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[Continued on next page]

(54) Title: ENDOPROSTHESIS COATING

(57) Abstract: An endoprosthesis, such as a stent, includes a chemical tie layer formed of polymer that enhance adherence of a coating, e.g. a drug eluting polymer coating, to a stent surface, e.g. made of ceramic.

FIG. 1A

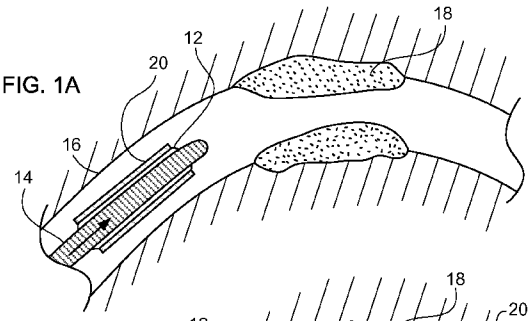


FIG. 1B

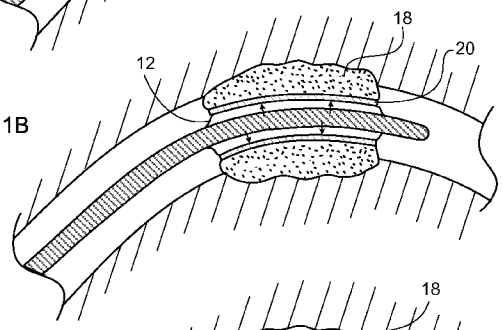
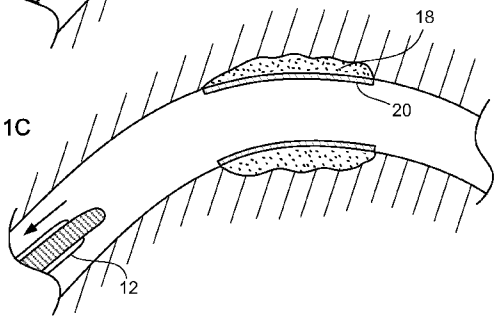


FIG. 1C



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ENDOPROSTHESIS COATING

TECHNICAL FIELD

The invention relates to endoprosthesis coating.

BACKGROUND

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

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

One method of installation involves expanding the endoprosthesis. The expansion mechanism used to install the endoprosthesis may include forcing it to expand radially. For example, the expansion can be achieved with a catheter that carries a balloon in conjunction with a balloon-expandable endoprosthesis reduced in size relative to its final form in the body. The balloon is inflated to deform and/or expand the endoprosthesis in order to fix it at a predetermined position in contact with the lumen wall. The balloon can then be deflated, and the catheter withdrawn. Stent delivery is further discussed in Heath, U.S. 6,290,721.

It is sometimes desirable for an endoprosthesis to contain a therapeutic agent, or drug which can elute into the body in a predetermined manner once the endoprosthesis is implanted.

SUMMARY

In an aspect, the invention features an endoprosthesis with a body including a ceramic on a surface thereof, a tie layer adhered to the ceramic, and a polymeric coating adhered to the tie layer.

In another aspect, the invention features a method of forming an endoprosthesis. The method includes forming a ceramic and a non-ceramic, non-metal overlayer on the ceramic such that, the ceramic has an Sdr of about 10 or less, and the layer is covalently bonded to the ceramic, or the ceramic has an Sdr of about 100 or greater, and the layer is non-covalently adhered to the ceramic, or the ceramic has an Sdr between about 10 and 100 and the layer is non-covalently adhered or covalently bonded to the ceramic.

Embodiments may include one or more of the following features. The ceramic has an Sdr of about 10 or less and an Sq of about 10 or less and the tie layer is covalently bonded to the ceramic. The ceramic has a globular morphology. The ceramic has surface oxygen content of about 80% or more and the tie layer is covalently bonded to the ceramic. The ceramic has an Sdr of about 120 to 200 and an Sq of about 20 or more and the tie layer is non-covalently adhered to the ceramic. The ceramic has a defined grain morphology. The ceramic has a surface oxygen content of about 80% or less and the tie layer is non-covalently adhered to the ceramic. The ceramic is an oxide. The ceramic is IROX. The tie layer is covalently bonded to the ceramic. The tie layer is non-covalently adhered to the ceramic. The tie layer is selected from silanes, phosphonates, and titanates. The polymeric coating includes a drug. The polymeric coating is adhered to the tie layer by covalent bonding. The polymeric coating is adhered to the tie layer by non-covalent adherence. The polymeric coating and the ceramic has an adhesion increased about 10% or greater by the tie layer. The polymeric coating and the ceramic has an adhesion increased about 50% or greater by the tie layer.

Embodiments may also include one or more of the following features. The method further includes forming a polymer layer on the overlayer. The ceramic having the Sdr of about 10 or less has a globular morphology. The ceramic having the Sdr of about 100 or greater has a defined grain morphology. The ceramic is an oxide. The ceramic is IROX. The covalent bond is formed through oxygen moieties of the ceramic. The overlayer is a silane, phosphate or titanate. The polymer layer includes a drug. The

polymer layer and the ceramic has an adhesion increased about 10% or greater by the overlayer. The polymer layer and the ceramic has an adhesion increased about 50% or greater by the overlayer through the covalent bond.

Aspects and/or embodiments may include one or more of the following advantages. An endoprosthesis, such as a stent, can be provided with a polymer coating, such as a drug eluting coating, that is strongly adhered to the stent to reduce flaking or delamination. The stent can include a ceramic material, and the polymer coating can be a material that has desirable drug release characteristics but non-optimal adhesion characteristics to the ceramic material. The adhesion can be enhanced without modifying drug delivery or biocompatibility characteristics. The stent can include a chemical tie layer directly on a ceramic surface, e.g. IROX, that has good adhesive characteristics to the ceramic. The tie layer also has good adhesive characteristics to a polymer. The tie layer can be selected in coordination with the morphology and composition of the ceramic. For example, for a relatively smooth morphology, the adhesive characteristics of the tie layer to the ceramic are selected to be increased, e.g. by covalent bonding. The adhesion strength, e.g. amount of covalent bonding or the degree of hydrophilicity can be increased, e.g., by increasing the concentration of bonding moieties at the surface, by e.g. increasing the oxygen content at the surface.

