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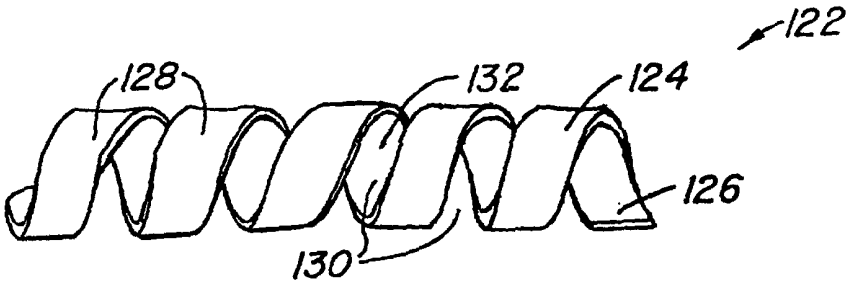

(57) Abstract: A prosthesis (122), for use within a hollow body structure of a patient, comprises a coiled body (105) having a radially-extending openings (113), the coiled body being movable from a radially-contracted state to a radially-expanded state. A material (124) extends along a coiled path algon the coiled body. A dispensable, biologically active agent (M, 147) is associated with at least one of the coiled body and material. The material may comprise a coiled sleeve of material having inner and outer surfaces (124B, 124A), the inner surface defining a sleeve interior (124C) containing the coiled body. The dispensable agent may be, for example, on the outer surface of the material, incorporated into the material to create an agent/material matrix, or on the inner surface of the material or within the sleeve interior. Structure may be used to delay the migration of the agent to the patient.

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BIOLOGICALLY ACTIVE AGENT DELIVERY APPARATUS AND METHOD

BACKGROUND OF THE INVENTION

[0001] The present invention provides devices and methods for the delivery of a biologically active agent by a coiled prosthesis, typically a covered coiled stent, to a target site within a hollow body structure of the patient, particularly within the vascular system for the treatment of cardiovascular and peripheral vascular disease, such as vascular stenoses and restenoses, dissections and other tissue separation conditions, aneurysms, and the like.

[0002] Research has been done to determine the causes and possible treatments of coronary restenosis following balloon angioplasty. Restenosis following balloon angioplasty is believed to result from several causes, including elastic recoil of the vessel, thrombus formation and cell wall growth. The article, *Chan, AW, Chew, DP, and Lincoff, AM,* Update on Pharmacology for Restenosis, *Current Interventional Cardiology Reports* 2001, 3:149-155, concludes that restenosis remains a major problem for percutaneous coronary intervention and that while drug-eluting stents may be found to be effective, larger clinical trials are needed.

[0003] The apparatus and methods of the present invention, however, are also useful for placement in other hollow body structures, such as the ureter, urethra, bronchus, biliary tract, gastrointestinal tract and the like, for the treatment of other conditions which may benefit from the introduction of a biologically active agent along with a reinforcing or protective structure within the body lumen. The prostheses will be placed endoluminally. As used herein, "endoluminally" will mean placement by percutaneous or cutdown procedures, wherein the prosthesis is transluminally advanced through the body lumen from a remote location to a target site in the lumen. In vascular procedures, the prostheses will typically be introduced "endovascularly" using a catheter over a guidewire under fluoroscopic, or other imaging system, guidance. The catheters and guidewires may be introduced through conventional access sites to the vascular system, such as through the femoral artery, or brachial and subclavian arteries, for access to the target site.

[0004] An endoluminal prosthesis typically comprises at least one radially expansible, usually cylindrical, body segment. By "radially expansible," it is meant that the body segment can be converted from a small diameter configuration (used for endoluminal placement) to a radially expanded, usually cylindrical, configuration which is achieved when the prosthesis is

implanted at the desired target site. The prosthesis may be non-resilient, e.g., malleable, thus requiring the application of an internal force to expand it at the target site. Typically, the expansive force can be provided by a balloon catheter, such as an angioplasty balloon for vascular procedures. Alternatively, the prosthesis can be self-expanding. Such self-expanding structures may be provided by a temperature-sensitive superelastic material, such as Nitinol, which naturally assumes a radially expanded condition once an appropriate temperature has been reached. The appropriate temperature can be, for example, a temperature slightly below normal body temperature; if the appropriate temperature is above normal body temperature, some method of heating the structure must be used. Another type of self-expanding structure uses resilient material, such as a stainless steel or superelastic alloy, and forming the body segment so that it possesses its desired, radially-expanded diameter when it is unconstrained, e.g., released from radially constraining forces of a sheath. To remain anchored in the body lumen, the prosthesis will remain partially constrained by the lumen. The self-expanding prosthesis can be delivered in its radially constrained configuration, e.g. by placing the prosthesis within a delivery sheath or tube and retracting the sheath at the target site. Such general aspects of construction and delivery modalities are well-known in the art.

[0005] The dimensions of a typical endoluminal prosthesis will depend on its intended use. Typically, the prosthesis will have a length in the range from 0.5 cm to 10 cm, usually being from about 0.8 cm to 5 cm, for vascular applications. The small (radially collapsed) diameter of cylindrical prostheses will usually be in the range from about 1 mm to 10 mm, more usually being in the range from 1.5 mm to 6 mm for vascular applications. The expanded diameter will usually be in the range from about 2 mm to 50 mm, preferably being in the range from about 3mm to 15mm for vascular applications and from about 25 mm to 45 mm for aortic applications.

[0006] One type of endoluminal prosthesis includes both a stent component and a graft-type covering component. These endoluminal prostheses are often called stent grafts. A stent graft is typically introduced using a catheter with both the stent and graft in contracted, reduced-diameter states. Once at the target site, the stent and graft are expanded. After expansion, the catheter is withdrawn from the vessel leaving the stent graft at the target site. Grafts may be made of, for example, PTFE, ePTFE or Dacron® polyester.

[0007] Grafts are used within the body for various reasons, such as to repair damaged or diseased portions of blood vessels such as may be caused by injury, disease, or an aneurysm. It has been found effective to introduce pores into the walls of the graft to provide ingrowth of tissue onto the walls of the graft. With larger diameter grafts, woven graft material is often used.

In small and large diameter vessels, porous fluoropolymers, such as ePTFE, have been found useful.

[0008] Coil-type stents can be wound about the catheter shaft in torqued compression for deployment. The coil-type stent can be maintained in this torqued compression condition by securing the ends of the coil-type stent in position on a catheter shaft. The ends are released by, for example, pulling on wires once at the target site. See, for example, U.S. Patent Nos. 5,372,600 and 5,476,505. Alternatively, the endoluminal prosthesis can be maintained in its reduced-diameter condition by a sleeve; the sleeve can be selectively retracted to release the prosthesis. A third approach is the most common. A balloon is used to expand the prosthesis at the target site. The stent is typically extended past its elastic limit so that it remains in its expanded state after the balloon is deflated and removed. One balloon expandable stent is the Palmaz-Schatz stent available from the Cordis Division of Johnson & Johnson. Stents are also available from Medtronic AVE of Santa Rosa, California and Guidant Corporation of Indianapolis, Indiana.

SUMMARY OF THE INVENTION

[0009] As used herein, biologically active agents include diagnostic and therapeutic agents, such as radiation-emitting agents used for imaging and/or therapy; compounds used to help prevent restenosis such as anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, and anti-proliferative drugs; apoptosis drugs; and light-activated drugs that intercalate into DNA or RNA strands (8-methoxypsoralen), cross-link into DNA or RNA strands (8-methoxysporalen plus UV light), or cause apoptosis (phthalocynine) or necrosis tin ethyl etiopurpurin) when activated with light. The following are examples of several of these groups of agents.

Anti-Inflammatory Drugs:

Aspirin or acetyl salicylic acid

Oral Corticosteroids (generic name followed by trademark in parentheses)-

Prednisone (Deltasone), methylprenisolone (Medrol), prednisolone solution (Pediapred, Prelone)

Inhaled Corticosteroids (generic name followed by trademark in parentheses)--

Flunisolide (AeroBid, AeroBid-M), triamcinolone (Azmacort), beclomethasone (Beclovent, Vanceril), budesonide (Pulmicort), fluticasone (Flovent), Nedocromil sodium (Tilade), Cromolyn sodium (Intal)

Nonsteroidal anti-inflamatory agents (generic names):

1. Diclofenac
2. Diflunisal‡
3. Etodolac †
4. Fenoprofen‡
5. Floctafenine *
6. Flurbiprofen ‡§
7. Ibuprofen ‡§
8. Indomethacin‡
9. Ketoprofen ‡
10. Meclofenamate †‡
11. Mefenamic Acid
12. Meloxicam ‡
13. Nabumetone
14. Naproxen ‡
15. Oxaprozin
16. Phenylbutazone ‡
17. Piroxicam ‡
18. Rofecoxib
19. Sulindac ‡
20. Tenoxicam *
21. Tiaprofenic Acid *
22. Tolmetin (‡

* Not commercially available in the U.S.
† Not commercially available in Canada
‡ Generic name product may be available in the U.S.

Anti-Thrombotic Drugs (generic names):

Anisindione Indications: Embolism, pulmonary; Embolism, pulmonary, prophylaxis; Thrombosis; Thrombosis, prevention

Antithrombin III (Human) Indications: Embolism; Thrombosis

Argatroban Indications: Thrombosis; Thrombocytopenia, secondary to heparin

Dicumarol Indications: Embolism, pulmonary; Embolism, pulmonary, prevention; Fibrillation, atrial, adjunct; Occlusion, coronary, adjunct; Thrombosis; Thrombosis, prevention

Heparin Sodium Indications: Coagulopathy, consumption; Dialysis, adjunct; Embolism, pulmonary; Embolism, pulmonary, prevention; Fibrillation, atrial, adjunct; Surgery, adjunct; Thrombosis; Thrombosis, prevention; Transfusion, adjunct

Lepirudin (rDNA) Indications: Thrombocytopenia, secondary to heparin; Thrombosis

Anti-Proliferative Drugs (generic name followed by trademark in parentheses):

Terazosin - (Hytrin) Antihypertensive, Benign prostatic hyperplasia therapy agent

Finasteride (Systemic) - (Propecia, Proscar) Benign prostatic hyperplasia therapy agent; hair growth stimulant, alopecia androgenetica (systemic)

Doxazosin (Systemic) - (Cardura) Antihypertensive, Benign prostatic hyperplasia therapy agent

Tamsulosin (Systemic) - (Flomax) Benign prostatic hypertrophy therapy agent

Prazosin (Systemic) - (Minipress) Antidote, to ergot alkaloid poisoning, Antihypertensive, Benign prostatic hyperplasia therapy agent, Vasodilator, congestive heart failure, Vasospastic therapy adjunct

More examples of anti-proliferative drugs (generic name followed by trademark name in parentheses):

Mitomycin for injection (Mutamycin); bleomycin sulfate for injection (Blenoxane); doxorubicin hydrochloride for injection (Adriamycin or Rubex or Doxorubicin hydrochloride); daunorubicin HCl (Cerubidine); dactinomycin for injection (Cosmegen); daunorubicin citrate (liposome) for injection (DaunoXome); doxorubicin HCl (liposome) for injection (Doxil), epirubicin hydrochloride for injection (Ellence); idarubicin hydrochloride for injection (Idamycin); plicamycin (Mithracin); pentostatin for injection (Nipent); mitoxantrone for injection (Novantrone); and valrubicin (Valstar).

[0010] A first aspect of the invention is directed to a prosthesis for use within a hollow body structure of a patient. The prosthesis comprises a coiled body having a radially-extending openings, the coiled body being movable from a radially-contracted state to a radially-expanded state. A material extends along a coiled path along the entire coiled body. A dispensable, biologically active agent is associated with at least one of the coiled body and material. The dispensable agent is dispensable into a hollow body structure of a patient. The material may comprise a coiled sleeve of material having inner and outer surfaces, the inner surface defining a sleeve interior containing the coiled body. The dispensable agent may be, for example, on the outer surface of the material, incorporated into the material to create an agent/material matrix, or on the inner surface of the material or within the sleeve interior. The prosthesis may comprise turns which either define gaps therebetween when in the radially-expanded state or which touch one another when in the radially-expanded state. The biologically active agent may be dispensable immediately or may be dispensed after a delay.

[0011] Another aspect of the invention is directed to a method for delivering a biologically active agent to a target site within a hollow body structure of a patient. The method comprises delivering a coiled prosthesis to target site while in a radially-contracted state; the prosthesis

includes a coiled body having radially-extending openings formed therethrough, material extending along a coiled path along the entire coiled body, and a dispensable, biologically active agent associated with at least one of the coiled body and material. The prosthesis is expanded to the radially-expanded state so to press the prosthesis against the wall of the hollow body structure. The agent is released into the hollow body structure. The prosthesis may be selected so that the material comprises a coiled sleeve of material having inner and outer surfaces, the inner surface defining a sleeve interior containing the entire coiled body. The agent may be, for example, on the outer surface of the material, incorporated into the material to create an agent/material matrix or on the inner surface of the material or within the sleeve interior. The dispensable agent may be selected from a group comprising: anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, and anti-proliferative drugs. The dispensable agent may be an anti-restenotic agent.

