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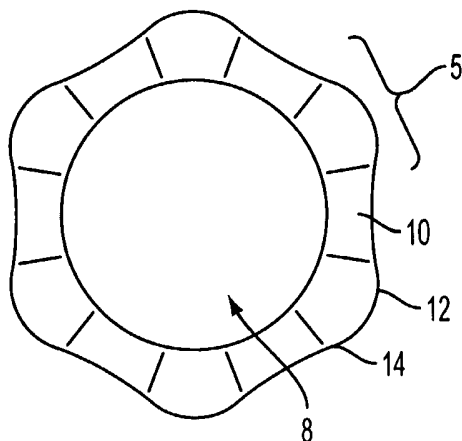
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[Continued on next page]

(54) Title: VARIABLE WALL ENDOVASCULAR STENT



(57) Abstract: An endovascular stent is disclosed  
with a variable thickness wall structure that provides  
increased longitudinal flexibility while retaining other  
desirable stent qualities, including radial strength equal  
to or greater than existing endovascular stents. In  
addition the variable thickness wall structure allows for  
increased surface area for the exterior stent walls, thus  
increasing the potential space available for therapeutic  
coatings.



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## **VARIABLE WALL ENDOVASCULAR STENT**

### **TECHNICAL FIELD**

[001] The present invention relates generally to the field of endovascular medical devices, and relates more specifically to a stent for use in supporting vascular tissue, and particularly, to a stent having improved longitudinal structural flexibility.

### **BACKGROUND ART**

[002] It is generally known to insert a resiliently expandable stent into a blood vessel to provide radial vascular support (hoop support) within the vessel in the treatment of atherosclerotic stenosis. For example, it is generally known to open a blocked cardiac blood vessel by known methods (e.g., balloon angioplasty or laser ablation) and to keep that blood vessel open using such a stent. These stents are generally formed of a biocompatible material, such as stainless steel, and have slots or holes cut therein or have an expansile mesh design, so that an operator may expand the stent after it has been deployed into a blood vessel.

[003] However, a conventional stent structure tends to be longitudinally inflexible (i.e., along a length of the stent), and therefore tends to be resistant to transverse deformation. As a result, the conventional stent tends

to straighten a blood vessel into which it is inserted because it resists conforming to the shape of a curved blood vessel path. Currently, there is some discussion in the art regarding a relationship between this tendency to straighten a blood vessel and the onset of restenosis (i.e., blood vessel reclosure).

**[004]** Conventional, longitudinally inflexible stents are disclosed in, for example, U.S. Patent No. 6,113,628 to Borghi. The stents discussed in this patent are not capable of achieving the longitudinal flexibility needed to prevent restenosis. These stents include distensible circumferential vascular support elements (sometimes referred to as “hoops” or “corrugated rings”) that are securely spaced from each other and from the ends of the stent so that they do not experience relative axial movement. The spacing between adjacent support elements in such conventional stent designs may be maintained by rigid connections or bridge elements (sometimes referred to in the art as “bridges”) that extend between adjacent support elements and/or a rigid connection between each support element and further may include at least one longitudinal rail extending from a first end of the stent to a second end of the stent. This type of secure, rigid spacing prevents the support elements from moving longitudinally along the rail(s) of the stent and prevents the stent from conforming to the curvature of the blood vessel in which it is deployed.

**[005]** It is known to use a stent for controlled, time release therapeutic agent delivery within a vessel. For example, this concept is discussed in U.S. Pat. No. 5,102,417 to Palmaz and U.S. Pat. No. 5,464,650 to Berg, et al., both of which are hereby incorporated by reference in their entirety.

These patents disclose different methods for applying agents, including therapeutic drugs, to a stent in order to reduce the incidence of restenosis, increase vascular healing and/or treat various conditions within the body in which the stent is deployed. However, the coatings of these stents are typically applied to an unexpanded stent. As a result, when the stent is expanded within the vessel, the coating is interrupted and separated, thereby causing portions of the stent to be left uncoated. This may result in an unreliable application of the agent within the vessel. Additionally, these stents and the coatings used to carry these agents may be very expensive to manufacture.

[006] Thus, the need exists for endovascular stents with increased longitudinal flexibility to reduce the incidence of restenosis. Moreover, the need exists for endovascular stent designs better disposed to therapeutic coating with improved reliability and manufacturing economy that provided by existing endovascular stent technology.

## **DISCLOSURE OF INVENTION**

[007] It is an object of the present invention to overcome, or at least alleviate, one or more of the difficulties or deficiencies associated with prior art endovascular stents. In that regard, the present invention provides devices and associated methods for the use of those devices to provide variable stent flexibility while retaining other desirable stent qualities.

[008] In that regard, the present invention fulfills in part the need to impart increased flexibility to an endovascular stent with radial strength equal to or greater than existing endovascular stents.

[009] Moreover, the present invention fulfills in part the need to impart increased flexibility to an endovascular stent with radio-opacity equal to or greater than existing endovascular stents.

[010] In addition, the present invention fulfills in part the need to impart increased surface area in the outer diameter of an endovascular stent over existing endovascular stents, thus increasing the surface area available for drug or other therapeutic coatings.

[011] These and other features, aspects, and other advantages of the present invention will become better understood with regard to the following drawings, description, and appended claims.

#### **BRIEF DESCRIPTION OF DRAWINGS**

[012] **FIG. 1** provides a perspective view of a longitudinal segment of a variable wall stent according to the present invention.

[013] **FIG. 2** provides a perspective view of a random cross-section of a variable wall stent according to the present invention.

#### **MODES FOR CARRYING OUT THE INVENTION**

[014] The present invention may be understood more readily by reference to the following detailed description of the preferred embodiments of the invention and the Examples included herein. However, before the preferred embodiments of the devices and methods according to the present invention are disclosed and described, it is to be understood that this invention is not limited to the exemplary embodiments described within this disclosure, and

the numerous modifications and variations therein that will be apparent to those skilled in the art remain within the scope of the invention disclosed herein. It is also to be understood that the terminology used herein is for the purpose of describing specific embodiments only and is not intended to be limiting.

[015] Unless otherwise noted, the terms used herein are to be understood according to conventional usage by those of ordinary skill in the relevant art. In addition to the definitions of terms provided below, it is to be understood that as used in the specification and in the claims, "a" or "an" may mean one or more, depending upon the context in which it is used.

[016] In an exemplary embodiment according to the present invention, a variable wall stent for deployment in a blood vessel or other anatomic lumen, comprises an elongated structure with a radial axis and a longitudinal axis, further defined by stent walls formed from distensible corrugated rings which are comprised of at least thin-walled corrugated ring elements and thick-walled corrugated ring elements that are joined by thin-walled stent bridges, and a stent lumen defined by and at least partially enclosed by said stent wall corrugated rings. In such an exemplary endovascular stent according to the present invention, the thin-walled corrugated ring elements allow for lowered resistance to radial distension of the stent after it has been deployed, the thick-walled corrugated ring elements maintain radial strength and radio-opacity of the stent, and the thin-walled stent bridges may be disposed to connect the stent wall corrugated rings, thereby allowing increased flexibility of the endovascular

stent along its longitudinal axis than if the stent were composed of thick-walled elements throughout.

[017] Moreover, in an exemplary embodiment of an endovascular stent according to the present invention, the pattern resulting from repeating locations of said thin-walled corrugated ring elements, thick-walled corrugated ring elements, and thin-walled stent bridges creates a scalloping effect on the outer or inner diameter of said stent wall corrugated rings, thereby increasing the surface area of the stent wall corrugated rings, and thus increasing the area potentially available for therapeutic coatings.

[018] Referring now to the drawings, in which like numerals indicate like elements throughout the several views, one embodiment of a variable wall endovascular stent according to the present invention is shown in **FIG. 1**. As shown in **FIG. 1**, a variable wall endovascular stent **100** comprises an elongated structure with both longitudinal and radial axes, in which stent wall corrugated rings **5** define and at least partially enclose a stent lumen **8**. The stent wall corrugated rings **5** are further comprised of at least two types of stent wall corrugated ring elements, thin-walled corrugated ring elements **10** and thick-walled corrugated ring elements **12**. In various embodiments according to the present invention, said stent wall corrugated rings may further comprise one or more additional stent wall elements, including transitional wall elements (not shown in **FIG.1**) which may connect adjacent thin-walled corrugated ring elements **10** and/or thick-walled corrugated ring elements **12**. Transitional wall elements are regions of varying thickness in which transitions in material thickness occur either gradually or abruptly. Thin-walled stent bridges **16** connect or join adjacent

stent wall corrugated rings **5** to form the variable wall endovascular stent **100**. The use of thin-walled stent bridges reduces the force required to bend the variable wall endovascular stent **100** along its longitudinal axis thus giving the stent added longitudinal flexibility.

[019] In some embodiments according to the present invention, the thin-walled stent bridges **16** are positioned so as to establish a linkage only between thick-walled corrugated ring elements **12**. In other embodiments, the thin-walled stent bridges **16** are positioned so as to establish a linkage only between thin-walled corrugated ring elements **10**. In yet another set of embodiments, the thin-walled stent bridges **16** are positioned so as to establish a linkage between a thin-walled corrugated ring element **10** and a thick-walled corrugated ring element **12**.

[020] In various embodiments according to the present invention, thin-walled corrugated ring elements **10** and thick-walled corrugated ring elements **12** may be discrete structures joined together to define the stent wall corrugated rings **5**. In yet other embodiments according to the present invention, the thin-walled corrugated ring elements **10** and thick-walled corrugated ring elements **12** may be continuous parts of the same structure, manufactured by machining or molding to provide variable thickness of the stent wall corrugated rings **5** at predetermined locations.

[021] The cross-sectional perspective view of an embodiment of a variable wall endovascular stent **100** is shown in **FIG. 2**, and the combined views of **FIGS. 1** and **2** may serve to more clearly understand the structure of the exemplary stent according to the present invention. In **FIG. 2**, it will be

noticed that the circumferential structure of the stent wall corrugated rings **5** is disposed in a continuously undulating fashion, in which thin-walled corrugated ring elements **10** and thick-walled corrugated ring elements **12** are interspersed at pre-determined locations throughout, and a stent lumen **8** is centrally defined. The thin-walled-corrugated ring elements **10** and thick-walled corrugated ring elements **12** may be discrete elements joined or fastened together, or they may be continuous elements of the same structure, varying only in thickness and location therein. In some embodiments according to the present invention, transitional stent wall elements **14** may be interspersed between the thin-walled corrugated ring elements **10** and thick-walled corrugated ring elements **12**. The exact thicknesses of the thick **12** and thin **10** walled corrugated ring elements will be determined by the specific application, and by the materials used to fabricate the stent wall corrugated ring elements. In an exemplary variable wall endovascular stent according to the present invention, the thin-walled corrugated ring elements **10** and thin-walled stent bridges **16** may have a thickness of from 10% to 90% of the thickness of the thick stent wall elements **12**.

[022] In some embodiments according to the present invention, hoops or corrugated stent rings may provide an undulating circumferential band of variable thickness, which may be joined to a plurality of like hoops or corrugated stent rings by thin-walled stent bridges **16** to form the variable wall endovascular stent **100**. In yet other embodiments of the present invention, there may be no complete, discernible stent hoops or rings, and the variable thickness wall structure may be provided in a spiraling or continuous fashion.