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

DESCRIPTION OF DRAWINGS

FIGS. 1A-1C are longitudinal cross-sectional views illustrating delivery of a stent in a collapsed state, expansion of the stent, and deployment of the stent.

FIG. 2A is a perspective view of a stent.

FIG. 2B is a schematic cross-sectional view of a portion of a stent.

FIG. 3 is a schematic cross-sectional view of a portion of a stent.

FIGS. 4A and 4B are micrographs of IROX morphologies.

Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

Referring to FIGS. 1A-1C, a stent 20 is placed over a balloon 12 carried near a distal end of a catheter 14, and is directed through the lumen 16 (FIG. 1A) until the portion carry the balloon and stent reaches the region of an occlusion 18. The stent 20 is then radially expanded by inflating the balloon 12 and compressed against the vessel wall with the result that occlusion 18 is compressed, and the vessel wall surrounding it undergoes a radial expansion (FIG. 1B). The pressure is then released from the balloon and the catheter is withdrawn from the vessel (FIG. 1C).

Referring to FIG. 2A, the stent 20 includes a plurality of fenestrations 22 defined in a wall 23. Stent 22 includes several surface regions, including an outer, or abluminal, surface 24, an inner, or adluminal, surface 26, and a plurality of cut-face surfaces 28. The stent can be balloon expandable, as illustrated above, or self-expanding stent. In embodiments, the stent includes a body made of e.g. a metal such as stainless steel, chrome, nickel, cobalt, tantalum, superelastic alloys such as nitinol, cobalt chromium, MP35N, and other metals. Suitable stent materials and stent designs are described in Heath '721, supra.

Referring to FIG. 2B, the stent 20 includes a body 21. On the abluminal and adluminal surfaces 24, 26 the stent includes a layer 23 of a material effective to enhance stent function, such as a ceramic, e.g. iridium oxide (IROX), that enhances stent endothelialization. The abluminal surface 24 further includes a coating 25 of a polymer that enhances function by, e.g. eluting a drug. The adherence of the coating 25 to the stent is enhanced by a chemical tie layer 27 which is bound tightly to the ceramic layer 23. The tie layer 27 includes a compound, e.g., a polymer, with good adhesion properties to both the ceramic and the polymer in the coating 25. For example, in embodimenis, the tie layer 27 includes compounds such as silanes which can form Si-O bonds with a ceramic surface or have non-covalently adhesive interactions with the surface. The silanes can be modified or derivatized for compatibility with the drug eluting polymer ("DEP") coating 25. For example, the silanes can be modified with moieties that adjust hydrophobicity/hydrophilicity for compatibility with the polymer coating 25 or moieties that cross-link with the polymer coating 25. A suitable drug eluting polymer is SIBS. Other suitable materials for layers 23, 25, and 27 are discussed below.

Referring to FIG 3, an expanded schematic view of a region of a stent, the stent body 21 includes at least one surface upon which a ceramic 23 lies. The surface of the ceramic includes oxygen moieties such as —OH and —O⁻. The hydrophilicity of the surface can be selected by controlling the surface concentration of oxygen moieties. A tie layer 27 formed of compounds 300 adheres to the ceramic through interactions or links 30 and a polymeric coating 25 formed of polymers 320 adheres to the tie layer through interactions or links 32. Links 30 and 32 can either be covalent bonding or a non-covalent adhesive interactions, such as electrostatic interactions, van de Waals forces or hydrogen bonds.

In embodiments, compound 300 is selected from a non-metal, non-ceramic material such as silanes, phosphonates, bisphosphonates, titanates, or mixtures or derivatives thereof. The compound 300 can adhere to the ceramic surface through one or more covalent bonds, such as Si-O, P-O or Ti-O bonds. In particular embodiments, di or tripodal linkages enhance the efficiency of the tie layer adhesion and thus the adhesion of the polymer coating to the ceramic.

In embodiments, compound 300 is derivatized to be compatible with hydrophilicity/hydrophobicity of the ceramic surface. For example, if the ceramic surface is hydrophilic, compound 300, can include some hydrophilic functional groups such as amine, hydroxyl, or carboxylic groups. In embodiments, lactic acid groups are used to enhance non-covalent adhesion to a hydrophilic surface. If the ceramic surface is hydrophobic, the compound 300 can include some hydrophobic functional groups such as alkyl, alkenyl, alkynyl, or aromatic groups. In some embodiments, compound 300 is a polymer precursor and may be polymerized to form a polymeric tie layer by, e.g., using plasma techniques such as plasma enhanced chemical vapor deposition ("PECVD"). In other embodiments, compound 300 is a polymer before it is applied to the ceramic surface. Suitable polymers or polymer precursors include polysilanes such as poly(phenylmethylsilane) and alkoxysilanes such as aminopropyltriethoxysilane and phenethyltrimethoxysilane. Compounds 300 may be applied to the ceramic surface by, e.g., rolling, dipping, spraying, or vapor deposition.

In embodiments, the tie layer is selected in coordination with the morphology and/or chemical compositions of the ceramic layer. Referring to FIGS. 4A and 4B,

micrographs of IROX coatings of different morphology are illustrated. Referring particularly to FIG. 4A, a relatively low roughness, smoother globular surface morphology that can enhance endothelialization is illustrated. Referring particularly to FIG. 4B, a defined grain, high roughness morphology is illustrated. The defined grain morphology provides increased surface area, and deep features which can enhance coating adhesion, whereas the globular morphology provides smaller surface area, which generally reduces adhesion. In embodiments, the tie layer is selected for stronger adhesion by, such as covalent bonding on smooth surfaces. To enhance covalent bonding, the surface compositions of the ceramic are formulated to such that they have increased bonding moieties in terms of oxygen content at the surface. Smoother globular surface morphology provides a surface which is tuned to facilitate endothelial growth by selection of its chemical composition and/or morphological features. Certain ceramics, e.g. oxides, can reduce restenosis through the catalytic reduction of hydrogen peroxide and other precursors to smooth muscle cell proliferation. The oxides can also encourage endothelial cell growth to enhance endothelialization of the stent. As discussed above, when a stent, is introduced into a biological environment (e.g., in vivo), one of the initial responses of the human body to the implantation of a stent, particularly into the blood vessels, is the activation of white blood cells. This activation causes a release of hydrogen peroxide, H_2O_2. The presence of H_2O_2 may increase proliferation of smooth muscle cells and compromise endothelial cell function, stimulating the expression of surface binding proteins which enhance the attachment of more inflammatory cells. A ceramic, such as IROX can catalytically reduce H_2O_2. The smoother globular surface morphology of the ceramic can enhance the catalytic effect and enhance growth of endothelial cells. Defined grain morphologies also allow for greater freedom of motion and are less likely to fracture as the stent is flexed in use and thus the matrix coating resists delamination of the ceramic from an underlying surface and reduces delamination of a possible overlaying coating. The stresses caused by flexure of the stent, during expansion or contraction of the stent or as the stent is delivered through a tortuously curved body lumen increase as a function of the distance from the stent axis. As a result, in embodiments, a morphology with defined grains is particularly desirable on abluminal

regions of the stent or at other high stress points, such as the regions adjacent fenestrations which undergo greater flexure during expansion or contraction.

