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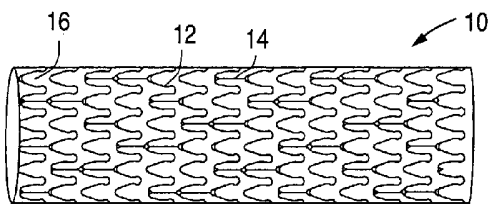
(54) Title: METHODS FOR MANUFACTURING A COATED STENT-BALLOON ASSEMBLY



(57) Abstract: Methods of coating a stent subsequent to mounting or crimping of the stent on a balloon of a catheter assembly are disclosed.

METHODS FOR MANUFACTURING A COATED STENT – BALLOON ASSEMBLY

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to methods for coating stents. In particular, the methods are directed to coating a stent mounted on a balloon of a catheter assembly.

Description of the Background

Stents are being modified to provide drug delivery capabilities. A polymeric carrier, impregnated with a drug or therapeutic substance is coated on a stent. The conventional method of coating is by, for example, applying a composition including a solvent, a polymer dissolved in the solvent, and a therapeutic substance dispersed in the blend to the stent by immersing the stent in the composition or by spraying the composition onto the stent. The solvent is allowed to evaporate, leaving on the stent strut surfaces a coating of the polymer and the therapeutic substance impregnated in the polymer. The dipping or spraying of the composition onto the stent can result in a complete coverage of all stent surfaces, i.e., both luminal (inner) and abluminal (outer) surfaces, with a coating. However, having a coating on the luminal surface of the stent can have a detrimental impact on the stent's deliverability as well as the coating's mechanical integrity. Moreover, from a therapeutic standpoint, the therapeutic agents on an inner surface of the stent get washed away by the blood flow and typically can provide for an insignificant therapeutic effect. In contrast, the agents on the outer surfaces of the stent are in contact with the lumen, and provide for the delivery of the agent directly to the tissues. Polymers of a stent coating also elicit a response from the body. Reducing the amount to foreign material can only be beneficial.

Briefly, an inflatable balloon of a catheter assembly is inserted into a hollow bore of a coated stent. The stent is securely mounted on the balloon by a crimping process. The balloon is inflated to implant the stent, deflated, and then withdrawn out from the bore of the stent. A polymeric coating on the inner surface of the stent can increase the coefficient of friction between the stent and the balloon of a catheter assembly on which the stent is crimped for delivery. Additionally, some polymers have a "sticky" or "tacky" consistency. If the polymeric material either increases the coefficient of friction or adherers to the catheter balloon, the effective release of the stent from the balloon after deflation can be compromised. If the stent coating adheres to the balloon, the coating, or parts thereof, can be pulled off the stent during the process of deflation and withdrawal of the balloon following the placement of the stent. Adhesive, polymeric stent coatings can also experience extensive balloon sheer damage post-deployment, which could result in a thrombogenic stent surface and possible embolic debris. The stent coating can stretch when the balloon is expanded and may delaminate as a result of such shear stress.

Accordingly, it is advantageous to eliminate the coating on the inner surface of the stent. Post crimping coating processes have been proposed for elimination of the coating on the inner surface of the stent. Briefly, subsequent to the mounting of the stent on the balloon, the stent can be dipped in the coating composition or the composition can be sprayed on the stent. Even though application of coating on the inner surface of the stent is eliminated, the coating is also deposited on the surface of the balloon between the stent struts. With this type of coating, the problems of adhesion of the stent to the balloon and formation of coating defects upon expansion, deflation and withdrawal of the balloon are not eliminated, and in effect, such problems could be further exasperated.

Coating of the stent prior to mounting of the stent on the balloon can also damage the coating on the outer surface of the stent. Stent crimping tools can cause coating defects on the

stent by applying too much pressure at various directions to a soft polymeric coating. Harder or brittle polymers can have coating failure or crack under crimping pressure. Stent crimping is a critical step in manufacturing in that stent retention depends on it. Stent crimping is the act of affixing the stent to the delivery catheter or delivery balloon so that it remains affixed to the catheter or balloon until the physician desires to deliver the stent at the treatment site. Current stent crimping technology is sophisticated. A short time ago, one process used a roll crimper. This damaged many polymer coatings due to its inherent shearing action. Next came the collet crimper using metal jaws that are mounted into what is essentially a drill chuck. The jaws move in a purely radial direction. This movement was not expected to shear the coating, because it applied forces only normal to the stent surface. But some stent geometries require that stent struts scissor together during crimping. In those geometries, even if the crimper imposes only normal forces, the scissor action of the stent struts imparts shear. Finally, the iris or sliding-wedge crimper imparts mostly normal forces with some amount of tangential shear.