[023] In various embodiments according to the present invention, the locations of thin-walled corrugated ring elements **10**, thick-walled corrugated ring elements **12**, and thin-walled stent bridges **16** may be pre-determined to allow for controlled stent distension and/or bending within desired parameters and at desired locations throughout the extent of the stent. In general, the thin-walled corrugated ring elements **10** allow for lowered resistance to distension of the stent after it has been deployed, the thick-walled corrugated ring elements **12** maintain the radial strength and radio-opacity of the stent, and thin-walled stent bridges **16** allow bending of the stent along its longitudinal axis.

[024] The pattern resulting from the repeating locations of thin-walled corrugated ring elements **10**, and thick-walled corrugated ring elements **12** may create a “scalloping” effect on the outer diameter of the stent wall corrugated rings **5**. Such a scalloping effect increases the outer surface area of the stent wall corrugated rings **5**, thereby increasing the area potentially available for therapeutic coatings. In alternate embodiments according to the present invention, the outer diameter surface of the stent may be maintained smooth, and the internal diameter of the stent may be “scalloped” similarly for maximal surface area delivery of a therapeutic coating within the inner surface of the stent.

[025] An exemplary embodiment according to the present invention, such as that shown in **FIGS. 1** and **2**, may be manufactured by standard extrusion molding, machining, microassembly, or laser machining technologies.

[026] In alternate embodiments according to the present invention, the variable wall stent may be round, ovoid, not round, or polygonal in its cross-sectional dimensions, and may have one or more lumens that may be central or offset in their placement therethrough.

[027] The stent wall corrugated ring and bridge elements according to the present invention may be fabricated from a variety of biocompatible materials, including metals, alloys, and metallic compounds (*e.g.*, metal oxides), polymers (*e.g.*, resins), amorphous materials (*e.g.*, ceramics, silica, and glassine), carbons (*e.g.*, pyrolytic carbon, such as the coating Carbofilm™, amorphous carbon, activated carbon, and fullerenes as described, *e.g.*, in WO 01/68158) and others. In general, suitable materials will exhibit biocompatibility, sufficient flexibility to navigate lumens during insertion, and the ability to contact and be secured relative to the vascular lumen wall. The term "biocompatible" refers to materials that do not have toxic or injurious effects on biological systems. Thus, the stents should not substantially induce inflammatory and neointimal responses. Any of the biocompatible materials discussed below may be used as the primary material to form the wall elements or other portions of the disclosed stents, or may be used to form a film, coating, or layer to cover a base material (*e.g.*, a metal) that may or may not be biocompatible. Coating techniques are known in the art and are described, *e.g.*, in U.S. Patent No. 6,153,252. If the stent material covers a base material that is itself biocompatible, complete coating of all exposed surfaces of the base material may not be necessary.

[028] Preferably, the stent wall corrugated ring elements **10**, **12**, and **14** and stent bridges **16**, along with other portions of the discussed stents, comprise biocompatible metals, metal alloys, and biocompatible polymers. For example, a type of biocompatible polymer usable with the stents according to the present invention includes the resilient polymeric materials disclosed in international publication WO 91/12779. Additional biocompatible metals and alloys include those disclosed, *e.g.*, in U.S. Patent Nos. 4,733,665; 4,800,882; 4,886,062; and 6,478,815. Such metals and alloys include, but are not limited to, silver, tantalum, stainless steel, annealed steel, gold, copper alloys, cobalt alloys (*e.g.*, cobalt-chromium-nickel alloys), titanium, tungsten, zirconium, niobium, iridium, and platinum. Shaped-memory metal alloys (*e.g.*, Nitinol, a super elastic titanium alloy) may also be used to form the wall elements discussed herein.

[029] Biocompatible polymers that are used with the stent wall elements of the present invention may be nonbioabsorbable, bioabsorbable in part, or substantially completely bioabsorbable. The stable, nonbioabsorbable polymers that may be used for stent wall and bridge construction are those generally exhibiting a low chronic tissue response. These include polyesters, polyamides, polyolefins (substituted or unsubstituted with *e.g.*, halides), polyurethanes (*e.g.*, polyurethane urea, segmented polyurethane urea/heparin) and silicones (*e.g.*, siliconeA, siliconeB, and silicone C) (*see, e.g.*, van Beusekom *et al.* Circulation 86(suppl 1):I-731, (1992) and Lincoff *et al.* J Am. Coll Cardiol 21: 886, 887 (1993)).

[030] Polyesters include *e.g.*, polyethylene terephthalate (PET) and polybutylene terephthalate (PBT). Other polyesters include polyethylene

terephthalate copolymers or polybutylene terephthalate copolymers using, as comonomers, saturated dibasic acids such as phthalic acid, isophthalic acid, sebacic acid, adipic acid, azelaic acid, glutaric acid, succinic acid, and oxalic acid; polyethylene terephthalate copolymers or polybutylene terephthalate copolymers using, as diol comonomers, 1,4-cyclohexanedimethanol, diethylene glycol, and propylene glycol; and blends thereof. Specific examples of these polyethylene terephthalate copolymers include polyethylene terephthalate/isophthalate (PET/I), polyethylene terephthalate/sebacate (PET/S), and polyethylene terephthalate/adipate (PET/A). Specific examples of the polybutylene terephthalate polymers include polybutylene terephthalate (PBT), polybutylene terephthalate/isophthalate (PBT/I), polybutylene terephthalate/sebacate (PBT/S), polybutylene terephthalate/adipate (PBT/A), polybutylene/ethylene terephthalate, and polybutylene/ethylene terephthalate/isophthalate. Also usable are polyesters that are copolymerized or modified with other third components in order to improve their physical characteristics. The polyester resins may be stretched either monoaxially or biaxially.

[031] Polyamides include, *e.g.*, polyamides, Nylon 66, polycaprolactam, and molecules of the form  $\text{--NH--(CH}_2\text{)}_n\text{--CO--}$  and  $\text{NH--(CH}_2\text{)}_x\text{--NH--CO--(CH}_2\text{)}_y\text{--CO}$ , wherein  $n$  is preferably an integer in from about 6 to about 13,  $x$  is an integer from about 6 to about 12, and  $y$  is an integer from about 4 to about 16.

[032] Polyolefins include, *e.g.*, polypropylene, polyethylene, polyisobutylene, polytetrafluoroethylene, expanded polytetrafluoroethylene, ethylene- $\alpha$ -olefin copolymers. Polyolefins also include copolymers of olefins and unsaturated glycidyl group-containing monomers, and terpolymers or multipolymers of olefins, unsaturated glycidyl group-containing monomers and ethylenically unsaturated monomers. Examples of olefins include propylene, butene-1, hexene-1, decene-1, octene-1. Examples of the unsaturated glycidyl group-containing monomers include *e.g.*, glycidyl esters such as glycidyl acrylate, glycidyl methacrylate, monoglycidyl itaconate, monoglycidyl butenetricarboxylate, diglycidyl butenetricarboxylate, and triglycidyl butenetricarboxylate; glycidyl esters of  $\alpha$ -chloroallyl, maleic acid, crotonic acid, and fumaric acid; glycidyl ethers such as vinyl glycidyl ether, allyl glycidyl ether, 2-methallyl glycidyl ether, glycidyloxyethyl vinyl ether, and styrene-*p*-glycidyl ether; and *p*-glycidylstyrene. In addition to olefins, other ethylenically unsaturated monomers of the invention may also be used to form homo- or copolymers. Such monomers include, *e.g.*, vinyl esters and  $\alpha$ - and  $\beta$ -ethylenically unsaturated carboxylic acids and derivatives thereof. Examples include vinyl esters such as vinyl acetate; vinyl propionate; vinyl benzoate; acrylic acid; methacrylic acid and esters thereof, such as methyl, ethyl, propyl, butyl, 2-ethylhexyl, cyclohexyl, dodecyl, and octadecyl acrylates or methacrylates; maleic acid; maleic anhydride; itaconic acid; fumaric acid; maleic mono and diesters; vinyl chloride; vinyl ethers such as vinyl methyl ether and vinyl ethyl ether; and acrylic amides.

[033] Other useful nonbioabsorbable polymers include poly(meth)acrylates, polyalkyl oxides (polyethylene oxide), polyvinyl alcohol homo- and

copolymers (*e.g.*, PVA foams, polyethylene vinyl alcohol), polyethylene glycol homo- and copolymers, polylysine, polyoxamers, polysiloxanes (*e.g.*, polydimethylsiloxane), polyethyloxazoline, and polyvinyl pyrrolidone, as well as hydrogels such as those formed from crosslinked polyvinyl pyrrolidinone and polyesters (*e.g.*, polyvinyl pyrrolidone/cellulose esters and polyvinyl pyrrolidone/poly urethane). Further nonbioabsorbable polymeric materials include acrylic polymers (*e.g.*, methacrylate) and copolymers, vinyl halide polymers and copolymers (*e.g.*, polyvinyl chloride), polyvinyl ethers (*e.g.*, polyvinyl methyl ether), polyvinylidene halides (*e.g.*, polyvinylidene fluoride and polyvinylidene chloride), polymethylidene maleate, polyacrylonitrile, polyvinyl ketones, polyvinyl aromatics (*e.g.*, polystyrene), polyvinyl esters (*e.g.*, polyvinyl acetate), copolymers of vinyl monomers with each other and olefins (*e.g.*, ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins and ethylene-vinyl acetate copolymers), alkyd resins, polycarbonates, polyoxymethylenes, polyimides, polyethers, epoxy resins, rayon, rayon-triacetate, cellulose, cellulose acetate, cellulose acetate butyrate, cellophane, cellulose nitrate, cellulose propionate, cellulose ethers (*e.g.*, carboxymethyl cellulose and hydroxyalkyl celluloses), cellulose esters, and combinations thereof.

[034] Bioabsorbable polymers may also be used for the stent wall and bridge elements and other parts of the stents of the present invention. Bioabsorbable polymers are advantageous in that stents or portions thereof formed from these materials may be absorbed into the body and therefore do not require physical removal. Bioabsorbable polymers include, for example, those found in Tanquay *et al.* (Contemp. Intervention. Tech.

12(4):699-713, (1994)). Bioabsorbable polymers differ from nonbioabsorbable polymers in that they may be degraded into substantially non-toxic biodegradation products, while used in *in vivo* therapy. Degradation generally involves breaking down the polymer into its monomeric subunits. For example, the ultimate hydrolytic breakdown products of a poly(phosphonate) are phosphonate, alcohol, and diol, all of which are potentially non-toxic. The rate of degradation of bioabsorbable polymers is related to various polymer properties, such as permeability, water solubility, crystallinity, and physical dimensions.

[035] Bioabsorbable polymers include various types of aliphatic polyesters, polyorthoesters, polyphosphazenes, poly(amino acids), copoly(ether-esters), polyalkylene oxalates, polyamides, poly(iminocarbonates), polyoxaesters, polyamidoesters, polyoxaesters containing amido groups, poly(anhydrides), poly(hydroxybutyrates), poly(phosphate-esters), polyurethanes, polyanhydrides, biomolecules, and blends thereof.

