RADIOPAQUE BIODEGRADABLE METALLIC SCAFFOLD WITH A NON-BIODEGRADABLE COATING, AND WHICH INCLUDES RADIAL SUPPORT RINGS AND RESILIENTLY FLEXIBLE, PREFERENTIALLY FRACTURABLE AXIAL LINKS THEREBETWEEN

TECHNICAL FIELD

The present disclosure relates to a scaffold structure implantable in an anatomical lumen of a living human or animal body. More particularly, the present disclosure is directed to an implantable scaffold structure including a biodegradable metallic scaffold that carries a non-biodegradable material, layer, or coating that insulates, separates, or isolates the metallic scaffold from a radiopaque material, layer, or coating. The scaffold structure is formed to include multiple radial support segments, sections, or rings, between which resiliently flexible and preferentially fracturable axial coupling / decoupling members or links are disposed.

BACKGROUND

Various types of scaffold structures (e.g., vascular stents) have been designed for implantation into the lumens of anatomical vessels or ducts of living bodies. From a structural integrity versus time perspective, such scaffold structures can broadly be categorized as (a) non-resorbable scaffolds, which retain their compositional integrity throughout the time they reside within the anatomical lumen in which they are implanted; or (b) bioresorbable scaffolds, which gradually deteriorate or break down over time as a result of exposure to the environment in the lumen. More particularly, with respect to bioresorbable scaffolds, substantially all of the material(s) incorporated into the scaffold can be biodegraded into materials that can be resorbed (i.e., metabolized and/or excreted by a living body). For bioresorbable vascular scaffolds, one of the most important asserted benefits is “vessel restoration”, i.e., the gradual degradation of mechanical strength of the scaffold, thus freeing the vessel from the scaffold’s underlying frame or cage structure, to enhance the flexibility and health of the vessel after angioplasty.

Obtaining adequate radiopacity such that an implanted scaffold is visible during one or more types of medical imaging procedures, such as angiography, is of great importance, particularly because the material(s) that form the scaffold’s underlying frame or cage may

be radiolucent. Typically, a scaffold that is formed of a radiolucent material is transformed into a radiopaque scaffold by carrying one or more radiopaque materials, such as by way of a radiopaque coating or layer applied to the scaffold's cage.

With respect to non-degradable metallic scaffolds in which the underlying metallic scaffold frame or cage is formed of a radiolucent material, technologically early art described in U.S. Patent 6,174,329 is directed to the application of a radiopaque gold coating to a very thin walled (<80 micrometer) metallic, non-degradable stent. A "protective layer" is then applied which is asserted to act as "a mechanical barrier which protects against mishandling, electrochemical reaction that causes galvanic corrosion, and adverse blood and tissue response". This protective layer has a first polymer adhesion layer formed "from the Silane group" or a plasma deposited "polymer from a gaseous organic such as Methane, Xylene, or gases from the Silane or Titanate group. The protective layer further includes thereupon a second "biocompatible and blood compatible" material which is a polymer, a metal, or a ceramic". An adhesion layer is used to prevent "stretching and straining" of the protective layer during flexing of the stent. In another embodiment, the previously described protective layer is first applied to cover the stent and the radiopaque layer is applied to partially or completely cover the protective layer. In this embodiment, the radiopaque layer is said to be "scratch resistant and biocompatible".

FIG. 1 shows portions of a stent constructed as described in U.S. Patent 6,174,329. Unfortunately, in a stent constructed in this manner, an outermost radiopaque coating, even when applied in a very thin layer, tends to be very fragile and brittle, as indicated in FIG. 1. It can be seen from FIG. 1 that there is a problem with excessive flaking of an unprotected radiopaque coating during delivery and expansion of the stent when the radiopaque coating comprises the outermost coating layer of the stent.

Additional prior art related to the foregoing includes U.S. Patent 7,077,837, which describes a metallic stent that is coated with three metallic layers via atomic bombardment, an adhesive layer, a radiopaque layer, and a protective biocompatible layer; and U.S. Patent 6,355,038, which describes a metallic stent with a biocompatible radiopaque coating consisting of particles of radiopaque material dispersed in a polymer.

With respect to bioresorbable scaffolds, most biodegradable materials that have useful properties after implantation in an internal lumen (e.g., biocompatibility, maintenance of adequate mechanical strength over a required healing period, favorable processing properties, etc…) have inadequate radiopacity, particularly for the construction of vascular stents having a typical wall thickness in the range of 60-180 micrometers. This has led the development of bioresorbable scaffolds having radiopaque coatings applied thereto.

For instance, U.S. Patent 7,951,194 describes a bioresorbable polymer scaffold with a radiopaque coating containing radiopaque particles dispersed in a biodegradable coating, and a topcoat layer of biodegradable polymer. U.S. Patent 9,265,866 describes a bioresorbable scaffold with a polymer coating that contains radiopaque particles. The particles are made from two dissimilar metals, which leads to galvanic corrosion of the particles.

After a bioresorbable magnesium (Mg) scaffold that has a radiopaque material which is directly in contact with the Mg has been implanted in a vessel, galvanic corrosion rapidly leads to significant restenosis. For instance, FIG. 2 is an angiographic image of a Mg scaffold having a radiopaque material directly in contact with the Mg, and which further includes an outer protective layer, at an *in vivo* post-implantation time of 4 weeks. As indicated in FIG. 2, due to galvanic corrosion, a large amount of restenosis has occurred in the region in which the scaffold was implanted, despite the outer protective layer.

A key property that must be considered in the design of bioresorbable scaffolds is the scaffold degradation or resorption rate, particularly with respect to (i) a target or desired length of time that the scaffold should continue to provide sufficient structural integrity in order for vessel healing to occur, and (ii) the extent to which the products of premature scaffold degradation can adversely affect vessel healing.

For instance, it is known that certain Mg alloys have favourable properties for the development of biodegradable metallic scaffolds. However, when formed into the shape of a scaffold, e.g., when formed as a metallic frame or cage structure, these alloys degrade

undesirably rapidly *in vivo*, resulting in structural failure and/or inadequate mechanical support during the vessel healing phase. (*Int. J. Mol. Sci.* **2011,** *12*, 4250-4270). As a result, coatings have been proposed to slow the scaffold degradation rate. For example, U.S. Patent 8,507,101, U.S. Patent Publication 20130218265, and U.S., Patent Publication 20140228968 describe surface treatments to the body of a Mg scaffold, which are asserted to increase scaffold corrosion resistance. U.S. Patent Publication 20100076544 describes a bioresorbable metal scaffold surrounded by a polymeric coating that has a slower degradation rate than the underlying metal scaffold. U.S. Patent 9,474,637 describes a high molecular weight, acid-generating polymer coating which is said to reduce the degradation rate of a bioresorbable polymeric scaffold. In one embodiment, the coating may also contain a therapeutic substance. The AMS-3 bioresorbable Mg scaffold, as manufactured by the Biotronik company (*Int. J. Mol. Sci.* **2011**, 4258) and described in U.S. Patent Publication 20090240323, uses a fast degrading polymer coating to reduce the degradation rate of its Mg body or core structure. In one embodiment, the polymer coating may contain a therapeutic substance to reduce restenosis or thrombosis during the healing phase. Lu *et al*. (*Colloids Surf. B Biointerfaces* **2010**, *83*, 23–28) reported the fabrication of bioresorbable AZ81 Mg alloy stent coated with a composite multi-layer biodegradable film for controlling the biodegradation rate of the Mg alloy.

Not surprisingly to individuals having ordinary skill in the art, the teachings of the bioresorbable scaffold art are overwhelmingly directed toward applying biodegradable coatings to reduce the degradation rate of the base or core scaffold material. However, devices manufactured with biodegradable anti-corrosion coatings as described in the prior art do not adequately slow the scaffold degradation rate, as the described coatings do not maintain adequate physical and chemical isolation of the base material of the scaffold body from fluid entry. Moreover, following the flexing and implantation of a scaffold with a biodegradable coating, localized rapid corrosion of the base scaffold material can occur, which results in undesirably early scaffold failure, and accompanying increases in tissue inflammation and restenosis.

FIG. 3 shows an idealized degradation time and radial strength curves for a commercially available Mg bioresorbable scaffold or stent. As indicated in FIG. 3, scaffolding decreases

significantly around 3 months, which is still too fast because it occurs before sufficient tissue healing has occurred. Additionally, the degradation products from the implanted scaffold structure significantly affect the healing of the vessel while the vessel is still in a fragile state. Furthermore, even if the idealized degradation time were achieved for the entire implanted structure, this bioresorbable stent is already well along in its degradation process while the vessel is still healing, which may take typically 9 - 12 months in a diseased blood-carrying vessel of the human anatomy. Moreover, the outer biodegradable coating can be easily damaged during handling, stent insertion, and expansion, resulting in early coating failure, much faster degradation, structural failure, excessive release of degradation products, inflammation, and restenosis.

FIG. 4A shows an intraluminal optical coherence tomography (OCT) image of a newly implanted commercially available Mg bioresorbable scaffold in a human coronary artery. The short bright lines tangent to the lumen diameter with the trailing shadows are images of the stent struts. FIG. 4B shows an early failure of the same implant at 4 months due to biodegradable coating failure and undesirably rapid degradation, leading to breakup of the stent struts, and resulting in severe restenosis and vessel failure.

Another undesirable aspect of known biodegradable coatings intended to slow down stent degradation is undesirable or unpredictable breakdown of the coating across various, different, or particular regions of the stent over. FIG. 5 is a collection of OCT showing time progress of strut degradation in a bioresorbable stent with a prior art biodegradable coating, where there is heterogeneous progression of strut degradation, undesirably resulting in variable radial support by different portions of the stent over time.

With respect to the radial support of an injured vessel during the scaffold degradation process, it is important to maintain the radial strength of the implant until the vessel is fully healed. Prior art bioresorbable scaffolds largely fail in this regard, degrading prematurely, losing radial strength and releasing excess degradation products, causing inflammation, and restenosis.

Bioresorbable scaffolds have been proposed which lose axial strength more rapidly than they lose radial strength after implant. The persistence of axial strength after stent implantation is undesirable because it interferes with vessel flexure, which is part of vessel healing and the normal functioning of a healthy blood vessel. Restricted axial flexure of the vessel caused by the presence of the scaffold further interferes with smooth blood flow patterns inside the vessel lumen, which may be a trigger for intraluminal thrombus. U.S. Patent Publication 20090208555 describes a biodegradable coating for bioresorbable implants, where the coating is biodegradable polymer which may be selectively applied to slow down the degradation rate of only certain portions of the implant. U.S. Patent Publication 201100076319 describes a bioresorbable Mg scaffold with a biodegradable, fluid permeable polymer wrap. The scaffold has interconnecting elements which are have smaller cross section than the radial support elements, which is asserted to allow for faster degradation of the interconnecting elements that provide axial strength. U.S. Patent 8,425,587 describes a bioresorbable stent containing straight links between axially spaced radial support bands. Some of the straight links are modified to contain failure points adapted to break before the radial support bands. However, due to the presence of the interconnecting straight links between the rings, the unexpanded stent has poor axial flexibility prior to link failure, including during delivery and deployment.