To use a roll crimper, first the stent is slid loosely onto the balloon portion of the catheter. This assembly is placed between the plates of the roll crimper. With an automated roll crimper, the plates come together and apply a specified amount of force. They then move back and forth a set distance in a direction that is perpendicular to the catheter. The catheter rolls back and forth under this motion, and the diameter of the stent is reduced. The process can be broken down into more than one step, each with its own level of force, translational distance, and number of cycles. With regard to a stent with a drug delivery coating, this process imparts a great deal of shear to the stent in a direction perpendicular to the catheter or catheter wall. Furthermore, as the stent is crimped, there is additional relative motion between the stent surface and the crimping plates. As a result, this crimping process tends to damage the stent coating.

The collet crimper is equally conceptually simple. A standard drill-chuck collet is equipped with several pie-piece-shaped jaws. These jaws move in a radial direction as an outer ring is turned. To use this crimper, a stent is loosely placed onto the balloon portion of a catheter and inserted in the center space between the jaws. Turning the outer ring causes the jaws to move inward. An issue with this device is determining or designing the crimping endpoint. One scheme is to engineer the jaws so that when they completely close, they touch and a center hole of a known diameter remains. Using this approach, turning the collet onto the collet stops crimps the stent to the known outer diameter. While this seems ideal, it can lead to problems. Stent struts have a tolerance on their thickness. Additionally, the process of folding non-compliant balloons is not exactly reproducible. Consequently, the collet crimper exerts a different amount of force on each stent in order to achieve the same final dimension. Unless this force, and the final crimped diameter, is carefully chosen, the variability of the stent and balloon dimensions can yield stent coating or balloon damage.

Furthermore, although the collet jaws move in a radial direction, they move closer together as they crimp. This action, combined with the scissoring motion of the struts, imparts tangential shear on the coatings that can also lead to damage. Lastly, the actual contact surfaces of the collet crimper are the jaw tips. These surfaces are quite small, and only form a cylindrical surface at the final point of crimping. Before that point, the load being applied to the stent surface is discontinuous.

In the sliding wedge or iris crimper, adjacent pie-piece-shaped sections move inward and twist, much like the leaves in a camera aperture. This crimper can be engineered to have two different types of endpoints. It can stop at a final diameter, or it can apply a fixed force and allow the final diameter to float. From the discussion on the collet crimper, there are advantages in applying a fixed level of force as variabilities in strut and balloon dimension will not change the

crimping force. The sliding wedges impart primarily normal forces, which are the least damaging to stent coatings. As the wedges slide over each other, they impart some tangential force. But the shear damage is frequently equal to or less than that of the collet crimper. Lastly, the sliding wedge crimper presents a nearly cylindrical inner surface to the stent, even as it crimps. This means the crimping loads are distributed over the entire outer surface of the stent.

All current stent crimping methods were developed for all-metal stents. Stent metals, such as stainless steel, are durable and can take abuse. When crimping was too severe, it usually damaged the underlying balloon, not the stent. But polymeric coatings present different challenges.

The methods of the present invention provide for a solution by coating the outer surfaces of the stent post crimping or mounting of the stent to the balloon.

SUMMARY

A method of manufacturing a coated stent – balloon assembly is provided, comprising mounting a stent on a balloon of a catheter assembly; followed by forming a stent coating on the stent, wherein the section of the balloon surface over which the stent is mounted is free from any stent coating.

A method of manufacturing a coated stent – balloon assembly is provided, comprising forming a sacrificial layer on the balloon of a catheter assembly; followed by mounting a stent on a balloon, the stent including a struts separated by gaps; followed by forming a stent coating on the stent; followed by removal of the sacrificial layer.

A method of manufacturing a coated stent – balloon assembly is provided, comprising mounting a stent on a balloon, the stent including a struts separated by gaps; followed by forming a sacrificial layer on the balloon in the areas of the gaps between struts of the stent; followed by

forming a coating on the stent; followed by removing the sacrificial layer, wherein the coating material remains on an outer surface of the stent.

BRIEF DESCRIPTION OF THE FIGURES

The figures have not been drawn to scale and, in particular, layers of Figures 3A-3E as well as 4A-4E have been over and under emphasized for illustrative purposes.

Figure 1 illustrates a stent;

Figure 2 illustrates a stent mounted on a balloon or expandable member of a catheter assembly;

Figure 3A-3E are steps for coating a stent mounted on a balloon in accordance with one embodiment of the invention; and

Figure 4A-4E are steps for coating a stent mounted on a balloon in accordance with one embodiment of the invention.

DETAILED DESCRIPTION

Figure 1 illustrates a conventional stent 10. The embodiments of the invention should not be limited to the stent pattern illustrated in Figure 1 as other types of stents can be coated by the methods described herein. Stent 10 is illustrated to have a scaffolding network which include struts 12 connected by elements 14 so as to have gaps 16 between struts 12. For ease of discussion, elements 14 can also be considered struts. Stents can be balloon expandable or self-expandable and can be used in a variety of medical applications and not just cardiovascular applications. The stent can be made from a metallic material, a polymeric material, such as those that are bioabsorabable, degradable, or erodable in kind, or a combination of both metallic material and polymers.