[036] Bioabsorbable polyesters may be used and are described, *e.g.*, in Pitt *et al.*, "Biodegradable Drug Delivery Systems Based on Aliphatic Polyesters: Application to Contraceptives and Narcotic Antagonists", Controlled Release of Bioactive Materials, 19-44 Richard Baker ed., (1980). Aliphatic polyesters include homopolymers and copolymers of lactides (including lactic acid and D-,L-, and meso lactide),  $\epsilon$ -caprolactone, glycolide (including glycolic acid and lactide/glycolide copolymers), hydroxybutyrate, hydroxyvalerate, dioxanone (*e.g.*, para-dioxanone), trimethylene carbonate (and its alkyl derivatives), 1,4-dioxepan-2-one, 1,5-dioxepan-2-one, 6,6-dimethyl-1,4-dioxan-2-one, and polymer blends

thereof. Bioabsorbable polyorthoesters may also be used and are described *e.g.*, by Heller *et al.*, "Release of Norethindrone from Polyortho Esters", Polymer Engineering Sci., 21:11, 727-31 (1981) and also by Heller in *Handbook of Biodegradable Polymers*, edited by Domb, Kost and Wisemen, Hardwood Academic Press (1997) p. 99-118. Polyorthoesters include, *e.g.*, polyglycolic acid and polylactic acid such as poly-L-lactic acid (PLLA); poly D,L-lactic acid; and poly-D-lactic acid. Bioabsorbable polyphosphazenes are described, *e.g.*, by Dunn *et al.*, in U.S. Patent Nos. 5,340,849; 5,324,519; 5,278,202; and 5,278,201. Polyphosphazenes, co-, ter- and higher order mixed monomer based polymers made from L-lactide, D,L-lactide, lactic acid, glycolide, glycolic acid, para-dioxanone, trimethylene carbonate and  $\epsilon$ -caprolactone, are described by Allcock in *The Encyclopedia of Polymer Science*, Vol. 13, p. 31-41, Wiley Intersciences, John Wiley & Sons (1988) and by Vandorpe, Schacht, Dejardin and Lemmouchi in the *Handbook of Biodegradable Polymers*, edited by Domb, Kost and Wisemen, Hardwood Academic Press (1997), p. 161-182. Poly(amino acids) and pseudo-poly(amino acids) are described, *e.g.*, by Pulapura *et al.*, "Trends in the Development of Bioresorbable Polymers for Medical Applications," J. of Biomaterials Appl., 6:1, 216-50 (1992); Poly(iminocarbonate) is described, *e.g.*, in Kemnitzer and Kohn, *Handbook of Biodegradable Polymers*, edited by Domb, Kost and Wisemen, Hardwood Academic Press (1997), p. 251-272. Copoly(ether-esters) include, *e.g.*, PEO/PLA and others described by Cohn and Younes, Journal of Biomaterials Research, Vol. 22 (1998), p. 993-1009, and by Cohn, Polymer Preprints (ACS Division of Polymer Chemistry) Vol. 30(1), (1989) p. 498. Polyalkylene oxalates include those described in U.S. Patent Nos. 4,208,511; 4,141,087; 4,130,639; 4,140,678; 4,105,034; and 4,205,399.

Polyanhydrides include those resulting from the polymerization of diacids of the form  $\text{HOOC}-\text{C}_6\text{H}_4-\text{O}-(\text{CH}_2)_m-\text{O}-\text{C}_6\text{H}_4-\text{COOH}$  where  $m$  is an integer from about 2 to about 8 and also include copolymers resulting from the copolymerization of these diacids with aliphatic alpha-omega diacids of up to 12 carbons. As is known in the art, the monomer ratios in polyanhydride copolymers may be varied so that the resulting copolymer is surface eroding. Polyoxaesters, polyoxaamides, and polyoxaesters containing amines and/or amido groups are described in one or more of U.S. Patent Nos. 5,464,929; 5,595,751; 5,597,579; 5,607,687; 5,618,552; 5,620,698; 5,645,850; 5,648,088; 5,698,213 and 5,700,583. Bioabsorbable poly(phosphate-esters), *e.g.*, poly(phosphates), poly(phosphonates) and poly(phosphites), are described, *e.g.*, by Penczek *et al.*, Handbook of Polymer Synthesis, Chapter 17: "Phosphorus-Containing Polymers", p. 1077-1132 (Hans R. Kricheldorf ed., 1992) and in U.S. Patent No. 6,153,212. Bioabsorbable polyurethanes are described, *e.g.*, by Bruin *et al.*, "Biodegradable Lysine Diisocyanate-based Poly-(Glycolide-co-ε-Caprolactone)-Urethane Network in Artificial Skin", Biomaterials, 11:4, 291-95 (1990). Bioabsorbable polyanhydrides are described, *e.g.*, by Leong *et al.*, "Polyanhydrides for Controlled Release of Bioactive Agents", Biomaterials, 7:5, 364-71 (1986).

[037] Polymeric biomolecules may also advantageously be used with the stent wall and bridge elements or other portions of the stents according to the present invention. Polymeric biomolecules include naturally occurring materials that may be enzymatically degraded in the human body or those that are hydrolytically unstable in the human body. Such materials include albumin, alginate, gelatin, acacia, cellulose dextran, ficoll, hydroxyethyl

cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, carboxyethyl cellulose, carboxymethyl cellulose, fibrin, fibrinogen, collagen, elastin, dextran sulfate and absorbable biocompatible polysaccharides such as chitosan, deacetylated chitosan, starch, fatty acids (and esters thereof), glucosylglycerols and hyaluronic acid.

[038] Other useful materials include bioabsorbable elastomers, preferably aliphatic polyester elastomers. In the proper proportions aliphatic polyester copolymers are elastomers. If used as coating materials, elastomers advantageously adhere well to the metal portions of the stent and may withstand significant deformation without cracking. Examples of suitable bioabsorbable elastomers are described in U.S. Patent No. 5,468,253. Preferred bioabsorbable biocompatible elastomers are based on aliphatic polyesters, including elastomeric copolymers of  $\epsilon$ -caprolactone and glycolide (preferably having a mole ratio of  $\epsilon$ -caprolactone to glycolide from about 35:65 to about 65:35); elastomeric copolymers of  $\epsilon$ -caprolactone and lactide, including L-lactide, D-lactide and blends thereof or lactic acid copolymers (preferably having a mole ratio of  $\epsilon$ -caprolactone to lactide from about 35:65 to about 90:10); elastomeric copolymers of p-dioxanone (1,4-dioxan-2-one) and lactide including L-lactide, D-lactide and lactic acid (preferably having a mole ratio of p-dioxanone to lactide from about 40:60 to about 60:40); elastomeric copolymers of  $\epsilon$ -caprolactone and p-dioxanone (preferably having a mole ratio of  $\epsilon$ -caprolactone to p-dioxanone from about 30:70 to about 70:30); elastomeric copolymers of p-dioxanone and trimethylene carbonate (preferably having a mole ratio of p-dioxanone to trimethylene carbonate from about 30:70 to about 70:30); elastomeric

copolymers of trimethylene carbonate and glycolide (preferably having a mole ratio of trimethylene carbonate to glycolide from about 30:70 to about 70:30); elastomeric copolymers of trimethylene carbonate and lactide including L-lactide, D-lactide, and blends thereof; or lactic acid copolymers (preferably having a mole ratio of trimethylene carbonate to lactide from about 30:70 to about 70:30) and blends thereof.

**[039]** The present invention also includes introducing an agent into a body using one of the above-discussed stents. In a preferred embodiment, the agent(s) is carried by one or more of the stent wall and/or bridge elements and released within the body over a predetermined period of time. Local delivery of an agent is advantageous in that its effective local concentration is much higher when delivered by the stent than that normally achieved by systemic administration. The stent wall corrugated ring elements **10**, **12**, and **14** and stent bridges **16**, which are relatively inelastic in their transverse strength properties, may carry one or more of the above-referenced agents for applying to a vessel as the vessel moves into contact with the agent carrying stent wall elements after deployment of the stent within the vessel.

**[040]** The above-discussed stents may deliver one or more known agents, including therapeutic and pharmaceutical agents, such as a drug, at a site of contact with a portion of the vasculature system or when released from a carrier as is known. These agents may include any known therapeutic drugs, antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents and proteins used for the treatment, prevention, diagnosis, cure, or mitigation of disease or illness; substances that affect the structure of

function of the body; and prodrugs, which become biologically active or more active after placement in a given physiological environment. Agents may include medicaments, vitamins, mineral supplements. The agents may also include any of those disclosed in U.S. Patent No. 6,153,252 to Hossainy et al. and U.S. Patent No. 5,833,651 to Donovan et al., both of which are hereby incorporated by reference in their entirety.

**[041]** Preferred agents usable with the stent wall and bridge elements disclosed herein are those that inhibit restenosis through any of a variety of approaches and include anti-inflammatory immuno-modulators including dexamethasone, m-prednisolone, interferon  $\gamma$ -1b, leflunomide, sirolimus, everolimus, tacrolimus, mycophenolic acid, mizoribine, cyclosporine, rapamycin, and tranilast; antiproliferatives including QP-2, taxol, actinomycine, methotrexate, angiopeptin, vincristine, mitomycin, statins, CMYC antisense, ABT-578, RestenASE, 2-chlorodeoxyadenosine, PCNA ribozyme, paclitaxel, rapamycin, everolimus and tacrolimus; migration inhibitors/ECM-modulators including batimastat, prolyhydroxylase inhibitors, halofuginone, C-proteinase inhibitors, probucol, rapamycin, everolimus and tacrolimus; and agents that promote healing and reendothelialization including BCP671, VEGF, and estrogen. Additional agents, such as those discussed below, may also be used.