U.S. Patent 7,811,622 describes a bioresorbable polymer scaffold structure in which a non-porous coating is applied over the scaffold, where the non-porous coating can be non-degradable; a bioactive layer is applied over the non-porous coating specifically for carrying a bioactive material; and a porous coating is applied over the bioactive layer for controlling the release of the bioactive material. The bioactive layer can include a radiopaque agent therein. However, a porous coating that allows radiopaque particles such as tantalum (Ta) particles to leach out of the bioactive layer may lead to unpredictable or undesirable tissue response. For instance, as shown by W. Van Oeveren *et al*. (*Prog. in Biomed. Res.* **2000**, 3, 211-214), in clinical studies a high incidence of thrombotic complications could occur after Ta stent implantation if anticoagulation and anti-platelet therapy was insufficient.

A need exists for an improved implantable scaffold structure that exhibits resorbability, which overcomes at least some of the aforementioned shortcomings of prior art scaffold structures.

SUMMARY

Aspects of the present disclosure are directed to scaffold (e.g., stent) structures or devices that are introducible or implantable into a lumen of an anatomical passage, channel, conduit, vessel, or duct of a living body, and which overcome at least some of the aforementioned shortcomings of the prior art.

More particularly, various embodiments in accordance with the present disclosure are directed to an implantable, ready for implantation, or implanted biodegradable scaffold structure or device that provides the same benefits as a bioresorbable scaffold, while not being fully bioresorbable. That is, an implantable scaffold structure in accordance with multiple embodiments of the present disclosure includes bioresorbable or biodegradable materials, but is not entirely composed of bioresorbable or biodegradable materials. For instance, an implantable scaffold or stent structure in accordance with an embodiment of the present disclosure includes some biodegradable materials, or mostly biodegradable materials (e.g., in some embodiments, the thickness of non-biodegradable materials is 20 micrometers / microns or less, such as 10 micrometers or less (e.g., between approximately 0.1 – 10 micrometers, 0.1 – 7.5 micrometers, 0.1 – 5 micrometers, 0.1 – 4 micrometers, 0.1 – 3 micrometers, 0.1 - 2.5 micrometers, 0.1 – 2 micrometers, 0.5 – 4 micrometers, 0.5 – 3 micrometers, 0.5 – 2.5 micrometers, 0.5 – 2 micrometers, 1 – 4 micrometers, 1 – 3 micrometers, or 1 – 2 micrometers) on each of an inner or inward facing surface and outer or outward facing surface of an underlying biodegradable metallic scaffold). Such embodiments can actually achieve the intended objective of “vessel restoration” and provide essentially the same type of functionality as a fully bioresorbable scaffold, but with significantly or greatly improved degradation time profiles relative to a time period desired or required for significant tissue healing to occur. Moreover, such embodiments provide the added benefit of substantially lower or reduced release of inflammatory degradation products because some of the materials of the scaffold structure are non-degradable.

An implantable, ready for implantation, or implanted scaffold or stent structure in accordance with various embodiments of the present disclosure includes: (a) a biodegradable metallic scaffold or stent formed from a magnesium (Mg) alloy, which provides an underlying or base material composition or material that establishes a scaffold or stent body corresponding to or defining a frame or cage structure; (b) a first material composition or material, coating, or layer (e.g., in the form of one or more polymers) carried by the scaffold or stent body that substantially reduces the *in vivo* degradation rate of the base material, and which is a durable, i.e., non-degradable, conformal material composition or material, coating, or layer relative to the scaffold or stent body; and (c) one or more additional material compositions, coatings, or layers to increase the radiopacity of the stent, while also (i) preventing flaking of radiopaque material(s) from the scaffold or stent structure, and/or (ii) releasing or delivering a therapeutic substance (e.g., an anti-restenotic drug).

A biodegradable metallic scaffold or stent structure in accordance with embodiments of the present disclosure includes a biodegradable metallic stent body carrying a coating (e.g., a non-biodegradable polymer coating) that substantially reduces and predictably and/or uniformly controls the degradation rate of the underlying scaffold or stent body throughout various or different sections of the biodegradable metallic scaffold or stent body. A biodegradable metallic scaffold or stent structure in accordance with embodiments of the present disclosure provides a sufficiently long degradation time (or a sufficiently slow degradation rate) to allow an anatomical lumen or vessel into which the scaffold or stent structure has been introduced or implanted to substantially heal prior to any significant loss of scaffold or stent radial strength or significant release of degradation products.

A biodegradable metallic scaffold or stent structure in accordance with embodiments of the present disclosure is visible under X-ray fluoroscopy by way of additionally carrying a radiopaque material, coating, or layer, wherein the radiopaque layer is protected from flaking and mechanical abrasion during stent insertion, delivery, and expansion.

In various embodiments, a biodegradable metallic scaffold or stent structure is compressible and expandable, and includes multiple radial support structures that are initially coupled or

joined together by way of non-linear, curved, curvilinear, or bent axial coupling members or links that are at least slightly resilient with respect to axial displacement of the radial support structures. Such a biodegradable metallic scaffold or stent structure exhibits increased or increasing post-implant axial flexibility by way of increased or increasing decoupling of radial support structures from each other, such as by way of preferential breakage or rupture of the axial coupling members in response to forces (e.g., repeated compressive forces) imparted thereto after implantation. The materials, coatings, or layers carried by the metallic scaffold or stent are stretchably, flexibly, and/or slidably carried by, overlaid upon, or attached to the metallic scaffold or stent body, and are sufficiently stretchable and malleable to allow for the decoupling of the radial support structures without compromising the intended functions of slowing degradation time, providing increased radiopacity, preventing flaking, and/or releasing a therapeutic agent.

A biodegradable metallic stent structure in accordance with an embodiment of the present disclosure is sufficiently flexible in its unexpanded state when attached to an angioplasty balloon to be easily delivered to an atherosclerotic lesion through tortuous vessel anatomy. In particular embodiments, fewer than approximately 10%, or less than about 5%, of the aforementioned axial coupling members rupture or are broken in response to compressive forces experienced thereby during stent structure implantation.

In the text that follows, particular representative embodiments in accordance with the present disclosure are described primarily with respect to their implantation in portions of the human cardiovascular system, e.g., for use in treating atherosclerotic lesions of the human cardiovascular system. In view of the description herein and the associated drawings, individuals having ordinary skill in the relevant art will understand that embodiments in accordance with the present disclosure can also be applied to other passages within the human body, including one or more of lumens within the urinary tract, respiratory tract, biliary tract, or digestive tract.

In accordance with an aspect of the present disclosure, a scaffold structure is provided which is implantable into an anatomical lumen of a human or animal body. The scaffold structure is an elongate structure having a length. A central axis is definable through or

internal to the elongate scaffold structure along its length. The scaffold structure as-manufactured includes, is formed as, or consists essentially of, or consists of: an elongate biodegradable metallic scaffold that provides a frame or cage structure; a non-porous inner coating disposed over the biodegradable metallic scaffold, wherein the inner coating includes a non-biodegradable polymer that conformally encases the scaffold, such that an inner surface of the inner coating is disposed adjacent to and in contact with the scaffold; a non-porous outer coating comprising a biodegradable or non-biodegradable polymer, the outer coating having an outer or outermost surface (e.g., an exposed outer surface); and a radiopaque material disposed external to the inner coating and internal to the outer or outermost surface (e.g., the exposed outer surface) of the outer coating along the scaffold structure's length, wherein the inner coating electrochemically isolates the radiopaque material from the scaffold.

The inner coating can include or be a resilient, pinhole free parylene sheath that conformally coats the scaffold and which exists in slidable and/or flexible contact with the scaffold.

The radiopaque material can include or be a coating of Tantalum or Platinum that forms a continuous material layer sandwiched between the inner coating and the outer coating.

The radiopaque material can include or be a multiplicity of radiopaque particles dispersed within the outer coating.

The outer coating can include one or more of parylene C, polylactic acid, polyglycolic acid, copolymers of lactic and glycolic acid, polycaprolactone, parylene, polymethacrylate, cyanoacrylates, polyvinylidene fluoride (PVDF), Poly(hydroxyalkanoate) (PHA), and polyurethane, and copolymers of polyurethane.

The outer coating can carry a therapeutic substance, e.g., an anti-restenosis drug, which can be selected from the group of paclitaxel and its derivatives (e.g., taxane derivatives of paclitaxel), or mTOR inhibitors of the LIMUS family.

The scaffold can include or be formed as a plurality of radial support rings axially disposed along the length of the scaffold structure, wherein the central axis of the scaffold structure extends through each radial support ring, and wherein each radial support ring includes: a pair of axially adjacent struts radially disposed about the central axis; and a plurality of bridge members, wherein each bridge member couples each of the pair of adjacent struts; and a plurality of preferentially fracturable links (e.g., preferentially fracturable axial links configured for axial coupling radial support rings) wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one bent or curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples.

Portions of the inner coating that overlay the preferentially fracturable links can be configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links.

At least some of the plurality of preferentially fracturable links can have an omega shape along their length.

At least some of the bridge members can be a straight structure that extends in a direction parallel to the central axis.

In accordance with a further aspect of the present disclosure, a scaffold structure is provided which is implantable into an anatomical lumen of a human or animal body. The scaffold structure is an elongate structure having a length. A central axis is definable through or internal to the elongate scaffold structure along its length. The scaffold structure as-manufactured includes, is formed as, consists essentially of, or consists of: (a) an elongate biodegradable metallic scaffold that provides a frame or cage structure, wherein the scaffold includes, is formed as, consists essentially of, or consists of: (i) a plurality of radial support rings axially disposed along the length of the scaffold, wherein the central axis of the scaffold extends through each radial support ring, and wherein each radial support ring includes, is formed as, consists essentially of, or consists of: a plurality

(e.g., a pair) of axially adjacent struts radially disposed about the central axis; and a plurality of bridge members, wherein each bridge member couples each of the plurality of adjacent struts; and (ii) a plurality of preferentially fracturable links (e.g., preferentially fracturable axial links), wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one bent or curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples; (b) a non-porous inner coating disposed over the biodegradable metallic scaffold, wherein the inner coating comprises a non-biodegradable polymer that conformally encases the scaffold, such that an inner surface of the inner coating is disposed adjacent to and in contact with the scaffold; (c) an outer coating comprising a biodegradable or non-biodegradable polymer, the outer coating having an outer or outermost surface (e.g., an exposed outer surface); and a radiopaque material disposed external to the inner coating and internal to the outer or outermost surface (e.g., the exposed outer surface) of the outer coating along the scaffold structure's length, wherein the inner coating electrochemically isolates the radiopaque material from the scaffold, and wherein the outer coating isolates the radiopaque material from the scaffold structure's external environment.