Figure 2 illustrates a stent 10 mounted on a balloon 18 of a catheter assembly 20. Figure 2 illustrates a stent with a different pattern than the one in Figure 1.

Referring to Figures 3A-3E, a method is illustrated for coating a stent in accordance with one embodiment of the invention. Figure 3A is a partial cross section of balloon 18 having an outer face 22. On or over outer face 22 is deposited a sacrificial coating layer 24. The term "on" is intended to be used broadly, such that, for example a layer on a stent or a balloon is not intended to mean, unless otherwise specifically stated, surface contact between the layer and the stent or the layer and the balloon such that an intermediary layer or layers can be included. Subsequent to the deposition of the sacrificial coating layer 24, a stent, which in one embodiment, is free from any coating can be mounted or crimped on balloon 18 (for example, using SC700 MSI Stent Crimping Equipment, available from Machine Solutions, Inc., Flagstaff, AZ) . Figure 3C depicts struts 12 of the stent having gaps 16. A stent press can be used to further compress a stent to provide firmer engagement with balloon 18 (for example, using FFS700 MSI Balloon Form/Fold/Set Equipment, available from Machine Solutions, Inc.). In some embodiments, the stent can include a coating layer; however, this coating layer can be subject to damage during the crimping process. The damage can be cured by subsequent coating applications. Figure 3D illustrates a stent coating 26 being uniformly applied over struts 12 and sacrificial layer 24. In some embodiments, a more selective coating process can be chosen to minimize application of the coating substance into gaps 16. Selective coating processes, such as those using an ink-jet type or micro-injector can limit the coating application to the outer surfaces of struts 12. Application of stent coating material is intended to include application of a single layer or multiple layers such that each layer can be the same or included different components and material. For example, some layers can be free of therapeutic substances or can be made from different polymeric materials. Prior to deposition of the stent coating material, a cleaning application, such as air-blasting, can be applied to the surface of struts 12 to clean off any residues or contaminants. In

some embodiments, a wash can be employed as the cleaning application with the caveat that the wash does not remove sacrificial layer 24. The wash can be a non-solvent for sacrificial layer 24. Sacrificial layer 24 is removed, as illustrated in Figure 3E causing the removal of coating 26 in gap regions 16. Surface 22 of balloon 18 can be free from any coating layer 26, at least in gaped regions 16 between struts 12. In some embodiments, crimping applies enough pressure to struts 12 so as to push the inner surface of struts 12 against outer surface 22 of balloon. As a result, sacrificial layer 24 is completely or substantially removed beneath struts 12. In some embodiments, sacrificial layer 24 can remain beneath struts 12 and eventually washed away in the body. This is applicable if sacrificial layer 24 is made from a bio-friendly material, such as materials that are non-toxic and non-inflammatory, and can be readily processed and eliminated by the body. In other embodiments, sacrificial layer 24 can be bioactive or include a bioactive material so as to provide therapeutic, prophylactic, and/or ameliorative effect for the patient. Once the stent is released, such agents can also be locally released into the system. In other embodiments, depending on the severity of the process of the removal of sacrificial layer 24, layer 24 under struts 12 can also be removed. Pressure can then be applied to the stent for firmer engagement with balloon 18.

In accordance with another embodiment, referring to Figures 4A-4E, a stent is first mounted or crimped on balloon 18 and optionally further pressed as described above. The stent can optionally have a coating disposed thereon, but preferably is without a coating. Figure 4B illustrates struts 12 on balloon 18. Sacrificial layer 24 is selectively deposited in gaps 16 on surface 22 of balloon 18 such that outer surface of struts 12 are not covered by layer 24. In some embodiments, deposition technique used could also cover struts 12 or there could be some incidental material deposited on struts 12. In such embodiments, an added step of removing sacrificial layer 24 over outer surface of struts 12 is required. This can be accomplished by, for example, application of a gas (e.g., forced air) or by scrapping. Stent coating 26 is then deposited

on the stent-balloon assembly. Removal of sacrificial layer 24 facilitates removal of stent coating 26 in gaps 16 but not stent coating 26 on struts 12. Surface 22 of balloon 18 is free from stent coating material between struts 12 in gaped regions 16.

The application of the stent coating 26 should not allow for removal or dissolution of sacrificial layer 24. Some of sacrificial layer 24 may be incidentally removed but sufficient amount of layer 24 should be left behind so as to adequately remove the unwanted stent coating 26 portions. For example, if the coating material for the stent includes a solvent, this solvent should act as a non-solvent for sacrificial layer 24. Additionally, if a fluid is used to remove sacrificial layer 24, the fluid should be a non-solvent for the coating layer 26 so as not to remove or adversely affect the coating layer 26 of the stent.