The morphology of the surface of the ceramic is characterized by its visual appearance, its roughness, and/or the size and arrangement of particular morphological features such as local maxima. Referring particularly to FIG. 4A, in embodiments, the surface is characterized by a more continuous surface having a series of shallow globular features. The globular features are closely adjacent with a narrow minima between features. In embodiments, the surface resembles an orange peel. The diameter of the globular features is about 100nm or less, and the depth of the minima, or the height of the maxima of the globular function is e.g. about 50nm or less, e.g. about 20nm or less.

Referring particularly to FIG. 4B, in embodiments, the surface is characterized by definable sub-micron sized grains. The grains have a length, L, of the of about 50 to 500nm, e.g. about 100-300nm, and a width, W, of about 5nm to 50nm, e.g. about 10-15nm. The grains have an aspect ratio (length to width) of about 5:1 or more, e.g. 10:1 to 20:1. The grains overlap in one or more layers. The separation between grains can be about 1-50 nm. In particular embodiments, the grains resemble rice grains. In other embodiments, the surface has characteristics between high aspect ratio definable grains and the more continuous globular surface and/or has a combination of these characteristics. For example, the morphology can include a substantially globular base layer and a relatively low density of defined grains. In other embodiments, the surface can include low aspect ratio, thin planar flakes. The morphology type is visible in FESEM images at 50 KX.

The roughness of the surface can also be characterized by the average roughness, Sa, the root mean square roughness, Sq, and/or the developed interfacial area ratio, Sdr. The Sa and Sq parameters represent an overall measure of the texture of the surface. Sa and Sq are relatively insensitive in differentiating peaks, valleys and the spacing of the various texture features. Surfaces with different visual morphologies can have similar Sa and Sq values, indicating the insensitivity of the Sa and Sq parameters. For a surface type, the Sa and Sq parameters indicate significant deviations in the texture characteristics. Sdr is expressed as the percentage of additional surface area contributed by the texture as compared to an ideal plane the size of the measurement region. Sdr

further differentiates surfaces of similar amplitudes and average roughness. Typically Sdr will increase with the spatial intricacy of the texture whether or not Sa changes.

In embodiments, the ceramic has a defined grain morphology. The Sdr is about 100 or more, e.g. about 120 to 200. In addition or in the alternative, the morphology has an Sq of about 20 or more, e.g. about 20 to 30. In other embodiments, the ceramic has a globular surface morphology. The Sdr is about 10 or less, e.g. about 1 to 8. The Sq is about 10 or less, e.g. about 1 to 5. In still other embodiments, the ceramic has a morphology between the defined grain and the globular surface, with Sdr and Sq values between the ranges above, e.g. an Sdr of about 1 to 200 and/or an Sq of about 1 to 30. The Sa, Sq, and Sdr can be calculated from AFM data. The uniformity of the morphology can be within about +/- 20% or less, e.g. +/- 10% or less within a 1μm × 1μm square. In a given stent region, the uniformity is within about +/- about 10%, e.g. about 1%. For example, in embodiments, the ceramic exhibits high uniformity over the entire surface side of the stents, such as the entire abluminal or adluminal surface, or a portion of a surface side, such as the center 25% or 50% of the surface. The high uniformity provides predictable, tuned therapeutic and mechanical performance of the ceramic.

In embodiments, the ceramics are also characterized by surface composition, composition as a function of depth, and crystallinity. In particular, the amounts of oxygen or nitride in the ceramic is selected for a desired catalytic effect on, e.g., the reduction of H_2O_2 in biological processes. The composition of metal oxide or nitride ceramics can be determined as a ratio of the oxide or nitride to the base metal. In particular embodiments, the ratio is about 2 to 1 or greater, e.g. about 3 to 1 or greater, indicating high oxygen content of the surface. In other embodiments, the ratio is about 1 to 1 or less, e.g. about 1 to 2 or less, indicating a relatively low oxygen composition. In particular embodiments, low oxygen content globular morphologies are formed to enhance endothelialization. In other embodiments, high oxygen content defined grain morphologies are formed, e.g., to enhance adhesion and catalytic reduction. Composition can be determined by x-ray photoelectron spectroscopy (XPS). Depth studies are conducted by XPS after FAB sputtering. The crystalline nature of the ceramic can be characterized by crystal shapes as viewed in FESEM images, or Miller indices as

determined by x-ray diffraction. In embodiments, defined grain morphologies have a Miller index of <101>. Globular materials have blended amorphous and crystalline phases that vary with oxygen content. Higher oxygen content typically indicates greater crystallinity. Further discussion of ceramics and ceramic morphology and computation of roughness parameters is in provided in U.S. Patent Application Serial Nos. 11/752,772 and 11/752,736 [Attorney Docket Nos. 10527-805001 and 10527-801001] and appendices, filed May 23, 2007. Other suitable ceramics include metal oxides and nitrides, such as of iridium, zirconium, titanium, hafnium, niobium, tantalum, ruthenium, platinum and aluminum. The ceramic can be crystalline, partly crystalline or amorphous. IROX is further discussed in Alt, U.S. 5,980,566 and USSN 10/651,562 filed August 29, 2003. The ceramic layer 23 can be, e.g. 10-50 μm in thickness.

In any of the morphologies, the tie layer can be bonded covalently or adhered non-covalently to the ceramic. In the case of globular or intermediate morphologies, the bond or adhesion strength is selected to be enhanced. For example, if the ceramic surface is hydrophilic, the tie layer that includes hydrophilic compatible moieties is seleted to enhance adhesion. In particular embodiments, the adhesion is enhanced by covalent bonding. In embodiments, in the case of defined grain morphologies, the tie layer can be non-covalently or covalently adhered.

