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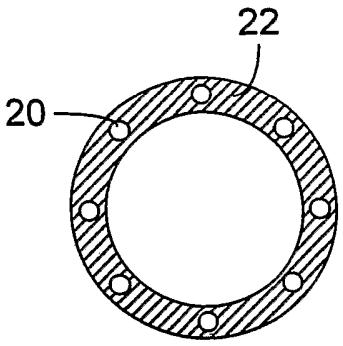
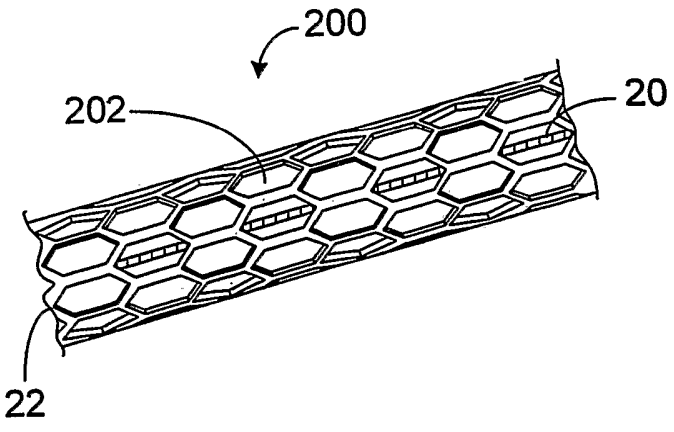
(54) Title: IMPLANTABLE ENDOPROSTHESIS AND METHODS OF DELIVERING





(57) Abstract: A tubular endoprosthesis including a polymeric material is disclosed. The endoprosthesis has a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal. The endoprosthesis can be further expanded to a second expanded position within the cavity or lumen. The endoprosthesis may have apertures that enlarge upon expansion and embedded longitudinal struts that prevent shortening of the prosthesis.

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IMPLANTABLE ENDOPROSTHESIS AND METHODS OF DELIVERING

TECHNICAL FIELD

This invention relates to implantable medical devices, and methods of delivering the same.

BACKGROUND

The body includes various passageways such as arteries, other blood vessels, and other body lumens. These passageways sometimes become occluded or weakened. For example, the passageways can be occluded by a tumor, restricted by plaque, or weakened by an aneurysm. When this occurs, the passageway can be reopened or reinforced, or even replaced, with a medical endoprosthesis. An endoprosthesis is typically a tubular member that is placed in a lumen in the body. Examples of endoprosthesis include stents and covered stents, sometimes called "stent-grafts".

An endoprosthesis can be delivered inside the body by a catheter that supports the endoprosthesis in a compacted or reduced-size form as the endoprosthesis is transported to a desired site. Upon reaching the site, the endoprosthesis is expanded, for example, so that it can contact the walls of the lumen.

In some cases, passageways can become re-occluded, a phenomenon often called "restenosis." After restenosis, often another endoprosthesis is deployed within the first endoprosthesis to re-open the passageway.

SUMMARY

This invention relates to implantable medical devices, and methods of delivering the same.

Generally, an endoprosthesis is described that can be deployed into a cavity or lumen in a collapsed position, and then reverted to a first expanded position larger than the collapsed position to support the cavity or lumen. At a later time, e.g., after restenosis of the cavity or lumen, the endoprosthesis can be further expanded.

In one aspect, the invention features a tubular endoprosthesis, e.g., a stent, that includes a polymeric material. The endoprosthesis has at least one longitudinal element embedded in a wall of the endoprosthesis. The endoprosthesis has a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen, e.g., a vascular or a non-vascular lumen, in a mammal. The endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen by heating to a second temperature higher than the first temperature.

In some embodiments, the endoprosthesis is substantially circular in transverse cross-section.

In some embodiments, the longitudinal element includes a metal, e.g., stainless steel. Longitudinal elements can be, e.g., monofilaments and/or multifilament. In embodiments in which the longitudinal elements are monofilaments, the monofilaments can have a circular transverse cross-section, e.g., having a diameter of from about 0.0005 inch to about 0.010 inch. The endoprosthesis can include, e.g., from about two to about twelve longitudinal elements. In some implementations, the longitudinal element extends substantially along an entire longitudinal length of the endoprosthesis.

In some embodiments, the wall includes an aperture or many apertures. The aperture or apertures can be, e.g., circular in transverse cross-section. In some implementations, the longitudinal elements are disposed longitudinally across apertures.

In some embodiments, the tubular endoprosthesis includes a coating that includes a therapeutic agent. In some embodiments, the coating is on an outer surface of the endoprosthesis. In specific embodiments, the coating is an outer surface of the endoprosthesis, and the therapeutic agent also is dispersed generally throughout the polymeric material. The therapeutic agent can be chosen, e.g., to prevent restenosis. For example, the therapeutic agent can be paclitaxel. The polymeric material can also include a radio-opaque agent and/or a thermal conductor, e.g., boron nitride.

In some embodiments, the polymeric material includes a natural polymer, e.g., zein, casein, gelatin, gluten, serum albumin, collagen, polysaccharides, polyhyaluronic acid, poly(3-hydroxyalkanoate)s, alginate, dextran, cellulose, collagen or mixtures of

these polymers. In some implementations, the polymeric material includes a synthetic polymer, e.g., chemical derivatives of collagen, chemical derivatives of cellulose, polyphosphazenes, poly(vinyl alcohols), polyamides, polyacrylates, polyalkylenes, polyacrylamides, polyalkylene glycols, polyalkylene oxides, polyalkylene terephthalates, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polyesters, degradable polymers, polyester amides, polyanhydrides, polycarbonates, polyorthoesters, polylactides, polyglycolides, polysiloxanes, polyurethanes, cellulose derivatives or mixtures of these polymers. In some embodiments, polymeric material includes mixtures of natural and synthetic polymers. In some embodiments, the polymeric material is cross-linked.

In specific embodiments, the tubular endoprosthesis has a collapsed transverse dimension and a collapsed longitudinal length, both measured at the collapsed position. The first expanded position has a first expanded transverse dimension that is at least fifty percent larger than the collapsed transverse dimension and a first expanded longitudinal length that is at least fifty percent of the collapsed longitudinal length.

In other specific embodiments, the endoprosthesis has a first expanded transverse dimension and a first expanded longitudinal length, both measured at the first expanded position. The second expanded position has a second expanded transverse dimension that is at least twenty-five percent larger than the first expanded transverse dimension and a second expanded longitudinal length that is at least fifty percent of the first expanded longitudinal length.

In another aspect, the invention features a method of treating a cavity or lumen in a mammal. The method includes inserting, into the cavity or lumen in the mammal, a tubular endoprosthesis that includes a polymeric material. The endoprosthesis has at least one longitudinal element embedded in a wall of the endoprosthesis and has a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal. The endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen in the mammal by heating to a second temperature higher than the first

temperature. The inserted endoprosthesis is heated to the first temperature to revert the collapsed position to the first expanded position.

In some embodiments, the method further includes heating the inserted endoprosthesis to the second temperature to further expand the endoprosthesis to the second expanded position. The heating can be performed, e.g., with a liquid. For example, heating can be performed by a delivery tube, e.g., a balloon catheter, that includes a warmed liquid.

In some embodiments, the first temperature is, e.g., from about 37 °C to about 55 °C and the second temperature is, e.g., from about 40 °C to about 75 °C.

In some embodiments, the lumen is a vascular lumen.

In another aspect, the invention features a method of treating a cavity or lumen in a mammal. The method include inserting, into the cavity or lumen in the mammal, a tubular endoprosthesis that includes a polymeric material. The endoprosthesis has a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal. The endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen in the mammal by heating to a second temperature higher than the first temperature. The inserted endoprosthesis is heated to the first temperature to revert the collapsed position to the first expanded position, and then the inserted endoprosthesis is heated to the second temperature to further expand the endoprosthesis to the second expanded position.

In another aspect, the invention features an endoprosthesis that includes a polymeric material having at least one longitudinal element embedded in a wall of the endoprosthesis.

In some embodiments, the endoprosthesis includes from about two to twelve longitudinal elements.

