which have been demonstrated both as basic components[15, 41] including batteries, sensors, passive components (capacitor, inductor, antenna, and resistor)[42, 43], and active components (diode and MOSFET)[43, 44], and as simply functional systems[45, 46].

Bioresorbable electronics can potentially make incredible strides in the next few years, and hold the promise of making revolutionary advances in health care and environmental protection, resulting in enormous social and economic impacts. Currently, it is estimated that there are annually 16 million surgical procedures performed in acute care hospitals in the United States[47]. These procedures account for ~0.5 million infections annually and nearly four million extra hospital days, as well as $2 billion in increased health care costs[48]. Bioresorbable electronics can be used to conduct internal post-surgical monitoring of organ, tissue, implant, and wound health without the need for surgery to remove them, thus reducing the risk of infection and complications during and after the surgical processes. With regard to environmental protection, increasing demands for electronic gadgets have accelerated the rate of obsolescence, leading to volumes of expended electronic waste (25 million tons yr^{-1})[49], the majority (82%) of which ends up in landfills[50]. The electronic waste in landfills undergoes extremely slow degradation processes, releasing toxic materials such as lead[51], mercury[52], and brominated flame retardants[53] that pollute ground water and soil[54, 55]. Bioresorbable circuits can be used to replace current built-to-last circuits, and can degrade without releasing harmful toxins, allowing rapid recycling of electronic components on the circuits and further reduction in environmental pollution due to unsustainable recycling procedures[56, 57]. The scope of this text mainly involves presenting constituent materials for bioresorbable biomedical implants in general, with the emphasis on materials that have been used in making bioresorbable electronics, including metals, polymers, inorganic compounds, and semiconductors (Figure 1). The biological effects and dissolution mechanisms of these materials are also presented, along with representative devices that demonstrate recent achievements in bioresorbable electronics.

2 *Materials used in Bioresorbable Devices*

Bioresorbable devices can be made of various bioresorbable materials including metals, nonmetals, and semiconductors. These

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materials possess varied water dissolution rates and biological effects, and are used with doses designed to allow tolerable amounts of the dissolution products of these materials in the body[58–60]. For bioresorbable electronics, most of the materials are used as thin films or membranes with thickness ranging from tens of nanometers to micrometers to match the life span of specific devices and to facilitate dissolution.

2.1 Metals

Bioresorbable metals typically include magnesium (Mg), zinc (Zn), molybdenum (Mo), calcium (Ca), and sodium (Na), all of which can react with water molecules through hydrolysis to generate products such as $Mg(OH)_2$, $Zn(OH)_2$, H_2MoO_4, $Ca(OH)_2$, and NaOH. Some of the dissolution products corrode slowly in aqueous conditions, but react with chloride ions in physiological conditions to produce metal chlorides and hydrogen gas. The reported daily tolerable rate of hydrogen gas release in human bodies is 10 μL cm^{-2}[61], which can be used to determine the proper dose and dissolution rate of the bioresorbable metals. The bioresorbable metals are known to be relatively non-cytotoxic in limited quantities, and present naturally in human bodies as vital elements for cell functions.

2.1.1 Mg

Magnesium (Mg) is the second most abundant element in cellular systems, and is involved in all metabolic pathways. It stabilizes DNA and chromatin structures, and acts as an essential cofactor in almost all enzymatic systems related to DNA processing[62]. In addition, Mg^{2+} acts in the formation of biological apatite, which determines the extent of bone fragility, bone healing, and regeneration. Mg offers high specific strength and an elastic modulus that is similar to human bone. As a result, Mg is traditionally used as bone grafts[63, 64] and fixation[65, 66]. In addition, its high biocompatibility leads to its intensive use for intervascular stents for the treatment of arterial disease[67–69] (Figure 3a). Mg is the major composition material in bioresorbable electronics, and has been frequently used to make conductive traces, electrodes, and