To assist in the retention of sacrificial layer 24, an adhesive can be applied to surface of balloon or an adhesive can be combined with the sacrificial layer material. An adhesive can be especially useful if sacrificial layer 24 is deposited in a dry powder form as opposed to a solution or suspension. Representative examples of suitable adhesives include fibrin glue, cyanoacrylate, FocalSeal® (polyethylene glycol based synthetic hydrogel), carboxymethyl cellulose, gelatin-resorcin-formaldehyde glue, silk elastin, tropoelastin added with an *in situ* cross-linker such as lysoyl peroxidase, and water soluble chitosan.

Sacrificial layer 24 can be made from or can include any substance that is capable of removing or disintegrating the coating material. Removal can be in bulk from. "Bulk form" refers to fragments of coating material as opposed to individual particles of coating material. Representative examples of material include oligosaccharides and polysaccharides such as sucrose (including caramel), dextrose, glucose and heparin; ionic salts such as sodium chloride, potassium chloride, copper sulfate, sodium bicarbonate and iodine salt; amino acids such as glycine; and polymers such as hyaluronic acid, poly(ethylene glycol) or polymers listed below. In one embodiment, the substance can be an active agent, drug or co-drug, including agents listed below.

In some embodiments, the substance is made of a low molecular weight material, for example, a material that can be easily eliminated and discharged by the body or a material having a molecular weight less than 60 Daltons. In yet another embodiment, the substance includes ionic molecules.

In some embodiment of the present invention, sacrificial layer 24 can include or be made from a hydrophilic material. A substance is classified as "hydrophilic" or "hydrophobic" depending on the value of the substance's Hildebrand solubility parameter. The term "Hildebrand solubility parameter" is defined as a parameter δ indicating the cohesive energy density of a substance. The δ parameter is determined as follows:

$$\delta = (\Delta E/V)^{1/2}$$

where δ is the solubility parameter, $(cal/cm^3)^{1/2}$; ΔE is the energy of vaporization, cal/mole; and V is the molar volume, cm^3/mole. "Hydrophilic" refers to a substance that has a Hildebrand solubility parameter equal to or greater than 8.5, 9, 9.5, 10, 10.5, 11, or alternatively 11.5 $(cal/cm^3)^{½}$.

In yet another embodiment, sacrificial layer 24 can be made from or include a material capable of absorbing a fluid. The substance can be a hydrogel. "Hydrogel" is intended to include a cross-linked polymer, via covalent, ionic, or hydrogen bonding, to form a three-dimensional open lattice structure which is capable of absorbing and entrapping water molecules to form a gel. Representative examples of hydrogels include poly(ethylene glycol), N-isopropylacrylamide, polyoxyethylene-polyoxypropylene block copolymers, poly(acrylic acid) grafted pluronic copolymers, chitosan grafted pluronic copolymer, elastin mimetic polypeptides, and combinations and mixtures thereof.

Sacrificial layer 24 and/or stent coating layer 26 can be deposited by spraying (e.g., EFD 780S spray device with VALVEMATE 7040 control system manufactured by EFD Inc., East Providence, RI), dipping, brushing, micro-injection, and the like. The deposition can be

automated such as a micro-injection dispenser programmed to follow the pattern of the stent or to deposit sacrificial layer 24 in gaps 16 between stent struts 12 but not on outer surface of struts 12. An automated system is disclosed in U.S. Patent No. 6,395,326. Masking techniques, as is known to one having ordinary skill in the art, can also be used for selective coating of a stent or balloon 18. Sacrificial layer 24 can be applied in dry powder form. Dry powder refers to a mass of particles that contains less than about 10%, less than 5%, less than 1%, less than 0.1%, or 0% residual fluid (e.g., solvent(s) or water). Alternatively, sacrificial layer 24 can be applied as a wet or semi-wet coating. For example, layer 24 material can be mixed with or dispersed in a liquid medium as particles, or can be partially or completely dissolved in a liquid carrier. If the material is combined with a liquid for deposition, the liquid can be allowed to evaporate before the application of the coating material. In some embodiments, however, it may be beneficial to apply the coating material to a wet or semi-wet sacrificial layer 24. This may allow sacrificial layer 24 to more effectively remove unwanted portions of coating layer 26. Wet and semi-wet coatings include 0.1%, 1%, 5%, or 10% or more water or solvent(s). Dry form can contain less than about 10%, less than 5%, less than 1%, less than 0.1%, or 0% residual fluid (e.g., solvent(s) or water). In some embodiments, it is preferred that the coating layer 26 be applied to a dry sacrificial layer 24.