Embodiments may have one or more of the following advantages. The endoprotheses described herein can be deployed into a cavity or lumen in a collapsed position, and then reverted to a first expanded position larger than the collapsed position to support the cavity or lumen. At a later time, e.g., after restenosis of the cavity or

lumen, the endoprosthesis can be further expanded, often without the need for secondary angioplasty. In some implementations, the endoprosthesis can be further expanded from outside the body. Many of the embodiments also show a reduced foreshortening and improved radio-opacity which can, e.g., improve placement of the endoprosthesis within a cavity or lumen.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, and advantages of the invention will be apparent from the description and drawings and from the claims.

DESCRIPTION OF DRAWINGS

Fig. 1 is a perspective view of an endoprosthesis in a collapsed position.

Fig. 1A is a cross-sectional view of the endoprosthesis shown in Fig. 1, taken along 1A-1A.

Fig. 2 is a perspective view of the endoprosthesis shown in Fig. 1 in a first expanded position.

Fig. 3 is a perspective view of the endoprosthesis shown in Fig. 1 in a second expanded position.

Figs. 4 and 5 are cross-sectional views of an endoprosthesis within an occluded lumen in a first and second expanded position, respectively.

Figs. 6-8 are mixed views of an endoprosthesis delivery system, the views being side views away from an occlusion, and cross-sectional proximate the occlusion.

Figs. 9A and 9B are perspective views of apertured endoprotheses.

Fig. 10A is a perspective view of an alternative endoprosthesis with two end portions in expanded positions.

Fig. 10 B is a cross-sectional view of an alternative endoprosthesis having a three-layer wall.

Fig. 11 is a perspective view of an alternative endoprosthesis having different wall thicknesses along its longitudinal length.

Figs. 11A and 11B are cross-sectional views of the endoprosthesis shown in Fig. 11, taken along 11A-11A or 11B-11B, respectively.

Fig. 12 is a perspective view of an alternative endoprosthesis having longitudinal ribs.

Fig. 12A is a cross-sectional view of the endoprosthesis shown in Fig. 12, taken along 12A-12A.

DETAILED DESCRIPTION

Generally, an endoprosthesis is described herein that can be deployed into a cavity or lumen of a mammal in a collapsed position at onset of stenosis, and then reverted to a first expanded position larger than the collapsed position to support an occluded cavity or lumen. After onset of restenosis, the endoprosthesis can be further expanded to a second expanded position larger than the first expanded position within the cavity or lumen to further support the cavity or lumen.

Referring to Figs. 1-5, an elongated, circular transverse cross-section tubular endoprosthesis 10, e.g., a stent, includes a polymeric material and has eight longitudinal elements 20 embedded in a wall 22. Endoprosthesis 10 has a collapsed position 30 that can be reverted to a first expanded position 32 larger than the collapsed position 30 by heating to a first temperature subsequent to insertion of endoprosthesis 10 into a cavity 42 or lumen 42′ in a mammal, e.g., a human. Endoprosthesis 10 can be further expanded to a second expanded position 36 larger than the first expanded position 32 within the cavity 42 or lumen 42′ by heating to a second temperature higher than the first temperature.

Longitudinal elements 20 can reduce endoprosthesis foreshortening during expansion from collapsed position 30 to first expanded position 32 or second expanded position 36. In addition, longitudinal elements 20 can serve as markers to aid in the delivery of endoprosthesis 10 when the elements include a radio-opaque material.

Referring now to Figs. 6-8, an implantable medical endoprosthesis delivery system 100 includes an inner member 120 and an outer member 140 surrounding inner member 120. Endoprosthesis 10 is positioned between inner member 120 and outer member 140. The delivery system 100 includes a distal end 160 dimensioned for insertion into a body cavity 42 or lumen 42′ (e.g., an artery of a human) and a proximal end 180 that resides outside the body of a subject, and that contains at least one port 181 and lumens for manipulation by a physician. A guide wire 200 with a blunted end 220 is

inserted into a body cavity 42 or lumen 42′ by, for example, making an incision in the femoral artery, and directing guide wire 200 to a constricted site 43 of cavity 42 or lumen 42′ (e.g., an artery constricted with plaque) using, for example, fluoroscopy as a position aid. After guide wire 200 has reached constricted site 43 of body cavity 42 or lumen 42′, inner member 120, endoprosthesis 10 in collapsed position 30, and outer member 140 are placed over the proximal end of guide wire 200. Inner member 120, endoprosthesis 10 and outer member 140 are moved distally over guide wire 200 and positioned within cavity 42 or lumen 42′ so that endoprosthesis 10 is adjacent constricted site 43 of cavity 42 or lumen 42′. When ready to deploy, outer member 140 is moved proximally, exposing endoprosthesis 10.

Endoprosthesis 10 having collapsed position 30 is then reverted to a first expanded position 32 larger than the collapsed position 30 by heating to a first temperature subsequent to insertion of the endoprosthesis 10 into the cavity 42 or lumen 42′. Outer member 140, inner member 120 and guide wire 200 are removed from cavity 42 or lumen 42′, leaving endoprosthesis 10 in first expanded position 32 engaged with constricted site 43 (Figs. 4 and 8). After restenosis of cavity 42 or lumen 42′, endoprosthesis 10 can be further expanded to a second expanded position 36 larger than the first expanded position 32 within the cavity 42 or lumen 42′ by heating to a second temperature higher than the first temperature. Further expansion to the second expanded position 36 is shown in Fig. 5. Other suitable delivery systems, methods of making delivery systems and components thereof are known. For example, those systems, methods and components described by Thompson, U.S. Patent No. 6,623,491, Lau, U.S. Patent No. 6,620,193, Svensson, U.S. Patent No. 6,620,191, Euteneuer, U.S. Patent No. 6,610,069, Fiedler, U.S. Patent No. 6,605,109, Markling, U.S. Patent No. 4,321,226 and Sahatjian, WO 2004032799, the contents of each of which is hereby incorporated by reference herein in its entirety.

In some implementations, heating to the first or second temperature is performed by a liquid in a tube, e.g., a balloon catheter. Heating can also be performed with radiation, e.g., infrared radiation, or radio-frequency radiation. In addition, heating can be performed using magnetic induction. In some embodiments, the first temperature is,

e.g., from about 37 °C to about 55 °C, and the second temperature is, e.g., 40 °C to about 75 °C.

In specific implementations, heating to the second temperature is performed from outside the body of the mammal, e.g., using magnetic induction.

Longitudinal element 22 can be made of, e.g., a metal (e.g., stainless steel), a plastic (e.g., a polyamide), or a composite material. When radio-opacity is desirable, longitudinal element 22 can be radio-opaque. Longitudinal element 22 can be, e.g., in the form of a monofilament, e.g., a circular transverse cross-section monofilament that has a diameter of from about 0.0005 inch to about 0.010 inch, e.g., from about 0.001 inch to about 0.008 inch, or from about 0.002 inch to about 0.005 inch. Longitudinal element 22 can be, e.g., in the form of a multifilament, e.g., a melt-spun multifilament, having, e.g., from about 3 threads to about 250 threads, e.g., from about 5 threads to about 144 threads. The threads making up the multifilament can include a single type of material, e.g., nylon, or can include a variety of different materials, e.g., threads of nylon and stainless steel, or threads of nylon and polyester.

In some implementations, tubular endoprosthesis 10 includes from about 1 to about 50 longitudinal elements 22, e.g., from about 4 to about 30 longitudinal elements, or from about six to about 24 longitudinal elements.

In some implementations, longitudinal element(s) 22 extend(s) substantially along an entire longitudinal length of endoprosthesis 10.

Materials, e.g., polymeric materials, that can be used to make endoprosthesis 10 having a collapsed position that can be reverted to a first expanded position, and then expanded further to a second expanded position are known. Suitable polymeric materials, e.g., homopolymers, block copolymers, and blends thereof, have been described by Langer, U.S. Patent Nos. 6,388,043 and 6,720,402, the contents of each of which is hereby incorporated by reference herein in its entirety.

In some embodiments, the polymeric material used to make endoprosthesis 10 can include a hard segment (H) and two distinct soft segments (S_1 and S_2).