**[042]** Non-limiting examples of agents include those within the following therapeutic categories: analgesics, such as nonsteroidal anti-inflammatories (NSAIDs), steroidal anti-inflammatories, COX 2 selective inhibitors, opiate agonists and salicylates; angiogenesis inhibitors; antiasthmatics; antihistamines/antipruritics, such as H<sub>1</sub>-blockers and H<sub>2</sub>-blockers; anti-

infectives, such as anthelmintics, anti-anaerobics, antibiotics, aminoglycoside antibiotics, antifungal antibiotics, macrolide antibiotics, miscellaneous  $\beta$ -lactam antibiotics, penicillin antibiotics, quinolone antibiotics, sulfonamide antibiotics, tetracycline antibiotics, antimicrobials, antibacterials, antimycobacterials, antituberculosis antimycobacterials, antiprotozoals, antimalarial antiprotozoals, antiviral agents, anti-retroviral agents, scabicides, and urinary anti-infectives; antiarthritics; antifibrinolytics; antineoplastics, such as alkylating agents, antimetabolites, purine analog antimetabolites, pyrimidine analog antimetabolites, hormonal antineoplastics, natural antineoplastics, antibiotic natural antineoplastics, and vinca alkaloid natural antineoplastics; calcium regulators; autonomic agents, such as anticholinergics, xanthines, mast cell stabilizers, antimuscarinic anticholinergics, ergot alkaloids, parasympathomimetics, cholinergic agonist parasympathomimetics, cholinesterase inhibitor parasympathomimetics, sympatholytics,  $\alpha$ -blocker sympatholytics,  $\beta$ -blocker sympatholytics, sympathomimetics, and adrenergic agonist sympathomimetics; cardiovascular agents, such as antianginals,  $\beta$ -blocker antianginals, calcium-channel blocker antianginals, nitrate antianginals, antiarrhythmics, cardiac glycoside antiarrhythmics, class I, II, III, or IV antiarrhythmics, antihypertensive agents,  $\alpha$ -blocker antihypertensives, angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives,  $\beta$ -blocker antihypertensives, calcium-channel blocker antihypertensives, central-acting adrenergic antihypertensives, diuretic anti-hypertensive agents, peripheral vasodilator anti-hypertensives, anti-lipidemics, inotropes, cardiac glycoside inotropes, and thrombolytics/fibrinolytics; dermatological agents, such as antihistamines, anti-inflammatory agents, corticosteroid anti-inflammatory agents, and antipruritics/local anesthetics; electrolytic

and renal agents, such as acidifying agents, alkalinizing agents, diuretics, carbonic anhydrase inhibitor diuretics, loop diuretics, osmotic diuretics, potassium-sparing diuretics, thiazide diuretics, electrolyte replacements, and uricosuric agents; enzymes, such as pancreatic enzymes and thrombolytic enzymes; gastrointestinal agents, such as anti-diarrheals, antiemetics/antinauseants, gastrointestinal anti-inflammatory agents, salicylate gastrointestinal anti-inflammatory agents, anti-ulcer/anti-reflux agents, antacid anti-ulcer agents, gastric acid-pump inhibitor anti-ulcer agents, gastric mucosal anti-ulcer agents, H<sub>2</sub>-blocker anti-ulcer agents, cholelitholytic agents, digestants, emetics, laxatives and stool softeners, and prokinetic agents; enzyme inhibitors; general anesthetics, such as halogenated anesthetics, barbiturate anesthetics, benzodiazepine anesthetics, and opiate agonist anesthetics; hematological agents, such as antianemia agents, hematopoietic antianemia agents, coagulation agents, anticoagulants, hemorheologic agents, hemostatic coagulation agents, antiplatelet agents, thrombolytic enzyme coagulation agents, and plasma volume expanders; hormones, hormone modifiers, and thyroid hormones, such as abortifacients, adrenal agents, adrenal corticosteroids, androgens, anti-androgens, antidiabetics, sulfonylurea antidiabetic agents, antihypoglycemic agents, progestins, estrogens, fertility agents, oxytocics, parathyroid agents, pituitary hormones, antithyroid agents, thyroid hormones, and tocolytics; immunobiologic agents, such as immunoglobulins, immunosuppressives, toxoids, and vaccines; local anesthetics, such as amide local anesthetics and ester local anesthetics; musculoskeletal agents, such as anti-gout anti-inflammatory agents, corticosteroid anti-inflammatory agents, immunosuppressive anti-inflammatory agents, salicylate anti-inflammatory agents, skeletal muscle

relaxants, neuromuscular blocker skeletal muscle relaxants, and reverse neuromuscular blocker skeletal muscle relaxants; anti-apoptotics; neurological agents, such as anticonvulsants, barbiturate anticonvulsants, benzo-diazepine anticonvulsants, anti-migraine agents, anti-parkinsonian agents, anti-vertigo agents, opiate agonists, and opiate antagonists; ophthalmic agents, such as anti-glaucoma agents,  $\beta$ -blocker anti-glaucoma agents, miotic anti-glaucoma agents, mydriatics, adrenergic agonist mydriatics, antimuscarinic mydriatics, ophthalmic anesthetics, ophthalmic anti-infectives, ophthalmic aminoglycoside anti-infectives, ophthalmic macrolide anti-infectives, ophthalmic quinolone anti-infectives, ophthalmic sulfonamide anti-infectives, ophthalmic tetracycline anti-infectives, ophthalmic agents, ophthalmic corticosteroid anti-inflammatory agents, and ophthalmic nonsteroidal anti-inflammatory drugs; psychotropic agents, such as antidepressants, heterocyclic anti-depressants, monoamine oxidase inhibitors (MAOIs), selective serotonin re-uptake inhibitors (SSRIs), tricyclic antidepressants, antimanics, antipsychotics, phenothiazine antipsychotics, anxiolytics, sedatives, and hypnotics, barbiturate sedatives and hypnotics, benzodiazepine anxiolytics, sedatives, and hypnotics, and psychostimulants; respiratory agents, such as antitussives, bronchodilators, adrenergic agonist bronchodilators, antimuscarinic bronchodilators, expectorants, mucolytic agents, respiratory anti-inflammatory agents, and respiratory corticosteroid anti-inflammatory agents; toxicology agents, such as antidotes, heavy metal antagonists/chelating agents, substance abuse agents, deterrent substance abuse agents, and withdrawal substance abuse agents; minerals; vitamins, such as vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, and vitamin K; amino acids; and proteins, such as

antibodies (*e.g.*, monoclonal antibodies, polyclonal antibodies, and antibody fragments).

[043] The following are examples of agents within the various therapeutic categories discussed above that may be used alone or with another one or more of these agents:

[044] Analgesics include, *e.g.*, para-aminophenol derivatives (*e.g.*, acetaminophen), indole and indene acetic acids (*e.g.*, etodalac), heteroaryl acetic acids (*e.g.*, diclofenac and ketorolac), arylpropionic acids (*e.g.*, ibuprofen), anthranilic acids (*e.g.*, mefenamic acid and meclofenamic acid), enolic acids (*e.g.*, tenoxicam and oxyphenthatrizone), nabumetone, gold compounds (*e.g.*, gold sodium thiomalate), buprenorphine, propoxyphene hydrochloride, propoxyphene napsylate, meperidine hydrochloride, hydromorphone hydrochloride, morphine, oxycodone, codeine, dihydrocodeine bitartrate, pentazocine, hydrocodone bitartrate, levorphanol, diflunisal, trolamine salicylate, nalbuphine hydrochloride, mefenamic acid, butorphanol, choline salicylate, butalbital, phenyltoloxamine citrate, methotrimeprazine, cinnamedrine hydrochloride, meprobamate, ketoprofen, flurbiprofen, naproxen, ramifenazone, meloxicam, fluazacort, celecoxib, rofecoxib, valdecoxib, nepafenac, ISV-205; angiogenesis inhibitors include, *e.g.*, angiostatin (plasminogen fragment), vascular endothelial cell growth factor (VEGF), fibroblast growth factor (FGF), nitric oxide donors, antiangiogenic antithrombin III, cartilage-derived inhibitor (CDI), CD59 complement fragment, endostatin (collagen XVIII fragment), fibronectin fragment, gro-beta, heparinases, heparin hexasaccharide fragment, human

chorionic gonadotropin (hCG),  $\alpha$ -,  $\beta$ -, and  $\gamma$ -interferon, interferon inducible protein (IP-10), interleukin-12, kringle 5 (plasminogen fragment), metalloproteinase inhibitors (TIMPs), 2-methoxyestradiol, placental ribonuclease inhibitor, plasminogen activator inhibitor, platelet factor-4 (PF-4), prolactin 16kD fragment, proliferin-related protein (PRP), retinoids, tetrahydrocortisol-S, thrombospondin-1 (TSP-1), transforming growth factor-beta (TGF-b), vasculostatin, vasostatin (calreticulin fragment), apolipoprotein E, TBC-2576; antiasthmatics include, *e.g.*, ketotifen and traxanox; antidepressants include, *e.g.*, nefopam, oxypertine, amoxapine, trazodone, maprotiline, phenelzine, desipramine, nortriptyline, tranlycypromine, fluoxetine, doxepin, imipramine, imipramine pamoate, isocarboxazid, trimipramine, and protriptyline; antidiabetics include, *e.g.*, biguanides (*e.g.*, metformin), sulfonylurea derivatives (*e.g.*, tolbutamide, chlorpropamide, acetohexamide, tolazamide, and glimepiride),  $\alpha$ -glucosidase inhibitors (*e.g.*, acarbose), thiazolidinediones (*e.g.*, troglitazone), and metglinide analogs (*e.g.*, repaglinide); antihypertensive agents include, *e.g.*, propranolol, propafenone, oxyprenolol, reserpine, trimethaphan, phenoxybenzamine, pargyline hydrochloride, deserpidine, diazoxide, guanethidine monosulfate, minoxidil, rescinnamine, sodium nitroprusside, rauwolfia serpentina, alseroxylon, and phentolamine; antineoplastics include, *e.g.*, cladribine (2-chlorodeoxyadenosine), nitrogen mustards (*e.g.*, cyclophosphamide, mechlorethamine, melphalan, and chlorambucil), ethylenimines and methylmelamines (*e.g.*, hexamethylmelamine and thiotepa), alkyl sulfonates (*e.g.*, busulfan), nitrosoureas (*e.g.*, streptozocin, carmustine (BCNU), methyl-CCNU and analogs), trazenes (*e.g.*, dacarbazine (DTIC)), platinum coordination complexes (*e.g.*, carboplatin and cisplatin), procarbazine, hydroxyurea,

mitotane, aminoglutethimide, camptothecin phenesterine, paclitaxel, docetaxel, vinca alkaloids (*e.g.*, vinblastine, vincristine, and vinorelbine), epidipodophyllotoxins (*e.g.*, etoposide (VP-16) and teniposide), tamoxifen, and pipsosulfan; anxiolytics include, *e.g.*, lorazepam, buspirone, prazepam, chlordiazepoxide, oxazepam, clorazepate dipotassium, hydroxyzine pamoate, hydroxyzine hydrochloride, alprazolam, droperidol, halazepam, chlormezanone, and dantrolene; enzyme inhibitors include, *e.g.*, selegiline or its hydrochloride salt, lazabemide, rasagiline, moclobemide, entacapone, tolcapone, nitecapone, Ro 40-7592, clozapine, risperidone, olanzapine, and quetiapine; immunosuppressives include, *e.g.*, calcineurin inhibitors (*e.g.*, cyclosporine and tacrolimus (FK-506)), antiproliferative/antimetabolic agents (*e.g.*, sirolimus, QP-2, taxol, actinomycin, dactinomycin, daunorubicin, angiopeptin, mitomycin, bleomycin, doxorubicin, epirubicin, mitomycin, idarubicin, anthracyclines, mitoxantrone, plicamycin, CMYC antisense, ABT-578, RestenASE, 2-chloro deoxyadenosine, PCNA ribozyme, rapamycin, folic acid analogs (*e.g.*, methotrexate), fluorouracil (5-FU), floxuridine, cytarabine, mercaptopurine, thioguanine, pentostatin, cyclophosphamide, thalidomide, chorambucil, leflunomide, batimastat, and mizoribine), everolimus, azathioprine, cytoxan, mycophenolic acid, mycophenolate mofetil, and tranilast; antimigraine agents include, *e.g.*, ergotamine, isometheptene mucate, and dichloralphenazone; sedatives and hypnotics include, *e.g.*, barbiturates (*e.g.*, pentobarbital and secobarbital), flurazepam hydrochloride, triazolam, and midazolam; calcium-channel blocker antianginals include, *e.g.*, nifedipine and diltiazem; nitrate antianginals include, *e.g.*, nitroglycerin, isosorbide dinitrate, pentaerythritol tetranitrate, and erythrityl tetranitrate; antipsychotics include, *e.g.*, haloperidol, loxapine succinate, loxapine