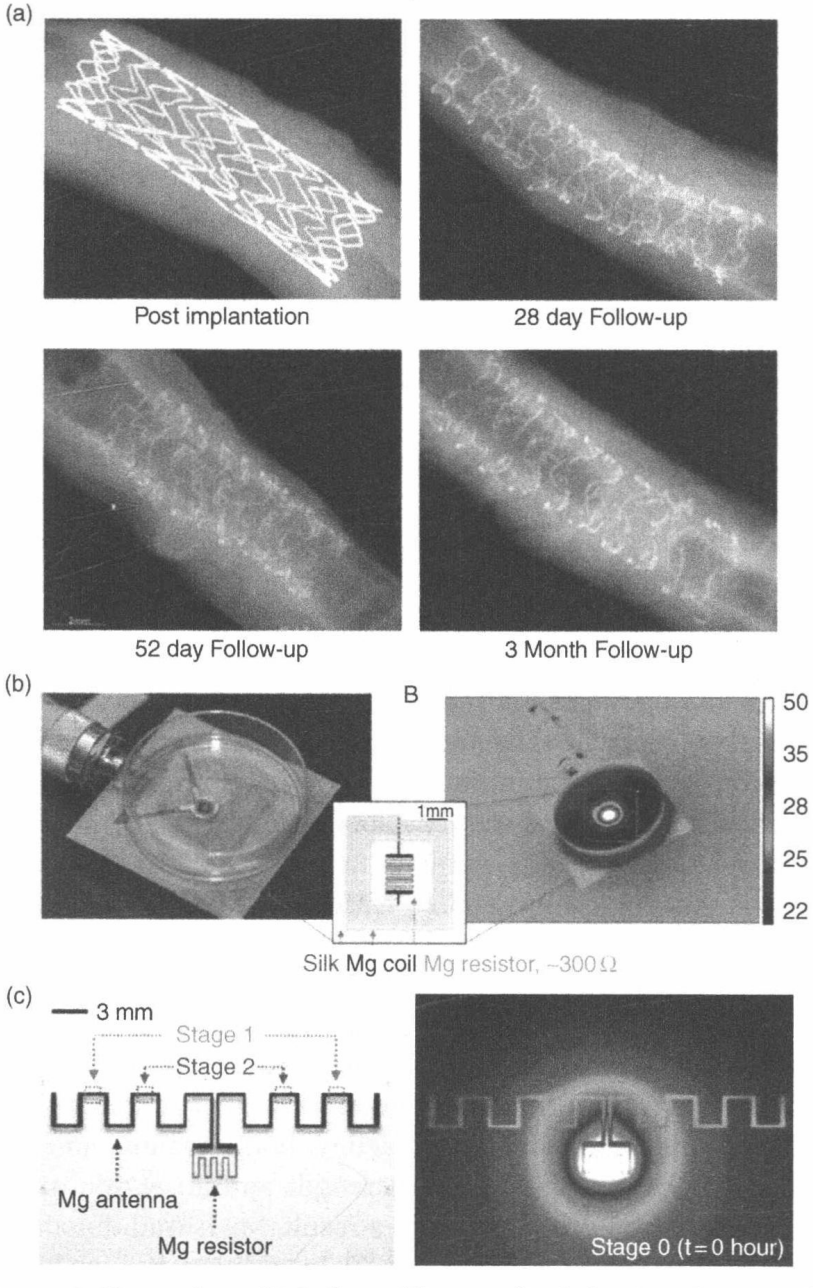

Figure 3. Examples of Mg-based biomedical devices that can be used as (a) bioresorbable stents (reprinted with permission from Ref.[68], copyright 2008 Elsevier Inc.), (b) wirelessly actuated heaters for wound care (reprinted with permission from Ref.[70],

passive components including capacitors, antennas, resistors, and coils[15, 42, 44, 70] (Figures 3b and 3c).

Mg possesses rapid *in vivo* corrosion and dissolution rates. When exposed to water, unprotected Mg will produce magnesium hydroxide ($Mg(OH)_2$)[71], which dissolves slowly in water and forms a surface coating on the Mg, causing a reduced corrosion rate of Mg. However, $Mg(OH)_2$ can react with Cl^- in biological environments to form highly soluble Mg chloride ($MgCl_2$) and hydrogen (H_2) gas. The following reactions can be used to summarize the corrosion reactions of Mg: $Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2$; (1) $Mg + 2Cl^- \rightarrow MgCl_2$; (2) $Mg(OH)_2 + 2Cl^- \rightarrow MgCl_2$[72, 73]. Song and Song measured the corrosion rate of Mg in stimulated body fluid (SBF) using a weight loss measurement approach, and obtained a daily dissolution rate of 19–44 mg cm^{-2}, which could be reduced by half when adding phosphate into the SBF[74]. At the reported dissolution rate, the surface areas of the Mg implants are limited to 9–21 cm^2, considering that the daily exposure limit of Mg for an average 60-kg adult is about 350–400 mg[75]. Additional influences from the environment can alter the dissolution behavior of Mg by means of different physicochemical parameters (e.g. pH, ion concentrations, oxygen). In addition, dissolution of Mg is connected with the immunological response from the localized tissues due to direct and intimate contact. For example, implanted Mg wires exhibited high corrosion when placed in direct contact with the arterial wall but were not corroded after exposure to blood in the arterial lumen for 3 weeks[76].