In some embodiments, sacrificial layer 24 can be removed by application of a removal fluid. Application can be by dipping or spraying. As indicated above, this fluid should be a non-solvent for the stent coating. Representative examples of fluids that can be used to remove layer 24 include water; alcohols including monohydric alcohols such as methanol, isopropyl alcohol and ethanol, dihydric alcohols and polyols; acetone; supercritical fluids such as supercritical carbon dioxide; and mixtures thereof. In one embodiment, the fluid is a mixture of supercritical carbon dioxide and one or more of methanol, isopropyl alcohol, ethanol and acetone. In another embodiment, the fluid is a mixture of water and an alcohol (e.g., 80/20 % (w/w) water:alcohol).

Preferably, the removal fluid is water or water-based. The fluid should be able dissolve sacrificial layer 24 or cause it to swell. In one embodiment, ultrasonic treatment or other vibrating type treatments can be employed to facilitate removal of layer 24. Post processing rinsing or application of an inert gas or air can be used to remove debris. It is believed that stent coating 26 which is in contact with sacrificial layer 26 will fail due to an interruption in the film structure by the swelling force or pressure. The selected duration of fluid exposure can depend on a variety of factors, such as the temperature, characteristics or type of the coating material, characteristics or type of the sacrificial layer, the potency of the removal fluid, the desired rate of removal, the cohesive and adhesion forces present on the coating, among other factors. For example, removal can be facilitated by deionized water at 37 deg. C or at room temperature. The duration of the fluid exposure, for instance, can be from about 1 second to about 24 hours at ambient temperature.

Other means of removal are also included with the embodiments of the inventions. For example, laser application can be used to remove sacrificial layer 24 for removal of layer 26. Sacrificial layer 24 can be of the type that absorbs a great amount of energy and/or disintegrates readily so as to promote removal of coating layer 26.

In some embodiments, sacrificial layer 24 should have a relatively high coefficient of extinction, which allows the material to burn quickly and easily. The coefficient of extinction k is defined by:

$$k = \{Ln(I_0/I_f)\} / h$$

Where k = coefficient of extinction (cm^{-1})
I_0 = initial intensity
I_f = final intensity
h = distance at final intensity (cm)

A suitably high coefficient of extinction k can be greater than or equal to 1×10^4 cm^{-1}. Such materials may be particularly suitable for preventing melting defects when sacrificial layer 24 is removed using a laser.

Applying a coating material to a stent mounted on a balloon has significant advantages. As noted previously, in conventional coating techniques, stents are coated with a polymer before the stents are mounted on a delivery device. Because some of the polymers used in conventional techniques are brittle, these polymers are not able to withstand the pressure applied to the stents during mounting or crimping methods. The selective coating techniques of the present invention therefore allow a stent to be coated after the stent has been mounted on the delivery device thereby avoiding the need to subject the coating to the mounting and crimping processes. Therefore, one is able to select from a greater number of available polymers, even those that might prove to be too brittle for the convention processes.

The stent coating material can include one or a combination of a polymer (or polymers) or a therapeutic agent (or agents), with or without a fluid carrier or a solvent. Stent coating 26 can include layer(s) of pure polymer(s) or layer(s) of pure agent(s) or drug(s). Layer 26 can include multiple layers such a primer layer, a drug-reservoir layer, and a topcoat layer.

Examples of polymers that can be used include, but are not limited to, ethylene vinyl alcohol copolymer; polybutylmethacrylate; poly(ethylene-co-vinyl acetate); poly(vinylidene fluoride-co-hexafluororpropene); poly(hydroxyvalerate); poly(L-lactic acid); polycaprolactone; poly(lactide-co-glycolide); poly(hydroxybutyrate); poly(hydroxybutyrate-co-valerate); polydioxanone; polyorthoester; polyanhydride; poly(glycolic acid); poly(D,L-lactic acid); poly(glycolic acid-co-trimethylene carbonate); polyphosphoester; polyphosphoester urethane; poly(amino acids); cyanoacrylates; poly(trimethylene carbonate); poly(iminocarbonate); copoly(ether-esters) (e.g., PEO/PLA); polyalkylene oxalates; polyphosphazenes; biomolecules, such as fibrin, fibrinogen, cellulose, starch, collagen and hyaluronic acid; polyurethanes; silicones; polyesters; polyolefins; polyisobutylene and ethylene-alphaolefin copolymers; acrylic polymers and copolymers; vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride and

polyvinylidene chloride; polyacrylonitrile; polyvinyl ketones; polyvinyl aromatics, such as polystyrene; polyvinyl esters, such as polyvinyl acetate; copolymers of vinyl monomers with each other and olefins, such as ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins, and ethylene-vinyl acetate copolymers; polyamides, such as Nylon 66 and polycaprolactam; alkyd resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins; polyurethanes; rayon; rayon-triacetate; cellulose acetate; cellulose butyrate; cellulose acetate butyrate; cellophane; cellulose nitrate; cellulose propionate; cellulose ethers; and carboxymethyl cellulose. KRATON G-1650 can also be used. KRATON is manufactured by Shell Chemicals Co. of Houston, Texas, and is a three block copolymer with hard polystyrene end blocks and a thermoplastic elastomeric poly(ethylene-butylene) soft middle block. KRATON G-1650 contains about 30 mass % of polystyrene blocks.