The tie layer is also selected for compatibility with the polymer 320. The polymer 320 adheres to the tie layer through either covalent bonding or non-covalent interactions, such as electrostatic interactions, van de Waals forces, or hydrogen bonds, all of which are schematically represented by links 32 in FIG 3. Similar to that discussed above, the tie layer compounds 300 can be derivatized for compatibility with the DEP. For example, if the DEP is hydrophobic, the tie layer can include hydrophobic moieties. For example, if SIBS (styrene-isobutylene-styrene copolymer) is used, compound 300 can include phenyl groups, e.g. as phenylalkenyl silane, to enhance adherence of SIBS to the tie layer. In particular embodiments, for more hydrophilic polymers, the tie layer is a more hydrophilic silane, e.g. amino alkoxy silane. In particular embodiments, polymer 320 may include reactive end groups such as hydroxyl, carboxyl, halide, and amine groups which react readily with silanes, e.g. amino alkoxy silane and as a result, the polymer is covalently bonded to the tie layer. Examples of silanes are available from

Gelest, Inc. and more examples of phosphonates are disclosed by Van Alsten, Langmuir, 15, 7605-7614 (1999). PECVD of silanes is disclosed in more detail by Long, U.S. Publication No. 2003/0170605. Formation of silane layer is discussed further in Duwez, Nature Nanotechnology, 1, 122-125 (2006) and J. Neurophysiol 93, 1659-1670 (2005). The enhancement of polymer-ceramic adhesion due to the tie layer can be tested by standard test methods for adhesion, e.g., Peel test, ASTM D 2197 (scrape adhesion) or ASTM D 3359 (tape test). For example, the standard adhesion tests can tell whether a failure of an adhesive joint is cohesive or adhesive, or what fraction of material remains on a substrate, or the force or energy required to cause the failure. More specifically, as an example, after a standard test, the amount of polymer remaining on a ceramic surface that has a tie layer can be compared to that on the ceramic surface without the tie layer. In embodiments, with the chemical tie layer, the adhesion between the polymer and the ceramic is increased by about 10% or greater, e.g., in terms of amount of polymer remaining on the ceramic after the test. In particular embodiments, the adhesion between polymer and the ceramic is increased by about 50% or greater due to the chemical tie layer. In embodiments, compatibility of two different compounds or materials can be characterized by Differential Scanning Calorimetry (DSC) miscibility test, or contact angle experiments. In embodiments, the contact angle of the tie layer and the ceramic is about 90° or less, preferably 20° or less. In embodiments, DSC analysis can examine the miscibility of two compounds by detecting change of the glass transition peaks since incompatible mixtures will exhibit separate glass transition or melting peaks for each component whereas compatible mixtures will exhibit only one peak that is typically different from the individual component peaks. The drug-eluting polymer or polymer precursor can be applied to the tie layer by, e.g., rolling, dipping, spraying, or vapor deposition. In embodiments, the tie layer can be patterned to increase its surface area. Patterning is further discussed in detail in U.S. Patent Application Serial No. 11/776,320 [Attorney Docket No. 10527-807001] filed contemporaneously herewith, the entire contents of which is hereby incorporated herein by reference.

Suitable drug eluting polymers may be hydrophilic or hydrophobic, and may be selected, without limitation, from polymers including, for example, polycarboxylic acids, cellulosic polymers, including cellulose acetate and cellulose nitrate, gelatin,

polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyanhydrides including maleic anhydride polymers, polyamides, polyvinyl alcohols, copolymers of vinyl monomers such as EVA, polyvinyl ethers, polyvinyl aromatics such as polystyrene and copolymers thereof with other vinyl monomers such as isobutylene, isoprene and butadiene, for example, styrene-isobutylene-styrene (SIBS), styrene-isoprene-styrene (SIS) copolymers, styrene-butadiene-styrene (SBS) copolymers, polyethylene oxides, glycosaminoglycans, polysaccharides, polyesters including polyethylene terephthalate, polyacrylamides, polyethers, polyether sulfone, polycarbonate, polyalkylenes including polypropylene, polyethylene and high molecular weight polyethylene, halogenerated polyalkylenes including polytetrafluoroethylene, natural and synthetic rubbers including polyisoprene, polybutadiene, polyisobutylene and copolymers thereof with other vinyl monomers such as styrene, polyurethanes, polyorthoesters, proteins, polypeptides, silicones, siloxane polymers, polylactic acid, polyglycolic acid, polycaprolactone, polyhydroxybutyrate valerate and blends and copolymers thereof as well as other biodegradable, bioabsorbable and biostable polymers and copolymers. Coatings from polymer dispersions such as polyurethane dispersions (BAYHDROL.RTM., etc.) and acrylic latex dispersions are also within the scope of the present invention. The polymer may be a protein polymer, fibrin, collage and derivatives thereof, polysaccharides such as celluloses, starches, dextrans, alginates and derivatives of these polysaccharides, an extracellular matrix component, hyaluronic acid, or another biologic agent or a suitable mixture of any of these, for example. In one embodiment, a suitable polymer is polyacrylic acid, available as HYDROPLUS.RTM. (Boston Scientific Corporation, Natick, Mass.), and described in U.S. Pat. No. 5,091,205, the disclosure of which is hereby incorporated herein by reference. U.S. Pat. 5,091,205 describes medical devices coated with one or more polyiocyanates such that the devices become instantly lubricious when exposed to body fluids. Another polymer is a copolymer of polylactic acid and polycaprolactone. Suitable polymers are discussed in U.S. Publication No. 20060038027.

The polymer is preferably capable of absorbing a substantial amount of drug solution. When applied as a coating on a medical device in accordance with the present invention, the dry polymer is typically on the order of from about 1 to about 50 microns

thick. In the case of a balloon catheter, the thickness is preferably about 1 to 10 microns thick, and more preferably about 2 to 5 microns. Very thin polymer coatings, e.g., of about 0.2-0.3 microns and much thicker coatings, e.g., more than 10 microns, are also possible. It is also within the scope of the present invention to apply multiple layers of polymer coating onto a medical device. Such multiple layers are of the same or different polymer materials.