The rapid corrosion rate of Mg in the electrolytic physiological environment is one of the greatest limitations for its use in

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Caption for Figure 3. (cont.)

copyright 2011 National Academy of Sciences), and (c) frequency tunable antenna, whose frequency can be changed by partially dissolving antenna structures (reprinted with permission from Ref.[42], copyright 2015 John Wiley and Sons).

long-term implantable applications. However, this issue can be handled by introducing bioresorbable surface coatings. Typical surface coating materials for Mg include calcium phosphate[77, 78], polycaprolactone[79], silicon carbide (SiC)[80], and silicon dioxide (SiO_2)[81], which are deposited onto Mg implants through soaking[77, 78], electrodeposition[82], spraying[79], chemical vapor deposition[80], and physical vapor deposition[83, 84]. By adjusting the coverage and thickness of the coating, the preferential degradation area and rate can be programmed to allow function transformation[42] during different dissolution periods (Figure 3c) and varied working times to adapt to specific implantation needs[85].

The dissolution rate and mechanical strength of Mg can also be tuned by adding bioresorbable alloying elements. An appropriate alloying composition can improve the corrosion resistance, mechanical properties, and ease of manufacture of Mg-based materials. Researchers have developed binary alloys containing two bioresorbable metals such as Mg–Ca[86], Mg–Zn[87], Mg–Nd[88], and Mg–Gd[89], all of which offer moderate resistance to corrosion (2 mm yr^{-1}) and mechanical yield strength (<150 MPa). Improved corrosion resistance and mechanical strength can be achieved by introducing multi-element Mg-based alloys. A notable example is the Mg–Zn–Ca alloy, within which Ca improves the corrosion resistance of the alloy and Zn increases the strength of the alloy[90]. A Young's modulus of ~40 GPa and glass transition temperatures in the range 119–129 °C can be achieved by properly selecting the ratio of individual elements in the alloy[91].

2.1.2 Zn

Zinc (Zn) is another essential element for human beings, and is a promising alternative to Mg owing to its slower dissolution rate in biological environments[92]. Zn participates in several basic biological functions in human bodies, such as cell growth[93], protein synthesis[94], and DNA replication[95]. Deficiency of Zn may result in skeletal growth retardation and alteration in bone tissue calcification[96, 97]. *In vivo* experiments involving implanting zinc wires in the abdominal aortas of rats indicated low cellular density

and lack of smooth-muscle cells adjacent to the implant interface, suggesting an anti-proliferation effect and the prevention of restenosis from zinc implants[98].

Zn offers much slower corrosion rates in biological environments compared with Mg. According to the standard electrode potential, i. e. Mg (-2.37 V)[99] <Zn (-0.763 V)[100]<Fe (0.440 V)[101], Zn has a corrosion rate faster than Fe, but slower than Mg. Four Zn wire samples were implanted in the abdominal aorta of a Sprague-Dawley rat for 1.5, 3, 4.5, or 6 months, respectively. The wires showed uniform corrosion behavior for the first 3 months, and severe, localized corrosion after 4.5 months (Figure 4a). Dissolution rates quantified from measuring the reduction of cross-sectional areas have shown that the average annual corrosion rate of Zn wires varied from ~12 μm yr^{-1} in the first month to ~50 μm yr^{-1} after implantation for 6 months[102] (Figure 4b). Another study that involved immersing a Zn coupon 6 mm in diameter and 2 mm in thickness in SBF at pH=7 (37 °C) for 14 days further confirms that the annual corrosion rate of Zn is ~50 μm yr^{-1}[103]. Such corrosion rates are much slower than those of Mg, and result in an average daily release of ~0.1 mg cm^{-2} of zinc implants, limiting the surface area of Zn implants to be less than 80–250 cm^2, based on the recommended dietary intake of 8–25 mg day^{-1}[104]. Compared to SBF, Zn exhibits less noble dissolution behavior and reduced dissolution rate after immersion in whole blood for 72 h. The reduced dissolution rate of Zn in whole blood is considered to result from the passivation effect from the biomolecules and inorganic dissolution products[104]. Hydrolysis of Zn generates $Zn(OH)_2$, which is again slightly soluble in water, but can dissolve readily in biological solutions that contain Cl^- ions.