In other embodiments, a polymer blend of a first multiblock copolymer and a second multiblock copolymer is utilized to make endoprosthesis 10 . The first multiblock copolymer includes a hard segment (H_1) with a relatively high transition temperature

(T_{trans}), e.g., glass transition temperature or melting temperature, and a soft segment (S'_1) with a relatively low T_{trans}. The second multiblock copolymer includes a different hard segment (H_2) with a relatively low T_{trans} and the same soft segment (S'_1) as in the first multiblock copolymer. Since the soft segments (S'_1) in both the first and second multiblock copolymers are identical, the polymers are miscible in each other. The resulting blend has three transition temperatures, one for the hard segment (H_1) of the a first multiblock copolymer, one for hard segment (H_2) of the second multiblock copolymer, and one for the soft segment (S'_1).

In a specific embodiment, endoprosthesis 10 can be fashioned from a polymer composition having a hard segment (H'), a first soft segment (S''_1), and a second soft segment (S''_2). The first soft segment (S''_1) has a T_{trans} at least 10 °C lower than T_{trans} of the hard segment (H'), and at least 10 °C above T_{trans} of the second soft segment (S''_2). The composition is shaped, e.g., extruded or molded, into the form of the second expanded position 36 (Fig. 3) at a temperature above T_{trans} of the hard segment (H'). Cooling the endoprosthesis to a temperature below that of T_{trans} of the first soft segment (S''_1), but above that of the second soft segment (S''_2), enables shaping, e.g., by compression, into the form of the first expanded position 32 (Fig. 2). Cooling below T_{trans} of the second soft segment (S''_2) enables shaping the endoprosthesis into the form of collapsed position 30 (Fig. 1). Now, heating the endoprosthesis above T_{trans} of the second soft segment (S''_2) reverts the collapsed position 30 (Fig. 1) to the first expanded position 32 (Fig 2). Heating the endoprosthesis in the first expanded position 32 above T_{trans} of the first soft segment (S''_1) expands the endoprosthesis from the first expanded position 32 to the second expanded position 36 (Fig. 3). Finally, heating above T_{trans} of the hard segment (H') causes the endoprosthesis to lose all shapes in memory.

Suitable polymers can have an elastic modulus of about 60,000 or 70,000 psi or more at 25°C (ASTM D638M), e.g., from about 100,000 to about 250,000 or more, e.g., from about 250,000 to about 500,000 or more, e.g., from about 500,000 to about 1,000,000 or more.

The polymers can be thermoplastic, thermoset, crystalline or amorphous. The polymers or portions of the polymers, e.g., a polymer segment or block, can be degradable, natural, or synthetic.

Natural polymers or polymer portions include, for example, zein, casein, gelatin, gluten, serum albumin, collagen, polysaccharides, polyhyaluronic acid, poly(3-hydroxyalkanoate)s, alginate, dextran, cellulose and collagen. Synthetic polymers or polymer portions include, for example, chemical derivatives of collagen, chemical derivatives of cellulose, polyphosphazenes, poly(vinyl alcohols), polyamides, polyacrylates, polyalkylenes, polyacrylamides, polyalkylene glycols, polyalkylene terephthalates, polyvinyl ethers, polyvinyl esters and polyvinyl halides, polyvinylpyrrolidone, polyesters. Degradable polymers or polymer portions include, for example, polyester amides, polyanhydrides, polycarbonates, polyorthoesters, polylactides, polyglycolides, polysiloxanes, polyurethanes and cellulose derivatives.

Generally, any of the above polymers can be cross-linked during their polymerization, or after their polymerization in a secondary step. The polymers can be cross-linked by application of radiation such as e-beam, UV, gamma, x-ray radiation or by heat-activated chemical crosslinking techniques, utilizing azo compounds or peroxides, e.g., organic peroxides, e.g., benzoyl peroxide. Radiation techniques provide the advantage that the polymer typically does not have to be substantially heated to achieve crosslinking. For e-beam radiation, an exposure of about 200-300, e.g. 250 kilograys, typically provides sufficient crosslinking.

Tubular endoprosthesis 10 can include a coating, e.g., a polymeric coating applied to an exterior surface of endoprosthesis 10, that includes a therapeutic agent. In some embodiments, the polymeric material from which endoprosthesis 10 is made includes a therapeutic agent dispersed therein. The therapeutic agent can, for example, prevent restenosis. In a specific embodiment, the medicament is paclitaxel.

In general, a therapeutic agent can be a genetic therapeutic agent, a non-genetic therapeutic agent, or cells. Therapeutic agents can be used singularly, or in combination. Therapeutic agents can be, for example, nonionic, or they may be anionic and/or cationic in nature.

Exemplary non-genetic therapeutic agents include: (a) anti-thrombotic agents such as heparin, heparin derivatives, urokinase, and PPack (dextrophenylalanine proline arginine chloromethylketone); (b) anti-inflammatory agents such as dexamethasone, prednisolone, corticosterone, budesonide, estrogen, sulfasalazine and mesalamine; (c) anti-neoplastic/antiproliferative/anti-miotic agents such as paclitaxel, 5-fluorouracil, cisplatin, vinblastine, vincristine, epothilones, endostatin, angiostatin, angiopeptin, monoclonal antibodies capable of blocking smooth muscle cell proliferation, and thymidine kinase inhibitors; (d) anesthetic agents such as lidocaine, bupivacaine and ropivacaine; (e) anti-coagulants such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, hirudin, antithrombin compounds, platelet receptor antagonists, anti-thrombin antibodies, anti-platelet receptor antibodies, aspirin, prostaglandin inhibitors, platelet inhibitors and tick antiplatelet peptides; (f) vascular cell growth promoters such as growth factors, transcriptional activators, and translational promotors; (g) vascular cell growth inhibitors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; (h) protein kinase and tyrosine kinase inhibitors (e.g., tyrphostins, genistein, quinoxalines); (i) prostacyclin analogs; (j) cholesterol-lowering agents; (k) angiopoietins; (l) antimicrobial agents such as triclosan, cephalosporins, aminoglycosides and nitrofurantoin; (m) cytotoxic agents, cytostatic agents and cell proliferation affectors; (n) vasodilating agents; (o) agents that interfere with endogenous vasoactive mechanisms; (p) inhibitors of leukocyte recruitment, such as monoclonal antibodies; (q) cytokines, and (r) hormones.

Exemplary genetic therapeutic agents include anti-sense DNA and RNA as well as DNA coding for: (a) anti-sense RNA, (b) tRNA or rRNA to replace defective or deficient endogenous molecules, (c) angiogenic factors including growth factors such as acidic and basic fibroblast growth factors, vascular endothelial growth factor, epidermal growth factor, transforming growth factor α and β, platelet-derived endothelial growth factor, platelet-derived growth factor, tumor necrosis factor α, hepatocyte growth factor and insulin-like growth factor, (d) cell cycle inhibitors including CD inhibitors, and (e)

thymidine kinase ("TK") and other agents useful for interfering with cell proliferation. Also of interest is DNA encoding for the family of bone morphogenic proteins ("BMP's"), including BMP-2, BMP-3, BMP-4, BMP-5, BMP-6 (Vgr-1), BMP-7 (OP-1), BMP-8, BMP-9, BMP-10, BMP-11, BMP-12, BMP-13, BMP-14, BMP-15, and BMP-16. Currently preferred BMP's are any of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6 and BMP-7. These dimeric proteins can be provided as homodimers, heterodimers, or combinations thereof, alone or together with other molecules. Alternatively, or in addition, molecules capable of inducing an upstream or downstream effect of a BMP can be provided. Such molecules include any of the "hedgehog" proteins, or the DNA's encoding them.

Vectors for delivery of genetic therapeutic agents include viral vectors such as adenoviruses, gutted adenoviruses, adeno-associated virus, retroviruses, alpha virus (Semliki Forest, Sindbis, etc.), lentiviruses, herpes simplex virus, replication competent viruses (e.g., ONYX-015) and hybrid vectors; and non-viral vectors such as artificial chromosomes and mini-chromosomes, plasmid DNA vectors (e.g., pCOR), cationic polymers (e.g., polyethyleneimine, polyethyleneimine (PEI)), graft copolymers (e.g., polyether-PEI and polyethylene oxide-PEI), neutral polymers PVP, SP1017 (SUPRATEK), lipids such as cationic lipids, liposomes, lipoplexes, nanoparticles, or microparticles, with and without targeting sequences such as the protein transduction domain (PTD).