[0012] A further aspect of the invention is directed to a method for making a prosthesis for use at a target site within a hollow body structure of a patient. The method comprises determining at least one therapy for a patient; and selecting a prosthesis suitable for the at least one therapy. The prosthesis comprises a coiled body with radially-extending openings, the material extending along a coiled path along the entire coiled body, and first and second dispensable, biologically active agents for the therapy, the first and second agents being associated with at least one of the coiled body and the material. The selecting step is carried out so that at least some of the first agent is releasable that the target site within the hollow body structure prior to start of release of the second agent at the target site.

[0013] A still further aspect of the invention is directed to a method for making a prosthesis for use at a target site within a hollow body structure of a patient. The method comprises placing a length of a material in contact with a mixture of a carrier and a dispensable, biologically active agent. At least a substantial portion of the carrier is removed from the mixture leaving the agent in contact with the material to create an agent-laden material. The agent-laden material is then combined with a radially-expandable stent to create a prosthesis suitable for use within a hollow body structure of the patient. The material may be a porous material, such as ePTFE. The method may further comprise selecting a length of porous sleeve material as the porous material, the porous sleeve material comprising inner and outer surfaces, the inner surface defining a sleeve interior containing the entire stent following the combining step. The placing step may be carried out by placing the mixture into the sleeve interior; thereafter the removing step may be carried out by draining away excess amounts of the mixture and then at least partially drying the length of material. The dispensable agent may be selected from a group comprising: anti-

inflammatory drugs, anti-thrombotic/anti-platelet drugs, and anti-proliferative drugs. The dispensable agent may be an anti-restenotic agent.

[0014] An advantage of the invention is the ability to coat the stent/graft with the biologically active material on one surface while the opposing surface remains biologically active material-free. By coating only the surface of the device that comes into intimate contact with the wall of the lumen being treated, the device becomes more efficient. In the case of vascular application, the biologically active material coated onto the surface of the device that comes into intimate contact with the flowing blood of the vessel is wasted material because it is "washed" from the surface of the device and flows to an area of the body not being treated. Coating one side of the device would increase the efficiency of biologically active material delivery.

[0015] A further advantage of the invention is that it provides for drug delivery using a covered stent in a very flexible manner. This flexibility is at least in part provided by the coiled nature of the stent used. This permits, for example, vascular sidebranch access for drug delivery which otherwise would not be possible. The use of a stent body having radially-extending openings covered by graft material helps promote a good tissue ingrowth, when compared with a solid stent body, when the prosthesis is permanently implanted within the hollow body structure.

[0016] A still further advantage is the surface area of the stent graft that comes into intimate contact with the inner wall of the vessel is much greater than standard stents, but not so much that it covers up side branch vessels as with grafts. The increased surface area contact may lead to delivery of more drug; therefore, the drug eluting stent may be more efficient (deliver more drug to the target site with less drug delivered to undesired areas) than standard drug delivery stents.

[0017] A still another aspect of the invention is directed to a covered, coiled agent delivery prosthesis that includes a coiled, radially-expandable prosthesis body comprising an outer surface. A porous covering overlies the outer surface. The agent is associated with the porous covering in one of several ways. One way is for the porous covering and agent to form a porous covering/agent matrix. Other ways include having the agent be a layer above or below the porous covering. Some type of structure may be used to delay the migration of the agent to the patient. One way of doing so is to use a protective layer, which covers the prosthesis body, porous covering, and agent. The protective layer may be removed, either by being biodegradable, or by being at least partially pulled off of the structure. The agent may be an integral part of a biodegradable material so that the agent is exposed only when the

biodegradable material biodegrades. The agent may also be housed within biodegradable micro encapsulation material.

[0018] Another aspect of the invention is directed to a method for delivering an agent to a patient. The method can be carried out by directing a covered, coiled, agent-delivery prosthesis, including a agent associated with a porous covering which overlies a coiled, radially-expandable prosthesis, to a target site. This is followed by waiting for the protective material, which is shielding the agent, to be effectively removed from the prosthesis subassembly, thereby exposing the agent. The agent is then permitted to migrate from the prosthesis subassembly for interaction with the patient.

[0019] An advantage of the invention is that it provides for agent delivery using a covered prosthesis in a manner, which is very flexible. This flexibility is at least in part provided by the coiled nature of the prosthesis used. This permits, for example, vascular sidebranch access for agent delivery which otherwise would not be possible.

[0020] Other features and advantages of the invention will appear from the following description in which the preferred embodiments have been set forth in detail in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] Fig. 1 illustrates a stent blank used to create a coiled stent such as those shown in Figs. 3, 4 and 5A;

[0022] Figs. 1A-1D illustrate four additional designs of stent blanks;

[0023] Fig. 1E shows a coiled stent made from the stent blank of Fig. 1B;

[0024] Fig. 2 illustrates a stent blank similar to that of Fig. 1 but having different thicknesses along its length;

[0025] Fig. 3 illustrates a stent graft in a radially expanded condition, the stent graft including a stent similar to that shown in Fig. 1 covered with a sleeve of porous graft material, the stent graft having a central turn with a greatly increased pitch for placement at a branching intersection;

[0026] Fig. 3A is an enlarged cross-sectional view of a prosthesis taken along line 3A-3A of Fig. 3;

[0027] Fig. 3B is a simplified side view illustrating the introduction of a mixture of a carrier and a biologically active agent into the interior of a sleeve of a porous graft material;

[0028] Fig. 4 illustrates a stent graft similar to that of Fig. 3 but in which one end of the stent graft has much greater radially expanded diameter than the other portion to accommodate a vessel having different internal diameters;

[0029] Fig. 5 illustrates an alternative embodiment to the stent graft of Fig. 3 in which the stent graft has a large expanded diameter and also has the one turn with the greater pitch at one end of the stent graft;

[0030] Fig. 5A shows a stent graft similar to that of Fig. 3 but with generally evenly-spaced turns;

[0031] Figs. 5B and 5C illustrate stent grafts made from the stent blank of Fig. 1C;

[0032] Figs. 5D-5I are three enlarged, partial cross-sectional views of three different covered, coiled drug-delivery stents;

[0033] Fig. 6A is an overall view of the distal end of a three-shaft deployment catheter used to deploy the stent grafts of Figs. 3-5;

[0034] Fig. 6B is an end view of the shafts of 6A;

[0035] Fig. 6C is an embodiment similar to the catheter of Fig. 6A but including only inner and outer shafts;

[0036] Fig. 6D illustrates a proximal end adapter mounted to the proximal end of the catheter of Fig. 6C;

[0037] Fig. 6E illustrates an alternative embodiment of the catheter of Fig. 6C;

[0038] Figs. 6F and 6G are simplified side and cross-sectional views of a further alternative embodiment of the catheter of Figs. 6A and 6B;

[0039] Fig. 7A illustrates the stent graft of Fig. 3 tightly wrapped about the distal end of the catheter of Figs. 6A and 6B and placed within a vessel with the intermediate portion of the stent graft at the intersection of the main and branching vessels;

[0040] Fig. 7B illustrates the release of the proximal half of the stent graft;

[0041] Fig. 7C illustrates the release of the distal half of the stent graft prior to the removal of the catheter shafts;

[0042] Fig. 7D illustrates the stent graft of Fig. 5C tightly wrapped about a placement catheter;

[0043] Fig. 7E illustrates the stent graft of Fig. 7D with the distal end of the stent graft released from the catheter and the proximal end of the stent graft releasably secured to the catheter at two positions;

[0044] Figs. 8 and 9 illustrate the placement of radiopaque marks at different positions along a coiled ladder-type stent having a central turn with a greatly increased pitch;

[0045] Fig. 10 illustrates one example of a radiopaque marker shaped to permit the determination of the orientation of the prosthesis as well as its location; and

[0046] Fig. 11 illustrates of the stent graft of Fig. 5B within the true lumen of the aortic arch at the entry of an aortic dissection, an alternative aortic dissection being shown in dashed lines.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

[0047] Fig. 1 illustrates a stent blank 104 used to create a coiled stent similar to that shown in Figs. 3, 4 and 5A. Stent blank 104 includes a main body portion 106 and first and second end portions 108. Main body portion 106 includes side edge or rail elements 110 connected by connector or rung elements 112 to define openings 113 therethrough. Rung elements 112 are, as shown in Fig. 1, at an angle to rail elements 110 so that when stent blank 104 is formed into a coiled stent and tightly wrapped about an introducer catheter, such as in Fig. 7A, rung elements 112 are axially-extending so that they lie flat for a tighter wrap.

[0048] End portions 108 are thinner and thus more flexible than main body portion 106. In addition, end portions 108 have an inwardly tapering portion 114 terminating at a blunt tip 115. The shape of end portions 108 and the lessened stiffness of the end portions, compared to body portion 106, help to prevent tissue trauma during use. This type of coiled stent in which the end portions 108 are less stiff than the main body portion 106 can find particular utility in stabilizing a traumatic injury site within a patient, such as in the case of a dissection, flap or false lumen. End portion 108 could also be stiffer than main body portion; this embodiment may be useful, for example, when treating occlusive disease on either side of a branch vessel.

[0049] Fig. 2 illustrates a stent blank 104A similar to stent blank 104 of Fig. 1 but in which main body portion 106A has three different radial stiffnesses. That is, main body portion 106A has a first, central longitudinal section 116 of a first, greater stiffness, and second and third longitudinal sections 118, 120 on either side of first section 116. Sections 118, 120 are successively thinner and thus have successively lower radial stiffnesses when stent blank 104A is formed into a coiled stent. End portion 108A acts as the fourth longitudinal section with the least radial stiffness of any of the sections in this embodiment. Instead of a set of generally discrete radial stiffnesses, the radial stiffness could vary continuously along at least part of the length of stent blank 104A, and then along the resulting stent body.

[0050] In addition to providing less traumatic end portions 108, 108A, a coiled prosthesis formed from either of stent blanks 104, 104A, when uncoiling, will have a tendency to open up first in the center, because of the greater stiffness at the center, followed by the ends. This helps

to reduce the degree to which the end portions 108, 108A are dragged along the surface of the vessel or other hollow body structure as the prosthesis is released.

[0051] Figs. 1A-1D illustrate four different designs of stent blanks 104B–104E. Each of these different stent blanks has at least three rail elements 110 with connector or rung elements 112 extending between the rail elements. In the Figs. 1A-1C embodiments connector elements 112 are aligned while in the 1D embodiment they are offset. The angles of connector elements 112 are such that when the stent blanks are formed into a tight coil during introduction, connector elements 112 are generally axially extending so they lie flat for a tighter wrap. Fig. 1E illustrates a coiled stent 105C made from stent blank 104C with one or more radiopaque markers 121 used to facilitate deployment. Stent blanks 104B-104E are relatively wide so to increase the radial force the coiled stents can apply to the walls of the hollow body organ within which they are to be placed. It has been found that reducing the number of turns for a stent graft having the same axial length helps to increase the user's control of the stent graft during placement. This is important in certain situations, such as when treating a dissection, in particular a vascular dissection such as the aortic dissection shown in Fig. 11 and discussed below. Also, as discussed above, the ends of stent blanks 104B-104E may be rounded or thinned in shape to cause a reduction in the radial force applied at the ends of the stent to help prevent vessel deformation at the ends of the stent.

[0052] When the stent blank is coiled, to act as the body of a coiled prosthesis, as illustrated in Figs. 3-5C, the openings 113 in the stent are radially extending openings as illustrated in Fig. 1E. While openings 113 are shown as generally quadrilateral openings, they may be of other shapes, such as oval or circular or octagonal with a combination of straight and curved sides.

[0053] Figs. 3, 4, 5 and 5A illustrate four stent graft embodiments 122, 122A, 122B, 122C. Stent graft 122 includes a ladder-type coiled stent formed from stent blank 104 and covered with tubular graft material 124. That is, graft material 124, see Fig. 3A, acts as a sleeve of material having an outer surface 124A and an inner surface 124B, the inner surface defining a sleeve interior 124C housing the entire stent 104A. Graft material 124 is preferably porous PTFE or ePTFE or Dacron® polyester. The ends 126 of graft material 124 are sealed, or for example, by using an adhesive or by placing a suitable heat seal material, such as FEP (fluorinated ethylene propylene) or other thermoplastic materials, between the layers of the graft material 124 and applying heat and pressure. The porous nature of the graft material permits sealing in this manner in spite of the inert nature of PTFE. In addition, a direct bond of the PTFE to itself, via a process known as sintering, may be employed. Other methods for sealing ends 126 could also be used. One or both of outer and inner surfaces 124A, 124B may be coated or graft material 124

may be otherwise treated to make the surface substantially impervious to the passage of blood therethrough. While it is presently preferred that graft material 124 completely enclose the stent, graft material may be a single layer and extend along a coiled path along only one side of the coiled body of the stent.