Portions of the inner coating that overlay preferentially fracturable links can be configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links.

In accordance with another aspect of the present disclosure, an elongate scaffold is provided, which is implantable into an anatomical lumen of a human or animal body. The elongate scaffold has a length, and a central axis is definable through or internal to the elongate scaffold along its length. As-manufactured, the scaffold includes, is formed as, consists essentially of, or consists of: a plurality of radial support rings axially disposed along the length of the scaffold, wherein the central axis of the scaffold extends through each radial support ring, and wherein each radial support ring includes, is formed as, consists essentially of, or consist of: a plurality (e.g., a pair) of axially adjacent struts radially disposed about the central axis; and a plurality of bridge members, wherein each bridge member

couples each of the plurality of axially adjacent struts; and a plurality of preferentially fracturable links (e.g., preferentially fracturable axial links), wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples.

At least some of the plurality of preferentially fracturable links can have an omega shape along their length.

At least some of the bridge members can have a straight structure that extends in a direction parallel to the central axis.

In accordance with an aspect of the present disclosure, a process for manufacturing or providing a biodegradable implantable or implanted metallic scaffold structure configurable or configured for implantation into a mammalian body includes or consists essentially of: providing an elongate biodegradable metallic scaffold having (a) preferentially fracturable links, and (b) radial support rings that are disposed along the scaffold's length and which are coupled by way of the preferentially fracturable links (e.g., preferentially fracturable axial links), wherein the preferentially fracturable links are intentionally (i) configured to be structurally weaker than the radial support rings along at least one spatial direction, and (ii) preferentially fracturable or breakable relative to the radial support rings in response to physical stresses or deformations exerted upon the scaffold; providing or disposing a non-porous first covering or coating over the scaffold, wherein the first covering or coating includes or is a non-biodegradable polymer that conformally encases the scaffold, thereby conformally encasing the scaffold's preferentially fracturable links and radial support rings, such that an inner surface of the first covering or coating is disposed adjacent to and in contact with the scaffold, wherein portions of the first covering or coating that overlay preferentially fracturable links are configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links; providing or disposing a radiopaque material external to exposed, external, or outer surfaces of the

first covering or coating along at least portions of the scaffold structure's length; and providing or disposing a non-porous second covering or coating including a biodegradable or non-biodegradable polymer over exposed, external, or outer surfaces of the radiopaque material over the scaffold structure's length, wherein the first covering or coating electrochemically isolates the radiopaque material from the scaffold.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 shows portions of a magnesium (Mg) stent constructed with a radiopaque coating as described in U.S. Patent 6,174,329, which results in a radiopaque coating exhibiting flaking or peeling away from the Mg stent.

FIG. 2 is an angiographic image of a Mg scaffold having a radiopaque material directly in contact with the Mg, and which further includes an outer protective layer, at an *in vivo* post-implantation time of 4 weeks, showing a large amount of restenosis in the region in which the scaffold was implanted, despite the outer protective layer.

FIG. 3 shows an idealized degradation time and radial strength curves for a commercially available Mg bioresorbable scaffold or stent.

FIG. 4A shows an intraluminal optical coherence tomography (OCT) image of a newly implanted commercially available Mg bioresorbable scaffold in a human coronary artery.

FIG. 4B shows an early failure of the implanted scaffold of FIG. 4A at 4 months due to biodegradable coating failure and undesirably rapid degradation, leading to breakup of scaffold struts, and resulting in severe restenosis and vessel failure.

FIG. 5 is a collection of OCT images showing time progress of strut degradation in a commercially available bioresorbable stent with a prior art biodegradable coating, where there is heterogeneous progression of strut degradation, undesirably resulting in variable radial support by different portions of the stent over time.

FIG. 6A is a perspective schematic illustration of a scaffold structure in accordance with an embodiment of the present disclosure.

FIG. 6B is a top schematic illustration showing portions of the scaffold structure of FIG. 6A.

FIG. 7A is a cross-sectional schematic illustration of a portion of a scaffold structure corresponding to FIGs. 6A – 6B, showing an organization of multiple coatings accordance with a first set of embodiments of the present disclosure, taken along line A – A' of FIG. 6A.

FIG. 7B is a cross-sectional schematic illustration of a portion of a scaffold structure corresponding to FIGs. 6A – 6B, showing another organization of multiple coatings in accordance with a second set of embodiments of the present disclosure, taken along line A – A' of FIG. 6A.

FIG. 8 is a magnified image showing portions of a scaffold structure in accordance with an embodiment of the present disclosure, which has undergone scaffold expansion, and for which no obvious cracking or flaking or peeling is apparent.

FIG. 9 is an *in vivo* angiographic image of a Mg biodegradable scaffold structure corresponding to FIGs. 6A, 6B, and 7A, which has been implanted in a porcine coronary artery, at a time of 4 weeks post-implantation.

FIG. 10A is a Faxitron (X-ray) image of a scaffold structure in accordance with an embodiment of the present disclosure, after 4 weeks of implantation *in vivo* in a porcine coronary artery, showing several broken or dismantled preferentially fracturable links (e.g., preferentially fracturable axial links).

FIG. 10B is an Optical Coherence Tomography (OCT) image in the vessel where the scaffold structure of FIG. 10A is located, demonstrating excellent patency and freedom from restenosis at 4 weeks post-implantation.

FIG. 10C is another Faxitron (X-ray) image of a scaffold structure in accordance with an embodiment of the present disclosure, after 12 weeks of implantation *in vivo* in a porcine coronary artery, showing further dismantling of the preferentially fracturable links.

FIG. 10D is a 12 week post-implantation OCT image of the vessel where the scaffold structure of FIG. 10C is located, where the results again demonstrate unobstructed blood flow and freedom from restenosis.

DETAILED DESCRIPTION

The FIGs. included herewith show aspects of non-limiting representative embodiments in accordance with the present disclosure for purpose of illustration and to aid understanding. Particular structural elements shown in one or more FIGs. may not be to scale or precisely to scale relative to each other. The depiction of a given element or consideration or use of a particular element number in a particular FIG. or a reference thereto in corresponding descriptive material can encompass or relate to a categorically related, the same, an equivalent, or an analogous structure, element, sub-element, or element number identified in another FIG. or descriptive material associated therewith. The presence of "/" in a FIG. or text herein is understood to mean "and/or" unless otherwise indicated. Herein, the recitation of a particular numerical value or value range, and use of the term approximately or about in association therewith, is understood to include or be numerical values within +/- 20%, +/- 15%, +/- 10%, +/- 5%, +/-2.5%, +/- 2%, +/- 1%, +/- 0.5%, or +/- 0% of the recited numerical value or value range. The term essentially can indicate a percentage greater than or equal to 90%, for instance, 92.5%, 95%, 97.5%, 99%, or 100%.

As used herein, the term set corresponds to or is defined as a non-empty finite organization of elements that mathematically exhibits a cardinality of at least 1 (i.e., a set as defined herein can correspond to a unit, singlet, or single element set, or a multiple element set), in accordance with known mathematical definitions (for instance, in a manner corresponding to that described in An Introduction to Mathematical Reasoning: Numbers, Sets, and Functions , "Chapter 11 : Properties of Finite Sets" (e.g., as indicated on p. 140), by Peter J. Eccles, Cambridge University Press (1998)). Thus, a set includes at least one element. In general, an element of a set can include or be one or more portions of a system, an

apparatus, a device, a structure, an object, a process, a physical parameter, or a value depending upon the type of set under consideration.

Overview

Various embodiments in accordance with the present disclosure are directed to a scaffold structure or device (e.g., a stent structure or device) that is implantable in a lumen of a living body (e.g., a lumen or anatomical passage, such as a portion of the cardiovascular system, of a human or animal body), and which as-manufactured includes: (i) a biodegradable, radiolucent scaffold body which provides or establishes a frame or cage that serves as a structural foundation or substrate upon or outside of which (ii) a first, inner, or innermost material composition, material, coating, layer, or film resides, which includes a non-biodegradable material, and which isolates, separates, and/or insulates (e.g., electrochemically insulates) the scaffold body from each of (iii) a radiopaque material composition, material, coating, layer, or film, and (iv) an outer, outermost, protective, or anti-flaking material composition, material, coating, layer, or film, which includes an outer or outermost surface (e.g., an exposed outer surface) that forms the outer or outermost surface of the scaffold structure.

For purpose of simplicity and brevity, in the description that follows, the scaffold body or the frame or cage corresponding thereto or defined thereby may be referred to as a scaffold; the inner material composition, material, coating, layer, or film may be referred to as an inner coating; and the outer material composition, material, coating, layer, or film may be referred to as an outer coating, in a manner readily understood by individuals having ordinary skill in the relevant art.

As individuals having ordinary skill in the relevant art will readily comprehend, a scaffold structure or device is typically an elongate structure having a length (e.g., a predetermined, as-designed, or as-manufactured average or uncompressed length). A lengthwise, longitudinal, or central axis can be defined extending along the scaffold structure's length. The scaffold structure has an expanded or maximum cross-sectional area or diameter (e.g., an average diameter) perpendicular to its central axis. As used herein, the term axial refers

to a direction along or parallel to the central axis; and the term radial refers to a direction transverse or perpendicular to the central axis.

In an as-manufactured scaffold structure or device in accordance with an embodiment of the present disclosure, the inner coating covers, blankets, sheaths, encapsulates, or encases the scaffold (e.g., the inner coating blankets, encapsulates, or encases the entirety of the scaffold, that is, all surfaces of the scaffold that were exposed to the scaffold's surrounding environment prior to the application of the inner coating to the scaffold), such that the scaffold itself resides beneath, under, or internal to the inner coating. The inner coating of the as-manufactured scaffold structure is thus a non-porous coating. The inner coating physically isolates the scaffold from one or more other coatings or materials that reside over or which are applied or deposited external to or outside or on top of the inner coating. More particularly, the scaffold resides beneath or under the inner coating (e.g., entirely underneath the inner coating); and the inner coating is disposed beneath or under the radiopaque coating or material(s) and the outer coating. The inner coating electrochemically insulates or isolates the scaffold from electrochemical corrosion that would otherwise occur (e.g., in the presence of water and/or other body fluids) if the radiopaque coating or material(s) were in direct contact with the scaffold. Thus, the inner coating establishes a physical barrier (e.g., an electrochemical barrier) with respect to electron transfer between the scaffold and the radiopaque coating or radiopaque material(s).