Cells for use include cells of human origin (autologous or allogeneic), including whole bone marrow, bone marrow derived mono-nuclear cells, progenitor cells (e.g., endothelial progenitor cells), stem cells (e.g., mesenchymal, hematopoietic, neuronal), pluripotent stem cells, fibroblasts, myoblasts, satellite cells, pericytes, cardiomyocytes, skeletal myocytes or macrophage, or from an animal, bacterial or fungal source (xenogeneic), which can be genetically engineered, if desired, to deliver proteins of interest.

In addition to therapeutic agents, any of the polymers mentioned may be filled with a non-therapeutic agent, for example, nanoparticles of clay and silica to, for example, increase the modulus of the plastic. Dispersing agents and/or compatibilizing agents may be used, for example, to improve the blending of polymers and the blending

of polymers with fillers. Dispersing agents and/or compatibilizing agents include, for example, ACRAWAX® (ethylene bis-stearamide), polyurethanes and ELVALOY® (acrylic-functionalized polyethylene).

In specific embodiments, the filler is a radio-opaque agent, e.g., bismuth carbonate or barium sulfate. In other specific embodiments, the polymeric material includes a thermal conductor, e.g., a boron nitride.

Endoprosthesis 10 can be bio-absorbable or non-bioabsorbable, and can be used in, e.g., a vascular or a non-vascular lumen or cavity. Examples of non-vascular lumens include the esophagus, the prostate, a ureteral lumen or a lumen in the biliary system.

Referring back now to Figs. 1-3, endoprosthesis 10 can be of any desired size. Depending on the application, endoprosthesis 10 in collapsed position (Fig. 1) can, e.g., have a length L_1 from about 3 mm and about 75 mm, an outer diameter OD_1 from about 1 mm to about 20 mm, and a wall thickness W_1 of from about 1 mm to about 5 mm. Depending on the application, endoprosthesis 10 in first expanded position 32 can, e.g., have a length L_2 of from about $0.6L_1$ to about $0.95L_1$, an outer diameter OD_2 from about $1.2OD_1$ to about $3OD_1$, and a wall thickness W_2 from about $0.5W_1$ to about $0.9W_1$. After further expansion, endoprosthesis 10 in second expanded position 36 can, e.g., have a have a length L_3 of from about $0.6L_2$ to about $0.95L_2$, an outer diameter OD_3 from about $1.2OD_2$ to about $3OD_2$, and a wall thickness W_3 from about $0.5W_2$ to about $0.9W_2$.

In specific embodiments, a coronary endoprosthesis can, e.g., have a first expanded diameter of from about 2 mm to about 6 mm, a peripheral endoprosthesis can, e.g., have a first expanded diameter of from about 5 mm to about 24 mm and a gastrointestinal and/or urological endoprosthesis can, e.g., have a first expanded diameter of from about 6 mm to about 30 mm. In other specific embodiments, a neurological endoprosthesis can, e.g., have a first expanded diameter of from about 1 mm to about 12 mm, an abdominal aortic aneurysm (AAA) endoprosthesis or a thoracic aortic aneurysm (TAA) endoprosthesis can, e.g., have a first expanded diameter of from about 20 mm to about 46 mm, and a renal endoprosthesis can, e.g., have a first expanded diameter of from about 8 mm to about 12 mm.

When it is desirable, endoprosthesis 10 can be configured for reduced foreshortening. For example, endoprosthesis 10 in collapsed position 30 can have a

collapsed transverse dimension OD_1 and a collapsed longitudinal length L_1, such that after heating above the first temperature and expansion to the first expanded position 32, that is at least about fifty percent larger than the collapsed transverse dimension, a first expanded longitudinal length L_2, decreases by less than about fifty percent, measured relative to the collapsed longitudinal length. In addition, after heating above the second temperature and expansion to the second expanded position 36 having a second expanded transverse dimension OD_3 that is at least about twenty-five percent larger than the first expanded transverse dimension OD_2, a second expanded longitudinal length L_3, measured at the second expanded position, decreases by less than about twenty-five percent, measured relative to the first expanded longitudinal length.

Referring now to Figs. 9A and 9B, each tubular endoprosthesis 200, 206 includes longitudinal elements 20 embedded in wall 22, and each endoprosthesis 200, 206 has a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen, and that can be further expanded to a second expanded position larger than the first expanded position within the cavity or lumen by heating to a second temperature higher than the first temperature. In addition, each endoprosthesis 200, 206 includes a plurality of apertures 202, 208 defined in wall 22. As shown, endoprosthesis 200 has apertures 202 that are hexagonal in shape, and endoprosthesis 206 has apertures 208 that are square in shape. Also, in each embodiment 200, 206 each longitudinal element is disposed longitudinally across some of the apertures 202, 208 such that the longitudinal element effectively bifurcates some of the apertures. The embodiments of Figs. 9A and 9B exhibit reduced foreshortening during expansion for two reasons. First, as described above, we have discovered that embedding a longitudinal element generally reduces endoprosthesis foreshortening during expansion. In addition, apertures reduce foreshortening because during expansion, the apertures defined in the wall of the endoprosthesis can be stretched. Having longitudinal elements bifurcating some of the apertures allows the polymeric material of the endoprosthesis to "fill-in" around the wire during compression. In addition, this arrangement provides for increased strength and prevents tissue from growing through the apertures.

The endoprosthesis described herein can be formed by a variety of techniques known in the art. For example, some embodiments are desirably formed by extrusion or co-extrusion, while other embodiments are desirably formed by molding, e.g., injection molding, co-molding, compression molding, or casting. For molded embodiments, longitudinal elements are embedded in a wall by placing the elements on a mold insert. Apertures can be formed by laser ablation or by forming the apertures in the wall of the endoprosthesis as the endoprosthesis is molded.

A number of embodiments of the invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention.

For example, while in some embodiments tubular endoprosthesis 10 has a transverse cross-section that is circular, in some embodiments its transverse cross-section is non-circular. For example, it can be elliptical or polygonal, e.g., square, pentagonal, hexagonal or octagonal.

While Figs. 9A and 9B show hexagonal and square apertures, wall 22 can include an aperture of other shapes, e.g., circular or elliptical. Other polygonal shapes are also possible, including pentagonal and octagonal.

While in some embodiments, the collapsed position is substantially an entire longitudinal length of the endoprosthesis, in other embodiments, only a portion of the endoprosthesis is in a collapsed position, e.g., 10 percent, 20 percent or 40 percent of the overall length of the endoprosthesis.

While in some embodiments, the expanded position is substantially an entire longitudinal length of the endoprosthesis, in other embodiments, only a portion of the endoprosthesis is in an expanded position. Referring to Fig. 10A, an endoprosthesis 260 has been expanded from a collapsed position so that only end portions 262 and 264 are in an expanded position.

While in some embodiments the wall of the tubular endoprosthesis includes only a single layer, in some embodiments, the wall includes more than one layer, e.g., 2, 3, 5 or 7 layers. For example, referring to Fig. 10B, an endoprosthesis 270 is shown that includes a wall that includes three layers 280, 282 and 284. Longitudinal element 20 is

embedded in layer 280 of wall 22. Each layer may be made of the same material or each layer may be made of a different material.

While some endoprotheses have been shown that have a longitudinally constant wall thickness, in some embodiments, the wall thickness is longitudinally non-constant. In addition, while some endoprotheses have been shown that have a constant outer diameter, in some embodiments the outer diameter is non-constant. Referring to Figs. 11, 11A and 11B, a tubular endoprosthesis 290 has a constant inner diameter ID, but a non-constant outer diameter. The outer diameter is varied by varying wall thickness of the endoprosthesis as shown in Figs. 11A and 11B. As shown, section 292 has a thicker wall than section 294. Varying the wall thickness improves lateral flexibility which enables the endoprosthesis, e.g., to be used in lumens and cavities with high curvature.