Therapeutic or bioactive agents can include any agent which is a therapeutic, prophylactic, diagnostic agent, and/or ameliorative. These agents can have anti-proliferative or anti-inflammmatory properties or can have other properties such as antineoplastic, antiplatelet, anti-coagulant, anti-fibrin, antithrombonic, antimitotic, antibiotic, antiallergic, antioxidant as well as cystostatic agents. Examples of suitable therapeutic and prophylactic agents include synthetic inorganic and organic compounds, proteins and peptides, polysaccharides and other sugars, lipids, and DNA and RNA nucleic acid sequences having therapeutic, prophylactic or diagnostic activities. Nucleic acid sequences include genes, antisense molecules which bind to complementary DNA to inhibit transcription, and ribozymes. Some other examples of other bioactive agents include antibodies, receptor ligands, enzymes, adhesion peptides, blood clotting factors, inhibitors or clot dissolving agents such as streptokinase and tissue plasminogen activator, antigens for immunization, hormones and growth factors, oligonucleotides such as antisense oligonucleotides and ribozymes and retroviral vectors for use in gene therapy. Examples of anti-proliferative agents include rapamycin and its functional or structural derivatives, 40-*O*-(2-

hydroxy)ethyl-rapamycin (everolimus), and its functional or structural derivatives, paclitaxel and its functional and structural derivatives. Examples of rapamycin derivatives include methyl rapamycin (ABT-578), 40-*O*-(3-hydroxy)propyl-rapamycin, 40-*O*-[2-(2-hydroxy)ethoxy]ethyl-rapamycin, and 40-*O*-tetrazole-rapamycin. Examples of paclitaxel derivatives include docetaxel. Examples of antineoplastics and/or antimitotics include methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, doxorubicin hydrochloride (e.g. Adriamycin® from Pharmacia & Upjohn, Peapack N.J.), and mitomycin (e.g. Mutamycin® from Bristol-Myers Squibb Co., Stamford, Conn.). Examples of such antiplatelets, anticoagulants, antifibrin, and antithrombins include sodium heparin, low molecular weight heparins, heparinoids, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist antibody, recombinant hirudin, thrombin inhibitors such as Angiomax ä (Biogen, Inc., Cambridge, Mass.), calcium channel blockers (such as nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonists, lovastatin (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug, brand name Mevacor® from Merck & Co., Inc., Whitehouse Station, NJ), monoclonal antibodies (such as those specific for Platelet-Derived Growth Factor (PDGF) receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitors, suramin, serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), nitric oxide or nitric oxide donors, super oxide dismutases, super oxide dismutase mimetic, 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (4-amino-TEMPO), estradiol, anticancer agents, dietary supplements such as various vitamins, and a combination thereof. Examples of anti-inflammatory agents including steroidal and non-steroidal anti-inflammatory agents include tacrolimus, dexamethasone, clobetasol, combinations thereof. Examples of such cytostatic substance include angiopeptin, angiotensin converting enzyme inhibitors such as captopril (e.g. Capoten® and

Capozide® from Bristol-Myers Squibb Co., Stamford, Conn.), cilazapril or lisinopril (e.g. Prinivil® and Prinzide® from Merck & Co., Inc., Whitehouse Station, NJ). An example of an antiallergic agent is permirolast potassium. Other therapeutic substances or agents which may be appropriate include alpha-interferon, bioactive RGD, and genetically engineered epithelial cells. The foregoing substances can also be used in the form of prodrugs or co-drugs thereof. The foregoing substances are listed by way of example and are not meant to be limiting. Other active agents which are currently available or that may be developed in the future are equally applicable.

Representative examples of solvents that can be combined with the polymer and/or active agent include chloroform, acetone, water (buffered saline), dimethylsulfoxide, propylene glycol methyl ether, iso-propylalcohol, n-propylalcohol, methanol, ethanol, tetrahydrofuran, dimethylformamide, dimethylacetamide, benzene, toluene, xylene, hexane, cyclohexane, pentane, heptane, octane, nonane, decane, decalin, ethyl acetate, butyl acetate, isobutyl acetate, isopropyl acetate, butanol, diacetone alcohol, benzyl alcohol, 2-butanone, cyclohexanone, dioxane, methylene chloride, carbon tetrachloride, tetrachloroethylene, tetrachloro ethane, chlorobenzene, 1,1,1-trichloroethane, formamide, hexafluoroisopropanol, 1,1,1-trifluoroethanol, and hexamethyl phosphoramide, and a combination thereof.