Zn has been used as a single construction material for stents[98, 102, 105, 106] and scaffolds[107] (Figure 4c), or used as an alloying material when combined with Mg[87, 108] or Ca[109]. Applications of Zn in bioresorbable electronics range from electrodes[38, 110] for batteries and sensors to micro/nano fillers[111] for conductive pastes (Figure 4d).

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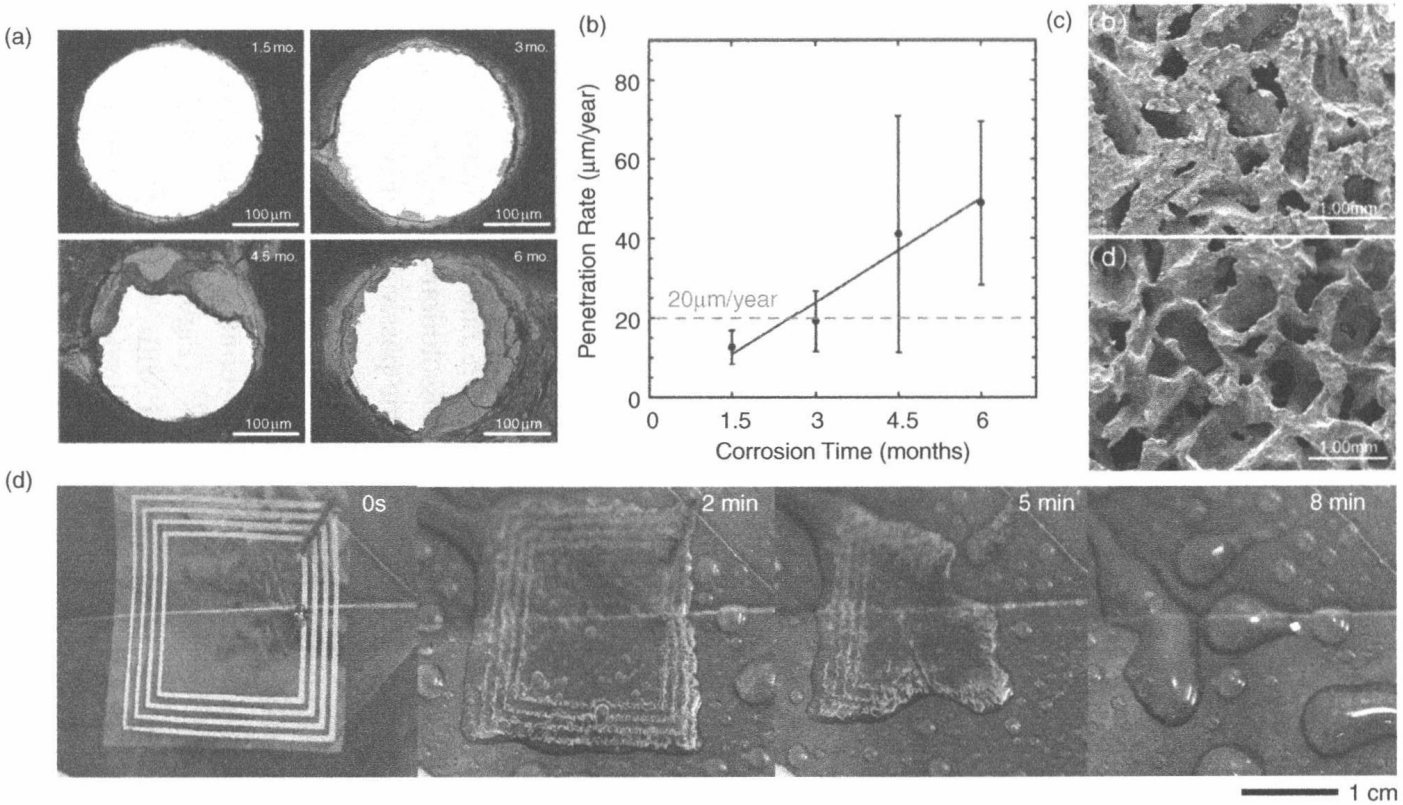

Figure 4. Zn as a bioresorbable material. (a) Representative backscattered electron images of cross-sectional areas from Zn implants after being implanted in a Sprague-Dawley rat for 1.5, 3, 4.5, and 6 months