While some endoprotheses have been shown that have a transversely constant wall thickness, in some embodiments, the wall thickness is transversely non-constant. Referring to Figs. 12 and 12A, endoprosthesis 300 includes a wall that is in the shape of a sprocket in transverse cross-section. The wall has thick areas 302 and thin areas 304 that extend longitudinally along a length of endoprosthesis 300. This type of endoprosthesis reduces lateral flexibility and increases strength when that is desirable.

A number of embodiments of have been described. Still other embodiments are within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A tubular endoprosthesis comprising a polymeric material, the endoprosthesis having at least one longitudinal element embedded in a wall of the endoprosthesis, the endoprosthesis having a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal, wherein the endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen in the mammal by heating to a second temperature higher than the first temperature.

2. The tubular endoprosthesis of claim 1, wherein the endoprosthesis is substantially circular in transverse cross-section.

3. The tubular endoprosthesis of claim 1, wherein the longitudinal element comprises a metal.

4. The tubular endoprosthesis of claim 3, wherein the metal comprises stainless steel.

5. The tubular endoprosthesis of claim 1, wherein the longitudinal element is a monofilament.

6. The tubular endoprosthesis of claim 5, wherein the monofilament is circular in transverse cross-section, having a diameter of from about 0.0005 inch to about 0.010 inch.

7. The tubular endoprosthesis of claim 1, wherein the longitudinal element is a multifilament.

8. The tubular endoprosthesis of claim 1, wherein the endoprosthesis includes from two to twelve longitudinal elements.

9. The tubular endoprosthesis of claim 1, wherein the longitudinal element extends substantially along an entire longitudinal length of the endoprosthesis.

10. The tubular endoprosthesis of claim 1, wherein the wall includes at least one aperture.

11. The tubular endoprosthesis of claim 10, wherein the aperture is circular in transverse cross-section.

12. The tubular endoprosthesis of claim 10, wherein the longitudinal element is disposed longitudinally across the aperture.

13. The tubular endoprosthesis of claim 1, wherein the tubular endoprosthesis includes a coating comprising a therapeutic agent.

14. The tubular endoprosthesis of claim 13, wherein the coating is on an outer surface of the endoprosthesis.

15. The tubular endoprosthesis of claim 13, wherein the coating is an outer surface of the endoprosthesis, and wherein the therapeutic agent also is dispersed generally throughout the polymeric material.

16. The tubular endoprosthesis of claim 13, wherein the therapeutic agent prevents restenosis.

17. The tubular endoprosthesis of claim 13, wherein the therapeutic agent is paclitaxel.

18. The tubular endoprosthesis of claim 1, wherein the polymeric material includes a radio-opaque agent.

19. The tubular endoprosthesis of claim 1, wherein the polymeric material includes a thermal conductor.

20. The tubular endoprosthesis of claim 19, wherein the thermal conductor is a boron nitride.

21. The tubular endoprosthesis of claim 1, wherein the polymeric material comprises a polymer that is selected from the group consisting of natural polymers, zein, casein, gelatin, gluten, serum albumin, collagen, polysaccharides, polyhyaluronic acid, poly(3-hydroxyalkanoate)s, alginate, dextran, cellulose, collagen, synthetic polymers, chemical derivatives of collagen, chemical derivatives of cellulose, polyphosphazenes, poly(vinyl alcohols), polyamides, polyacrylates, polyalkylenes, polyacrylamides, polyalkylene glycols, polyalkylene oxides, polyalkylene terephthalates, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polyesters, degradable polymers, polyester amides, polyanhydrides, polycarbonates, polyorthoesters, polylactides, polyglycolides, polysiloxanes, polyurethanes, cellulose derivatives, and mixtures thereof.

22. The tubular endoprosthesis of claim 1, wherein the endoprosthesis has a collapsed transverse dimension and a collapsed longitudinal length, both measured at the collapsed position, and wherein the first expanded position has a first expanded transverse dimension that is at least fifty percent larger than the collapsed transverse dimension and a first expanded longitudinal length that is at least fifty percent of the collapsed longitudinal length.

23. The tubular endoprosthesis of claim 1, wherein the endoprosthesis has a first expanded transverse dimension and a first expanded longitudinal length, both measured at the first expanded position, and wherein the second expanded position has a second expanded transverse dimension that is at least twenty-five percent larger than the first expanded transverse dimension and a second expanded longitudinal length that is at least fifty percent of the first expanded longitudinal length.

24. A method of treating a cavity or lumen in a mammal, the method comprising:

inserting, into the cavity or lumen in the mammal, a tubular endoprosthesis comprising a polymeric material, the endoprosthesis having at least one longitudinal element embedded in a wall of the endoprosthesis, the endoprosthesis having a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal, and wherein the endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen in the mammal by heating to a second temperature higher than the first temperature; and

heating the inserted endoprosthesis to the first temperature to revert the collapsed position to the first expanded position.

25. The method of claim 24, further comprising heating the inserted endoprosthesis to the second temperature to further expand the endoprosthesis to the second expanded position.

26. The method of claim 24, wherein the heating is performed with a liquid.

27. The method of claim 24, wherein the first temperature is from about 37 °C to about 55 °C.

28. The method of claim 24, wherein the second temperature is from about 40 °C to about 75 °C.

29. The method of claim 24, wherein the heating is performed by a delivery tube that includes a warmed liquid.

30. The method of claim 29, wherein the delivery tube is a balloon catheter.

31. The method of claim 24, wherein the lumen a vascular lumen.

32. An endoprosthesis comprising a polymeric material having at least one longitudinal element embedded in a wall of the endoprosthesis.

33. The endoprosthesis of claim 32, wherein the endoprosthesis includes from about two to twelve longitudinal elements.

34. A method of treating a cavity or lumen in a mammal, the method comprising:

inserting, into the cavity or lumen in the mammal, a tubular endoprosthesis comprising a polymeric material, the endoprosthesis having a collapsed position that can be reverted to a first expanded position larger than the collapsed position by heating to a first temperature subsequent to insertion of the endoprosthesis into a cavity or lumen in a mammal, and wherein the endoprosthesis can be further expanded from the first expanded position to a second expanded position within the cavity or lumen in the mammal by heating to a second temperature higher than the first temperature;

heating the inserted endoprosthesis to the first temperature to revert the collapsed position to the first expanded position; and then

heating the inserted endoprosthesis to the second temperature to further expand the endoprosthesis to the second expanded position.