The outer coating surrounds, covers, blankets, sheaths, encapsulates, or encases the radiopaque material(s) and the inner coating, and in multiple embodiments of the as-manufactured scaffold structure, physically isolates the radiopaque material(s) from the scaffold structure's external environment. The outer coating is typically a non-porous coating, although outer coating non-porosity is not required in all embodiments (i.e., in certain embodiments, the outer coating is porous). In several embodiments, radiopaque coating and the outer coating are separate or sequentially distinct coatings, e.g., corresponding to or defining two successive or adjacent (e.g., directly adjacent) material films or layers that are formed or applied sequentially or separately relative to each other, where each such material layer has a predetermined thickness and a distinct chemical

composition, and each such material layer is typically uniform or essentially uniform throughout its thickness with respect to its chemical composition. In other embodiments, at least one material suitable for forming an outer coating (e.g., a polymer material) is combined or blended with one or more radiopaque materials to form a radiopaque first outer coating, film, or layer, to or upon which another layer of outer coating material (e.g., the same or a different polymer material) that excludes the radiopaque material(s) is applied to form a non-radiopaque second outer coating, film, or layer. Taken together, the radiopaque first outer coating and the non-radiopaque second outer coating can be referred to or defined as a composite outer coating, film, or layer. The radiopaque first outer coating is typically a film or layer (e.g., a continuous film or layer) in which a polymer material having a predetermined thickness carries one or more types of radiopaque materials or particles (e.g., a multiplicity of radiopaque particles), such that the radiopaque materials or particles are incorporated, distributed, dispersed, or embedded in the polymer material. The non-radiopaque second outer coating is typically a non-porous film or layer that includes or is made of the same or a different polymer material.

A scaffold structure (e.g., an as-manufactured scaffold structure) can carry one or more therapeutic agents, or exclude any therapeutic agent, depending upon embodiment details. For instance, an outer coating or a composite outer coating can optionally carry one or more therapeutic agents or substances, e.g., to facilitate controlled drug elution, in a manner readily understood by individuals having ordinary skill in the relevant art. Thus, in some embodiments, in an as-manufactured scaffold structure the outer coating or composite outer coating includes a therapeutic agent therein, whereas in other embodiments the outer coating or composite outer coating excludes any therapeutic agent therein.

In an as-manufactured scaffold structure or device in accordance with multiple embodiments of the present disclosure, or immediately after the implantation thereof in a vessel, a non-porous outer coating or non-porous composite outer coating isolates the radiopaque material(s) from chemical species in the scaffold structure’s external environment.

In view of the foregoing, in a first set of embodiments of an as-manufactured scaffold structure or device, the scaffold includes or is formed of a biodegradable metal alloy or metal, e.g., magnesium (Mg) or a Mg alloy, over or on top of which a conformal, non-porous inner coating, e.g., of a type set forth herein, resides or is applied or deposited. A radiopaque coating resides or is applied or deposited over or on top of the inner coating, and an outer coating (e.g., non-porous outer coating) resides or is applied or deposited over or on top of the radiopaque coating. The outer coating has an outer or exterior surface that forms the outer or exterior surface of the as-manufactured scaffold structure (e.g., the exposed outer surface of the as-manufactured scaffold structure, which is exposed to the scaffold structure's external environment). The inner coating includes or is composed of at least one type of non-biodegradable material, which conformally covers and electrochemically insulates the scaffold from the radiopaque material(s) and thus prevents galvanic corrosion between the scaffold and the radiopaque material(s), while also preventing premature or undesirably rapid biodegradation of the scaffold (e.g., the Mg alloy) when the scaffold is in the presence of, exposed to, or in contact with body fluids. The radiopaque coating enables the scaffold structure to be visualized under fluoroscopy. The outer coating includes or is composed of a biodegradable and/or a non-biodegradable material that prevents the radiopaque coating from cracking and/or flaking or peeling away from or off of the scaffold, e.g., when the crimped scaffold structure is implanted into a vessel along a tortuous pathway, and/or expanded within the vessel during a scaffold structure implantation procedure.

In a second set of embodiments of an as-manufactured scaffold structure or device, the scaffold includes or is formed of a biodegradable metal alloy or metal, e.g., a Mg alloy, which is covered or coated with a conformal non-biodegradable inner coating, e.g., of a type set forth herein. Rather than having a radiopaque coating and an outer coating that are formed, applied, or deposited separately from each other as in the aforementioned first set of embodiments, the scaffold structure or device includes a composite outer coating of a type set forth herein that is applied over the inner coating; e.g., in the composite outer coating, particles of one or more high atomic weight materials that provide radiopacity are distributed or dispersed throughout a polymer material to form a radiopaque first outer coating, which is overlaid, encased, or encapsulated with the same or a different polymer

material (or a combination of polymer materials) to form a non-porous, non-radiopaque second outer coating. The composite outer coating, and in particular, the non-radiopaque second outer coating, has an outer or exterior surface that forms the outer or exterior surface of the as-manufactured scaffold structure (e.g., the exposed outer surface of the as-manufactured scaffold structure, which is exposed to the scaffold structure's external environment).

As further set forth below for particular representative embodiments in accordance with the present disclosure, the scaffold includes strut members or struts that are radially, annularly, or circumferentially disposed about or around the scaffold's central axis. The struts typically have a serpentine structure about or around the scaffold's central axis. Particular adjacent struts are selectively axially coupled or joined together by bridge members, elements, or links, such that predetermined groups of struts (e.g., particular pairwise-adjacent struts) that are coupled or joined together by way of bridge members form radial support structures, segments, sections, or rings. In an as-manufactured scaffold structure or device, along the scaffold's length, successive or adjacent radial support rings (e.g., pairwise-adjacent radial support rings) are axially coupled or joined together by preferentially breakable, fracturable, frangible, or rupturable links (e.g., preferentially fracturable axial links). In various embodiments, the preferentially fracturable links are at least somewhat flexible and/or resilient with respect to the motion or displacement of the radial support structures or rings coupled or joined thereby. As manufactured, the preferentially fracturable links are typically contiguous, one/single piece, or integral structures.

The preferentially fracturable links enable and accommodate at least some displacement (e.g., longitudinal, lengthwise, or axial displacement) of adjacent radial support rings relative to each other, and thus enable and accommodate at least some variability in spacing between adjacent radial support rings, particularly during scaffold structure expansion. In various embodiments, while intact and before the breakage or rupture thereof, a preferentially fracturable link can structurally correspond to or be defined as a type of flat spring structure. Thus, in an as-manufactured scaffold structure or device in accordance with an embodiment of the present disclosure, the scaffold structure includes multiple

radial support rings that are axially coupled or connected together by way of flat spring structures, where the flat spring structures include or are implemented as preferentially fracturable links.

The preferentially fracturable links are intentionally designed or structurally configured to include one or more rupture sections or regions that are structurally weaker or more prone to structural failure (e.g., in response to scaffold structure motion, deformation, or flexure, such as on a repeated or repetitive basis) than each strut and each bridge member. Hence, the weaker / weakest portions of a scaffold in accordance with various embodiments of the present disclosure are the rupture regions of the preferentially fracturable axial links. Such fracturable links are thus preferentially or more readily fracturable or more prone to structural failure compared to the fracturability or structural failure likelihood of the struts and the bridge members. Stated analogously, the preferentially fracturable links are intentionally designed such that they are more or much more likely to fracture (or fracture earlier) than the struts and the bridge members (e.g., in response to physical or mechanical stresses) exerted upon the scaffold structure. In a given preferentially fracturable link, its rupture region(s) can be provided by at least one bent, curved, or curvilinear portion or segment along the preferentially fracturable axial link's length. In multiple embodiments, at least some preferentially fracturable links generally exhibit or have an omega-type lengthwise profile or shape (e.g., a contiguous, one/single piece, or integral omega shape or profile); however, in other embodiments, at least some preferentially fracturable links can generally exhibit or have a c-shaped, u-shaped, v-shaped, w-shaped, s-shaped, or similar or other type of lengthwise profile or shape. In embodiments in which the preferentially fracturable links have an omega-type lengthwise shape, the height to width ratio of the omega shape is typically at least approximately 1.5.

The physical structure of the scaffold, and in particular the preferentially fracturable links coupling the scaffold's radial support rings, in combination with the physical nature, properties, or composition and organization of the coatings carried by the scaffold as set forth herein, enables the preferential axial decoupling of the scaffold's radial support rings (e.g., the preferential decoupling of particular or particular subsets of radial support rings)

over a predictable or controllable period of time before significant degradation (e.g., biodegradation) of the scaffold's strut elements and bridge members occurs.

The inner coating includes or is a non-biodegradable coating having sufficient thickness and uniformity relative to the topology of the scaffold such that the inner coating prevents scaffold biodegradation prior to the breakage of any preferentially fracturable links. More particularly, for an as-manufactured scaffold structure or device, the inner coating conformally covers the scaffold in a pinhole-free or essentially pinhole-free manner, and prevents the ingress of chemical species, which could or would cause scaffold material degradation, to or into the scaffold material. Prior to the breakage or rupture of any preferentially fracturable links, the inner coating over the entire scaffold structure or device thus prevents scaffold degradation. Just after the breakage of a given or first preferentially fracturable link (e.g., a first preferentially fracturable axial link) thereby forming a first broken link (e.g., corresponding to or forming two separate link pieces or segments that were formerly contiguous or integral), the previously covered but now uncovered cross-sectional area of this broken link (e.g., each exposed end or end portion of this broken axial link) is exposed to fluids (e.g., body fluids) or chemical species in the environment in which the scaffold structure or device resides, and thus portions of the scaffold at and along this broken link can begin to degrade (e.g., this broken link can begin to progressively biodegrade along its length, starting from its terminal ends or end portions). However, other preferentially fracturable links that have not yet broken, as well as other portions of the scaffold structure including the scaffold's radial support rings, remain covered by the inner coating, and are hence protected from direct exposure to environmental fluids or chemical species, while the degradation of exposed portions of the scaffold at, adjacent, and proximate to the first broken link progressively occurs. Because the exposed cross-sectional area of the first broken link is small or very small with respect to the surface area of the radial support rings that were formerly coupled or joined by first broken link, any progressive degradation of these radial support rings occurs gradually or very gradually, and/or in a predictable or generally predictable manner, over time.

Further to the foregoing, after multiple or many preferentially fracturable links have broken (e.g., after the implantation of the scaffold structure or device in a vessel, and after

particularly the scaffold has resided in the vessel for approximately 4-12 weeks or longer), more widespread scaffold degradation occurs in a manner analogous to that described above for the first broken link. Notwithstanding the presence of multiple or many broken links, in various embodiments in accordance with the present disclosure, the overall time required for scaffold degradation, an in particular the overall time required for the degradation of the scaffold's struts in each radial support ring, is significantly or very significantly longer than that for prior art scaffold structures (e.g., by at least a factor of approximately 2 – 4).