While particular embodiments of the present invention have been shown and described, it will be obvious to those skilled in the art that changes and modifications can be made without departing from this invention in its broader aspects. Therefore, the appended claims are to encompass within their scope all such changes and modifications as fall within the true spirit and scope of this invention.

CLAIMS

What is claimed is:

1. A method of manufacturing a coated stent – balloon assembly, comprising:

mounting a stent, having struts separated by gap regions, on a balloon of a catheter assembly; followed by

forming a stent coating on the stent, wherein areas of the balloon exposed by the gap regions of the stent are free from any stent coating.

2. The method of Claim 1, wherein mounting of the stent on the balloon comprises crimping of the stent on the balloon to as to firmly engage the stent to the balloon.

3. The method of Claim 1, further comprising:

forming a sacrificial layer on the balloon prior to mounting the stent on the balloon and wherein forming a stent coating comprises:

depositing a coating material on the stent;

removing the sacrificial layer from the balloon, wherein the coating material remains on an outer surface of the stent.

4. The method of Claim 3, wherein the sacrificial layer is removed by exposure of the balloon to a fluid.

5. The method of Claim 3, wherein the sacrificial layer includes a material selected from a group of an oligosaccharide, a polysaccharide, dextrose, glucose, heparin, an ionic salt, potassium chloride, copper sulfate, sodium bicarbonate, iodine salt, an amino acid, a polymer, an active agent, a drug or a co-drug.

6. The method of Claim 3, wherein the sacrificial layer includes a low molecular weight material.

7. The method of Claim 3, wherein the sacrificial layer includes a material having a Hildebrand solubility parameter equal to or greater than 8.5 $(cal/cm^3)^{1/2}$.

8. The method of Claim 3, wherein the sacrificial layer includes a hydrogel.

9. The method of Claim 8, wherein the hydrogel is selected from a group of poly(ethylene glycol), N-isopropylacrylamide, polyoxyethylene-polyoxypropylene block copolymer, poly(acrylic acid) grafted pluronic copolymer, chitosan grafted pluronic copolymer, elastin mimetic polypeptide, and combinations and mixtures thereof.

10. The method of Claim 1, wherein forming the stent coating comprises:

forming a sacrificial layer on the areas of the balloon exposed by the gap regions between struts of the stent; followed by

forming a coating on the stent; followed by

removing the sacrificial layer, wherein the coating material remains on an outer surface of the stent.

11. The method of Claim 10, wherein the sacrificial layer is removed by exposure of the balloon to a fluid.

12. The method of Claim 10, wherein the sacrificial layer includes a material selected from a group of an oligosaccharide, a polysaccharide, dextrose, glucose, heparin, an ionic salt, potassium chloride, copper sulfate, sodium bicarbonate, iodine salt, an amino acid, a polymer, an active agent, a drug or a co-drug.

13. The method of Claim 10, wherein the sacrificial layer includes a low molecular weight material.

14. The method of Claim 10, wherein the sacrificial layer includes a material having a Hildebrand solubility parameter equal to or greater than 8.5 $(cal/cm^3)^{1/2}$.

15. The method of Claim 10, wherein the sacrificial layer includes a hydrogel.

16. The method of Claim 15, wherein the hydrogel is selected from a group of poly(ethylene glycol), N-isopropylacrylamide, polyoxyethylene-polyoxypropylene block

copolymer, poly(acrylic acid) grafted pluronic copolymer, chitosan grafted pluronic copolymer, elastin mimetic polypeptide, and combinations and mixtures thereof.

17. A method of manufacturing a coated stent – balloon assembly, comprising:

forming a sacrificial layer on the balloon of a catheter assembly; followed by

mounting a stent on a balloon, the stent including a struts separated by gaps; followed by

forming a stent coating on the stent; followed by

removal of all or most of the sacrificial layer.

18. The method of claim 17, wherein some of the sacrificial layer beneath the struts of stent remains on the balloon subsequent to the removal of the sacrificial layer.

19. The method of claim 18, wherein the sacrificial layer includes an active agent or therapeutic substance.

20. A method of manufacturing a coated stent – balloon assembly, comprising:

mounting a stent on a balloon, the stent including a struts separated by gaps; followed by

forming a sacrificial layer on the balloon in the areas of the gaps between struts of the stent; followed by

forming a coating on the stent; followed by

removing the sacrificial layer, wherein the coating material remains on an outer surface of the stent.

