(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 October 2008 (16.10.2008)

PCT

(10) International Publication Number
WO 2008/124519 A2

(51) International Patent Classification:
*A61L 31/08* (2006.01) *A61L 31/16* (2006.01)
*A61L 31/14* (2006.01) *C23C 14/48* (2006.01)

(21) International Application Number:
PCT/US2008/059287

(22) International Filing Date: 3 April 2008 (03.04.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11/697,079 5 April 2007 (05.04.2007) US

(71) Applicant *(for all designated States except US)*: **BOSTON SCIENTIFIC SCIMED, INC.** [US/US]; One Scimed Place, Maple Grove, MN 55311-1566 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **WEBER, Jan** [NL/NL]; Holdaal 49, NL-6228 GJ Maastricht (NL).

(74) Agent: **BRUESS, Steven, C.**; Merchant & Gould P.C., P.O. Box 2903, Minneapolis, MN 55402-0903 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**
— *without international search report and to be republished upon receipt of that report*

WO 2008/124519 A2

(54) Title: STENTS WITH CERAMIC DRUG RESERVOIR LAYER AND METHODS OF MAKING AND USING THE SAME

(57) Abstract: A method of making a drug eluting stent comprises forming a porous stent body surface layer by ion implantation, applying a layer of ceramic particles on the porous layer and compressing the layer of ceramic particles. The layer of ceramic particles can be compressed to successively higher densities. Drugs can be loaded into the layer of ceramic materials at a relatively low density before the layer of ceramic materials is compressed to a higher density to achieve a desired low drug release rate.

# STENTS WITH CERAMIC DRUG RESERVOIR LAYER AND METHODS OF MAKING AND USING THE SAME

This application is being filed on 03 April 2008, as a PCT International Patent application in the name of Boston Scientific Scimed, Inc., a U.S. national corporation, applicant for the designation of all countries except the US, and Jan Weber, a citizen of the Netherlands, applicant for the designation of the US only, and claims priority to U.S. Utility Patent Application No. 11/697,079, filed April 5, 2007.

## Technical Field

This disclosure relates to stents and related methods. Specific arrangements also relate to methods and configurations of stents with drug reservoir layers that can be loaded with drugs at low temperatures.

## Background

Stents are prosthetic devices typically intraluminally placed by a catheter within a vein, artery, or other tubular body organ for treating conditions such as, occlusions, stenoses, aneurysms, dissection, or weakened, diseased, or abnormally dilated vessels or vessel walls, by expanding vessels or by reinforcing vessel walls. Stents can improve angioplasty results by preventing elastic recoil and remodeling of the vessel wall and treating dissections in blood vessel walls caused by balloon angioplasty of coronary arteries.

Stents are typically tubular and expandable from a collapsed state to an expanded state. In a typical operation to implant a stent, the stent is initially configured in the collapsed state, with a cross-sectional size sufficiently small for ease of passage to the intended site. After the stent reaches the intended site, the stent is typically deformed to increase its cross-sectional size to fully engage the stent with the surrounding tissues. The stent thereafter remains in place in the expanded state.

In some cases, stents are impregnated with drugs, i.e., therapeutic agents, to be released over time to treat various conditions. Drugs are typically dispersed in porous drug reservoir layers formed on the surfaces of metallic stent bodies. Bonding between the drug reservoir layers and the stent bodies is of

significant concern as the stents typically undergo significant deformation during deployment, and detachment of the drug reservoir layers from the stent bodies would generally be undesirable.

While conventional stent technology is relatively well developed, technologies related to drug-delivering stents are still being developed.

## Summary of the Disclosure

The present disclosure relates generally to methods of making stents with drug reservoir surface coating layers. In one configuration, a drug reservoir layer is made by applying a layer of ceramic particles, compressing the particles to a final density in successive stages and infusing the layer with drug between stages of compression.

A further aspect of the present disclosure relates to providing stent body having porous surface portions, and depositing a layer of ceramic particles over the porous surface portions, with a portion of the ceramic particles at least partially filling the open pores in the porous surface portions.

## Brief Description of the Drawings

Figure 1 is a schematic perspective view of an example stent constructed according to one aspect of the present disclosure.

Figure 2 is a schematic cross-sectional view of a portion of an example stent constructed according to one aspect of the present disclosure.