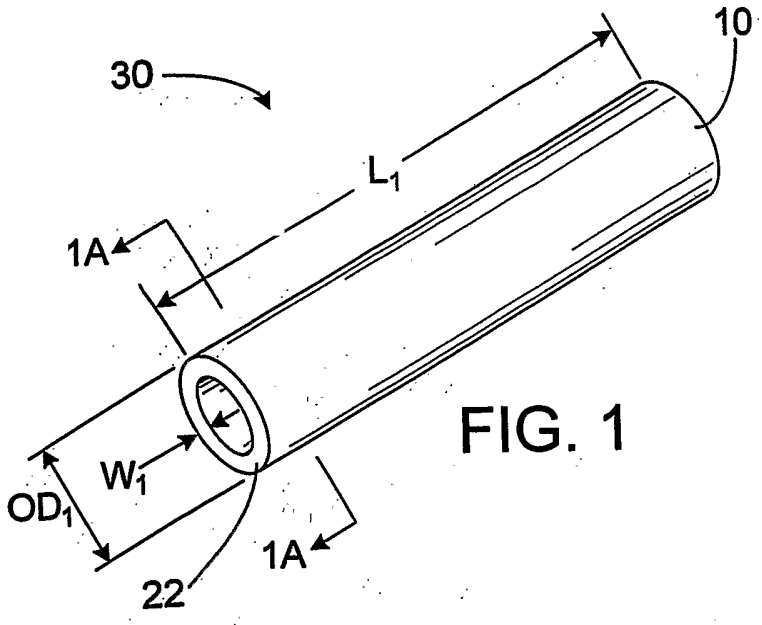

FIG. 1

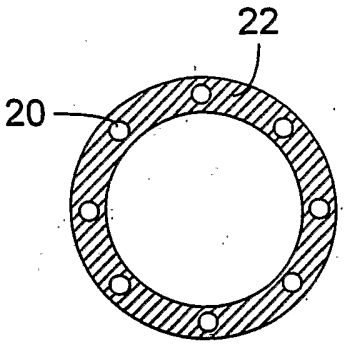

FIG. 1A

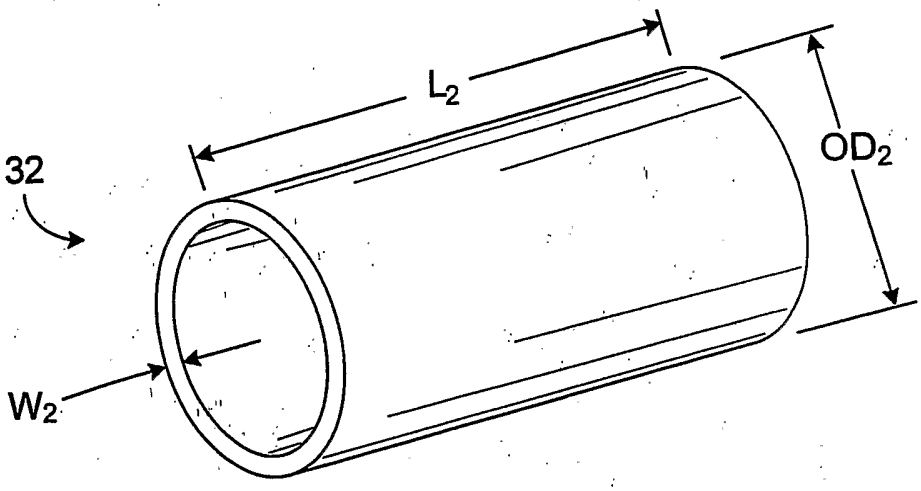

FIG. 2

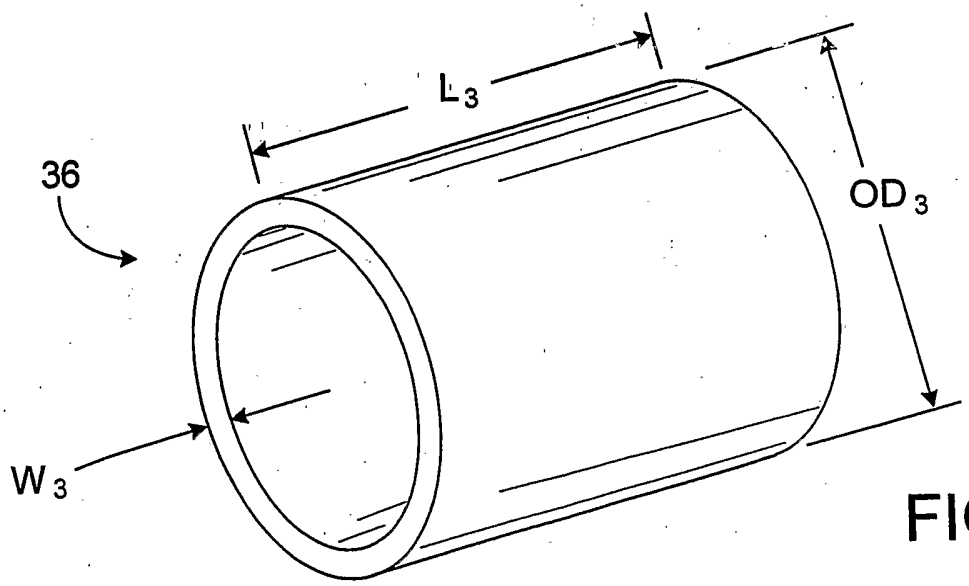

FIG. 3

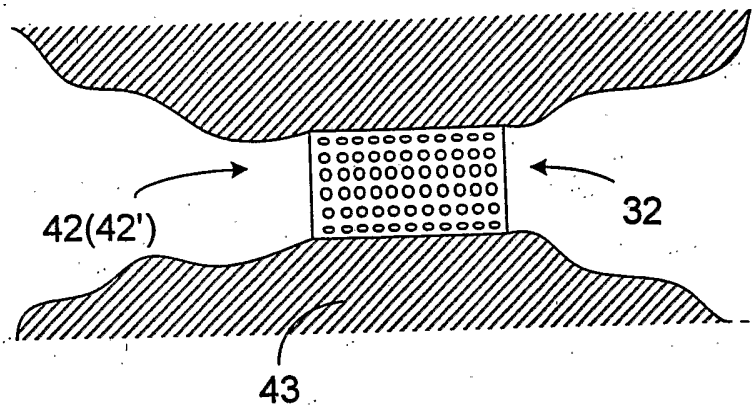

FIG. 4

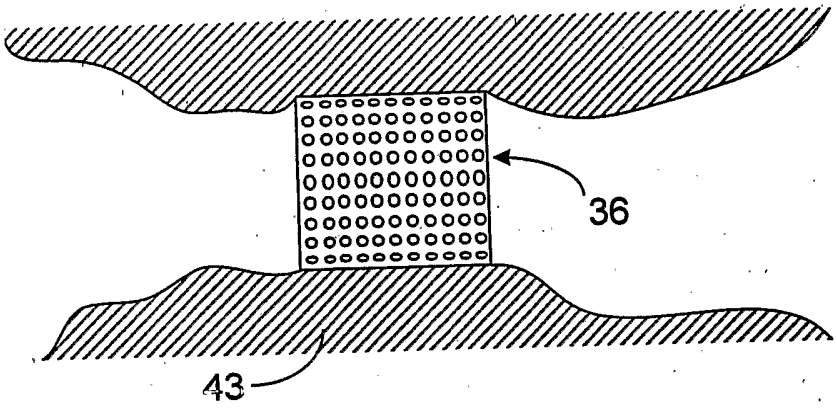

FIG. 5

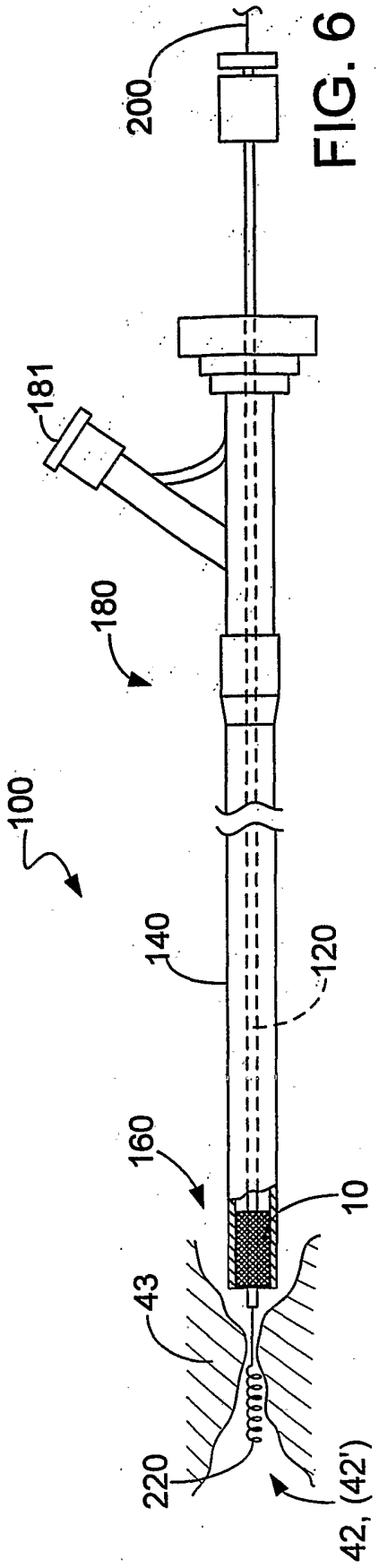

FIG. 6

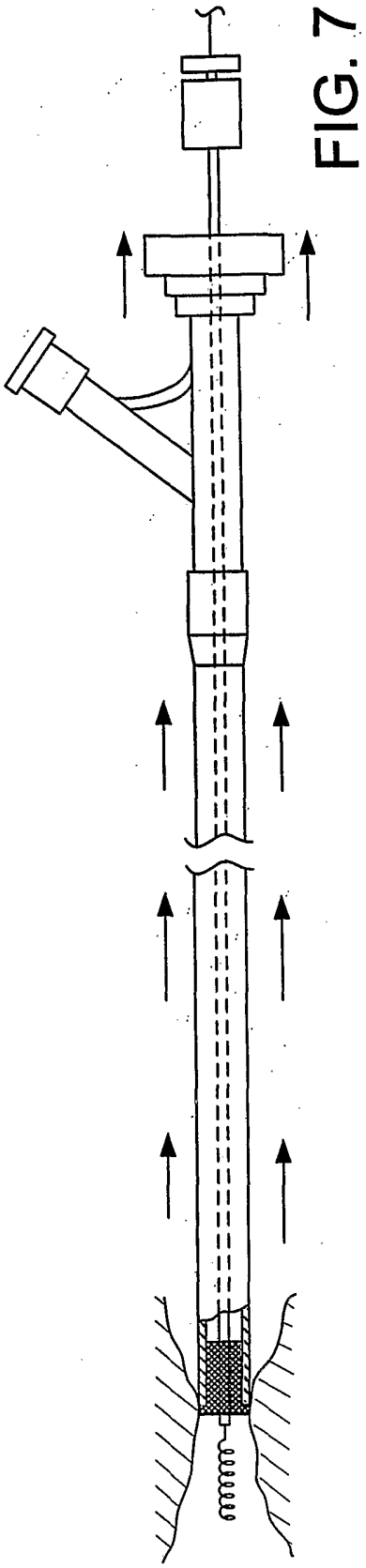

FIG. 7

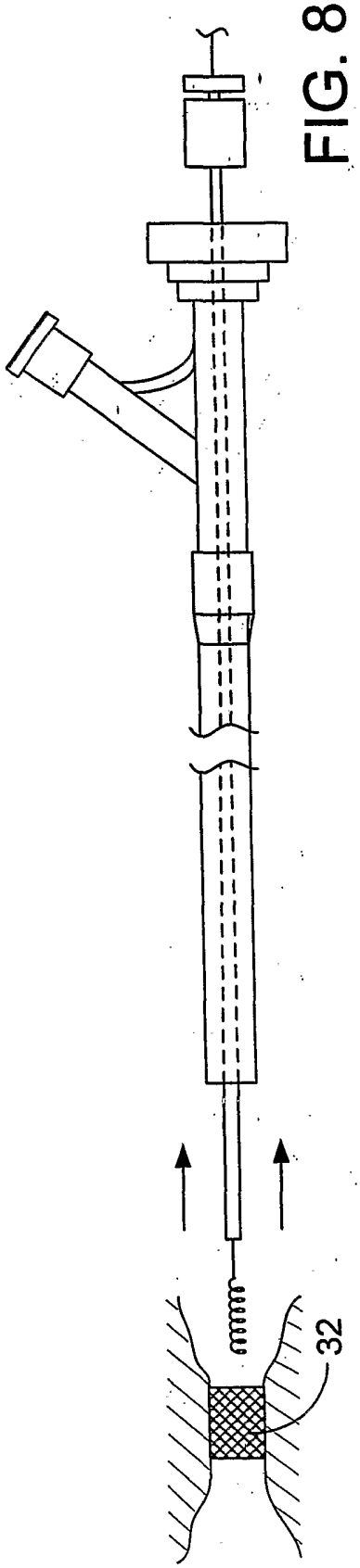

FIG. 8

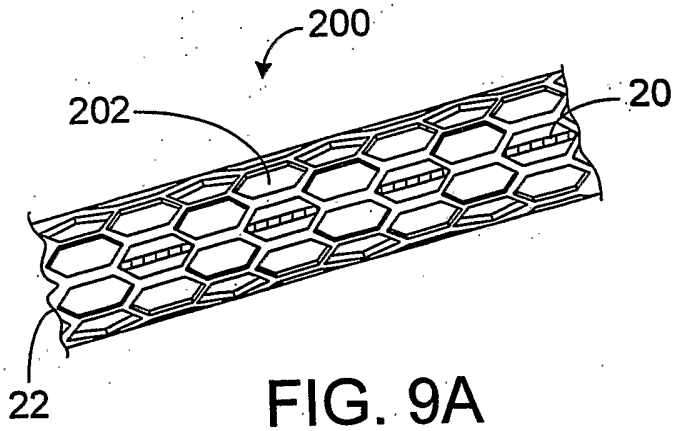

FIG. 9A

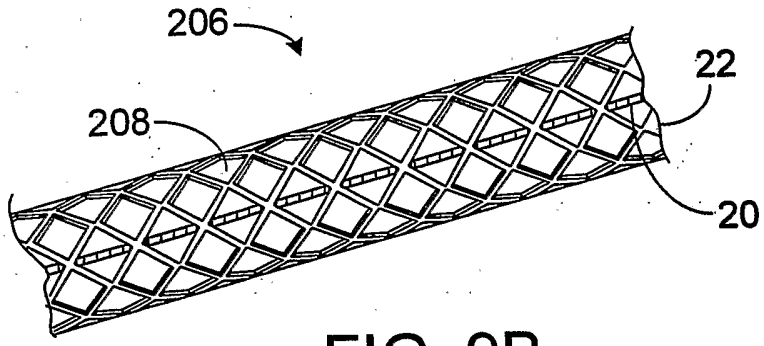

FIG. 9B

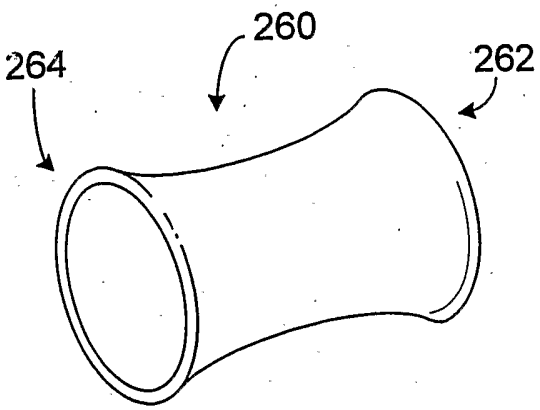

FIG. 10A

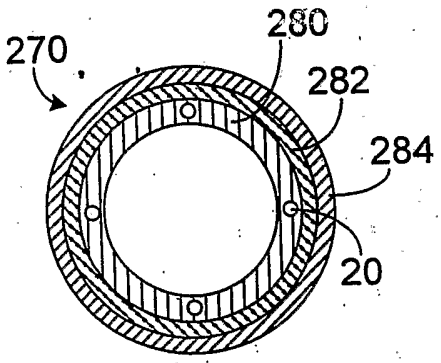

FIG. 10B

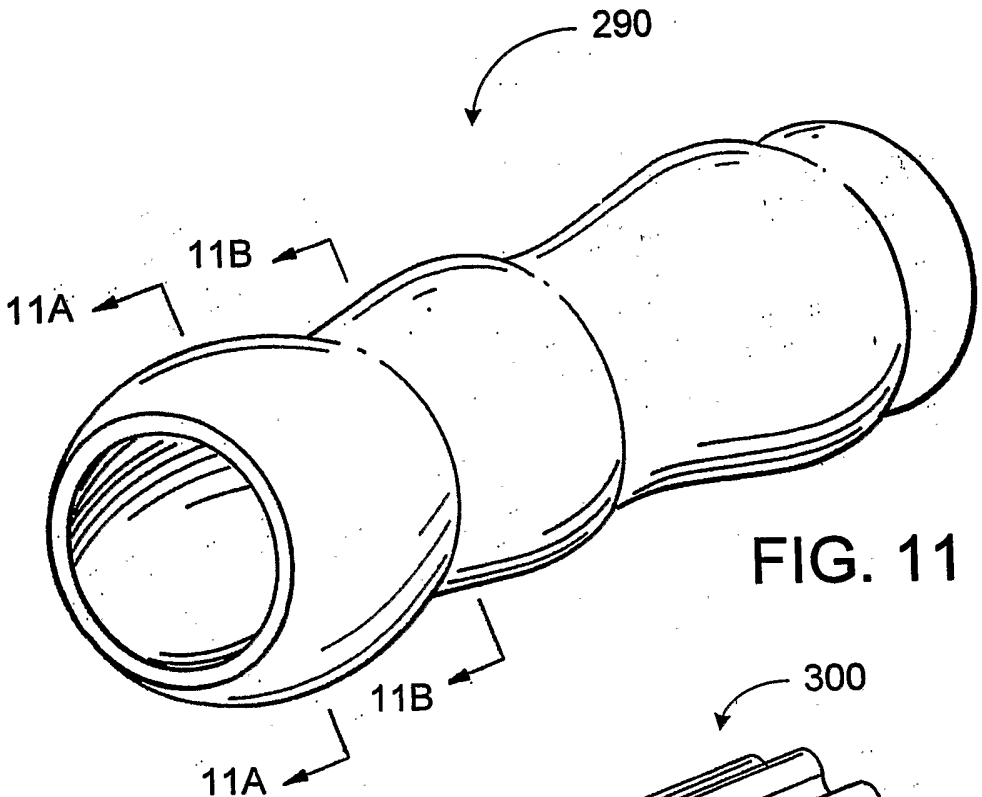

FIG. 11

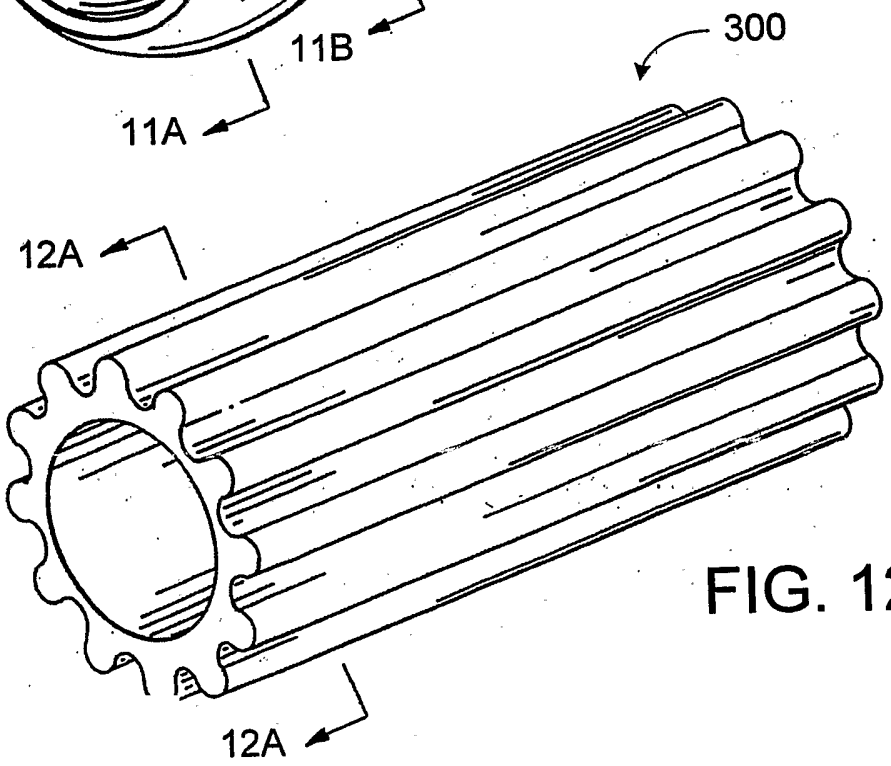

FIG. 12

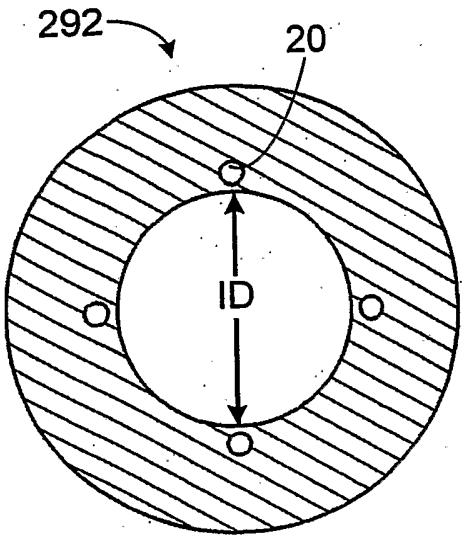

FIG. 11A

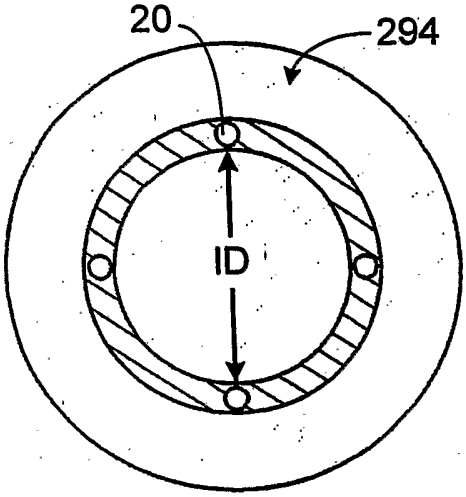

FIG. 11B