[0054] The stent grafts of Figs. 3-5C may be constructed for delivering a biologically active agent, if desired. Such covered, coiled drug delivery stents may be constructed in several ways. One way is to place one or more biologically active agents on one or both of outer and inner surfaces 124A, 124B of the sleeve of material 124 shown in Fig. 3A. A biologically active agent may also be on inner surface 124B or contained within sleeve interior 124C; such agent may be, for example, coated on the stent or may be captured between the stent and inner surface 124B. Another way is to incorporate the agent into graft material 124 to create an agent/material matrix. Such a matrix may be created by using a porous material for graft material 124. The porous graft material is then saturated with a mixture of a carrier, such as water or alcohol, and one or more agents. One way to do so is shown in Fig. 3B. A sleeve of graft material 124 has one end 124F knotted to close off that end while a syringe S is used to fill graft material 124 with the mixture M. When the mixture has fully saturated graft material 124, which is typically evident when the mixture seeps through the pores of graft material 124, the excess amounts of the mixture is drained and the now agent-laden graft material is at least partially dried. Another method is to manufacture the graft material with one or more agents interspersed therein. The agents may be, for example, microencapsulated to provide a time-release function for the agent. Time release may also be achieved by coating outer surface 124A with an appropriate biodegradable material.

[0055] Another way to deliver a biologically active agent will be described with reference to Figs. 5D-5I. Figs. 5D-5I are greatly enlarged cross-sectional views taken through covered, coiled drug delivery stents 145 – 145E. Fig. 5D illustrates a stent wall 139, having an outer surface 139A, covered by a porous covering 141, the porous covering covered by a protective coat 143. The porous covering, in this embodiment, is made of a porous covering/drug matrix, preferably using ePTFE as the porous covering. Protective coat 143 is preferably a biodegradable polymer. When the covered, coiled drug delivery stent 145 is in place within a patient, protective coat 143 begins to degrade so that after a period of time, the drug begins migration from the matrix to the patient.

[0056] Fig. 5E discloses a further embodiment of the covered, coiled drug-delivery stent 145A, with like references referring to like elements. Porous covering 141A in the embodiment of Fig. 5E is made of ePTFE, covered by a drug layer 147, which in turn is covered by protective coat 143. In the Fig. 5F embodiment, the arrangement of porous covering 141A and drug layer

147 is reversed from that of Fig. 5E so that drug layer 147 is between stent wall 139 and porous covering 141A. In each of these situations, the drug is permitted to migrate from the stent 145, 145A, 145B, for interaction with the patient after the protective coat 143 has sufficiently degraded to expose the drug. Porous covering 141 is sufficiently porous to permit the drug to pass therethrough in the embodiments of Figs 5D and 5F. Figs. 5G, 5H and 5I illustrate embodiments similar to Figs. 5D, 5E and 5F but with protective coat 143 removed.

[0057] Drug layer 147 may include various types of therapeutic and diagnostic pharmaceuticals including, for example, NO generators, paclitaxel, statins, taxol, heparin in its various forms, i.e., low molecular weights, thienopyridines, glycoprotein IIb/IIIb inhibitors, antiplatelet agents, fibrinolytics, anticoagulants, thrombolytics, abciximab, rapamycin, hirudin, VEGF, Hirulog, ticlopidine and clopidogrel, **as well as the biologically active agents listed above.** Stents 145, 145A or 145B are made to deliver drug to the patient by directing the drug delivery stent to a target site within the patient, waiting for a protective material, initially shielding the drug, to be effectively removed from the stent, thereby exposing the drug. This is followed by permitting the drug to migrate from the stent for interaction with the patient.

[0058] In some situations it may be desirable to make the prosthesis in manner so that at least first and second biologically active agents are carried by the prosthesis and released in a manner so that at least some of the first agent, for example at least half, is released prior to the start of the release of the second agent. This can be accomplished in several ways. A protective coat 143 may be placed between layers of the biologically active agent. The first agent may be applied over the second agent to cover, and thus initially prevent the release of, the second agent. One or both of the agents may be encapsulated in biodegradable coverings so to be released only after a period of time.

[0059] Coiled stent graft 122 includes a number of spaced apart turns 128 defining a generally helical gap 130 therebetween. The average width of helical gap 130 is equal to about 0% to 1200% of the average width of turns 128. For some applications the average width of gap of 130 is about 50% to 800% of the average width of turns 128 when stent graft 122 is deployed. For other applications, such as placement at dissections discussed below, gap 130 is closed, that is about 0%.

[0060] Stent graft 122 has a generally constant pitch except at its central region. The pitch of a central turn 132 of stent graft 122 is substantially greater than the pitch of its adjacent turns 128 to accommodate placement of stent graft 122 at the intersection of a main or first vessel and a branching vessel as will be discussed in more detail with reference to Figs. 7A-7C.

[0061] Fig. 4 illustrates a stent graft 122A in which a central turn 132A also has an increased pitch as opposed to adjacent turns 128A. However, the turns on one side of central turn 132A have a larger fully-expanded diameter than turns on the other side to accommodate transition between smaller and larger diameter vessels.

[0062] Fig. 5 illustrates a stent graft 122B designed for placement with the end turn 134 having a substantially greater pitch than its adjacent turn 128B. Stent graft 122B is used when one end of the stent graft is to be positioned at the intersection of main and branching vessels so that the stent graft extends to one side of the intersection as opposed to both sides as in the embodiments of Figs. 3 and 4. Fig. 5A illustrates stent graft 122C, which may be used at locations other than bifurcations, having generally uniformly spaced turns 128C.

[0063] Figs. 5B and 5C illustrate stent grafts 122C, 112D each made from stent blank 104D of Fig. 1C. Stent grafts 122C, 122D are designed and intended to have the edges 135 of adjacent turns 137 adjacent to one another. Such stent grafts as Figs. 5B and 5C are intended for use in treating aortic dissections. The combination of having the width of each turn being relatively wide compared to the diameter when in the radial expanded condition, plus the use of abutting or overlapping adjacent edges, combine to make such a stent graft useful when full surface coverage and reasonably higher outward radial force are desired. The width of turns 137 is measured perpendicular to edges 135. Also, fewer turns can make the stent graft easier to control and require fewer rotations of shafts 138, 142 prior to release from catheter 136. Stent grafts 122C, 122D may be characterized by having an average diameter to turns-width ratio, when in their radially expanded conditions, from about 0.1 to 1 to about 2.4 to 1. Stent grafts 122C, 122D may also be characterized by having an average turns-width to stent graft length ratio, when in their radially expanded conditions, from about 1 to 1 to about 1 to 4. In some situations it may not be necessary or desired to have connectors 112 be axially extending when in the tightly wound, radially contracted condition. In some cases connectors 112 could be replaced by other shapes of connectors, such as wave- or undulating-shaped connectors, v-shaped connectors, x-shaped connectors, etc.

[0064] Figs. 6A-6B illustrate a catheter 136 used for deploying the stent grafts of Figs. 3 and 4. Catheter 136 includes outer, intermediate and inner rotating, telescoping shafts 138, 140, 142 each having a distal end 144, 146, 148. Each of the shafts has a prosthesis portion holder 150, 150A, 150B at its distal end 144, 146, 148. Prosthesis portion holders 150, 150A, 150B include pull wires 152, 152A, 152B which pass along axially-extending lumens 154, 154A, 154B formed in the body of shafts 138, 140, 142, out of exit holes 156, 156A, 156B, across gaps 158, 158A, 158B and back into reinsertion openings 160, 160A, 160B. Pull wires 152, 152A, 152B pass

through and engage different portions of, for example, stent graft 122 and secure those portions of the stent graft to shafts 138, 140, 142. As shown in Fig. 7A, prosthesis portion holder 150B at distal end 148 of inner shaft 142 engages the distal end 166 of stent graft 122. Holders 150, 150A at distal ends 144, 144A of outer and intermediate shafts 138, 140 engage proximal end 168 and central turn 132 of stent graft 122, respectively. One or more of shafts 138, 140, 142 may be braided to enhance torquing stiffness to aid rotation.

[0065] Fig. 6C illustrates the distal end of a catheter 136A including only two shafts, outer shaft 138A and inner shaft 142A. Catheter 136A is typically used when placing an endoluminal prosthesis of the type which does not have a central turn with an increased pitch, such as those of Figs. 5, 5A, 5B and 5C, and thus does not need a catheter with an intermediate shaft.

[0066] Figs. 6D illustrates, in a simplified form, a proximal end adapter 170 mounted to the proximal end of catheter 136A of Fig. 6C. Proximal end adapter 170 includes distal and proximal portions 172, 176 through which catheter 136A passes. Proximal end adapter 170 provides for the rotation of either or both shafts 138A, 142A through the manipulation of thumb wheel 174 mounted to portion 176. A flip lever 175 extends from distal portion 172 and is movable between secured and released positions to either secure shafts 138A, 142A to one another or to permit shafts 138A, 142A to move axially relative to one another. Pull wires 152, 152B are normally secured to their respective shafts 138A, 142A by deployment knobs 178, 180; pulling on deployment knobs 178, 180 releases pull wires 152, 152B, respectively to permit the pull wires to be pulled to release the endoluminal prosthesis from the appropriate holder 150, 150B.

[0067] Figs. 6F and 6G illustrate a further three-shaft embodiment of the invention similar to the three -shaft embodiment of Figs. 6A and 6B. Instead of using lumens 154 to house pull wires 152, tubular members 162, 162A, 162B, typically hypotubes, could be secured to the outside of the shafts 138B, 140B, 142B. Gaps or breaks are provided at the distal ends of hypotubes 162, 162A, 162B to define the gaps 158, 158A, 158B.

[0068] Fig. 7A shows stent graft 122 of Fig. 3 tightly wrapped about catheter 136. Distal end 166, proximal end 168 and central turn 132 of stent graft 122 are secured to distal ends 148, 144 and 146 of inner, outer and intermediate shafts 142, 138 140 by prosthesis portions holders 150. Stent graft 122 is housed within a main vessel 182 with central turn 132 aligned with the intersection 184 of main vessel 182 and branching vessel 186. To help ensure proper placement of central turn 132 at intersection 184, stent graft 122 has one or more remote visualization markers at or adjacent to turn 132. Radiopaque markers 188, 190 192 are shown in Fig. 8 at distal, intermediate and proximal portions of the central turn 194 of stent 196. Radiopaque

markers may be shaped to provide information as to both location and orientation of stent 196 on the catheter. For example, radiopaque marker 190A of Fig. 9 has a broad central portion 190B extending between rail elements 110 and arm portions 190C extending along rail elements 110; this permits marker 190A to provide both location and orientation information about stent 196A. Orientation marker 190A is configured so that the viewer can determine whether the turn is facing the viewer or is away from the viewer based upon the marker's orientation. Various other marker shapes to provide both location and orientation can also be used.

[0069] Radiopaque markers may also be used on the placement catheter itself. For example, radiopaque markers 191, 193, 195 are used on shafts 138B, 140B, 142B aligned with their respective holders 150, 150A, 150B, as shown in Fig. 6F, to indicate the location of the holders. Radiopaque marker 193 is shown to be configured as an orientation specific marker to help in the proper placement of the prosthesis. Fig. 10 illustrates the shape of an orientation-specific radiopaque marker 197 which could be placed, for example, on shafts 138, 140, 142 at one or more of the holders 150 of the embodiments of Figs. 6A, 6C and 6E. Radiopaque or other remote visualization markers may also be used at other positions along the endoluminal prosthesis, such as at each end, or along the placement catheter.

[0070] Fig. 7B illustrates the release of proximal end 168 of stent graft 122 while Fig. 7C illustrates the subsequent release of distal end 166 of stent graft 122. It should be noted that central turn 132 remains secured to intermediate shaft 140 while the distal and proximal ends 166, 168 of stent graft 122 are released to ensure that the open region of central turn 122 remains facing intersection 184 to help ensure substantially unrestricted fluid flow between main vessel 182 and branching vessel 186. It should also be noted that prior to releasing the stent graft, the number of turns can be increased or decreased by the relative rotation of shafts 138, 140 and 142. Also, the length of stent graft 122 can be changed by the relative axial sliding motion among outer, intermediate and inner shafts 138, 140, 142. For example, instead of simply releasing proximal end 168 of stent graft 122 to the position shown in Fig. 7B, it may be desired to rotate outer shaft relative to intermediate shaft 140, keeping intermediate and inner shafts 140, 142 stationary so to unwind the proximal half of the stent graft to ensure that the stent graft is properly positioned prior to releasing the stent graft. Similarly, both outer shaft and inner shafts can be rotated while maintaining intermediate shaft stationary to create the expanded diameter condition of Fig. 7 prior to releasing any portion of the stent graft. In this way the physician can ensure that stent graft 122 is properly positioned, especially with respect to central turn 132. If necessary or desired, intermediate shaft 140 could be, for example, rotated relative to outer and inner shafts 138, 142 to help properly position or reposition central turn 132.

[0071] Fig. 7A also shows how by properly selecting the angle of connector elements 112 relative to side elements 110 for a placement catheter of a particular outside diameter, connector elements 112, indicated by dashed lines in Fig. 7A, will lie generally parallel to the axis of stent graft 122. This permits connector element 112 to lie closer to catheter 136, to provide a much smoother wrap when in its contracted, reduced-diameter state, than would result if connector elements were not generally parallel to the axis in such a state. This axial orientation can be contrasted with the off-axis orientation of connectors 112 when in the expanded diameter state of Fig. 7C. The smoother outer surface of stent graft 122 enhances the ease of insertion of the stent graft within a hollow body organ, such as blood vessel 182.