hydrochloride, thioridazine, thioridazine hydrochloride, thiothixene, fluphenazine, fluphenazine demayoate, fluphenazine enanthate, trifluoperazine, chlorpromazine, perphenazine, lithium citrate, and prochlorperazine; antimanics include, *e.g.*, lithium carbonate; antiarrhythmics include, *e.g.*, bretylium tosylate, esmolol, verapamil, amiodarone, encainide, digoxin, digitoxin, mexiletine, disopyramide phosphate, procainamide, quinidine sulfate, quinidine gluconate, quinidine polygalacturonate, flecainide acetate, tocainide, and lidocaine; antiarthritics include, *e.g.*, phenylbutazone, sulindac, penicillanine, salsalate, piroxicam, indomethacin, meclofenamate, ketoprofen, auranofin, aurothioglucose, tolmetin, and tolmetin sodium; anti-gout agents include, *e.g.*, colchicine and allopurinol; anticoagulants include *e.g.*, danaparoid, lepirudin, dicumarol, acenocoumarol, heparin, heparin salts (*e.g.*, heparin sodium), warfarin sodium, 4-hydroxycoumarin, phenprocoumon, indan-1,3 dione, anisindione, warfarin sodium, tissue factor pathway inhibitor (TFPI), tifacogin, ancrod, bromindione, clorindione, coumetarol, cyclocoumarol, 4-coumarinol, desirudin, dextran sodium sulfate, diphenadione, ethyl biscoumacetate, fluidione, hirudin, nadroparin calcium, nafamostat mesylate, oxazidione, phenindione, phosvitin, picotamide, sodium apolate, thrombocid, tiocloamarol, warfarin, aprosulate sodium, ART 123, bivalirudin, BMS 189090, BMS 186282, BMS 189664, BMS 191032, corsevin M, CS 747, curdlan sulfate, DPC 423, DX 9065a, efegatran, fondaparinux sodium, GR 144053, inogatran, LB 30057, melagatran, MR 33, napsagatran, NSL 9403, SR 90107, YM 75466, ZK 805412, ZK 807834, OGS 15435, JTV 803, LY 287045, P 8720, RE 1492, Ro 43-8857, S 18326, S 31214, SK 549, SB 249417, SR 123781A, and UK 156406; thrombolytics/fibrinolytics include, *e.g.*, urokinase, streptokinase, alteplase,

phosphorylcholine, plasmin, plasminogen, angiokinase, anistreplase, prourokinase, reteplase, saruplase, tissue plasminogen activator, actinokinase,  $\alpha$ 2-antiplasmin, antithrombin, E 6010, fibrolase, lys-plasminogen, lanoteplase, lumbrokinase, metalloproteinase, monteplase, PAI proteinase inhibitor, pamiteplase, staphylokinase, and tenecteplase; antifibrinolytics include, e.g., aminocaproic acid; hemorheologic agents include, e.g., pentoxifylline; antiplatelet agents include, e.g., aspirin, ticlopidine, abciximab, clopidogrel, eptifibatide, tirofiban, and glycoprotein IIb/IIIa inhibitors, argatroban, cilostazole, cloricromene, dalteparin, daltroban, defibrotide, dipyridamole, enoxaparin, iloprost, indobufen, isbogrel, lamifiban, lotrifiban nadroparin calcium, orbofiban, pamicogrel KBT 3022, plafibrade, picotamide, ozagrel, ramatroban, reviparin sodium, ridogrel, roxifiban, satigrel, sibrafiban, sulotroban, taprostene, ticlopidine, triflusal, amrinone, cilostamide, dialzep, enoximone, milrinone, naftazone, pimilprost, pimobendan, sarpogrelate, sulfinpyrazone, vapiprost, vesnarinone, xemilofiban, zaprinast, zeria Z 335, A 02131-1, camonagrel, maygrelor, DMP 728, DMP 802, elarofiban, EMD 122347 FK 633, FXV 673, ifetroban, L 734217, lefradafiban, MK 852, ON 579, R 99224, RGD 039, RGD 891, RPR 109891, Ro 48-3657, Ro 44-3888, S 1197, SDZ-GPI 562, SL 650472, SM 20302, SR 121566A, SR 121787A, TA 993, TAK 029, XV 454, XV 459, YC-1, aspalatone, BAY 41-2272, BM 531, BM 14515, C 186-65, CS 570, FR 158999, fradafiban, L 750034, linotroban, ME 3277, MED 27, NQ 12, NQ 301, NQ 304, NSL 9511, NSP 513, 4-pentynoic acid, 3-[[4-[[4-(aminomethyl)-phenyl]amino]-1,4-dioxobutyl]-amino]-ethyl ester, RE 2047, SCH 79797, SM 10906, SR 25989, TP 9201, XJ 735, XR 300, XU 057, XU 063, XU 065, Y 909, ZD 2486, and ZD 9583; anti-apoptotics include, e.g., CGP 3466, CEP-1347/KT-7515, TCH-

346, and WHI-P131; neurological agents include, *e.g.*, timolol, dapiprazole, levobunolol, betaxolol, befunolol, carteolol, metipranolol, AMO-140, bunazosin, adaprolol, ISV-208, L-653328, cetamolol, H-216/44, KRG-332, levobetaxolol, metazosin, NCX-904, NCX-905, guanethidine, brimonidine, apraclonidine, AGN-195795, AGN-191103, AGN-190532, AGN-192172, AGN-193080, AGN-190837, talipexole, thiourea, dipivefrin, epinephrine, phenylephrine, cocaine, hydroxyamphetamine, naphazoline, tetrahydrozoline, levodopa, levodopa/carbidopa, levodopa/benserazide, amantadine, sumanirole, pergolide, pramipexole, ropinirole, bromocriptine, lisuride or 9, 10 dihydrolisuride, apomorphine or N-propylnoraporphine, N-propyl noraporphine, PHNO, N-0437 (racemate) and N-9023 (purified negative enantiomer), cabergoline, ciladopa, ABT-431, lergotril, DIB1508Y, and ABT418m; selective serotonin re-uptake inhibitors (SSRIs) include, *e.g.*, paroxetine, and sertraline; anticonvulsants include, *e.g.*, valproic acid, divalproex sodium, phenytoin, phenytoin sodium, clonazepam, primidone, phenobarbital, carbamazepine, amobarbital sodium, methsuximide, metharbital, mephobarbital, mephentyoin, phensuximide, paramethadione, ethotoin, phenacemide, secobarbital sodium, clorazepate dipotassium, and trimethadione; anti-parkinsonian agents include, *e.g.*, ethosuximide; antihistamines/antipruritics include, *e.g.*, hydroxyzine, chlorpheniramine, brompheniramine maleate, cyproheptadine hydrochloride, terfenadine, clemastine fumarate, triprolidine, carbinoxamine, diphenylpyraline, phenindamine, azatadine, tripeleminamine, dexchlorpheniramine maleate, and methdilazine; calcium regulators include, *e.g.*, calcitonin and parathyroid hormone; antibacterials include, *e.g.*, amikacin sulfate, aztreonam, chloramphenicol, chloramphenicol palmitate, clindamycin, clindamycin palmitate, clindamycin phosphate,

metronidazole, gentamicin sulfate, lincomycin hydrochloride, tobramycin sulfate, vancomycin hydrochloride, polymyxin B sulfate, colistimethate sodium, and colistin sulfate; antibiotics include, *e.g.*, neomycin, streptomycin, chloramphenicol, cephalosporin, ampicillin, penicillin, tetracycline, and ciprofloxacin; antifungal antibiotics include, *e.g.*, griseofulvin, ketoconazole, itraconazole, amphotericin B, nystatin, and candicidin; antiviral agents include, *e.g.*, zidovudine (AZT), amantadine hydrochloride, ribavirin, and acyclovir; antimicrobials include, *e.g.*, cephalosporins (*e.g.*, cefazolin sodium, cephadrine, cefaclor, cephapirin sodium, ceftizoxime sodium, cefoperazone sodium, cefotetan disodium, cefuroxime sodium, cefotaxime sodium, cefadroxil monohydrate, cephalexin, cephalothin sodium, cephalexin hydrochloride monohydrate, cefamandole nafate, cefoxitin sodium, cefonicid sodium, ceforanide, ceftriaxone sodium, cefadroxil, and cefuroxime sodium), penicillins (*e.g.*, ampicillin, amoxicillin, penicillin G benzathine, cyclacillin, ampicillin sodium, penicillin G potassium, penicillin V potassium, piperacillin sodium, oxacillin sodium, bacampicillin hydrochloride, cloxacillin sodium, ticarcillin disodium, azlocillin sodium, carbenicillin indanyl sodium, penicillin G procaine, methicillin sodium, and nafcillin sodium), and erythromycins (*e.g.*, erythromycin ethylsuccinate, erythromycin, erythromycin estolate, erythromycin lactobionate, erythromycin stearate, and erythromycin ethylsuccinate), and tetracyclines (*e.g.*, tetracycline hydrochloride, doxycycline hyclate, minocycline hydrochloride, azithromycin, and clarithromycin); anti-infectives include, *e.g.*, GM-CSF; sympathomimetics include, *e.g.*, epinephrine hydrochloride, metaproterenol sulfate, terbutaline sulfate, isoetharine, isoetharine mesylate, isoetharine hydrochloride, albuterol sulfate, albuterol, bitolterolmesylate, isoproterenol

hydrochloride, epinephrine, and epinephrine bitartrate; anticholinergics include, *e.g.*, ipratropium bromide, benzhexol, trihexphenidyl, benzotropine, diphenhydramine hydrochloride, orphenadrine, chlorphenoxamine, amitriptyline, doxepin, imipramine, nortriptyline, biperiden, ethopropazine, procyclidine, cycrimine, and ethopropzaine; xanthines include, *e.g.*, aminophylline, dyphylline, metaproterenol sulfate, and aminophylline; mast cell stabilizers include, *e.g.*, cromolyn sodium; bronchodilators include, *e.g.*, salbutamol, budesonide, ketotifen, salmeterol, xinafoate, terbutaline sulfate, theophylline, nedocromil sodium, metaproterenol sulfate, flunisolide, and fluticasone proprionate; androgens include, *e.g.*, danazol, testosterone cypionate, fluoxymesterone, ethyltestosterone, testosterone enanthate, methyltestosterone; estrogens include, *e.g.*, estradiol, estropipate, and conjugated estrogens; progestins include, *e.g.*, methoxyprogesterone acetate, and norethindrone acetate; adrenal corticosteroids include, *e.g.*, cortisol, cortisone, oxandrolone, creatine, erythropeotin, dehydroepiandrosterone triamcinolone, betamethasone, betamethasone sodium phosphate, dexamethasone, dexamethasone sodium phosphate, dexamethasone acetate, prednisone, prednisolone, methylprednisolone acetate suspension, triamcinolone acetonide, hydrocortisone sodium succinate, triamcinolone hexacetonide, hydrocortisone, hydrocortisone cypionate, fludrocortisone acetate, paramethasone acetate, prednisolone tebutate, and prednisolone acetate; thyroid hormones include, *e.g.*, levothyroxine sodium; antihypoglycemic agents include, *e.g.*, human insulin, purified beef insulin, purified pork insulin, glyburide, chlorpropamide, glipizide, tolbutarnide, and tolazamide; anti-lipidemics include *e.g.*, antiatherosclerotics and antihypercholesteremics (*e.g.*, cholesteryl ester transfer protein (CETP)