Still further to the foregoing, the inner coating of the as-manufactured scaffold structure should be sufficiently thick such that immediately after implantation in a vessel and for an intended, desired, or target time period thereafter, it prevents galvanic corrosion between the radial support rings of the scaffold and the radiopaque material(s) used to provide scaffold structure radiopacity. However, the inner coating should not be so thick that it inhibits the gradual or very gradual biodegradation of the scaffold once an intended, desired, target, or sufficient extent of cell endothelization has taken place or is expected to have taken place in the vessel.

Across the time period during which the scaffold progressively degrades, endothelial tissue can grow around and/or into portions of the scaffold structure (e.g., around radial support rings or portions thereof that remain covered by the aforementioned coatings), such that non-degradable portions of the scaffold structure (e.g., the inner coating, and the radiopaque material(s)) become physically embedded or incorporated into vessel tissue. For instance, after vessel healing, the inner coating can remain as a thin biocompatible layer within vessel tissue.

In view of the foregoing, after the scaffold structure has been implanted in a vessel, (a) the axial decoupling mechanism by which the scaffold's radial support rings become physically decoupled or detached from each other, in conjunction with (b) the composition and organization of the coatings, significantly and predictably or controllably reduce or slow the scaffold's degradation rate, and cooperatively or synergistically aid or enable (i) the restoration of vessel flexibility and enhancement of the natural pulsatile function of the

vessel over time, and ensure that (ii) individual radial support rings provide sufficient radial support to the vessel during or over an intended, adequate, target, or predetermined period of time that intentionally corresponds to or is correlated with the likely or expected duration of the vessel's healing phase.

Embodiments in accordance with the present disclosure are applicable to endovascular treatment of vascular and non-vascular diseases in coronary arteries and various peripheral vessels including the tibial artery, superficial femoral artery, iliac artery, carotid artery, and renal artery. Embodiments in accordance with the present disclosure are also applicable to non-vascular treatment including the palliation of strictures of the bile ducts (Hepatic, Cystic, Common Bile, and Pancreatic) resulting from malignancy of the liver, pancreas, duodenum, biliary tree, or from various benign diseases.

Detailed Aspects of Particular Representative Embodiments

In general, the purpose of a biodegradable scaffold structure in accordance with an embodiment of the present disclosure is to provide temporary support for a body lumen or portions thereof for an intended, target, predetermined, or minimum time period, e.g., approximately 3 - 12 months or longer. This will restore the uninterrupted flow of blood and/or other body fluid(s) in the body lumen, and at the same time facilitate the formation of endothelial tissue around portions of the scaffold structure (which takes place across a 1-3 month time period according to animal tests), thereby enabling portions of the scaffold structure (e.g., non-resorbable portions of the scaffold structure) to be integrated into the vessel wall, while the scaffold itself slowly degrades and reduces its mechanical strength properties.

Depending upon embodiment details, a biodegradable or bioresorbable scaffold can include or be formed of a metallic material such as one or more of magnesium (Mg), iron (Fe), zinc (Zn), alloys of these metals, or similar materials. In various embodiments, the bioresorbable scaffold includes or is formed of a Mg alloy because of its low thrombogenicity and well-known biocompatibility, as Mg alloys have been used in many orthopedic and cardiovascular implant structures, devices, and applications. Suitable Mg alloys for use in embodiments in accordance with the present disclosure are described in U.S. Patent Nos.

9,522,219; 9,566,367; and 8,507,101, each of which is incorporated herein by reference in its entirety.

However, two main drawbacks of Mg have limited its use in bioresorbable scaffolds. First, the radiolucent nature of Mg makes it difficult for visualization during implantation and post-operative diagnosis. Second, Mg undergoes hydrolysis immediately upon contact with water and/or body fluids, and begins to breakdown into various degradation products that can be proinflammatory to surrounding tissues. With respect to commercially-available Mg-based scaffolds, despite protecting the Mg with a coating or layer of Polylactide-based polymer, isolated clinical cases of unintended / uncontrolled acute localized scaffold degradation (occurring over a time period of less than 6 months) have been reported, likely due to the polymer layer being partially compromised.

In order to address the radiolucent nature of Mg, a coating over the scaffold with a layer of a suitable high atomic weight element, compound, or material enables the scaffold to achieve sufficient radiopacity, but does not obstruct the visualization of radiopaque dye during fluoroscopy. The coating can be high atomic weight material such as tantalum (Ta), gold (Au), platinum (Pt), bismuth (Bi), iridium (Ir), or the like. Although Au has a better ductility property, the results of human clinical trials of a Au coated stent have demonstrated that the Au coated stent induced higher neointimal hyperplasia as compared to an uncoated stainless steel stent. Ta or Pt is thus a better choice for a radiopaque material or coating in various embodiments of the present disclosure, because of high atomic weight and density which contributes to radiopacity, as well as good or excellent biocompatibility.

Notwithstanding, for a reactive or biodegradable metal like Mg which has high electron potential (as compared to a non-degradable metal like 316L stainless steel or Nickel-Titanium alloy, which are commonly used to form stents), a direct coating of Ta onto Mg will cause significant galvanic effects, which would accelerate the corrosion of the Mg scaffold. Therefore, in accordance with multiple embodiments of the present disclosure, an inner or inner insulation coating between the scaffold and the radiopaque (e.g., Ta or Pt) coating or layer is applied to reduce or minimize the likelihood of scaffold galvanic corrosion.

Furthermore, on top of the radiopaque coating or layer, an outmost coating or outermost protective layer is applied to prevent the radiopaque (e.g., Ta or Pt) layer from cracking or flaking off.

FIGs. 6A – 6B and 7A – 7B show aspects of radiopaque metallic bioresorbable scaffold structures or devices (e.g., stent structures or devices) 10 in accordance with particular embodiments of the present disclosure. More specifically, FIG. 6A is a perspective schematic illustration of a scaffold structure 10, which includes or is formed from a scaffold that underlies a non-degradable inner coating, where the inner coating itself underlies a radiopaque coating or material(s) and an outer coating or composite outer coating, as further detailed below. As individuals having ordinary skill in the relevant art will readily understand, the scaffold structure 10 has a length (e.g., an average or predetermined uncompressed length), and a lengthwise, longitudinal, or central axis 5 can be defined therethrough along the scaffold structure's length. The scaffold structure 10 also has an expanded or maximum cross-sectional area or average cross-sectional area (e.g., a generally uniform or uniform cross-sectional area or diameter) along its length about the central axis 5. FIG. 6B is a top schematic illustration showing portions of the scaffold structure 10 of FIG. 6A.

FIG. 7A is a cross-sectional schematic illustration of a portion of a scaffold structure 10a in showing an organization of multiple coatings accordance with a first set of embodiments corresponding to FIGs. 6A – 6B, taken along line A – A' of FIG. 6A; and FIG. 7B is a cross-sectional schematic illustration of a portion of a scaffold structure 10b showing another organization of multiple coatings in accordance with a second set of embodiments corresponding to FIGs. 6A – 6B, taken along line A – A' of FIG. 6A.

As indicated in FIGs. 7A - 7B, the scaffold structure 10 of FIGs. 6A – 6B includes an underlying or innermost biodegradable metallic scaffold 100, e.g., which (a) forms an inner frame or cage that extends along the scaffold structure's length; (b) can be defined as the as-manufactured scaffold-structure's inner core; and (c) gives rise to the scaffold structure's overall lengthwise or longitudinal geometry or shape, in a manner readily understood by

individuals having ordinary skill in the relevant art. Generally, the scaffold 100 is fabricated or manufactured by known processes such as laser cutting from a tube, or mesh weaving using wires, in a manner also readily understood by individuals having ordinary skill in the relevant art.

Further with respect to lengthwise or longitudinal geometry, as indicated in FIGs. 6A, 6B, 7A, and 7B, the scaffold 100 and thus the scaffold structure 10 includes radially expandable / compressible struts 110 disposed about or around the central axis 5, which typically exhibit a serpentine shape or pattern about or around the central axis 5. Individual struts 110 contribute to the scaffold structure's radial strength. The struts 110 provide radial support to the walls of an anatomical passage or vessel in which the scaffold structure 10 is implanted, in a manner readily understood by individuals having ordinary skill in the relevant art.

Predetermined pairs of directly adjacent struts 110 are coupled or connected by bridge members 120 to form radial support rings 130, which further enhance or maximize the scaffold structure's radial strength. The bridge members 120 are typically linear or straight structures, which typically extend in a direction parallel to the central axis 5, though this need not be the case in all embodiments (e.g., portions of some bridge members 120 can be oriented at an angle with respect to the central axis 5). As indicated in FIG. 6A, in any given radial support ring 130, the two struts 110 thereof are coupled or connected (e.g., axially coupled or connected) by a total of six bridge members 120 disposed at predetermined positions about or around the central axis 5. Notwithstanding, in other embodiments, at least some radial support rings 130 can have fewer or additional bridge members 130 that couple or connect the struts 110 thereof. Also, while each radial support ring 130 has two struts 110 in FIG. 6A, in alternate embodiments one or more radial support rings 130 can include more than two struts 110 (e.g., three struts 110).

Radial support rings 130 that are directly adjacent to each other are longitudinally or axially coupled or connected to each other, i.e., coupled or connected along a direction extending parallel to the central axis 5, by way of intentionally / preferentially fracturable links, e.g., intentionally / preferentially fracturable axial links 140 (which for purpose of simplicity can

be referred to hereafter as preferentially fracturable links 140). Each preferentially fracturable link 140 includes or is a bent, curved, or curvilinear structure having at least one rupture region 142. In multiple embodiments, at least some preferentially fracturable links 140 are formed as contiguous, one/ single piece, or integral structures (e.g., each preferentially fracturable link 140 is a contiguous, one/single piece, or integral structure). In some embodiments, the rupture region 142 of a preferentially fracturable link 140 includes, provides, or forms a curvature inflection segment or vertex along the link 140; and the curvature inflection segments or vertices of one or more preferentially fracturable links 140 (e.g., each such link 140) can be oriented or pointed in a direction transverse or perpendicular to the central axis 5.