[0072] Fig. 7D illustrates stent graft 122D of Fig. 5C tightly wrapped about placement catheter, 136A of Fig. 6C with the proximal end of stent graft 122D secured to outer catheter shaft 138A and the distal end of stent graft 122D secured to inner catheter shaft 142A. Fig. 7E illustrates the structure of Fig. 7D after pull wire 152B has been pulled to release the distal end of stent graft 122D. Soon thereafter pull wire 152 will be pulled to release the proximal end of stent graft 122D from outer catheter shaft 138A. Because of the width of each turn of stent graft 122D, each pull wire 152, 152B passes through two positions 199 along an end of stent graft 122D to ensure that the stent graft lies tightly against catheter 136A during delivery.

[0073] As discussed above, stent graft 122D is placed in a radially contracted condition by rotating inner and outer catheter shafts 138A ,142A relative to one another. Once in position for deployment, catheter shafts 138A, 142A are rotated relative to each other to open stent graft 122D. Shafts 138A, 142A can also be moved longitudinally (axially) relative to one another to allow one to change the pitch and ensure that edges 135 of turns 137 of stent graft 122 will be adjacent to one another when fully deployed, as is often desired. At any point the operator can decide to retighten stent graft 122D, placing it in a radially contracted condition, to reposition the stent graft or change the pitch so long as pull wires 152, 152B have not been removed from the ends of the stent graft. Proper placement of the graft 122D, including ensuring that the edges lie adjacent to one another, can be aided by the used of radiopaque markers 121. See Fig. 1E.

[0074] Fig. 11 illustrates the placement of stent graft 122C within the true lumen 200 of an aortic arch 202 so to cover the entry 204 into a false lumen 206 created by an aortic dissection 208. Aortic dissections are of various type but all include a false lumen caused by separation of the lining, such as intimal lining 210, from the remainder of the wall, such as wall 212 of the hollow body structure, together with an entry formed through the separated lining into the false lumen. Aortic dissections, as well as other dissections, may be of the type with a single entry 204 or may include, for example, an entry and an exit. An alternative dissection 208A is

suggested by the dashed lines in Fig. 11 indicating an extension of aortic dissection 208 from the solid line portion down to an exit 214 adjacent bifurcation 216. While it may be possible to close both entry 204 and exit 214 using one or more stent grafts, it may not be necessary or desirable. Also, it may not be necessary to cover either the entrance and/or any exit to a false lumen with the stent graft to effectively treat the dissection. Stent graft 122C also has dashed lines indicating the locations of rail elements 110 and connector elements 112 of the stent.

[0075] Stent graft 122C is used with a thoracic level aortic dissection. Stent grafts may be used with dissections at other levels along aorta 218, such as at the abdominal level 220 or along the arch 222. When a stent graft is used at arch 222, or at other hollow body regions with one or more branches, stent grafts having one or more enlarged gaps, see Figs. 3, 4 and 7C, may be used to help prevent obstruction of the branching vessel.

[0076] Stent grafts, such as those of Figs. 5B and 5C, may be used to help repair various dissections other than aortic dissections. In particular, such stent grafts may be used for other types of vascular dissections and dissections in other hollow body organs within which dissections may be found. The dissections may be created as a result of non-penetrating trauma or invasive trauma as well as biological reasons, such as disease, stress, congenital disorders, etc.

[0077] Modification and variation can be made to the above described invention without departing from the subject of the invention as defined in the following claims. For example, connectors 112 could be oriented perpendicular to rail elements 110, graft material 124 could be placed upon only a portion of the underlying stent or on only one side of the underlying stent. Placement catheter 136 could include fewer or additional telescoping rotatable shafts. The telescoping shafts may not need to be coaxial shafts slidable within or over one another; the telescoping shafts could be, for example, solid and/or tubular elongate members positioned side-by-side. Holders 150 could be constructed differently; for example, if the sequence of releasing the prosthesis is known it may be possible to use a single pull wire instead of three separate pull wires.

[0078] Any and all patents, applications, and printed publications referred to above are incorporated by reference.

CLAIMS

1. A prosthesis, for use within a hollow body structure of a patient, comprising:

a coiled body having radially-extending openings formed therethrough, the body movable from a radially-contracted state to a radially-expanded state;

a material extending along a coiled path along the entire coiled body; and

a dispensable, biologically active agent associated with at least one of the coiled body and the material, said dispensable agent being dispensable into a hollow body structure of a patient.

2. The prosthesis according to claim 1 further comprising a delay-release material associated with the dispensable agent to delay the release of the dispensable agent into the hollow body structure.

3. The prosthesis according to claim 2 wherein the delay-release material comprises a biodegradable, delay-release layer.

4. The prosthesis according to claim 1 wherein the dispensable agent is microencapsulated using a biodegradable encapsulation material so as to delay migration of said drug from said prosthesis.

5. The prosthesis according to claim 1 further comprising removing a protective layer from said coiled body and material there with so that when removed, said dispensable agent may migrate from said prosthesis.

6. The prosthesis according to claim 5 wherein the protective layer comprises a biodegradable material so that said protective layer is removed when it biodegrades.

7. The prosthesis according to claim 5 wherein the protective layer comprises a sheath which can be pulled off the coiled body and material there with to remove the protective layer therefrom.

8. The prosthesis according to claim 1 wherein said body has longitudinally extending side members and cross members connecting said side members.

9. The prosthesis according to claim 1 wherein said body is made of metal.

10. The prosthesis according to claim 1 wherein said prosthesis comprises spaced apart turns defining gaps therebetween when in the radially-expanded state.

11. The prosthesis according to claim 1 wherein the prosthesis comprises turns, adjacent ones of said turns touching one another when in the radially-expanded state.

12. The prosthesis according to claim 1 wherein the material comprises a coiled sleeve of material having inner and outer surfaces, said inner surface defining a sleeve interior containing the entire coiled body.

13. The prosthesis according to claim 12 wherein the agent is located at and is dispensable from at least the following location: on the outer surface of the material, the outer surface being placeable against the hollow body structure when the body is in the radially-expanded state so the material may be located at and dispensable from only locations of intimate contact with the hollow body structure.

14. The prosthesis according to claim 12 wherein the agent is located at and is dispensable from at least the following location: incorporated into the material to create an agent/material matrix.

15. The prosthesis according to claim 12 wherein the agent is located at and is dispensable from at least the following location: on the inner surface of the material.

16. The prosthesis according to claim 12 wherein the agent is located at and is dispensable from at least the following location: within the sleeve interior.

17. The prosthesis according to claim 1 wherein the material has a radially-inwardly facing inner surface and a radially-outwardly facing outer surface, and material surrounding the body with said inner surface adjacent to the body and the outer surface placeable against the hollow body structure when the body is in the radially-expanded state.

18. The prosthesis according to claim 12 wherein the agent is located at and is dispensable from the outer surface of the material so to be located at and dispensable from only locations of intimate contact with the hollow body structure.

19. The prosthesis according to claim 1 further comprising first and second dispensable agents.

20. The prosthesis according to claim 19 wherein said first agent is layered on top of said second agent.

21. The prosthesis according to claim 19 wherein said first agent is dispensable prior to the start of dispensing of the second agent.

22. The prosthesis according to claim 19 wherein at least half of said first agent is dispensable prior to the start of dispensing of the second agent.

23. The prosthesis according to claim 1 wherein said material is a porous material.

24. The prosthesis according to claim 23 wherein said porous material comprises porous PTFE.

25. The prosthesis according to claim 23 wherein said porous material has an inner surface which is substantially impervious to the passage of blood therethrough.

26. The prosthesis according to claim 1 wherein the dispensable agent is selected from the group comprising: anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, anti-proliferative drugs, apoptosis-inducing drug, light activated drug, and biological materials.

27. The prosthesis according to claim 1 wherein the dispensable agent comprises an anti-restenotic agent.

28. A prosthesis, for use within a hollow body structure of a patient, comprising:

a coiled body having radially-extending openings formed therethrough, the body movable from a radially-contracted state to a radially-expanded state;

a coiled sleeve of material extending along a coiled path, the material having an inner surface and an outer surface and defining the sleeve interior containing the coiled body; and

a dispensable, biologically active agent on said outer surface of the material, said dispensable agent being dispensable into a hollow body structure of a patient.

29. The prosthesis according to claim 28 wherein the dispensable agent comprises an anti-restenotic agent.

30. The prosthesis according to claim 28 further comprising a delay-release material associated with the dispensable agent to delay the release of the dispensable agent into the hollow body structure.

31. The prosthesis according to claim 28 wherein said prosthesis comprises spaced apart turns defining gaps therebetween when in the radially-expanded state.

32. The prosthesis according to claim 28 wherein said material comprises porous PTFE.

33. A prosthesis, for use within a hollow body structure of a patient, comprising:

a coiled body having radially-extending openings formed therethrough, the body movable from a radially-contracted state to a radially-expanded state;

a coiled sleeve of material extending along a coiled path, the material having an inner surface and an outer surface and defining the sleeve interior containing the coiled body; and

a dispensable, biologically active agent incorporated into the material to create an agent/material matrix, said dispensable agent being dispensable into a hollow body structure of a patient.

34. The prosthesis according to claim 33 wherein the dispensable agent comprises an anti-restenotic agent.

35. The prosthesis according to claim 33 further comprising a delay-release material associated with the dispensable agent to delay the release of the dispensable agent into the hollow body structure.

36. The prosthesis according to claim 33 wherein said prosthesis comprises spaced apart turns defining gaps therebetween when in the radially-expanded state.

37. The prosthesis according to claim 33 wherein said material comprises porous PTFE.

38. A prosthesis, for use within a hollow body structure of a patient, comprising:

a coiled body having radially-extending openings formed therethrough, the body movable from a radially-contracted state to a radially-expanded state;

a coiled sleeve of material extending along a coiled path, the material having an inner surface and an outer surface and defining the sleeve interior containing the coiled body; and

a dispensable, biologically active agent on said inner surface of the material or within the sleeve interior, said dispensable agent being dispensable into a hollow body structure of a patient.

39. The prosthesis according to claim 38 wherein the dispensable agent comprises an anti-restenotic agent.

40. The prosthesis according to claim 38 further comprising a delay-release material associated with the dispensable agent to delay the release of the dispensable agent into the hollow body structure.

41. The prosthesis according to claim 38 wherein said prosthesis comprises spaced apart turns defining gaps therebetween when in the radially-expanded state.

42. The prosthesis according to claim 38 wherein said material comprises porous PTFE.

43. A method for delivering a biologically active agent to a target site within a hollow body structure of a patient, comprising:

delivering a coiled prosthesis to a target site within a hollow body structure of a patient, the prosthesis being in a radially-contracted state, the prosthesis comprising a coiled body having radially-extending openings formed therethrough, a material extending along a coiled path along the entire coiled body, and a dispensable, biologically active agent associated with at least one of the coiled body and the material;

radially expanding the prosthesis from the radially-contracted state to a radially-expanded state so to press the prosthesis against a wall of the hollow body structure; and

releasing the agent into the hollow body structure.

44. The method according to claim 43 further comprising selecting a prosthesis comprising a coiled body having longitudinally extending side members and cross members connecting said side members.

45. The method according to claim 43 wherein the radially expanding step is carried out with a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

46. The method according to claim 43 wherein the radially expanding step is carried out with a prosthesis comprising turns which touch one another when in the radially-expanded state.

47. The method according to claim 43 further comprising selecting a prosthesis in which the material comprises a coiled sleeve of material, said coiled sleeve of material having inner and outer surfaces, said inner surface defining a sleeve interior containing the entire coiled body.

48. The method according to claim 43 further comprising selecting a prosthesis in which the agent comprises first and second dispensable agents.

49. The method according to claim 48 further comprising selecting a prosthesis having said first agent layered on top of said second agent.

50. The method according to claim 48 wherein the releasing step is carried out so that at least a portion of said first agent is released prior to the start of release of the second agent.

51. The method according to claim 48 wherein the controllably releasing step is carried out so that at least half of said first agent is released prior to the start of release of the second agent.

52. The method according to claim 43 further comprising selecting a prosthesis comprising porous material as said material.

53. The method according to claim 52 wherein the selecting step is carried out by selecting a prosthesis with said porous material comprising ePTFE.

54. The method according to claim 52 wherein the selecting step is carried out by selecting a prosthesis with said porous material has a surface which is substantially impervious to the passage of blood therethrough.

55. The method according to claim 43 further comprising selecting a prosthesis having a delay-release material associated with the dispensable agent.

56. The method according to claim 55 wherein the selecting step is carried out by selecting a prosthesis in which the delay-release material comprises a biodegradable, delay-release material.

57. The method according to claim 55 wherein the selecting step is carried out by selecting a prosthesis in which the delay-release material comprises a delay-release layer covering the dispensable agent.

58. The method according to claim 55 wherein the selecting step is carried out by selecting a prosthesis in which the delay-release material is a component of a matrix of the dispensible agent and the delay-release material.

59. The method according to claim 55 wherein the selecting step is carried out by selecting a prosthesis in which the delay-release material comprises a biodegradable polymer.