inhibitors, such as those disclosed in U.S. Patent No. 6,458,850; ileal bile acid transport (IBAT) inhibitors, such as those disclosed in U.S. Patent No. 6,458,851; and HMG CoA reductase inhibitors, such as those disclosed in U.S. Patent No. 6,462,091), fibric acid derivatives (*e.g.*, clofibrate, fenofibrate, ciprofibrate, benzaifibrate, clinofibrate, binifibrate and gemfibrozil), and nicotinic acid derivatives (*e.g.*, nicotinic acid, niceritrol, and acipimox), dextrothyroxine sodium, probucol, pravastatin, atorvastatin, lovastatin, and niacin; antiulcer/antireflux agents include, *e.g.*, famotidine, cimetidine, and ranitidine hydrochloride; antiemetics/antinauseants include, *e.g.*, meclizine hydrochloride, nabilone, prochlorperazine, dimenhydrinate, promethazine hydrochloride, thiethylperazine, and scopolamine; collagen synthesis inhibitors include, *e.g.*, prolyl hydroxylase inhibitors, C-proteinase inhibitors, and halofuginone; vitamins include oil-soluble vitamins (*e.g.*, vitamins A, D, E, and K); amino acids include, *e.g.*, valine, leucine, and isoleucine; proteins include, *e.g.*, cyclophilin, antithymocyte globulin, immunoglobulin, muromonab-CD3, daclizumab, basiliximab, infliximab, etanercept, DNase, alginase, L-asparaginase, superoxide dismutase (SOD), lipase, metallothionine, apolipoprotein E, oxandrolone, creatine, dehydro epiandrosterone, platelet derived growth factor, fibrin, fibrinogen, collagen, interleukins 1 through 18, luteinizing hormone releasing hormone (LHRH), gonadotropin releasing hormone (GnRH), and transforming growth factor- $\beta$  (TGF- $\beta$ ), tumor necrosis factor- $\alpha$  and  $\beta$  (TNF- $\alpha$  and  $\beta$ ), nerve growth factor (NGF), growth hormone releasing factor (GHRF), epidermal growth factor (EGF), fibroblast growth factor homologous factor (FGFHF); hepatocyte growth factor (HGF); insulin growth factor (IGF), invasion inhibiting factor-2 (IIF-2), bone morphogenetic proteins 1-7 (BMP 1-7), somatostatin; thymosin- $\alpha$ -1, and  $\gamma$ -

globulin. Various biologically active forms of these proteins, including recombinant forms, mutants, complements, analogs, derivatives, and fragments are also contemplated. Other useful agents include nucleic acids (*e.g.*, sense or anti-sense nucleic acids encoding any therapeutically useful protein, including any of the proteins described herein).

[045] A description of other categories of useful agents and other individual agents may be found in Martindale, The Extra Pharmacopoeia, 30<sup>th</sup> Ed. (The Pharmaceutical Press, London 1993).

[046] Examples of other agents that may be delivered using the stent of the present invention include chlorhexidine, estradiol cypionate, estradiol valerate, flurbiprofen sodium, ivermectin, nafarelin, beta-glumay, bovine immunoglobulin, bovine superoxide dismutase, HIV-1 immunogen, human anti-TAC antibody, CD34 antibody, recombinant human growth hormone (r-hGH), recombinant human hemoglobin (r-Hb), recombinant human mecasermin (r-IGF-1), lenograstim (G-CSF), recombinant thyroid stimulating hormone (r-TSH), topotecan, aldesleukin, atenolol, epoetin alfa, leuprolide acetate, ceftriaxone, ceftazidime, oxaprozin, breveldin, valacyclovir, urofollitropin, famciclovir, flutamide, enalapril, mefformin, itraconazole, gabapentin, fosinopril, tramadol, lorazepam, follitropin, omeprazole, fluoxetine, lisinopril, tramadol, levofloxacin, zafirlukast, growth hormone, granulocyte stimulating factor, nizatidine, bupropion, perindopril, erbumine, adenosine, alendronate, alprostadil, benazepril, bleomycin sulfate, dexfenfluramine, fentanyl, flecainid, gemcitabine, glatiramer acetate, granisetron, lamivudine, mangafodipir trisodium, mesalamine, metoprolol fumarate, miglitol, moexipril, monteleukast,

octreotide acetate, olopatadine, paricalcitol, somatropin, sumatriptan succinate, tacrine, trovafloxacin, dolasetron, finasteride, isradipine, lansoprazole, terbinafine, pamidronate, didanosine, cisapride, venlafaxine, fluvastatin, losartan, imiglucerase, donepezil, valsartan, fexofenadine, BCP 671, adapalene, doxazosin mesylate, mometasone furoate, ursodiol, enalapril maleate, felodipine, nefazodone hydrochloride, valrubicin, albendazole, conjugated estrogens, medroxyprogesterone acetate, nicardipine hydrochloride, zolpidem tartrate, amlodipine besylate, ethinyl estradiol, rubitemay, amlodipine besylate/benazepril hydrochloride, etodolac, paroxetine hydrochloride, atovaquone, podofilox, betamethasone dipropionate, pramipexole dihydrochloride, Vitamin D<sub>3</sub> and related analogs, quetiapine fumarate, maydesartan, cilexetil, fluconazole, ritonavir, flumazenil, carbamazepine, carbidopa, ganciclovir, saquinavir, amprenavir, sertraline hydrochloride, carvedilol, halobetasolpropionate, sildenafil citrate, chlorthalidone, imiquimod, simvastatin, citalopram, irinotemay hydrochloride, sparfloxacin, efavirenz, cisapride monohydrate, tamsulosin hydrochloride, mofafinil, letrozole, terbinafine hydrochloride, rosiglitazone maleate, diclofenac sodium, lomefloxacin hydrochloride, tirofiban hydrochloride, telmisartan, diazepam, loratadine, toremifene citrate, dinoprostone, mefloquine hydrochloride,trandolapril, tretinoin, nelfinavir mesylate, indinavir, beclomethasone dipropionate, isotretinoin, tamoxifen citrate, nimodipine,latanoprost, travoprost, unoprostone, AL-10682, AL-3138, AGN-191976, PhXA-34, AL-16082, bimatoprost, ethanolamide, dorzolamide, brinzolamide, acetazolamide, methazolamide, L-662583, MK-927, L-693612, L-685393, mannitol, glycerol, isosorbide, physostigmine, echothiophate, acetylcholine, methacholine, pilocarpine, aceclidine, carbachol, demecarium, isofluorophate, memantine, iomerizine, H-7, SR-

43845, enalkiren, Y-39983, GPI-5693, anadamide, L-768242, L-759787, dextranabinol, collagenase ABC, iomefloxacin, iosartan, CS-088, mecobalamin, ISV-900, cardiotrophin-1, S-1033, D-22A, pentigetide, lerdelimumab, DE-085, SR-121463, org-34517, octamer, NNC-26-9100, KSR-592, A-75169, ethacrynate sodium, SDZ-GLC-756, rostaporphin, proxodolol, WIN-552122, OSA-8302, AL-16049, naboctate, L-696986, AL-4333A, vaninolol, PCA-50941, HGP-32, AGN-192836, AGN-191970, WP-934, ACC-9002, AL-4623A, AL-4414A, CK-119, alprenoxime, CBT-101, AGN-191151, H 21644, SL 1111, GPI-5232, eliprodil, tilisolol, lomerizine, riluzole, lamotrigine, dextromethorphan, EAAT2, topiramate, AP5, CPP, selfotel or CGS 19755, CGP 37849, CGP 39551, CGP 40116, NPC 17742, aptiganel/CNS 1102, dextromethorphan and enzyme inhibitor, FR 115427, ketamine, ketobemidone, methadone, dizocilpine or MK 801, PCP, pethidine, RPR-119990, LY-300164 or talampanel, CNQX, DNQX, LY 215490, NNC 079202 or NBQX, NS 257, GYKI 52466, cyclothiazide, IDRA 21, DCG-IV, glycine, AP4, t-ACPD, L-SOP, L-AP3, S-4C3HPG, S-4CPG, MAP-4, RS-M4CPG, N-(3-[5-chloro-1-(4-chlorophenyl)[indan-1-yl]propyl)-N-methylalanine, SR-57746A, T-588, 3,4 diaminopyridine, CPC-304, CPC-317, PD-176078, cephalosporin ceftriaxone, huperzine A, 10-methyl-huperzine A, 10,10 dimethyl huperzine A, huperzine B, nicotine, epibatidine, cytosine, lobeline, anabasine, CNTF, BDNF, rhIGF-1, myotrophin mecaseprin, Somatomedin C, GDNF, liatermin, neurturin, PEDF, FKBO-neuroimmunophilin ligands, AIT-082, leteprinim potassium, neotrofinT, emfilermin, CT-1, NT-3, NT-4/5, EHT 201, EHT 202, genistein, RX-77368, MK-771, JTP-2942, GPI-5000, ZVAD fink, 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt, nordihydroguaiaretic acid, L-655238, Bay-X-1005, ML-3000, zileuton, oxothiazolidine carboxylate,

ARR 17477, SOD, recombinant human CuZn-SOD, glutathione, glutathione peroxidase, catalase, nitric oxide synthase, vitamin E, vitamin C, selenium, acetylcysteine, seleginine, pycnogenol, co-enzyme Q10, beta carotene, PC 01, SC-55858, edaravone, iron (III) porphyrins, chromomycin, daunomycin, olivomycin, WP-631, DHEA, baclofen, tizandidine, dronabinol, diazepam, AVP-923, amitriptylene, fluvoxamine, sertraline, glycopyrrolate, copolamine, trihexyphenidyl, clonidine, propantheline, tropine, docusate sodium, tolterodine, TA-0910, ubiquinone, alpha lipoic acid, NAC, polyphenols, pregnenolone, threonine, methylcobalamin, metaxalone, tizanadine, carisoprodol, cyclobenzaprine, tramadol, potassium, calcium, zinc, magnesium, botulinum neurotoxin, succinylcholine, decamethonium, quinine, tetrahydromaynabinol, d-tubocurarine, atracurium, doxacurium, mivacurium, cistracurium besilate, pancuronium, pipecuronium bromide, rapacuronium bromide, rocuronium, vecuronium bromide, atracurium, suxamethonium, alcuronium, curare, metocurine, gallamine, nitrazepam, nordazepam, vigabatrin, procaine, chloroquine, glutathione, odansetron, memantadine, GPI-1046, eradoline U-69 593, KW 6002, remacemide, dextromethorphan, NS-2214, CD133 antigen, CD34 antigen and reboxetine.