The terms "therapeutic agent", "pharmaceutically active agent", "pharmaceutically active material", "pharmaceutically active ingredient", "drug" and other related terms may be used interchangeably herein and include, but are not limited to, small organic molecules, peptides, oligopeptides, proteins, nucleic acids, oligonucleotides, genetic therapeutic agents, non-genetic therapeutic agents, vectors for delivery of genetic therapeutic agents, cells, and therapeutic agents identified as candidates for vascular treatment regimens, for example, as agents that reduce or inhibit restenosis. By small organic molecule is meant an organic molecule having 50 or fewer carbon atoms, and fewer than 100 non-hydrogen atoms in total.

Exemplary therapeutic agents include, e.g., anti-thrombogenic agents (e.g., heparin); anti-proliferative/anti-mitotic agents (e.g., paclitaxel, 5-fluorouracil, cisplatin, vinblastine, vincristine, inhibitors of smooth muscle cell proliferation (e.g., monoclonal antibodies), and thymidine kinase inhibitors); antioxidants; anti-inflammatory agents (e.g., dexamethasone, prednisolone, corticosterone); anesthetic agents (e.g., lidocaine, bupivacaine and ropivacaine); anti-coagulants; antibiotics (e.g., erythromycin, triclosan, cephalosporins, and aminoglycosides); agents that stimulate endothelial cell growth and/or attachment. Therapeutic agents can be nonionic, or they can be anionic and/or cationic in nature. Therapeutic agents can be used singularly, or in combination. Preferred therapeutic agents include inhibitors of restenosis (e.g., paclitaxel), anti-proliferative agents (e.g., cisplatin), and antibiotics (e.g., erythromycin). Additional examples of therapeutic agents are described in U.S. Published Patent Application No. 2005/0216074. Polymers for drug elution coatings are also disclosed in U.S. Published Patent Application No. 2005/019265A.

The stents described herein can be configured for vascular, e.g. coronary and peripheral vasculature or non-vascular lumens. For example, they can be configured for

use in the esophagus or the prostate. Other lumens include biliary lumens, hepatic lumens, pancreatic lumens, uretheral lumens and ureteral lumens.

Any stent described herein can be dyed or rendered radiopaque by addition of, e.g., radiopaque materials such as barium sulfate, platinum or gold, or by coating with a radiopaque material. The stent can include (e.g., be manufactured from) metallic materials, such as stainless steel (e.g., 316L, BioDur® 108 (UNS S29108), and 304L stainless steel, and an alloy including stainless steel and 5-60% by weight of one or more radiopaque elements (e.g., Pt, Ir, Au, W) (PERSS®) as described in US-2003-0018380-A1, US-2002-0144757-A1, and US-2003-0077200-A1), Nitinol (a nickel-titanium alloy), cobalt alloys such as Elgiloy, L605 alloys, MP35N, titanium, titanium alloys (e.g., Ti-6Al-4V, Ti-50Ta, Ti-10Ir), platinum, platinum alloys, niobium, niobium alloys (e.g., Nb-1Zr) Co-28Cr-6Mo, tantalum, and tantalum alloys. Other examples of materials are described in commonly assigned U.S. Application No. 10/672,891, filed September 26, 2003; and U.S. Application No. 11/035,316, filed January 3, 2005. Other materials include elastic biocompatible metal such as a superelastic or pseudo-elastic metal alloy, as described, for example, in Schetsky, L. McDonald, "Shape Memory Alloys", Encyclopedia of Chemical Technology (3rd ed.), John Wiley & Sons, 1982, vol. 20. pp. 726-736; and commonly assigned U.S. Application No. 10/346,487, filed January 17, 2003.

The stent can be of a desired shape and size (e.g., coronary stents, aortic stents, peripheral vascular stents, gastrointestinal stents, urology stents, tracheal/bronchial stents, and neurology stents). Depending on the application, the stent can have a diameter of between, e.g., about 1 mm to about 46 mm. In certain embodiments, a coronary stent can have an expanded diameter of from about 2 mm to about 6 mm. In some embodiments, a peripheral stent can have an expanded diameter of from about 4 mm to about 24 mm. In certain embodiments, a gastrointestinal and/or urology stent can have an expanded diameter of from about 6 mm to about 30 mm. In some embodiments, a neurology stent can have an expanded diameter of from about 1 mm to about 12 mm. An abdominal aortic aneurysm (AAA) stent and a thoracic aortic aneurysm (TAA) stent can have a diameter from about 20 mm to about 46 mm. The stent can be balloon-expandable, self-expandable, or a combination of both (e.g., U.S. Patent No. 6,290,721).

In embodiments, the tie layer and drug-eluting layer are provided only on the abluminal surface, as illustrated. In other embodiments, these elements are provided as well or only on the adluminal surface and/or cut-face surfaces.

All publications, patent applications, patents, and other references mentioned herein are incorporated by reference herein in their entirety.

Still further embodiments are in the following claims.

WHAT IS CLAIMED IS:

1. An endoprosthesis, comprising:
a body including a ceramic on a surface thereof,
a tie layer adhered to the ceramic, and
a polymeric coating adhered to the tie layer.

2. The endoprosthesis of claim 1, wherein the polymeric coating includes a drug.

3. The endoprosthesis of claim 1, wherein the tie layer is covalently bonded to the ceramic.

4. The endoprosthesis of claim 1, wherein the tie layer is non-covalently adhered to the ceramic.

5. The endoprosthesis of claim 1, wherein the ceramic has an Sdr of about 10 or less and an Sq of about 10 or less and the tie layer is covalently bonded to the ceramic.

6. The endoprosthesis of claim 5, wherein the ceramic has a globular morphology.

7. The endoprosthesis of claim 1, wherein the ceramic has surface oxygen content of about 80% or more and the tie layer is covalently bonded to the ceramic.

8. The endoprosthesis of claim 1, wherein the ceramic has an Sdr of about 120 to 200 and an Sq of about 20 or more and the tie layer is non-covalently adhered to the ceramic.

9. The endoprosthesis of claim 8, wherein the ceramic has a defined grain morphology.

10. The endoprosthesis of claim 1, wherein the ceramic has a surface oxygen content of about 80% or less and the tie layer is non-covalently adhered to the ceramic.