60. The method according to claim 55 wherein the delay-release material comprises a protective layer, and further comprising removing the protective layer from the coiled body and material therewith thereby exposing the coiled body and material therewith.

61. The method according to claim 43 further comprising selecting a prosthesis comprising a dispensable agent selected from the group comprising: anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, anti-proliferative drugs, apoptosis-inducing drug, light activated drug, and biological materials.

62. The method according to claim 43 further comprising selecting an anti-restenotic agent as the dispensable agent.

63. A method for delivering a biologically active agent to a target site within a hollow body structure of a patient, comprising:

delivering a coiled prosthesis to a target site within a hollow body structure of a patient, the prosthesis being in a radially-contracted state, the prosthesis comprising a coiled body having radially-extending openings formed therethrough, a coiled sleeve of material extending along a coiled path, the coiled sleeve of material comprising inner and outer surfaces, said inner surface defining a sleeve interior containing the entire coiled body, and a dispensable, biologically active agent on the outer surface of the material;

radially expanding the prosthesis from the radially-contracted state to a radially-expanded state so to press the prosthesis against the wall; and

releasing the agent from the outer surface of the material and into the hollow body structure.

64. The method according to claim 63 further comprising selecting an anti-restenotic agent as the dispensable agent.

65. The method according to claim 63 wherein the releasing step comprises temporally controllably releasing the agent into the hollow body structure.

66. The method according to claim 63 wherein the radially expanding step is carried out with a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

67. The method according to claim 63 further comprising selecting a prosthesis comprising porous PTFE as said material.

68. A method for delivering a biologically active agent to a target site within a hollow body structure of a patient, comprising:

delivering a coiled prosthesis to a target site within a hollow body structure of a patient, the prosthesis being in a radially-contracted state, the prosthesis comprising a coiled body having radially-extending openings formed therethrough, a coiled sleeve of material extending along a coiled path, the coiled sleeve of material comprising inner and outer surfaces, said inner surface defining a sleeve interior containing the entire coiled body, and a dispensable, biologically active agent incorporated into the material to create an agent/material matrix;

radially expanding the prosthesis from the radially-contracted state to a radially-expanded state so to press the prosthesis against the wall; and

releasing the agent from the agent/material matrix and into the hollow body structure.

69. The method according to claim 68 further comprising selecting an anti-restenotic agent as the dispensable agent.

70. The method according to claim 68 wherein the releasing step comprises temporally controllably releasing the agent into the hollow body structure.

71. The method according to claim 68 wherein the radially expanding step is carried out with a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

72. The method according to claim 68 further comprising selecting a prosthesis comprising porous PTFE as said material.

73. The method according to claim 68 further comprising selecting a prosthesis in which the material comprises a coiled sleeve of material, said coiled sleeve of material having inner and outer surfaces, said inner surface opposite said coiled body, said inner surface defining a sleeve interior containing the entire coiled body.

74. A method for delivering a biologically active agent to a target site within a hollow body structure of a patient, comprising:

delivering a coiled prosthesis to a target site within a hollow body structure of a patient, the prosthesis being in a radially-contracted state, the prosthesis comprising a coiled body having radially-extending openings formed therethrough, a coiled sleeve of material extending along a coiled path, the coiled sleeve of material comprising inner and outer surfaces, said inner surface

defining a sleeve interior containing the entire coiled body, and a dispensable, biologically active agent on the inner surface of the material or within the sleeve interior;

radially expanding the prosthesis from the radially-contracted state to a radially-expanded state so to press the prosthesis against the wall; and

releasing the agent from the inner surface of the material and into the hollow body structure.

75. The method according to claim 74 further comprising selecting an anti-restenotic agent as the dispensable agent.

76. The method according to claim 74 wherein the releasing step comprises temporally controllably releasing the agent into the hollow body structure.

77. The method according to claim 74 wherein the radially expanding step is carried out with a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

78. The method according to claim 74 further comprising selecting a prosthesis comprising porous PTFE as said material.

79. A method for making a prosthesis for use at a target site within a hollow body structure of a patient comprising:

determining at least one therapy for a patient;

selecting a prosthesis suitable for said at least one therapy, said prosthesis comprising a coiled body having radially-extending openings formed therethrough, a material extending along a coiled path along the entire coiled body, and first and second dispensable, biologically active agents for said therapy, said first and second agents being associated with at least one of said coiled body and said material; and

said selecting step being carried out so that at least some of said first agent is releasable at a target site within a hollow body structure of a patient prior to the start of the release of the second agent at the target site.

80. The method according to claim 79 wherein the selecting step is carried out by selecting a prosthesis with a porous material as said material.

81. The method according to claim 80 wherein the selecting step is carried out with the porous material comprising ePTFE.

82. The method according to claim 80 wherein the selecting step is carried out by selecting a prosthesis with said porous material having a surface which is substantially impervious to the passage of blood therethrough.

83. The method according to claim 79 wherein the selecting step is carried out by selecting a prosthesis having said first agent layered on top of said second agent.

84. The method according to claim 79 wherein said to selecting step is carried out so that said first agent is releasable or over a first period and said second agent is releasable over a second period, said first and second periods at least partially overlapping.

85. The method according to claim 79 wherein the selecting step is carried out by selecting a prosthesis having a delay-release material associated with at least one of the first and second agents.

86. The method according to claim 85 wherein the selecting step is carried out by selecting a prosthesis in which the delay-release material comprises a biodegradable, delay-release layer.

87. The method according to claim 79 wherein the selecting step comprises selecting a prosthesis comprising dispensable agents selected from the group comprising: anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, anti-proliferative drugs, apoptosis-inducing drug, light activated drug, and biological materials.

88. The method according to claim 79 further comprising selecting anti-restenotic agents as the dispensable agents.

89. The method according to claim 79 wherein the selecting step comprises selecting a prosthesis in which the material comprises a coiled sleeve of material, said coiled sleeve of material having inner and outer surfaces, said inner surface defining a sleeve interior containing the entire coiled body, the selecting step being carried out with the agents being releasable from at least one of the following locations: the outer surface of the material, incorporated into the material to create an agent/material matrix, on the inner surface of the material, and within the sleeve interior.

90. The method according to claim 79 wherein the selecting step comprises selecting a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

91. A method for making a prosthesis for use at a target site within a hollow body structure of a patient comprising:

placing a length of a material in contact with a mixture of a carrier and a dispensable, biologically active agent;

removing at least a substantial portion of the carrier from the mixture leaving said agent in contact with the material to create an agent-laden material;

combining the agent-laden material with a radially-expandable stent to create a prosthesis suitable for use within a hollow body structure of a patient.

92. The method according to claim 91 wherein the placing step is carried out using a porous material as the material.

93. The method according to claim 92 wherein the placing step is carried out with the porous material comprising ePTFE.

94. The method according to claim 92 further comprising selecting a length of porous sleeve material as said porous material, said porous sleeve material comprising inner and outer surfaces, said inner surface defining a sleeve interior containing the entire stent following the combining step.

95. The method according to claim 94 wherein said placing step is carried out by placing said mixture into said sleeve interior.

96. The method according to claim 95 wherein the selecting step is carried out using a sleeve material having open ends, and the placing step comprises at least temporarily sealing one said open end.

97. The method according to claim 91 wherein said removing step is carried out by draining away excess amounts of said mixture and then at least partially drying said length of material.

98. The method according to claim 91 further comprising selecting an agent from the group comprising: anti-inflammatory drugs, anti-thrombotic/anti-platelet drugs, anti-proliferative drugs, apoptosis-inducing drug, light activated drug, and biological materials.

99. The method according to claim 91 further comprising selecting an anti-restenotic agent as the biologically active agent.

100. The method according to claim 91 wherein the combining step is carried out with a prosthesis comprising spaced apart turns defining gaps therebetween when in the radially-expanded state.

101. A covered, coiled drug delivery stent comprising:

a coiled, radially-expandable stent body comprising an outer surface;

a porous covering overlying the outer surface;

a drug associated with the porous covering; and

said stent, porous covering and drug constituting a stent subassembly.

102. The covered stent according to claim 101 wherein the stent body comprises spaced-apart parallel side elements joined by connector elements.

103. The covered stent according to claim 101 wherein the stent body is made of metal.

104. The covered stent according to claim 101 wherein the stent body is made of nickel-titanium.

105. The covered stent according to claim 101 wherein the porous covering comprises ePTFE.

106. The covered stent according to claim 101 wherein the drug and the porous covering comprises a drug/porous covering matrix.

107. The covered stent according to claim 101 wherein the drug is situated between the outer surface and the porous covering.

108. The covered stent according to claim 101 wherein the drug overlies the porous covering.

109. The covered stent according to claim 101 further comprising means for delaying migration of said drug from said stent subassembly.

110. The covered stent according to claim 109 wherein the drug migration delaying means comprise a drug/biodegradable material matrix wherein said drug is interspersed within a biodegradable material.

111. The covered stent according to claim 101 wherein the drug is micro-encapsulated using a biodegradable encapsulation material so as to delay migration of said drug from the stent subassembly.

112. The covered stent according to claim 101, further comprising a removable protective layer covering said stent subassembly so that when removed, said drug may migrate from said stent subassembly.

113. The covered stent according to claim 112 wherein the protective layer comprises a biodegradable material so that said protective layer is removed when it biodegrades.

114. The covered stent according to claim 113 wherein the biodegradable material comprises a biodegradable polymer.

115. The covered stent according to claim 112 wherein the protective layer comprises a sheath which can be pulled off of the stent subassembly to remove protective layer from the stent subassembly.

116. The covered stent according to claim 101 wherein the drug comprises one or more of the following:

NO generators, paclitaxel, statins, taxol, heparin in its various forms, i.e., low molecular weights, thienopyridines, glycoprotein IIb/IIIb inhibitors, antiplatelet agents, antithrombins, fibrinolytics, anticoagulants, thrombolytics, abciximab, rapamycin, hirudin, VEGF, Hirulog, ticlopidine and clopidogrel.

117. The covered stent according to claim 101 wherein the drug comprises taxol.

118. The covered stent according to claim 101 wherein the drug comprises heparin.

119. The covered stent according to claim 101 wherein the drug comprises rapamycin.

120. A covered, coiled drug delivery stent comprising:

a coiled, radially-expandable stent body comprising spaced-apart parallel side elements joined by connector elements and an outer surface;

a porous covering, comprising ePTFE, overlying the outer surface;

a drug associated with the porous covering;

said stent body, porous covering, and drug constituting a stent subassembly; and

a biodegradable protective layer covering said stent subassembly so that when said protective layer biodegrades, said drug may migrate from said stent subassembly.

121. A method for delivering a drug to a patient comprising:

directing a covered, coiled stent subassembly, comprising a drug associated with a porous covering which overlies a coiled, radially-expandable prosthesis, to a target site within a patient;

waiting for a protective material, initially shielding the drug, to be effectively removed from said stent subassembly thereby exposing said drug; and

permitting said the drug to migrate from said stent subassembly for interaction with the patient.

122. The method according to claim 121 wherein the directing step is carried out using a drug comprising at least one of the following:

NO generators, hirudin, Paclitaxel, Rapmycin, statins, taxol, heparin in its various forms, i.e., low molecular weights, thienopyridines, glycoprotein IIb/IIIb inhibitors, antiplatelet agents, antithrombins, fibrinolytics, anticoagulants, thrombolytics, abciximab, rapamycin, hirudin, VEGF, Hirulog, Ticlopidine and clopidogrel.

123. The method according to claim 121 wherein the directing step is carried out with the drug at at least one of the following locations: underlying the porous covering, overlying the porous covering and incorporated into the porous covering to create a drug/porous covering matrix.

124. The method according to claim 121 wherein the waiting step comprises waiting for a biodegradable material, initially enclosing the drug, to biodegrade thus exposing the drug.

125. The method according to claim 121 wherein the waiting step comprises waiting for the protective layer covering the subassembly to biodegrade.

126. The method according to claim 121 wherein the waiting step comprises waiting for a protective covering the subassembly to be at least partially pulled off of the stent.

127. The method according to claim 121 further comprising removing the stent subassembly from the patient following the permitting step.

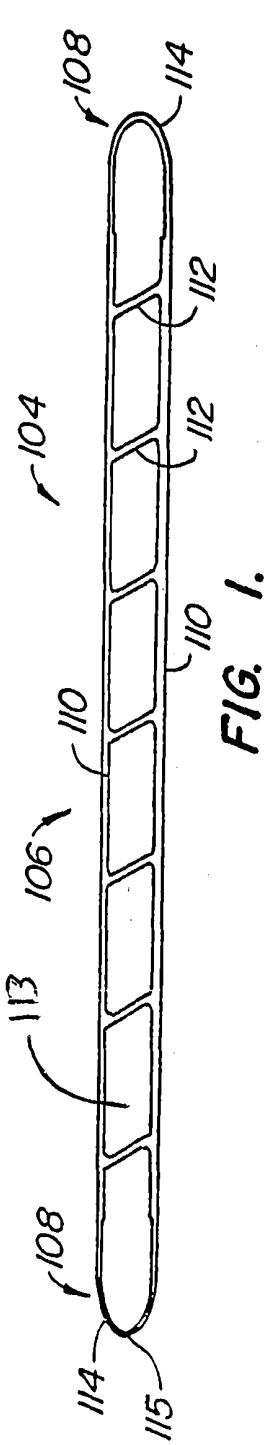

FIG. 1.