[047] In addition to the above agents, there are a number of viruses, live or inactivate, including recombinant viruses that may, with the stent of the present invention, be used to deliver nucleic acids to the vessel walls of a lumen. Disorders that may be treated using viral delivery are described in U.S. Patent No. 5,833,651. Examples of disorders that may be treated in this manner include, *e.g.*, cell proliferation resulting from stenosis (for example using suicide genes or targeting cell-cycle regulatory genes);

damage associated with myocardial infarction or aneurysms (targeting fibroblast growth factor or transforming growth factor  $\beta$  and protease respectively); atherosclerosis (for example, targeting high density lipoprotein); familial hypercholesterolemia (targeting the low density lipoprotein receptor), hypercoagulable states (targeting tissue-plasminogen activator), refractory diabetes mellitus (for example, targeting insulin) as well as diseases not necessarily associated with the vasculature, including, but not limited to, muscular dystrophy, cystic fibrosis, digestive disorders, maycer, inherited disease, colitis, benign prostatic hypertrophy, transplant rejection or transplant vasculopathy (targeting for example, leukocyte adhesion molecule or cytokines respectively), and the like. Treatment involves either the expression of a gene to provide a therapeutic effect to a cell or the expression of a gene to i) replace a mutated gene in a cell, ii) augment expression of a protein in a cell, or iii) inhibit a gene in a cell.

**[048]** Of the therapeutic categories specified above, one set of preferred categories are those associated with treating vascular conditions that may or are likely to require a stent. Other preferred categories are those associated with the prevention or treatment of restenosis or side effects (*e.g.*, infection) possibly accompanying stent insertion. Preferred therapeutic categories include hematological agents, preferably antiplatelet agents and anticoagulants; anti-infectives, preferably antimicrobials, antibacterials, antiviral agents, and antibiotics; immunobiologic agents, preferably immunosuppressives; proteins, preferably antibodies; cardiovascular agents, preferably anti-lipidemics, and thrombolytics/fibrinolytics; angiogenesis inhibitors; anti-apoptotics; antineoplastics; and collagen synthesis inhibitors.

[049] The above agents may be used in any known pharmaceutically acceptable form. The term “pharmaceutically acceptable” refers to the agents being appropriate for use *in vivo*. For example, pharmaceutically acceptable forms include various metallic ion and organic ion forms. Metallic ions include, but are not limited to, alkali metal ions, alkaline earth metal ions and other physiological acceptable metal ions. Exemplary ions include aluminum, calcium, lithium, magnesium, potassium, sodium and zinc ion forms, where the ions are in their usual valences. Preferred organic ions include protonated tertiary amines and quaternary ammonium cations, including in part, trimethylamine, diethylamine, N,N'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procaine.

[050] Also included as pharmaceutically acceptable forms are various acid forms of the above agents. Exemplary pharmaceutically acceptable acids include, without limitation, hydrochloric acid, hydroiodic acid, hydrobromic acid, phosphoric acid, sulfuric acid, methanesulfonic acid, acetic acid, formic acid, tartaric acid, maleic acid, malic acid, citric acid, isocitric acid, succinic acid, lactic acid, gluconic acid, glucuronic acid, pyruvic acid, oxalacetic acid, fumaric acid, propionic acid, aspartic acid, glutamic acid, and benzoic acid. Further pharmaceutically acceptable forms include various salt forms of the above agents. Illustrative pharmaceutically acceptable salts are prepared from formic, acetic, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, anthranilic, mesylic, stearic, salicylic, p-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic),

methanesulfonic, ethanesulfonic, benzenesulfonic, pantothenic, toluenesulfonic, 2-hydroxyethanesulfonic, sulfanilic, cyclohexylaminosulfonic, algenic,  $\beta$ -hydroxybutyric, galactaric and galacturonic acids.

[051] Other pharmaceutically acceptable salt forms are the base addition salt forms of the agents described above. Illustrative pharmaceutically acceptable base addition salts include metallic ion salts and organic ion salts. Preferred metallic ion salts include appropriate alkali metal (group Ia) salts, alkaline earth metal (group IIa) salts and other known physiological acceptable metal ions. Such salts may be made from the ions of aluminum, calcium, lithium, magnesium, potassium, sodium and zinc. Preferred organic salts may be made from tertiary amines and quaternary ammonium salts, including in part, trimethylamine, diethylamine, N,N'-dibenzylethylenediamine, chlorprocaine, choline, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procaine.

[052] Also, other pharmaceutically acceptable forms of the above agents include the various isomeric forms (*e.g.*, purified structural isomers; purified stereoisomers such as diastereomers and enantiomers; and purified racemates), tautomers, esters, amides and prodrugs of these agents.

[053] These agents may be applied using a known method such as dipping, spraying, impregnation or any other technique described in the above-mentioned patents that have been incorporated by reference. Applying the agents to the stent wall and bridge elements avoids the mechanical disruption that occurs when coated elastic support elements are expanded.

In this manner drug coatings applied to the stent wall and bridge elements may be used with support elements formed of materials that are otherwise unsuitable for coating.

**[054]** Any one or more of the above-discussed agents may be coated onto the stent wall corrugated ring elements **10**, **12**, and **14** and stent bridges **16**, and other parts if desired, of the stent in any conventional manner, such by a spray coating, vapor deposition, simple dip coating or, if a thicker coating of the therapeutic agent is desired, multiple dip coatings of the same or multiple agents. The agents may be applied directly onto the stent wall elements in multiple layers, in grooves formed into an outer surface of these wall and bridge elements using a conventional technique, such as molding, laser etching/cutting or chemical etching/cutting, recesses (inlays) formed in the outer surface of these wall and bridge elements or in openings formed through these wall and bridge elements by any of the above-mentioned techniques.

**[055]** Methods for spray coating a stent are described, *e.g.*, in U.S. Pat. Nos. 5,464,650 and 5,833,651. Alternatively, a thin film of a therapeutic agent may be molded over the stent framework, as described in U.S. Patent No. 4,866,062. Additionally, rapamycin analogs could be used on the wall and bridge elements to provide additional surface area for dry delivery of agents.

**[056]** In general, multiple dipping involves applying several thin layers of the agent, while in liquid form (*e.g.*, a solution, dispersion, or emulsion) of appropriate viscosity, and allowing each liquid layer to dry between

successive applications. Drying may be carried out simply by evaporation in air or promoted by heating, including baking or heat flashing, or even osmotic moisture removal, for example, by using a semipermeable membrane. Otherwise, the formation of a solid, adhering layer may be accomplished through chemical or biological transformations occurring on the stent surface as described, for example in U.S. Patent No. 4,548,736 where fibrin is solidified onto the stent by carrying out the clotting reaction between fibrinogen and thrombin.

[057] Active flow systems are also possible. For example, U.S. Patent No. 6,153,252 describes a method using fluid flow or movement through the passages in a perforated medical device to avoid the formation of blockages or bridges. The fluid flow may be created by using a perforated manifold inserted in the stent to circulate the coating fluid through the passages or by placing the stent on a mandrel or in a small tube that is moved relative to the stent during the coating process.

[058] The polymer embodiments described in this application can optionally include a therapeutic agent matrixed within the polymer used to construct the stent such that the polymer becomes the drug delivery vehicle. Such polymers can be further coated as described above to provide additional control on drug delivery or to provide additional or different therapeutic agents.

[059] Another possibility for incorporation of a therapeutic agent is through the use of an active material that promotes physical or chemical adsorption.

As described in WO 01/68158, an activated form of carbon known as a fullerene may promote the chemical binding of various biological agents (*e.g.*, antibodies) to the surface of the bridges, rails, and other stent wall elements for therapeutic delivery. In the same manner, various stent materials described previously (*e.g.*, polymeric materials) may be chemically modified, such as by the incorporation of a co-monomer, to introduce functional groups that chemically interact or bind to a given therapeutic agent.

**[060]** The stent wall corrugated rings, bridges and other stent wall elements may also be coated with a smooth nanoporous ceramic layer of aluminum oxide available from AlCove GmbH of Germany. This coating is suitable for releasing an agent such as those discussed above while provide the stent with high stability and flexibility. Such a coating may be used in place of a coating of one the discussed polymers.

**[061]** In yet another embodiment, each of the stent wall corrugated rings, bridges other stent wall elements may contain more than one agent that may be released either simultaneously, at completely different times or delivery may overlap in time. The release rates of the individual agents or of all agents may be customized for a particular patient or condition using biocompatible polymers and manufacturing methods described above. This would allow the delivery of drug to be optimized to the normal healing processes with the appropriate drug at the right concentration delivered at the desired point in time.

[062] The agents applied in separate layers may be the same agent, different agents with different time releases or different agents intended to be released simultaneously or in successive order. In either instance, barrier layers may cover the different layers of agents. For example, a first barrier layer could cover the wall element surface, a first drug layer could be applied on top of the barrier layer and a separation layer applied over the first drug layer. A second drug layer could be applied over the separation layer and then a cover layer could be applied over the second drug layer. More than two drug layers may be applied to the wall elements. The cover and separation layers may be chosen to provide predetermined and independent time release of the applied agents that they cover.

[063] The different agents discussed above may be applied on different wall or bridge elements or different portions of the same wall or bridge element. As a result, numerous combinations of agents may be applied to the bridge or wall elements. For example, each complete wall or bridge element or coated portion of a wall or bridge element may include one or more layers of the same or different agents. Hence, one wall or bridge element could be coated with different agent combinations at different locations along its length.

[064] In an alternative embodiment, both the stent wall elements and the bridges of a single stent carry one or more of the above-discussed agents. The agent(s) carried by the bridges may be the same as, or different from, the agents carried the stent wall elements. Additionally, the agent(s) carried by one or more of the stent wall elements may be carried by some of the

bridges, while the remaining stent wall elements may carry the same or different agents.

**[065]** It is contemplated that the various elements of the present invention may be combined with each other to provide the desired flexibility. For example, support element designs may be altered and various support element designs combined into a single stent with/without any one of the above-discussed wall elements. Similarly, the number, shape, composition and spacing of the stent wall elements may be altered to provide the stent with different properties. Additionally, the device may have varying numbers and placement of the bridge elements. The properties of any individual stent would be a function of the design, composition and spacing of the stent wall elements and bridges.

**[066]** Finally, while there have been shown and described and pointed out fundamental novel features of the present invention as applied to preferred embodiments thereof, it will be understood that various omissions and substitutions and changes in the form and details of the devices illustrated, and in their operation, and in the method illustrated and described, may be made by those skilled in the art without departing from the spirit of the invention as broadly disclosed herein. All of the above-discussed patents and publications are hereby expressly incorporated by reference as if they were written directly herein.

## CLAIMS

## WE CLAIM:

1. A variable wall stent for deployment in a blood vessel or other anatomic lumen, comprising:
  - an elongated structure with a radial axis and a longitudinal axis;
  - stent wall corrugated rings comprised of at least thin-walled corrugated ring elements and thick-walled corrugated ring elements;
  - one or more thin-walled stent bridges joining said stent wall corrugated rings; and
  - a stent lumen defined by and at least partially enclosed by said stent wall corrugated rings and thin-walled stent bridges.
2. The variable wall stent of claim 1 wherein said thin-walled corrugated ring elements allow for lowered resistance to distension of the stent along said radial axis after it has been deployed in said blood vessel or other anatomic lumen.
3. The variable wall stent of claim 2 wherein said thick-walled corrugated ring elements maintain radial strength and radio-opacity of the stent.
4. The variable wall stent of claim 3 wherein said thin-walled stent bridges allow increased flexibility of said stent along said longitudinal axis.