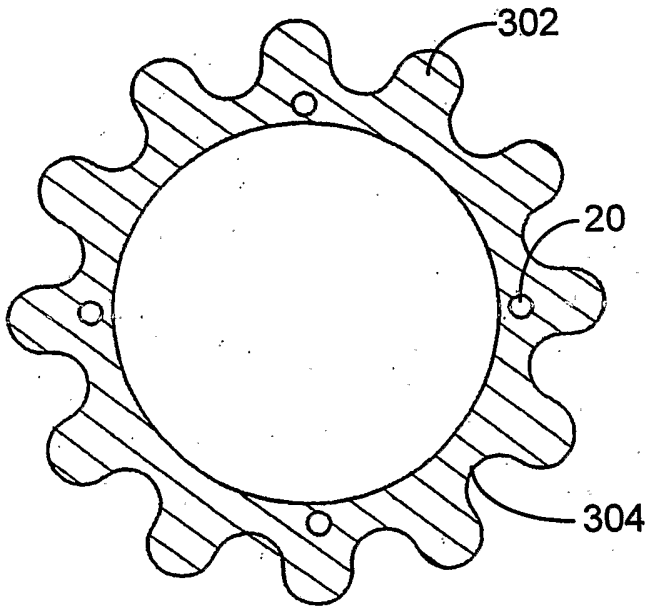

FIG. 12A

INTERNATIONAL SEARCH REPORT

Inte..... application No
PCT/US2005/044084

A. CLASSIFICATION OF SUBJECT MATTER
A61F2/06 A61F2/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/055198 A1 (LANGER ROBERT S ET AL) 20 March 2003 (2003-03-20) paragraphs [0013], [0017], [0037], [0040], [0130] - [0138]	1-23
Y	US 2003/045923 A1 (BASHIRI MEHRAN) 6 March 2003 (2003-03-06) paragraphs [0041], [0042]	1-23
Y	WO 03/015663 A (ROY, SUMIT) 27 February 2003 (2003-02-27) pages 3-4; claims 1,6; figures 1-4,8	1-23

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 April 2006	25/04/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Prechtel, A-K

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Inter al application No
PCT/US2005/044084

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2004/032799 A (SCIMED LIFE SYSTEMS, INC) 22 April 2004 (2004-04-22) page 4, lines 11-22 page 5, lines 7-9 page 8, line 23 - page 9, line 9 figures 1A-1D page 22, lines 27-29	10-23
Y	WO 98/25544 A (PURDUE RESEARCH FOUNDATION; BABBS, CHARLES, F; FEARNOT, NEAL, F; BADYL) 18 June 1998 (1998-06-18) page 15; figures 4A,4B	10-12
A	US 2002/128706 A1 (OSYPKA PETER) 12 September 2002 (2002-09-12) paragraphs [0003], [0004], [0017], [0018]	1-23
A	US 6 099 533 A (SHAH ET AL) 8 August 2000 (2000-08-08) the whole document	1-23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/044084

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 24-34
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery: Insertion of an endoprosthesis always involves a surgical act.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr al application No
PCT/US2005/044084

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