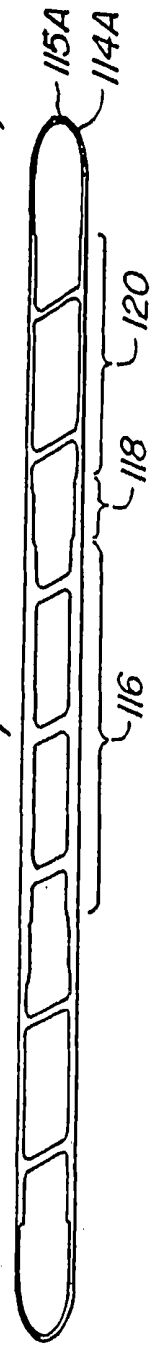

FIG. 2.

FIG. 5A.

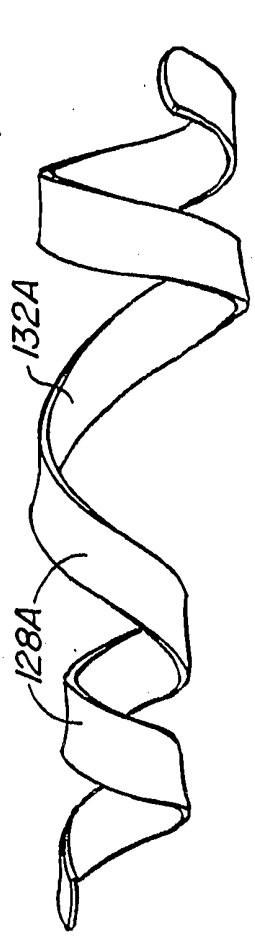

FIG. 4.

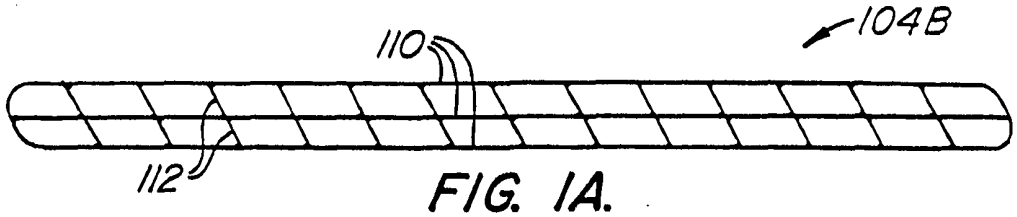

FIG. 1A.

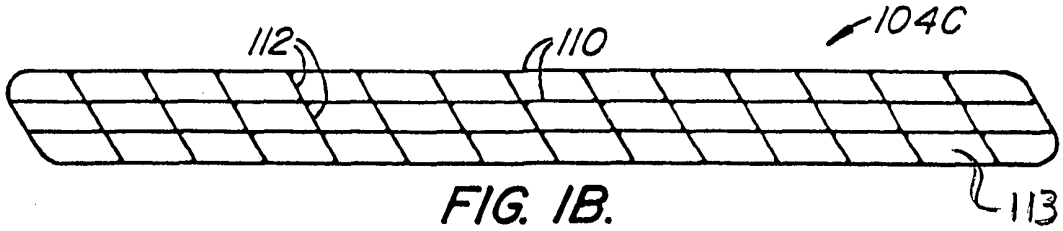

FIG. 1B.

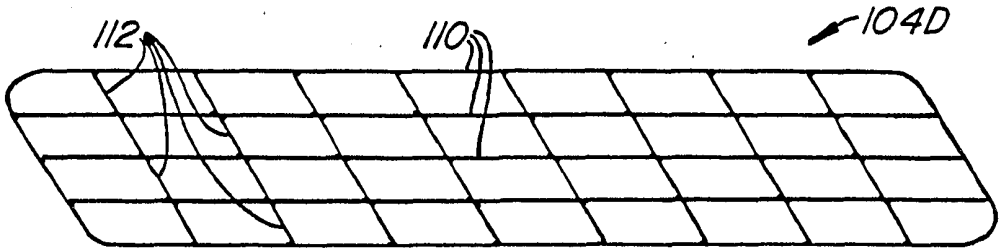

FIG. 1C.

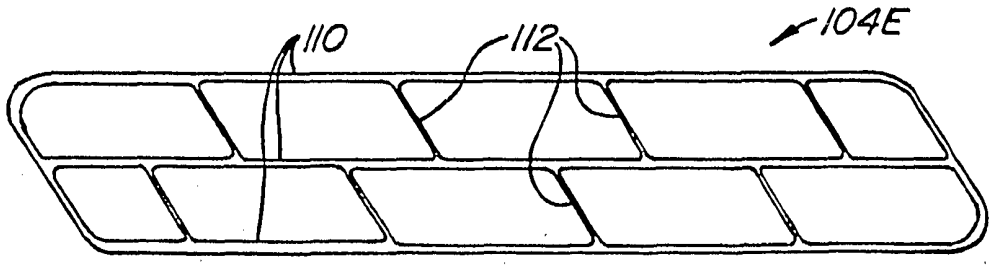

FIG. 1D.

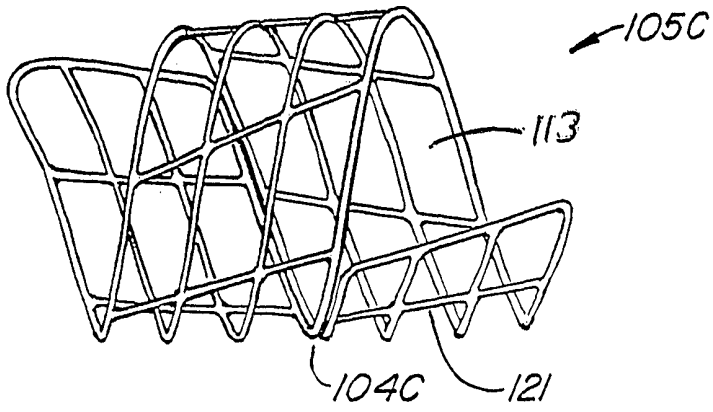

FIG. 1E.

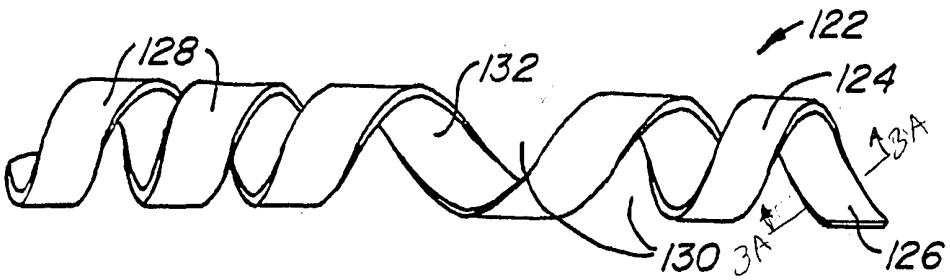

FIG. 3.

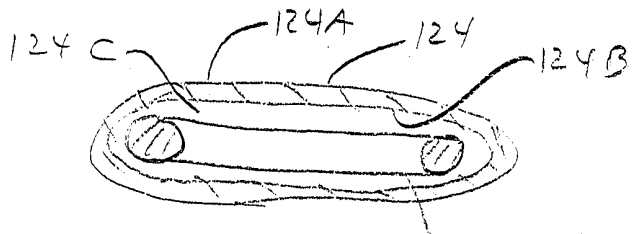

FIG. 3A

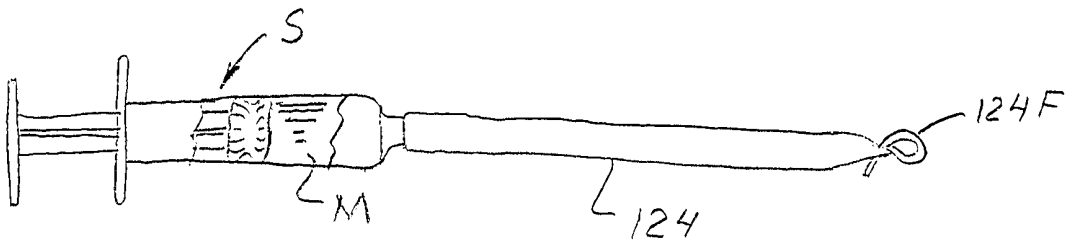

FIG. 3B

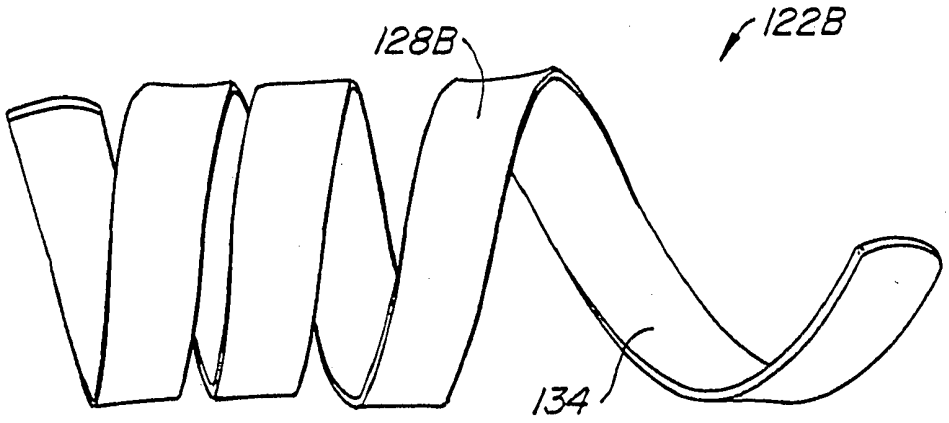

FIG. 5.

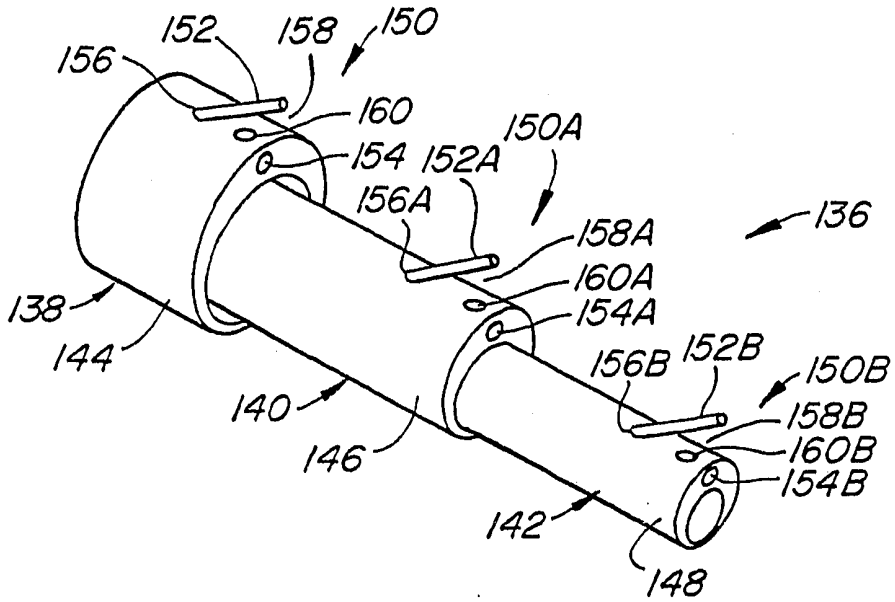

FIG. 6A.

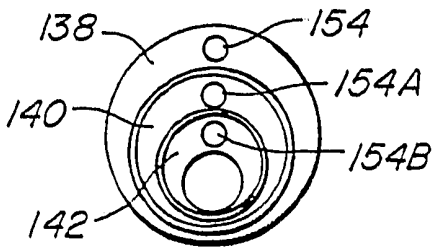

FIG. 6B.

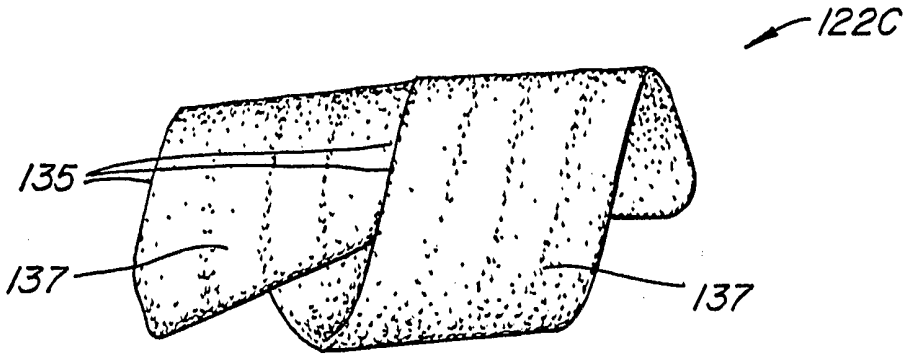

FIG. 5B.