In several embodiments, at least some preferentially fracturable links 140, or each preferentially fracturable link 140, includes or is formed to have a lengthwise shape or profile that corresponds or generally corresponds to or resembles an omega (Ω) shape, although preferentially fracturable links 140 can have other or additional types of lengthwise curved shapes or profiles in other embodiments. In representative embodiments such as shown in FIG. 6A – 6B in which the preferentially fracturable links 140 exhibit a lengthwise omega-type of shape, as indicated in FIG. 6B such preferentially fracturable links 140 can include a first or central rupture region 142 corresponding to a first, middle, or more gently curved portion of the omega shape, and one or more additional rupture regions 143 corresponding to additional, extremity, or more sharply curved portions of the omega shape. As shown in FIG. 6A, in some embodiments, pairwise adjacent radial support rings 130 are coupled or connected by a total of three preferentially fracturable links 140 disposed at predetermined locations about or around the central axis 5. Notwithstanding, in other embodiments, at least some pairwise adjacent radial support rings 130 can be coupled or connected by fewer or additional preferentially fracturable links 140.

When the scaffold structure 10 is expanded and deployed in a vessel, the scaffold 100, and in particular the struts 110 (and hence the radial support rings 130) and the preferentially fracturable links 140 undergo plastic deformation. In order to achieve an intended, desired, or target performance of the scaffold structure 10 in view of sustained radial strength, anti-

corrosion properties, radiopacity, body fluid / blood compatibility, and intended, desired, target, or optimum degradation rate, multiple coatings, layer, material compositions, or materials are applied over the scaffold, in a specific predetermined order.

More particularly, with reference to FIGs. 7A and 7B, an inner coating 20 is applied to coat the entirety of the exposed surface are of the scaffold 100, that is, both inward / internal facing surfaces (i.e., facing toward the central axis 5) and outward / external facing surfaces (i.e., facing away from the central axis 5) of the scaffold 100. The inner coating 20 should be sufficiently thick to prevent galvanic corrosion from taking place between the biodegradable metal (e.g., Mg) of the scaffold 100 and radiopaque material(s) that are carried by the scaffold structure 10. However, the inner coating 20 should not be so thick that it inhibits the intended gradual, very gradual, or predictably gradual degradation or breakdown of the biodegradable metal (e.g., Mg) scaffold 100 once sufficient cell endothelization has taken place in the vessel. In various embodiments, the inner coating 20 has a thickness (e.g., a generally uniform or uniform thickness) between approximately 0.1 to 10 micrometers (e.g., in some embodiments, less than or equal to: approximately 5 micrometers, or 4 micrometers, or 3 micrometers, or 2 micrometers; or between: approximately 0.1 – 3.0 micrometers, or approximately 0.5 – 3.0 micrometers, or approximately 1 – 3 micrometers). It is also important that the inner coating 20 not be too rigidly adhered or attached to the scaffold 100, but rather forms a stretchable or suitably stretchable / resilient sheath covering the scaffold 100 with adequate resilience during scaffold expansion, preferentially fracturable link deformation, and radial support ring detachment, as further detailed below.

As shown in FIG. 7A, a radiopaque coating 30 is applied or deposited on top of the inner coating 20. The radiopaque coating 30 typically has a thickness between approximately 1 – 10 micrometers. In this thickness range, the radiopaque coating provides sufficient radiopacity to allow the scaffold structure 10 to be seen under fluoroscopy, while maintaining a sufficiently thin coating that does not or does not significantly adversely affect the scaffold structure's mechanical properties, especially the expandability and flexibility of the scaffold 100.

The radiopaque coating 30 can be applied to the inner / internal and/or outer / external surface(s) of the scaffold 100 following the application of the inner coating 20 to the scaffold 100. The radiopaque coating 30 can be applied by way of magnetron sputtering, physical vapor deposition (PVD), chemical vapor deposition, dipping, ion implantation, or other techniques known in the art. A typical magnetron sputtering process for applying the radiopaque layer 30 involves fixing the scaffold 100 in a fixture that is electrically conductive, and then placing it in sputtering chamber that is subjected to a negative or vacuum pressure lower than $8x10^{-6}$ torr, e.g., typically lower than $4x10^{-7}$ torr, before commencing a radiopaque layer coating process, which typically involves multiple sputtering sessions. The radiopaque layer coating can be carried out at room temperature, with a rest period between each sputtering session of approximately 30 minutes in order to prevent the scaffold surface temperature from being elevated above a temperature of more than about $80^{o}C$. The entire radiopaque layer coating process, including attaining a target vacuum pressure, takes approximately 5-10 hours depending on the sputtering chamber size, and the sputtering target material condition and thickness.

An outer coating 40 is applied or deposited on top of the radiopaque coating 30. The outer coating 40 typically has a thickness between approximately 1 – 10 microns, and protects the radiopaque coating 30 from cracking and/or flaking off as the scaffold structure 10 is delivered through a tortuous vessel shape and subsequently expanded in the vessel at a lesion site. Depending upon embodiment details, the outer coating 40 can be a single layer coating, or a multi-layer coating.

The inner coating 20 is biocompatible and in various embodiments is non-biodegradable, and is able to provide sufficient insulation or electrochemical isolation between the scaffold 100 and the radiopaque coating 30 to prevent galvanic corrosion of the scaffold 100. The inner coating 20 can include or be one or more materials such as parylene, polymethacrylate and its copolymers, polyvinyl acetate, and polycaprolactone. In various embodiments, the inner coating 20 includes or is made of parylene, as it is important for the inner coating 30 to be a pinhole free, conformal layer. In prior art stent applications, parylene has been mainly used in conjunction with other surface treatments to form an adhesion layer to enhance the adhesion of a second polymer layer to the stent.

The outer coating 40 is biocompatible, and may or may not be biodegradable. The outer coating 40 provides protection for the radiopaque coating 30. The outer coating 40 can include or be formed of one or more polymeric materials, such as polylactic acid, polyglycolic acid, copolymers of lactic and glycolic acid, polycaprolactone, parylene, polymethacrylate, polyvinylidene fluoride (PVDF), poly(hydroxyalkanoate) (PHA), cyanoacrylates and its copolymers, and polyurethane and its copolymers. An additional or other material such as diamond-like carbon (DLC), which has good biocompatibility characteristics, is also suitable. In several embodiments, the outer coating 40 includes or is formed of parylene, as parylene is able to provide a pinhole free, conformal layer. In embodiments in which the outer coating 40 includes or is formed of polylactic acid, the outer coating 40 is able to provide sufficient protection for the radiopaque coating 30 so as to prevent the radiopaque coating 30 from flaking off during scaffold implantation and expansion. Due to the biodegradable nature of polylactic acid, upon sufficient endothelization around the scaffold structure 10, the polylactic acid of the outer coating 40 will slowly degrade, and hence will assist in the gradual degradation of the scaffold structure 10. The outer coating 40 can be applied by dip-coating, spray-coating, spin-coating, plasma deposition, pipetting, condensation, electrochemically, electrostatically, or other suitable techniques.

In some embodiments, the outer coating 40 or particular portions of the outer coating 40 can serve as a reservoir for one or more therapeutic substances or drugs that allow controlled release of the therapeutic agent(s). In several embodiments in which the outer coating 40 carries a therapeutic agent, the therapeutic agent is present within and/or upon the outer coating 40 along the entirety of the scaffold structure's length. In other embodiments, the therapeutic agent is carried by the outer coating 40 only along particular portions of the scaffold structure's length, but is absent or excluded from the outer coating 40 along other portions of the scaffold structure's length. For instance, the therapeutic agent can be present in the outer coating 40 over the radial support rings 130, but absent from the outer coating 40 over the preferentially fracturable links 140. In yet other embodiments, a first therapeutic agent can be carried by the outer coating 40 over particular portions of the scaffold structure's length, and a second therapeutic agent that is

different from the first therapeutic agent with respect to chemical composition and/or concentration can be carried by the outer coating 40 over other portions of the scaffold structure's length. For instance, the first therapeutic agent can be carried by the outer coating 40 over the radial support rings 130, and the second therapeutic agent can be carried by the outer coating 40 over the preferentially fracturable links 140.

FIG 7B shows another scaffold structure coating organization, in which the scaffold structure 10b has a composite outer coating over the inner coating 20, where the composite outer coating includes or is formed as a radiopaque first outer coating 35 and a non-radiopaque second outer coating 40. In the radiopaque first outer coating 35, radiopaque particles (e.g., Ta or Pt particles) are incorporated into or distributed or dispersed in a material (e.g., a polymer material). More particularly, in multiple embodiments the Ta or Pt particles a size of or ranging between approximately 0.1 - 10 microns are mixed (e.g., premixed) with a coating material such as polylactic acid, polyglycolic acid, copolymers of lactic and glycolic acid, polycaprolactone, parylene, polymethacrylate, cyanoacrylates, polyvinylidene fluoride (PVDF), poly(hydroxyalkanoate) (PHA), or polyurethane and associated copolymers. The polymer material with radiopaque particles distributed or dispersed therein can applied by a standard coating technique, such as dip-coating or spray-coating, to obtain a uniform coating thickness for the radiopaque first outer coating 35 onto or over the outer, exterior, or exposed surface(s) of the inner coating 20. Alternatively, the radiopaque first outer coating 35 can be formed by way of micro-pipetting of a polymer coating material with radiopaque particles distributed or dispersed therein onto or over the outer, exterior, or exposed surface(s) of the inner coating 20. The non-radiopaque second outer coating 40 is then applied over the radiopaque first outer coating 35, e.g., in a manner identical, essentially identical, or analogous to that described in the previous paragraph. The non-radiopaque second outer coating 40 is typically non-porous, and in various embodiments, the radiopaque first outer coating is also non-porous.

In an as-manufactured scaffold structure 10b such as that shown in FIG. 7B, the inner coating 20 prevents direct contact between the radiopaque particles of the radiopaque first outer coating 35 and the Mg scaffold 100, and hence prevents galvanic corrosion or unintended or excessive galvanic corrosion of the scaffold 100; and the non-radiopaque

second outer coating 40 prevents chemical substances or species in the scaffold structure's external environment from interacting with or contacting the radiopaque particles of the radiopaque first outer coating 35.

An important aspect of embodiments in accordance with the present disclosure is the organization or sequence of coatings carried by or applied to the biodegradable metallic scaffold 100, which is crucial for the clinical success of the biodegradable metallic scaffold 100 in order to avoid or prevent radiopaque material cracking and/or flaking, prevent unintended or excessive scaffold galvanic corrosion, and also to enable a controlled biodegradation or bioresorption / breakdown of the scaffold 100. As indicated in FIG. 7A, for several embodiments, the coating sequence is such that the inner coating 20 covers the scaffold 100, and the radiopaque coating 30 is sandwiched in between the inner coating 20 and the outer coating 40. In other embodiments, the coating sequence is such that the inner coating 20 is applied over the scaffold 100, and the composite outer coating is applied over the inner coating 20, e.g., by way of the application of the radiopaque first outer coating 35 over the inner coating 20, followed by the application of the non-radiopaque second outer coating 40 over the radiopaque first outer coating 35.