11. The endoprosthesis of claim 1, wherein the ceramic is an oxide.

12. The endoprosthesis of claim 1, wherein the ceramic is IROX.

13. The endoprosthesis of claim 1, wherein the tie layer is selected from silanes, phosphonates, and titanates.

14. The endoprosthesis of claim 1, wherein the polymeric coating is adhered to the tie layer by covalent bonding.

15. The endoprosthesis of claim 1, wherein the polymeric coating is adhered to the tie layer by non-covalent adherence.

16. The endoprosthesis of claim 3, wherein the polymeric coating and the ceramic has an adhesion increased about 50% or greater by the tie layer.

17. A method of forming an endoprosthesis, comprising:

forming a ceramic and a non-ceramic, non-metal overlayer on the ceramic such that,

the ceramic has an Sdr of about 10 or less, and the overlayer is covalently bonded to the ceramic, or

the ceramic has an Sdr of about 100 or greater, and the overlayer is non-covalently adhered to the ceramic, or

the ceramic has an Sdr between about 10 and 100 and the overlayer is non-covalently adhered or covalently bonded to the ceramic.

18. The method of claim 17, wherein the ceramic having the Sdr of about 10 or less has a globular morphology.

19. The method of claim 17, wherein the ceramic having the Sdr of about 100 or greater has a defined grain morphology.

20. The method of claim 17, wherein the ceramic is an oxide.

21. The method of claim 17, wherein the covalent bond is through oxygen moieties of the ceramic.

22. The method of claim 17, wherein the overlayer is a silane, phosphate or titanate.

23. The method of claim 17, further comprising forming a polymer layer on the overlayer.

24. The method of claim 23, wherein the polymer layer includes a drug.

25. The method of claim 23, wherein the polymer layer and the ceramic has an adhesion increased about 10% or greater by the overlayer.