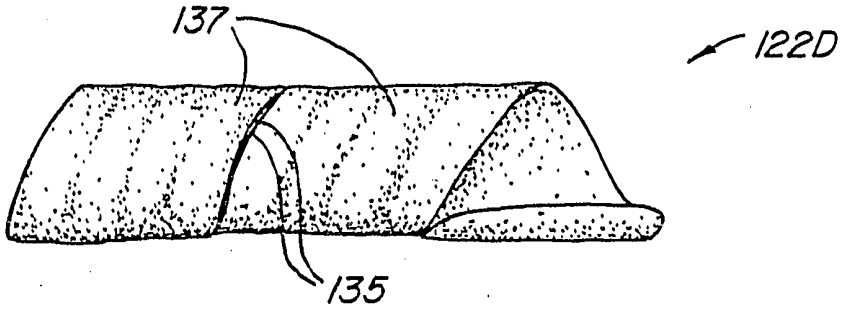

FIG. 5C.

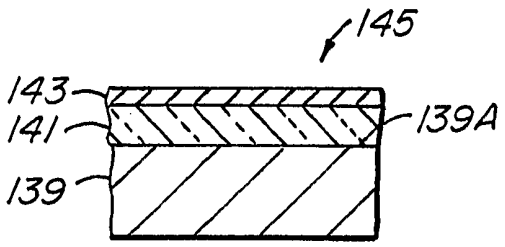

FIG. 5D.

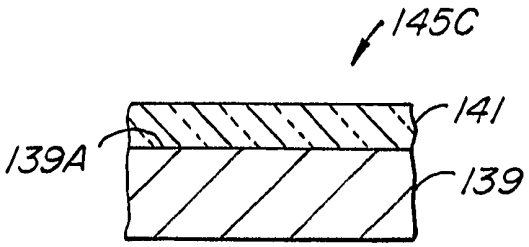

FIG. 5G.

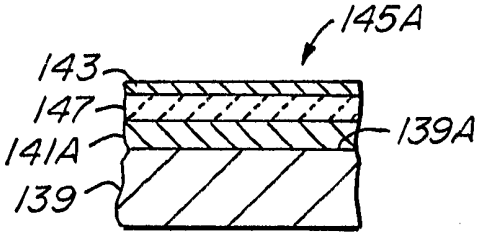

FIG. 5E.

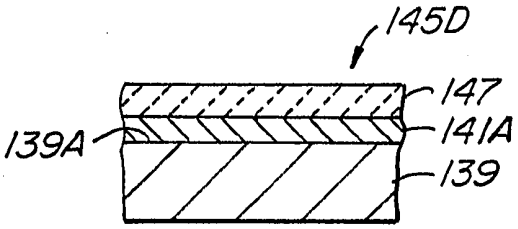

FIG. 5H.

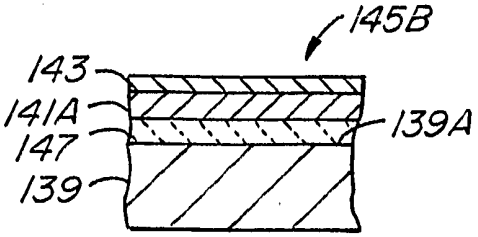

FIG. 5F.

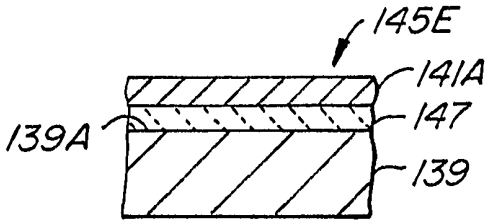

FIG. 5I.

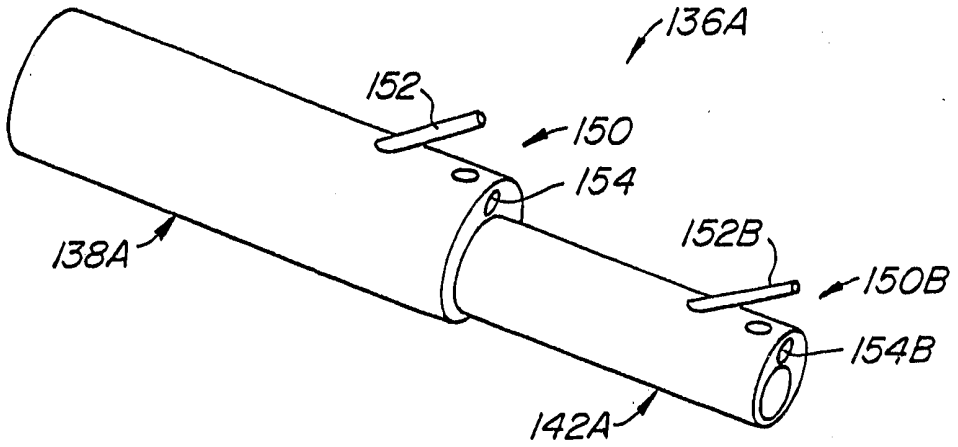

FIG. 6C.

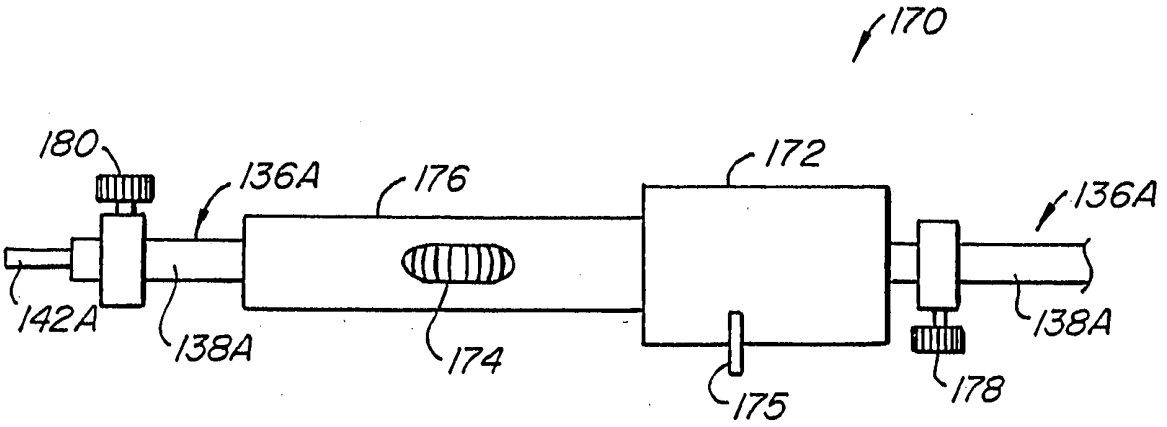

FIG. 6D.

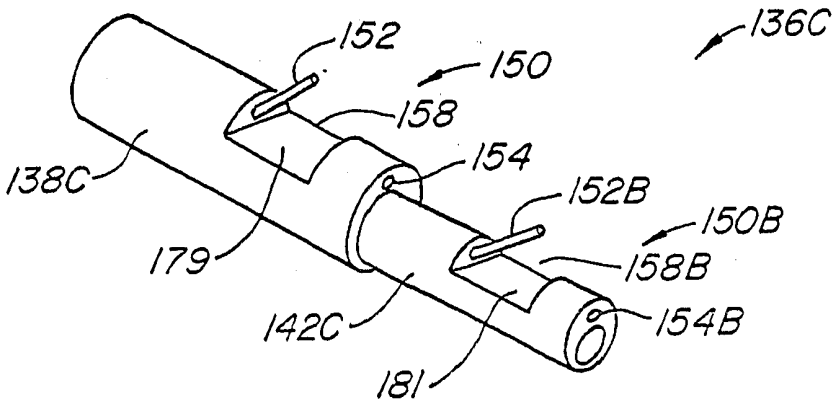

FIG. 6E.

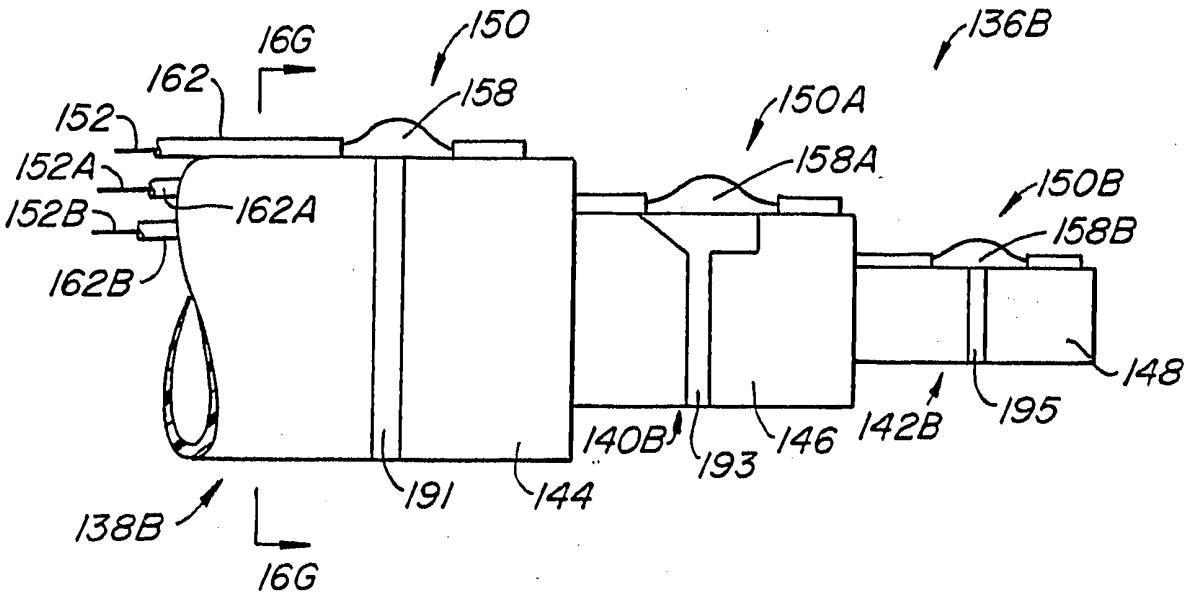
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FIG. 6F.

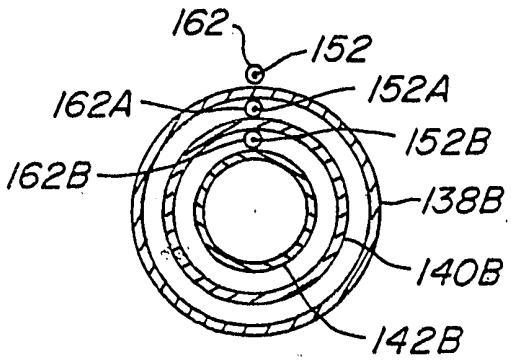
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FIG. 6G.

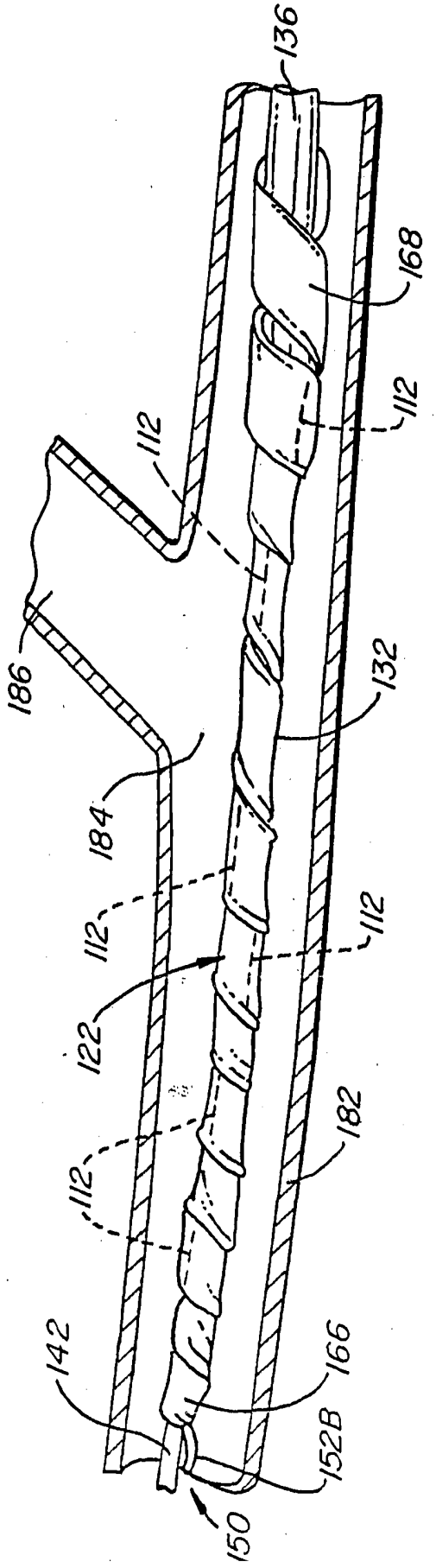

FIG. 7A.