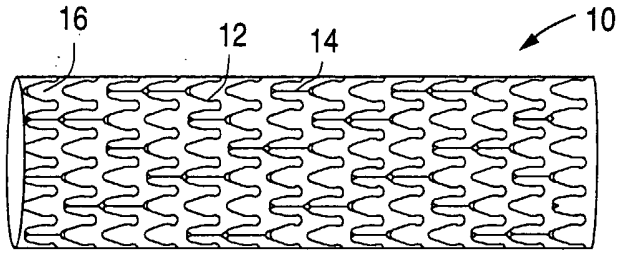


FIG. 1

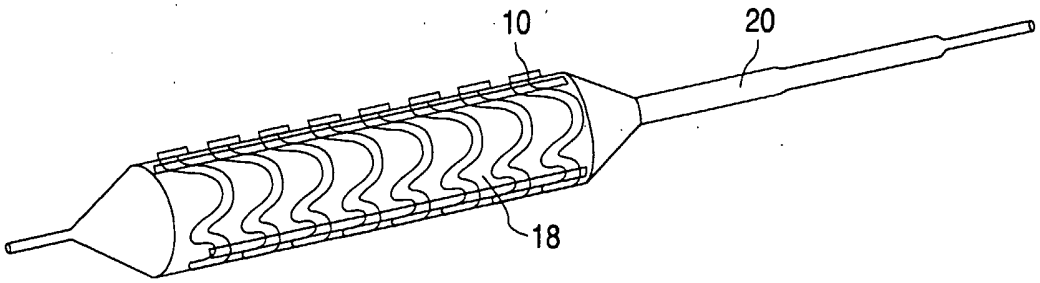


FIG. 2

FIG. 3A

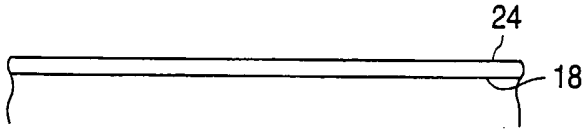


FIG. 3B

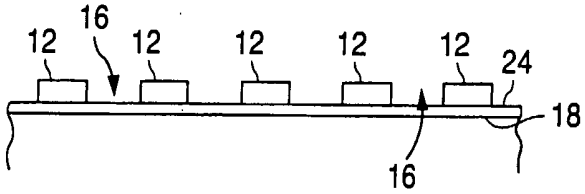


FIG. 3C

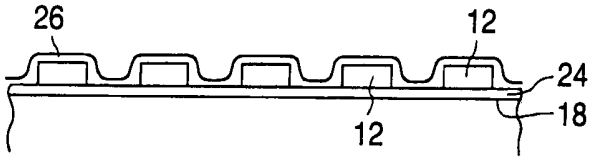


FIG. 3D

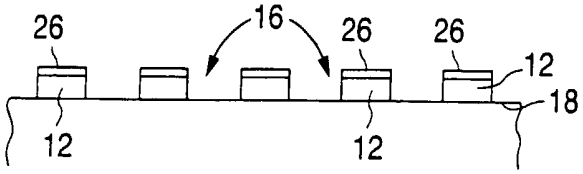


FIG. 3E

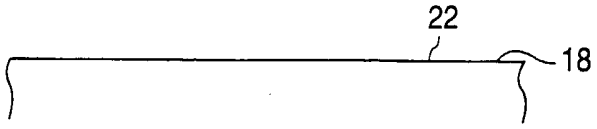


FIG. 4A

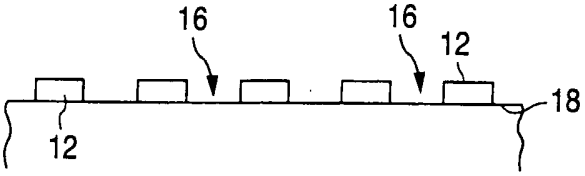


FIG. 4B

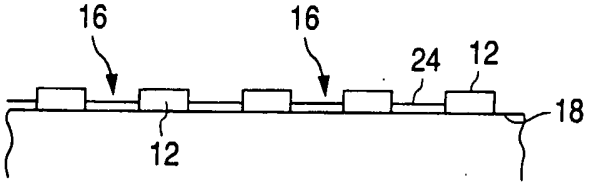


FIG. 4C

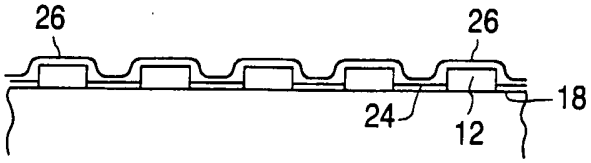


FIG. 4D

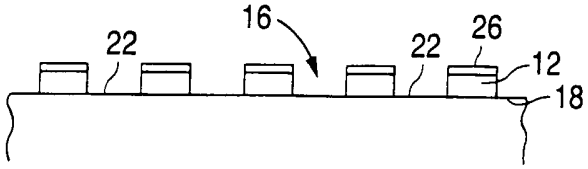


FIG. 4E