26. The method of claim 17, wherein the ceramic is IROX.

FIG. 1A

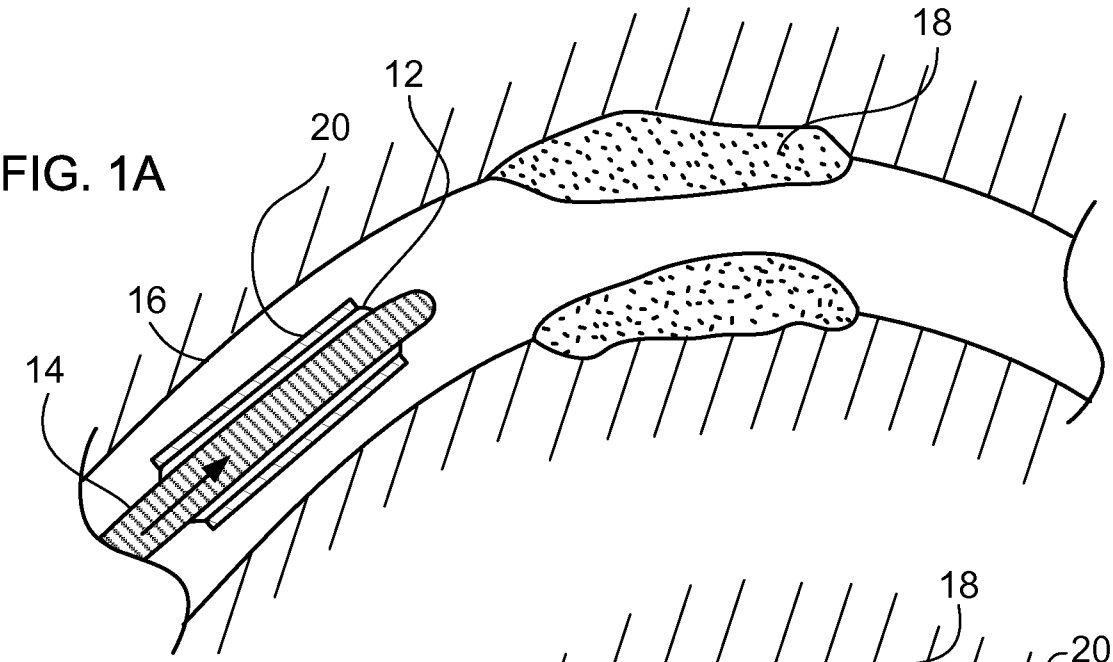


FIG. 1B

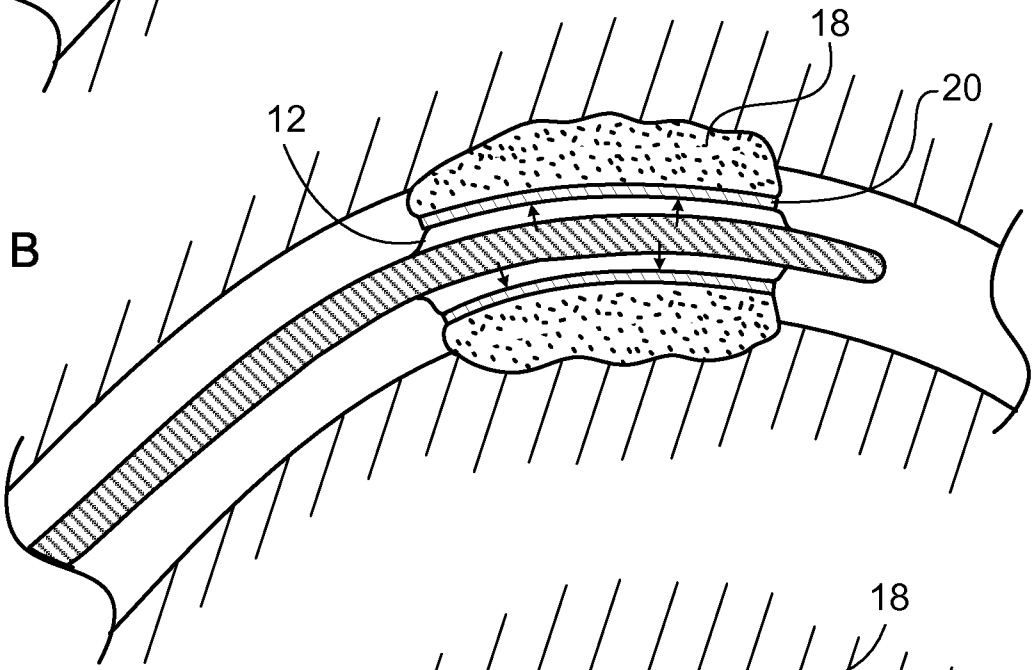
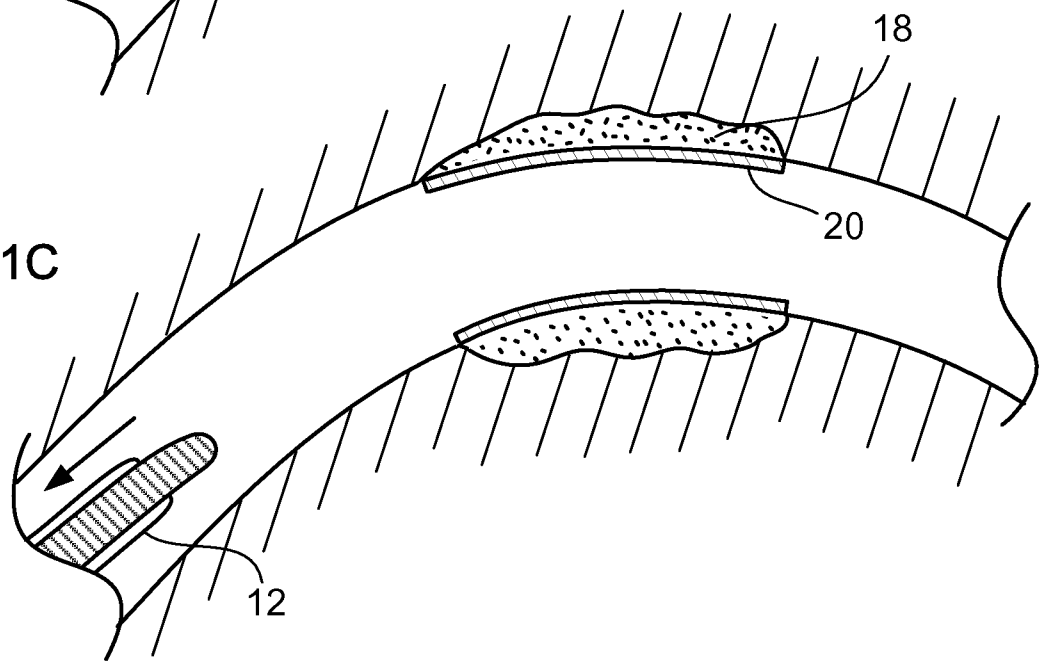