FIG. 8 is a magnified image showing portions of a scaffold structure 10 in accordance with an embodiment of the present disclosure, which has undergone scaffold expansion. As shown in FIG. 8, no obvious cracking or flaking is apparent, and thus the coatings carried by the scaffold 100 remain intact following scaffold expansion.

FIG. 9 is an *in vivo* angiographic image of a Mg biodegradable scaffold structure 10 in accordance with the embodiment shown in FIGs. 6A, 6B, and 7A, which has been implanted in a porcine coronary artery, at a time of 4 weeks post-implantation. As shown in FIG. 8, the coronary artery remains fully open, with no sign of vessel narrowing due to restenosis or excessive tissue response. It should be noted that after 12 weeks of *in vivo* implantation, the coronary artery remains also open with no sign of vessel narrowing due to restenosis or excessive inflammatory or other tissue response.

During an actual implantation procedure during which a scaffold structure 10 is implanted in a vessel, the scaffold structure 10 is crimped onto a balloon catheter and delivered through a guidewire, after which the scaffold structure 10 is subsequently expanded and deployed in the body vessel. In association with the implantation procedure, the scaffold structure 10 experiences or undergoes significant deformation. Following scaffold deployment in the vessel, the scaffold structure 10 experiences generally constant radial pressure, together with the natural pulsatile flexing of the vessel.

In conjunction with the time-extended and controlled degradation of portions of an *in vivo* implanted scaffold structure 10 by way of the combination and organization of coatings as described herein, preferential decoupling of certain regions of the scaffold structure 10, i.e., preferential decoupling of multiple radial support rings 130 by way of breakage, fracture, or rupture of preferentially fracturable links 140, was observed. When the scaffold structure 10 was expanded in diameter, the plastic deformation experienced by preferentially fracturable links 140 was significantly larger than that experienced by the struts 110, whereas the bridge members 120 remain relatively undeformed. With respect to omega-shaped preferentially fracturable links 140, the apex of the omega-shape was typically the area or portion of the preferentially fracturable links 140 that experienced the highest concentration of mechanical stress. In several embodiments in which the preferentially fracturable links 140 have an omega-type lengthwise shape, the height to width ratio of the omega shape is at least approximately 1.5.

FIG. 10A is a Faxitron (X-ray) image of a scaffold structure 10 in accordance with an embodiment of the present disclosure, after 4 weeks of implantation *in vivo* in a porcine coronary artery. As indicated in FIG. 10A, several broken or dismantled preferentially fracturable links 140 can be seen, while the strut 110 and the bridge members 120, and hence the radial support rings 130, remain intact. FIG. 10B is a corresponding Optical Coherence Tomography (OCT) image in the vessel where the scaffold structure 10 of FIG. 10A is located, demonstrating excellent patency and freedom from restenosis, and where the scaffold structure 10 was essentially completely or completely endothelized, at 4 weeks post-implantation. It has therefore been demonstrated that the breakage or dismantling of the preferentially fracturable links 140 does not lead to localized accelerated degradation of

the scaffold 100 (e.g., accelerated or significantly accelerated degradation of the radial support rings 130), which is prevented by the coatings in accordance with embodiments of the present disclosure, particularly by way of the inner coating 20 that is applied in the absence of or without surface adhesive treatments to the Mg scaffold 100 to thereby allow the inner coating 20 to act as an impermeable yet flexible and resilient sheath that can adapt to or flexibly / slidably accommodate the various movements of the scaffold 100 underlying the inner coating 20.

FIG. 10C is another Faxitron (X-ray) image of a scaffold structure 10 in accordance with an embodiment of the present disclosure, after 12 weeks of implantation *in vivo* in porcine coronary artery. The dismantling of the preferentially fracturable links 140 is clearly more pronounced at 12 weeks, while the struts 110 and the bridge members 120 (and hence the radial support rings 130) remain intact. FIG. 10D is a corresponding 12 week post-implantation OCT image of the vessel where the scaffold structure 10 is located, where the results again demonstrate unobstructed blood flow and freedom from restenosis.

In several embodiments (e.g., directed to cardiovascular applications), the mechanical strength of the preferentially fracturable links 140 is selected or established such that no more than approximately 5% of the preferentially fracturable links 140 break in association with or during a scaffold structure implantation procedure (e.g., as a result of scaffold structure expansion during implantation). Additionally, the mechanical strength of the preferentially fracturable links 140 can be selected or established such that approximately 20 – 40% (e.g., about 30%) of the of the preferentially fracturable links 140 become fractured at approximately 4 weeks post-implantation; and approximately 50% or more of the preferentially fracturable links 140 become fractured at approximately 12 weeks post-implantation. In some embodiments, each individual preferentially fracturable link 140 of the scaffold structure 10 can have an approximately identical mechanical strength; however, in other embodiments, some preferentially fracturable links 140 can be weaker than other preferentially fracturable links 140, e.g., in order to preferentially tailor or customize the likelihood or occurrence of adjacent radial support ring separation at different locations along the scaffold structure's length.

This unique radial support ring decoupling or disconnection mechanism provided by various embodiments of the present disclosure can quickly restored the flexibility, and enhance the natural pulsatile function of the vessel while the multiple coatings of the scaffold structure 10 ensure that as portions of the scaffold structure 10 biodegrade over time, the radial support rings 130 of the remaining scaffold structure 10 provide adequate radial support to the vessel.

In view of the foregoing, various embodiments of the present disclosure provide: (1) a biodegradable implantable or implanted metallic scaffold structure or scaffold such as a stent configurable or configured for implantation into a mammalian body, and having (a) first structural elements (e.g., preferentially fracturable links 140), and (b) second structural elements (e.g., ring-like or ring-type structures, such as radial support rings 130), wherein the first structural elements are intentionally (i) configured to be structurally weaker than the second structural elements along at least one spatial direction, and (ii) preferentially fracturable or breakable relative to the second structural elements in response to physical stresses or deformations exerted upon the scaffold (e.g., typical physical stresses or deformations that the scaffold structure is expected to experience post-implantation); and (2) a non-porous first or inner covering or coating disposed over the scaffold, wherein the first or inner covering or coating includes or is a non-biodegradable polymer that conformally encases the scaffold structure, such that an inner surface of the first or inner covering or coating is disposed adjacent to and in contact with the scaffold structure.

Portions of the first or inner covering or coating that overlay first structural elements of the scaffold are intentionally configured to tear, break, rupture, open, and/or become porous (e.g., by way of thinning and/or stretching) in response or subsequent to fracture or breakage of the first structural elements, thereby exposing portions (e.g., terminal or end portions, regions, or segments) of the fractured or broken first structural elements to a physical environment in which the scaffold structure resides, such as a biological environment in which biodegradation can occur by way of biological fluid incursion or biological fluid / chemical species contact with the fractured or broken first structural elements, which can enable gradual progressive biodegradation of portions of the scaffold

structure beginning at such fractured or broken first structural elements that are exposed to such an environment.

A radiopaque material can be disposed external to the first or inner coating along at least portions of the scaffold's length (e.g., along the entire or essentially entire length of the scaffold). A non-porous second or outer coating including a biodegradable or non-biodegradable polymer can be disposed over or external to outer surfaces of the radiopaque material over the scaffold's length (e.g., along the entire or essentially entire length of the scaffold). The first or inner coating electrochemically isolates the radiopaque material from the scaffold.

A manufacturing process for a biodegradable implantable or implanted metallic scaffold structure such as a stent configurable or configured for implantation into a mammalian body can include or consist essentially of:

providing a biodegradable metallic scaffold having or consisting essentially of (a) first structural elements (e.g., preferentially fracturable links 140), and (b) second structural elements (e.g., ring-like or ring-type structures, such as radial support rings 130), wherein the first structural elements are intentionally (i) configured to be structurally weaker than the second structural elements along at least one spatial direction, and (ii) preferentially fracturable or breakable relative to the second structural elements in response to physical stresses or deformations exerted upon the scaffold (e.g., typical physical stresses or deformations that the scaffold structure is expected to experience post-implantation);

providing or disposing a non-porous first or inner covering or coating over the scaffold, wherein the first or inner covering or coating includes or is a non-biodegradable polymer that conformally encases the scaffold, thereby conformally encasing the scaffold's first structural elements and second structural elements, such that an inner surface of the first or inner covering or coating is disposed adjacent to and in contact with the scaffold, and wherein portions of the first or inner covering or coating that overlay first structural elements of the scaffold are intentionally configured to tear, break, rupture, open, and/or become porous (e.g., by way of thinning and/or stretching) in response to fracture or breakage of the first structural

elements (thereby exposing portions of the fractured or broken first structural elements to a physical environment in which the scaffold structure resides, such as a biological environment in which biological fluid incursion or biological fluid / chemical species contact with such fractured or broken first structural elements can occur, which can enable gradual progressive biodegradation of portions of the scaffold structure beginning at such fractured or broken first structural elements that are exposed to such an environment);

providing or disposing a radiopaque material external to exposed, external, or outer surface(s) of the first or inner covering or coating along at least portions of the scaffold structure's length (e.g., along the entire or essentially the entire length of the scaffold or scaffold structure); and

providing or disposing a non-porous second or outer covering or coating including a biodegradable or non-biodegradable polymer over exposed, external, or outer surface(s) of the radiopaque material over the scaffold structure's length (e.g., along the entire or essentially entire length of the scaffold structure),

wherein the first or inner covering or coating electrochemically isolates the radiopaque material from the scaffold.

In view of the description herein and the accompanying FIGs., various embodiments in accordance with the present disclosure provide a biodegradable scaffold (e.g., a biodegradable metallic scaffold such as a biodegradable stent-like structure or stent) having: (1) preferentially fracturable structural elements or links (e.g., preferentially fracturable links 140) that are intentionally configured to be structurally weaker and hence more prone to fracture or breakage in response to physical stress(es) than ring-like or ring-type structures of the scaffold or scaffold structure, such as radial support rings 130, that are coupled or interconnected by the preferentially fracturable structural elements or links; and (2) a first or inner non-biodegradable inner covering or coating (e.g., inner coating 20) that conformally encases the scaffold, thereby conformally encasing the scaffold's preferentially fracturable structural elements or links and ring-like or ring-type structures, wherein the first or inner covering or coating has a thickness intentionally selected such that portions of the first or inner covering or coating which overlay first structural elements of the scaffold are intentionally configured to tear, break, rupture, open, and/or become porous (e.g., by

way of thinning and/or stretching) in response to or following fracture or breakage of the preferentially fracturable structural elements or links, thereby exposing portions of these fractured or broken structural elements to a physical environment in which the scaffold structure resides, such as a biological environment in which scaffold biodegradation can occur by way of biological fluid / chemical species incursion or biological fluid contact, which can enable gradual or controlled progressive biodegradation of portions of the scaffold beginning at such fractured or broken first structural elements that are exposed to such an environment.