5. The variable wall stent of claim 1 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are discrete structures joined together.
6. The variable wall stent of claim 5 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.
7. The variable wall stent of claim 1 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are continuous parts of the same structure.
8. The variable wall stent of claim 7 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.
9. The variable wall stent of claim 1 wherein the thickness of said thin-walled corrugated ring elements and said thin walled stent bridges is between 10% and 90% of the thickness of said thick-walled corrugated ring elements.
10. The variable wall stent of claim 1 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are comprised of biocompatible materials selected from among the group of biocompatible materials consisting of metals, metal alloys

bioabsorbable polymers, nonbioabsorbable polymers and combinations thereof.

11. The variable wall stent of claim 1 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with one or more therapeutic agents.
12. The variable wall stent of claim 11 wherein said therapeutic agents are selected from among the group of agents consisting of therapeutic drugs, antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents, medicaments, proteins, vitamins, mineral supplements.
13. The variable wall stent of claim 11 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with said therapeutic agents by a method selected from the group of coating methods consisting of spraying, vapor deposition, dipping, impregnation and combinations thereof.
14. The variable wall stent of claim 11 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.

15. The variable wall stent of claim 11 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.
16. The variable wall stent of claim 11 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in grooves formed on their outer surfaces.
17. The variable wall stent of claim 11 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in openings formed therethrough.
18. The variable wall stent of claim 10 wherein said bioabsorbable polymer or non-bioabsorbable polymer further comprises a therapeutic agent.
19. A variable wall stent for deployment in a blood vessel or other anatomic lumen having an increased surface area for therapeutic coatings, comprising:
  - an elongated structure with a radial axis and a longitudinal axis;
  - stent wall corrugated rings comprised of alternately placed thin-walled corrugated ring elements and thick-walled corrugated ring elements;

thin-walled stent bridges joining said stent wall corrugated rings; and

a stent lumen defined by and at least partially enclosed by said stent wall corrugated rings and thin-walled stent bridges;

whereby a pattern resulting from the alternating placement of said thin-walled corrugated ring elements and said thick-walled corrugated ring elements creates a scalloping effect on the diameter of said stent wall corrugated rings.

20. The variable wall stent of claim 19 wherein said scalloping effect is created on the inside diameter of said stent wall corrugated rings.
21. The variable wall stent of claim 19 wherein said scalloping effect is created on the outside diameter of said stent wall corrugated rings.
22. The variable wall stent of claim 19 wherein said thin-walled corrugated ring elements allow for lowered resistance to distension of the stent along said radial axis after it has been deployed in said blood vessel or other anatomic lumen.
23. The variable wall stent of claim 22 wherein said thick-walled corrugated ring elements maintain radial strength and radio-opacity of the stent.

24. The variable wall stent of claim 23 wherein said thin-walled stent bridges allow increased flexibility of said stent along said longitudinal axis.
25. The variable wall stent of claim 19 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are discrete structures joined together.
26. The variable wall stent of claim 25 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.
27. The variable wall stent of claim 19 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are continuous parts of the same structure.
28. The variable wall stent of claim 27 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.
29. The variable wall stent of claim 19 wherein the thickness of said thick-walled corrugated ring elements is at least .0001mm greater than the thickness of said thin-walled corrugated ring elements.
30. The variable wall stent of claim 19 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are comprised of

biocompatible materials selected from among the group of biocompatible materials consisting of metals, metal alloys bioabsorbable polymers, nonbioabsorbable polymers and combinations thereof.

31. The variable wall stent of claim 19 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with one or more therapeutic agents.
32. The variable wall stent of claim 31 wherein said therapeutic agents are selected from among the group of agents consisting of therapeutic drugs, antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents, medicaments, proteins, vitamins, mineral supplements.
33. The variable wall stent of claim 31 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with said therapeutic agents by a method selected from the group of coating methods consisting of spraying, vapor deposition, dipping, impregnation and combinations thereof.
34. The variable wall stent of claim 31 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.

35. The variable wall stent of claim 31 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.
36. The variable wall stent of claim 31 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in grooves formed on their outer surfaces.
37. The variable wall stent of claim 31 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in openings formed therethrough.
38. The variable wall stent of claim 30 wherein said bioabsorbable polymer or non-bioabsorbable polymer further comprises a therapeutic agent.
39. A variable wall stent for deployment in a blood vessel or other anatomic lumen, comprising:
  - an elongated structure with a radial axis and a longitudinal axis;
  - stent wall corrugated rings comprised of at least thin-walled corrugated ring elements and thick-walled corrugated ring elements defining at least one stent segment;

at least one thin-walled stent bridges joining each of said stent segments; and

a stent lumen defined by and at least partially enclosed by said stent wall corrugated rings and thin-walled stent bridges.

40. The variable wall stent of claim 39 wherein said thin-walled corrugated ring elements allow for lowered resistance to distension of the stent along said radial axis after it has been deployed in said blood vessel or other anatomic lumen.
41. The variable wall stent of claim 40 wherein said thick-walled corrugated ring elements maintain radial strength and radio-opacity of the stent.
42. The variable wall stent of claim 41 wherein said thin-walled stent bridges allow increased flexibility of said stent along said longitudinal axis.
43. The variable wall stent of claim 39 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are discrete structures joined together.
44. The variable wall stent of claim 43 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.

45. The variable wall stent of claim 39 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are continuous parts of the same structure.
46. The variable wall stent of claim 45 wherein said thin-walled corrugated ring elements and said thick-walled corrugated ring elements are joined by transitional wall elements.
47. The variable wall stent of claim 39 wherein the thickness of said thick-walled corrugated ring elements is at least .0001mm greater than the thickness of said thin-walled corrugated ring elements.
48. The variable wall stent of claim 39 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are comprised of biocompatible materials selected from among the group of biocompatible materials consisting of metals, metal alloys bioabsorbable polymers, nonbioabsorbable polymers and combinations thereof.
49. The variable wall stent of claim 39 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with one or more therapeutic agents.
50. The variable wall stent of claim 49 wherein said therapeutic agents are selected from among the group of agents consisting of

therapeutic drugs, antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents, medicaments, proteins, vitamins, mineral supplements.

51. The variable wall stent of claim 49 wherein said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges are coated with said therapeutic agents by a method selected from the group of coating methods consisting of spraying, vapor deposition, dipping, impregnation and combinations thereof.
52. The variable wall stent of claim 49 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.
53. The variable wall stent of claim 49 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in multiple layers.
54. The variable wall stent of claim 49 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in grooves formed on their outer surfaces.

55. The variable wall stent of claim 49 wherein said therapeutic agents are applied to said thick-walled corrugated ring elements, said thin-walled corrugated ring elements and said thin-walled stent bridges in openings formed therethrough.
56. The variable wall stent of claim 48 wherein said bioabsorbable polymer or non-bioabsorbable polymer further comprises a therapeutic agent.

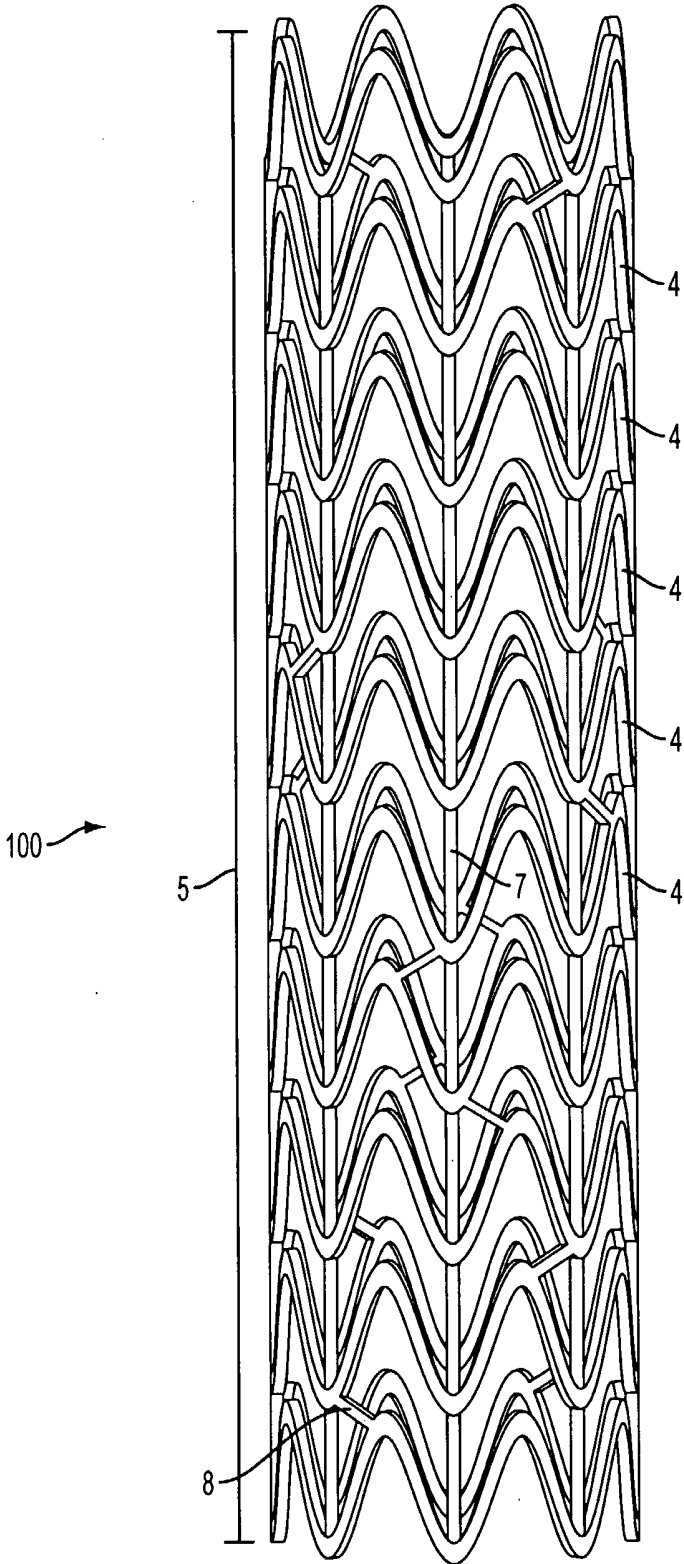


FIG. 1

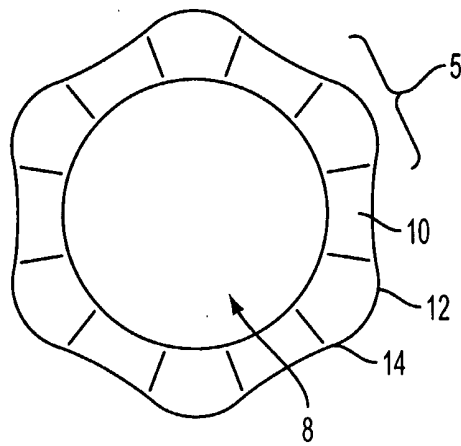


FIG. 2