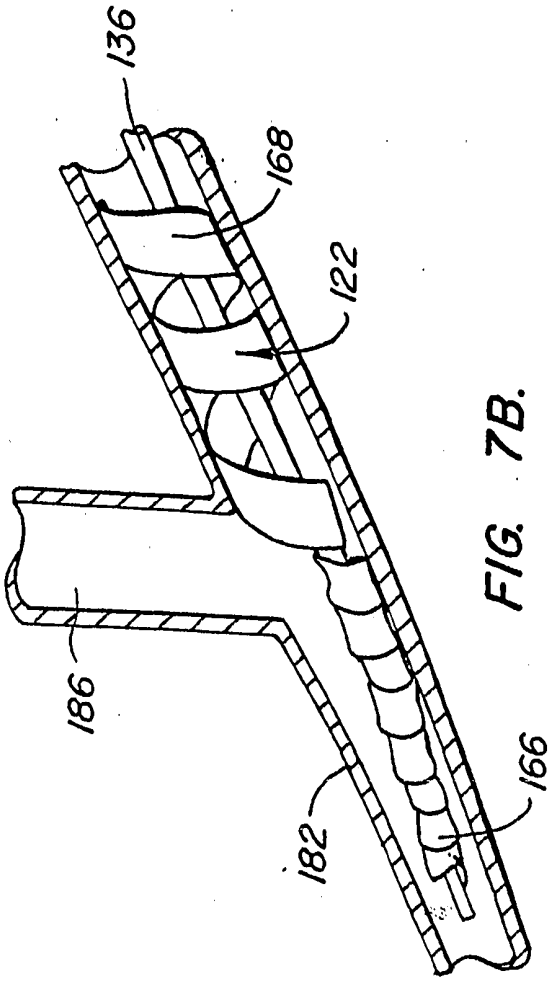
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FIG. 7B.

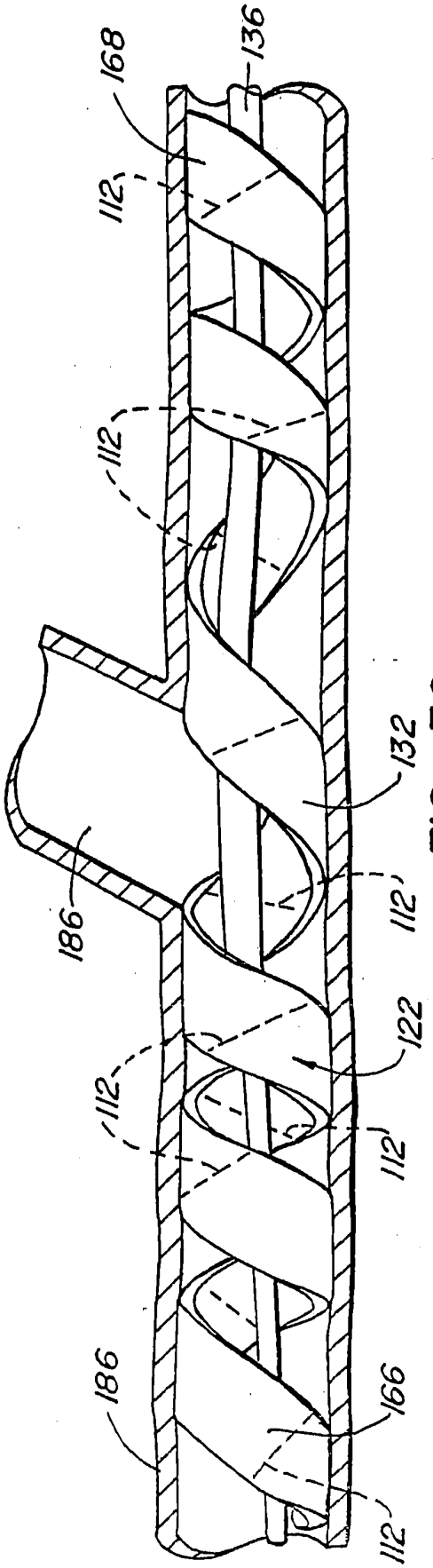
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FIG. 7C.

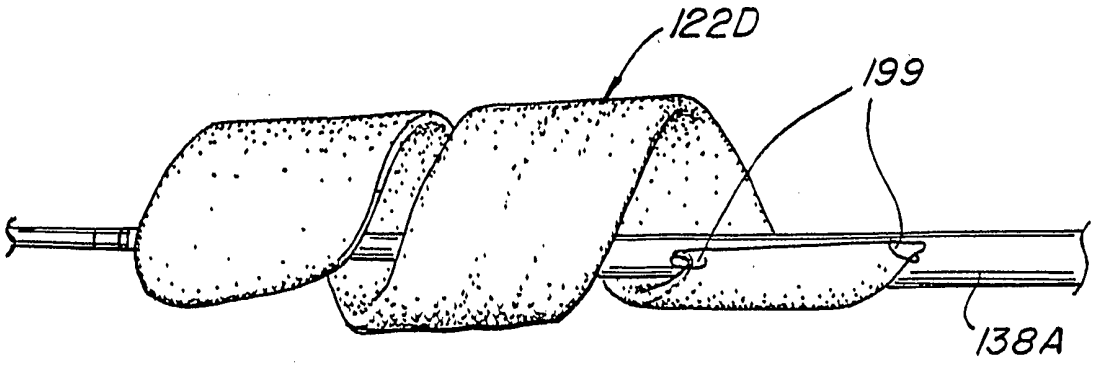

FIG. 7E.

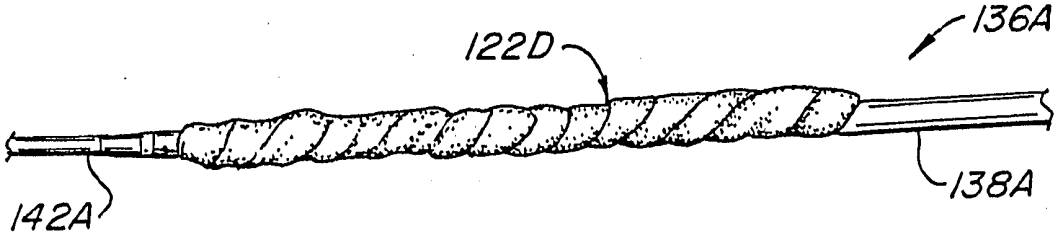

FIG. 7D.

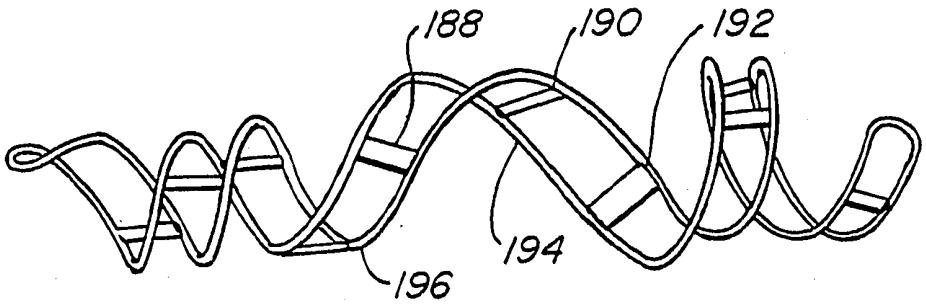

FIG. 8.

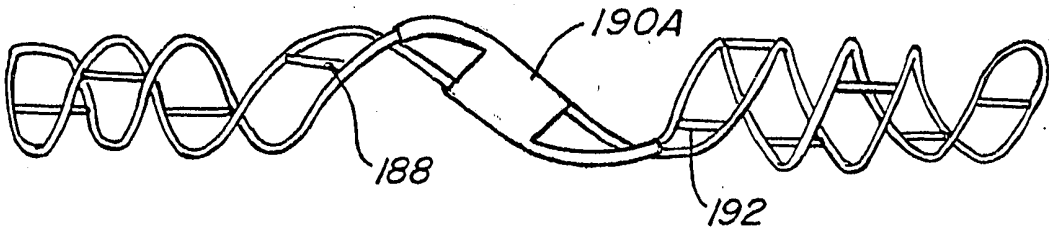

FIG. 9.

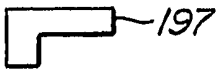

FIG. 10.

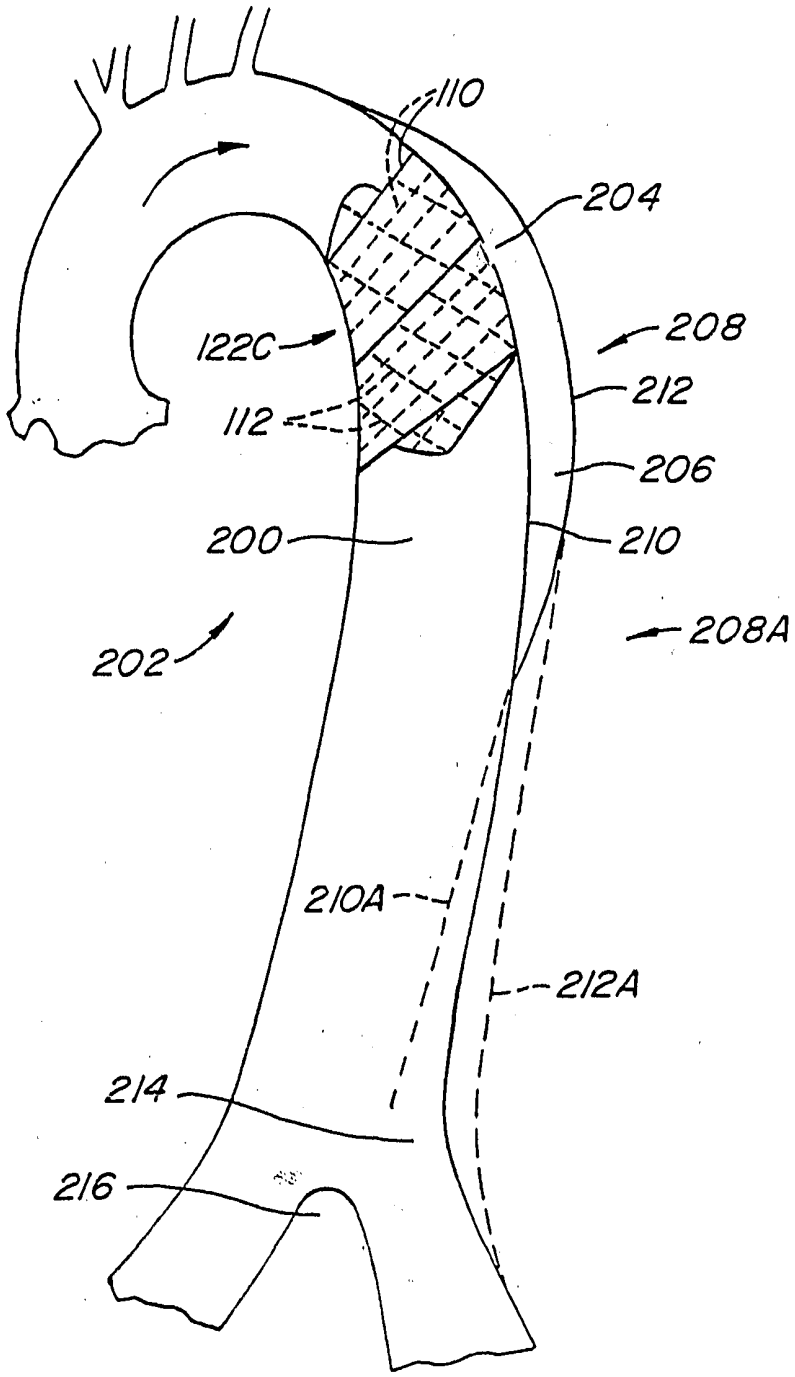

FIG. 11.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/49178

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61F 2/06
US CL :623/1.13,1.39,1.42,1.43,1.45,1.46
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)

U.S. : 623/1.13,1.39,1.42,1.43,1.45,1.46

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 practicable, search terms used)

WEST
text terms: stent, drug, medicine, sleeve, liner, biodegradable, taxol, rapamycin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,760,849 A (KROPF) 02 August 1988, Figs. 2, 5, col. 2, lines 60-68.	1-90, 101-127
Y	US 5,605,696 A (EURY et al) 25 February 1997, col. 2, lines 8-27, col. 3, lines 60-67, col. 5, l ines 19-28.	1-23,25-31,33-36,38-41 ,43-52, 54-66,68-71 ,73-77,79, 80,82-92, 94-104,106- 108-116, 118, 121-127
Y,P	US 6,273,913 A (WRIGHT et al) 14 August 2001, col. 3, lines 36-45, col. 4, lines 54-67, col. 5, lines 22- end of document.	1-18,23-47,52-78,91- 116, 118-127

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier document published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search 16 APRIL 2002	Date of mailing of the international search report 07 JUN 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Bruce Snow Telephone No. (703) 308-3255

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/49178

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,500,013 A (BUSCEMI et al) 19 March 1996, Fig. 4, col. 6, lines 29-37, col. 10-end of document.	101, 106-116, 118,121- 127
X	US 5,441,515 A (KHOSRAVI et al) 15 August 1995, Figs. 4, 5, 26, col. 4, lines 1, 2, col. 6, lines 44-49, col. 7, lines 29-38.	1,9-14,19, 20,26,27, 33,34,36,43,45,48, 49, 61,62,79, 87-90
X -- Y	US 5,873,904 A (RAGHEB et al) 23 February 1999, see entire document.	91-118,120-127 -------- 1-90