Various embodiments in accordance with the present disclosure thus synergistically utilize preferentially fracturable structural elements or links in combination with the first or inner non-biodegradable inner covering or coating of an appropriate thickness to intentionally modulate or control the exposure or permeability of portions of the base biodegradable scaffold material to biological fluid and/or chemical species incursion and/or contact, e.g., thus providing managed, slow / gradual, or very slow / very gradual intended biodegradation of the scaffold (e.g., including preferential biodegradation of particular portions of the scaffold, such as preferentially fracturable links 140 relative to other portion of the scaffold such as radial support rings 130) relative to or over an intended or target time period (e.g., approximately 4 – 12 weeks or longer).

In view of the foregoing, first or inner non-biodegradable inner covering or coating controls (e.g., intentionally / preferentially controls, in an intended, generally consistent, generally predictable, consistent, or predictable manner) access of chemical species, biological fluids, and/or saline to particular or intended portions of the underlying biodegradable scaffold (e.g., relative to an intended or target time period such as set forth above).

Further to the foregoing, in at least some embodiments, at least portions of the first or inner non-biodegradable inner covering or coating can be selected to have an appropriate thickness (e.g., between approximately 0.5 – 3 micrometers, approximately 1 – 3 micrometers, approximately 0.5 – 2.5 micrometers, or approximately 1 – 2.5 micrometers) such that stresses exerted upon remaining or still intact portions of the scaffold structure over a particular period of time (e.g., approximately 4 to 12 weeks or longer post-

implantation), including stresses exerted on as-yet unbroken preferentially fracturable structural elements or links and/or substantially intact, essentially intact, or intact portions of at least some ring-like or ring-type structures such as radial support rings 130, progressively, gradually, or very gradually stretch, thin, and/or render porous at least some regions or sites on the first or inner non-biodegradable inner covering or coating that overlay the remaining or still intact portions of the scaffold, thereby exposing or further exposing these portions of the scaffold to biological fluids / chemical species such that further progressive biodegradation of the scaffold occurs.

Additionally or alternatively, across the time period during which the scaffold progressively degrades, endothelial tissue can progressively grow around and/or into portions of the scaffold structure (e.g., around and/or into radial support rings 130 or portions thereof that remain significantly covered or covered by the non-biodegradable inner covering or coating), such that non-degradable portions of the scaffold structure (e.g., the inner covering or coating, and the radiopaque material(s)) become physically embedded or incorporated into vessel tissue. In some embodiments, such endothelial tissue growth can disrupt the continuity of portions of the first or inner non-biodegradable covering or coating and/or disrupt adherence of portions of the first or inner non-biodegradable covering or coating to the scaffold, thereby enabling further scaffold biodegradation. After vessel healing, the inner covering or coating can remain as a thin biocompatible layer within vessel tissue.

While aspects of the present disclosure have been described herein with respect to particular embodiments, it will be apparent to an individual having ordinary skill in the relevant art that adaptations or variations on the embodiments described herein can be made, which remain within the scope of the present disclosure and the following claims. For instance, the outer coating can be non-porous over portions of the scaffold structure corresponding to the radial support rings, but porous over portions of the scaffold structure corresponding to at least some preferentially fracturable links; and/or the scaffold structure can include radiopaque material(s) on top of the inner coating corresponding to the radial support rings, but can exclude radiopaque material(s) on top of the inner coating corresponding to the preferentially fracturable links.

CLAIMS

1. A scaffold structure implantable into an anatomical lumen of a human or animal body, the scaffold structure comprising an elongate structure having a length, and through which a central axis is definable along its length, wherein the scaffold structure as-manufactured comprises:

an elongate biodegradable metallic scaffold that provides a frame or cage structure;

a non-porous inner coating disposed over the biodegradable metallic scaffold, wherein the inner coating comprises a non-biodegradable polymer that conformally encases the scaffold, such that an inner surface of the inner coating is disposed adjacent to and in contact with the scaffold;

a non-porous outer coating comprising a biodegradable or non-biodegradable polymer, the outer coating having an outer surface; and

a radiopaque material disposed external to the inner coating and internal to the outer surface of the outer coating along the scaffold structure's length,

wherein the inner coating electrochemically isolates the radiopaque material from the scaffold.

2. The scaffold structure of claim 1, wherein inner coating comprises a resilient, pinhole free parylene sheath that conformally coats the scaffold and which exists in slidable and/or flexible contact with the scaffold.

3. The scaffold structure of claim 1 or 2, wherein the radiopaque material comprises a coating of Tantalum or Platinum that forms a continuous material layer sandwiched between the inner coating and the outer coating.

4. The scaffold structure of any one of claims 1 – 3, wherein the radiopaque material comprises a multiplicity of radiopaque particles dispersed within the outer coating.

5. The scaffold structure of any one of claims 1 – 4, wherein the outer coating comprises one of parylene C, polylactic acid, polyglycolic acid, copolymers of lactic and glycolic acid,

polycaprolactone, parylene, polymethacrylate, cyanoacrylates, polyvinylidene fluoride (PVDF), Poly(hydroxyalkanoate) (PHA), polyurethane, and copolymers of polyurethane.

6. The scaffold structure of any one of claim 1 – 5, wherein where the outer coating carries a therapeutic substance.

7. The scaffold structure of claim 6, wherein the therapeutic substance is an anti-restenosis drug, comprising at least one selected from the group of paclitaxel, taxane derivatives of paclitaxel, and mTOR inhibitors of the LIMUS family.

8. The scaffold structure of any one of claims 1 - 8, wherein the scaffold comprises:

a plurality of radial support rings axially disposed along the length of the scaffold structure, wherein the central axis of the scaffold structure extends through each radial support ring, and wherein each radial support ring comprises:

a pair of axially adjacent struts radially disposed about the central axis; and

a plurality of bridge members, wherein each bridge member couples each of the pair of adjacent struts;

and

a plurality of preferentially fracturable links, wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples.

9. The scaffold structure of claim 8, wherein portions of the inner coating that overlay the preferentially fracturable links are configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links.

10. The scaffold structure of claim 9, wherein at least some of the plurality of preferentially fracturable links have an omega shape along their length.

11. The scaffold structure of claim 10, wherein each bridge member is a straight structure that extends in a direction parallel to the central axis.

12. A scaffold structure implantable into an anatomical lumen of a human or animal body, the scaffold structure comprising an elongate structure having a length, and through which a central axis is definable along its length, wherein the scaffold structure as-manufactured consists essentially of:

an elongate biodegradable metallic scaffold that provides a frame or cage structure;

a non-porous inner coating disposed over the biodegradable metallic scaffold, wherein the inner coating comprises a non-biodegradable polymer that conformally encases the scaffold, such that an inner surface of the inner coating is disposed adjacent to and in contact with the scaffold;

a non-porous outer coating comprising a biodegradable or non-biodegradable polymer, the outer coating having an outer surface; and

a radiopaque material disposed external to the inner coating and internal to the outer surface of the outer coating along the scaffold structure's length,

wherein the inner coating electrochemically isolates the radiopaque material from the scaffold.

13. A scaffold structure implantable into an anatomical lumen of a human or animal body, the scaffold structure comprising an elongate structure having a length, and through which a central axis is definable along its length, wherein the scaffold structure as-manufactured comprises:

an elongate biodegradable metallic scaffold that provides a frame or cage structure, wherein the scaffold comprises:

a plurality of radial support rings axially disposed along the length of the scaffold, wherein the central axis of the scaffold extends through each radial support ring, and wherein each radial support ring comprises:

a pair of axially adjacent struts radially disposed about the central axis; and

a plurality of bridge members, wherein each bridge member couples each of the pair of adjacent struts;

and

a plurality of preferentially fracturable links, wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples;

a non-porous inner coating disposed over the biodegradable metallic scaffold, wherein the inner coating comprises a non-biodegradable polymer that conformally encases the scaffold, such that an inner surface of the inner coating is disposed adjacent to and in contact with the scaffold;

an outer coating comprising a biodegradable or non-biodegradable polymer, the outer coating having an outer surface; and

a radiopaque material disposed external to the inner coating and internal to the outer surface of the outer coating along the scaffold structure's length,

wherein the inner coating electrochemically isolates the radiopaque material from the scaffold.

14. The scaffold structure of claim 13, wherein portions of the inner coating that overlay the preferentially fracturable links are configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links.

15. An elongate scaffold implantable into an anatomical lumen of a human or animal body, the scaffold having a length along which a central axis is definable, wherein the as-manufactured scaffold comprises:

a plurality of radial support rings axially disposed along the length of the scaffold, wherein the central axis of the scaffold extends through each radial support ring, and wherein each radial support ring comprises:

a pair of axially adjacent struts radially disposed about the central axis; and

a plurality of bridge members, wherein each bridge member couples each of the pair of adjacent struts;

and

a plurality of preferentially fracturable links, wherein each preferentially fracturable link has a length, wherein each preferentially fracturable link couples a pair of adjacent radial support rings, and wherein each preferentially fracturable link includes at least one bent or curved rupture region that is mechanically weaker than each strut and each bridge member of the adjacent radial support rings that it couples.

16. The scaffold structure of claim 15, wherein at least some of the plurality of preferentially fracturable links have an omega shape along their length.

17. The scaffold structure of claim 15 or 16, wherein each bridge member is a straight structure that extends in a direction parallel to the central axis.

18. A method for manufacturing a biodegradable implantable or implanted metallic scaffold structure configurable or configured for implantation into a mammalian body, the method comprising:

providing an elongate biodegradable metallic scaffold having (a) preferentially fracturable links, and (b) radial support rings that are disposed along the scaffold's length and which are coupled by way of the preferentially fracturable links, wherein the preferentially fracturable links are intentionally (i) configured to be structurally weaker than the radial support rings along at least one spatial direction, and (ii) preferentially fracturable or breakable relative to the radial support rings in response to physical stresses or deformations exerted upon the scaffold;

providing or disposing a non-porous first covering or coating over the scaffold, wherein the first covering or coating includes or is a non-biodegradable polymer that conformally encases the scaffold, thereby conformally encasing the scaffold's preferentially fracturable links and radial support rings, such that an inner surface of the first covering or coating is disposed adjacent to and in contact with the scaffold, wherein portions of the first covering or coating that overlay the preferentially fracturable links are configured to tear, break, rupture, open, and/or become porous in response to fracture or breakage of the preferentially fracturable links;

providing or disposing a radiopaque material external to exposed, external, or outer surfaces of the first covering or coating along at least portions of the scaffold structure's length; and

providing or disposing a non-porous second covering or coating including a biodegradable or non-biodegradable polymer over exposed, external, or outer surfaces of the radiopaque material over the scaffold structure's length,

wherein the first covering or coating electrochemically isolates the radiopaque material from the scaffold.