FIG. 1C



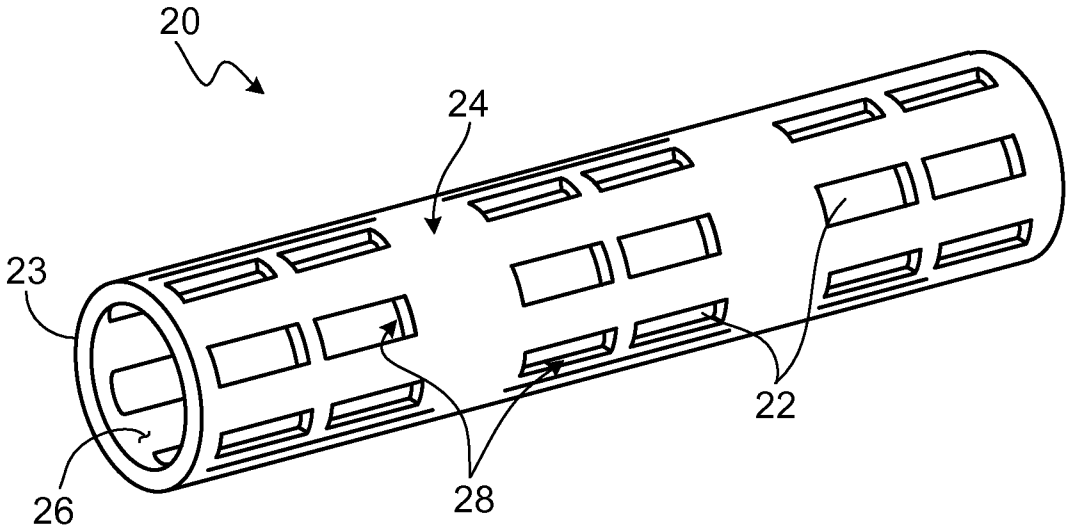


FIG. 2A

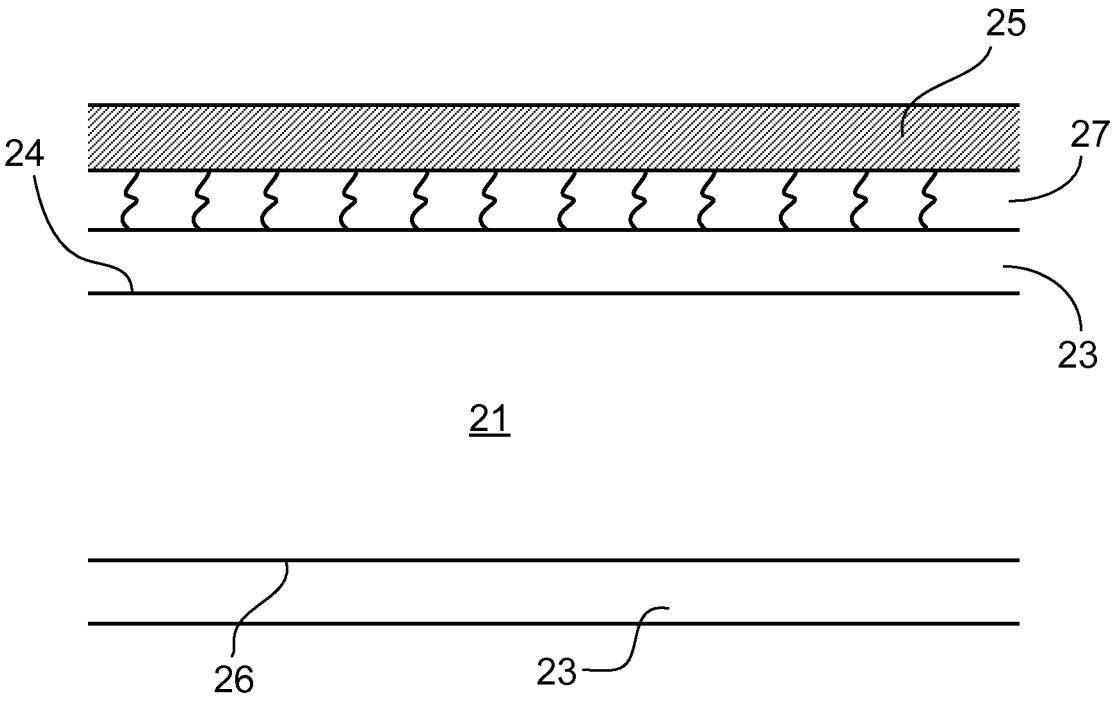
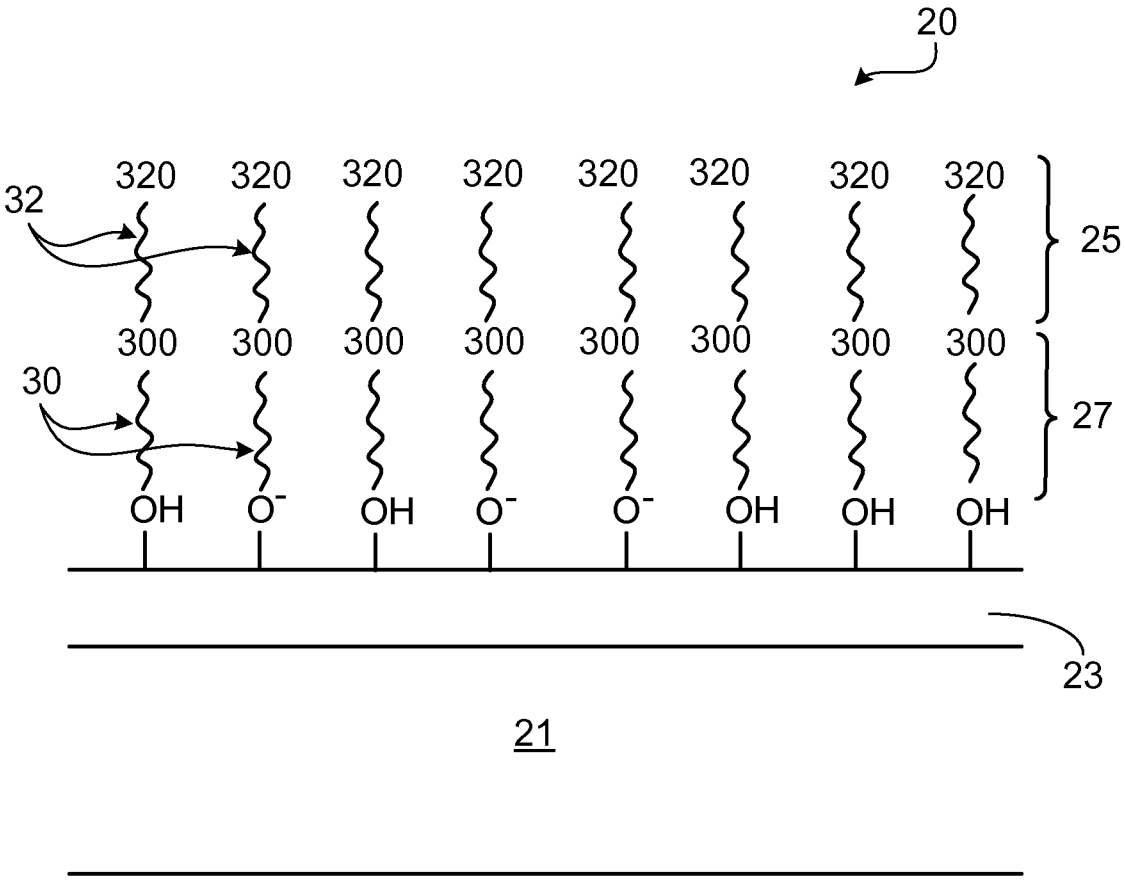


FIG. 2B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OH
OH
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21

FIG. 3

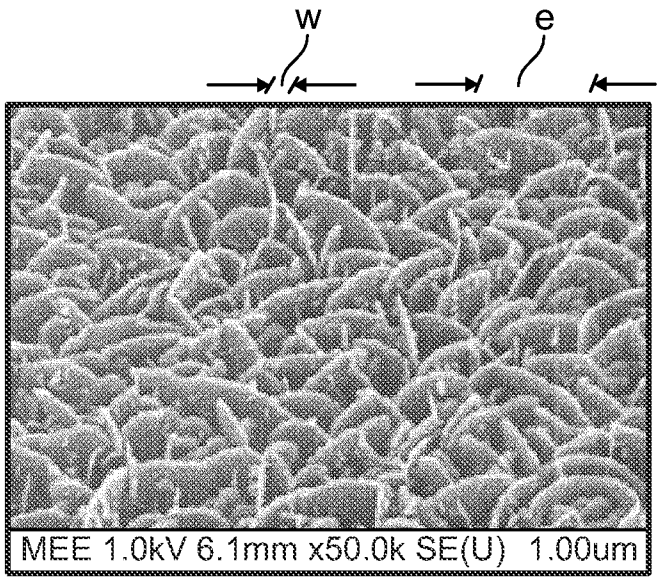
w
e
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FIG. 4A

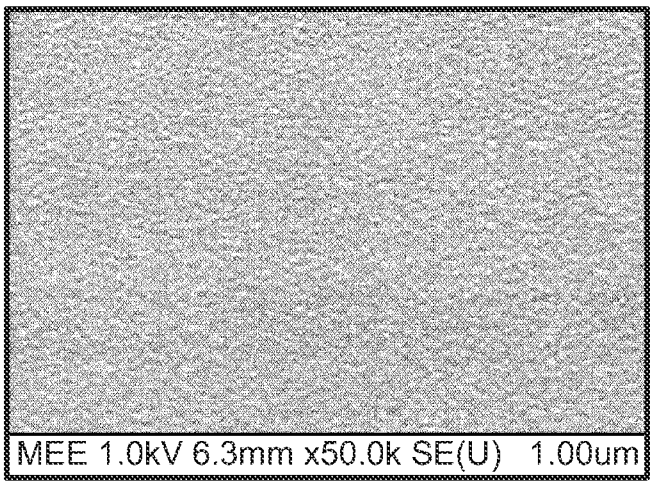
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FIG. 4B