Figure 3(a) is a scanning electron micrographs of porous surface portions of stainless steel. The porous structures are produced by argon bombardment. The scale bar represents approximately 10 micrometers.

Figure 3(b) is a magnified view (magnification = 2×) of a portion of the micrograph in Figure 3(a).

Figure 3(c) is a magnified view (magnification = 8×) of a portion of the micrograph in Figure 3(a).

Figure 4 is a schematic diagram showing an apparatus for compression of a layer of ceramic particles on the abluminal surface portions of a stent.

## Detailed Description

I. Overview

This disclosure relates to making stents having ceramic reservoir surface layers formed on stent bodies.

Stents are typically implanted intraluminally in tubular body organs, such as blood vessels, to expand or strengthen the portion of the organ where the stent is placed. Drug eluting stents typically have surface portions capable of storing drugs and releasing the drugs at particular rates. Porous ceramic drug reservoir layers coating stent bodies are desirable in many applications because of the biocompatibility exhibited by many ceramic materials. It is desirable to have ceramic drug reservoir layers that are sufficiently thick (e.g., on the order of a few micrometers or thicker) to achieve useful drug storage capacities. In some applications, it is also desirable to have substantially polymer-free ceramic drug reservoir layers.

There are a number of difficulties in making stents with ceramic drug reservoir layers. First, it is often difficult to achieve good bonding between porous ceramic layers to the underlying stent bodies, which are typically metallic. Second, it is often difficult to load drugs into a porous network structure of a ceramic drug reservoir layer. Although certain chemical processes using organic substances, such as polymers, can be used to aid the loading of drugs into the ceramic drug reservoir layers, the subsequent processes, such as heating to drive off the organic substances, are often detrimental to the drugs. Third, ceramic layers of adequate thicknesses for drug eluting stents and made by traditional methods can sometimes be prone to cracking, especially when the stent is deformed in the deployment process.

The example processes disclosed in the present disclosure overcome at least some of the above-mentioned difficulties in producing stents with ceramic drug reservoir surface layers. In one aspect of the present disclosure, porous surface portions of stent body material are produced by ion implantation, and a layer of ceramic particles are deposited on the porous surface portions and partially compressed into the open pores to form a strong bond between the layer of ceramic particles and the stent body. In another aspect of the present disclosure, Drugs are dispersed into the layer of ceramic particles after the layer of ceramic particles is

compressed to a first density, and the layer is further compressed to a higher density thereafter to achieve a designed drug release rate.

II. Example Processes and Configurations

A process for making a stent with drug reservoir coating layers is now described with reference to an example stent 20 in Figures 1 and 2. The stent 20 is shown in an at least partially expanded state. The stent 20 has the form of a tubular member defined by a plurality of bands 22 and a plurality of connectors 24 that extend between and connect adjacent bands. During use, bands 22 are expanded from an initial, smaller cross-sectional size to a larger one to contact stent 20 against a wall of a vessel, thereby expanding or strengthening the vessel. A stent can be expanded using a variety of methods. For example, one or more balloons can be used to expand a stent. A self-expanding stent can also be compressed into a collapsed state and held in the collapsed state by a sheath prior to implantation, and unsheathed and permitted to expand at the implantation site. Examples of self-expanding stents include stents made of memory metals, which are flexible and collapsible from a predefined shape at room temperature but regains the predefined shape above certain critical temperature. Connectors 24 provide stent 20 with flexibility and conformability so that the stent can adapt to the contours of the vessel.

As shown in Figure 2, the stent 20 comprises a stent body 26 with an adluminal (toward lumen) surface 28 and abluminal (away from lumen; or toward vessel wall) surface 30. In an example method of the present disclosure, a surface, such as the abluminal surface 30 of the stent body 26 is treated, for example, by ion implantation, to produce a layer 38 of porous structure. A coating of ceramic particles is then deposited on the layer 38 of porous structure by, for example, spraying a suspension of the particles in water or an organic solvent, to the treated surface 30 or by dipping the treated surface 30 in such a suspension. The coating is then dried. Subsequent deposition and drying steps can be carried out to stack additional coatings of ceramic particles to form a combined layer of ceramic particles on the porous layer of the stent body 26. After the deposition steps, the layer of ceramic particles is compressed by, for example, a mechanical press with a solid surface. In one aspect of the present disclosure, the layer of ceramic particles

is compressed to a first density. A drug is then dispersed into the layer. The layer is then further compressed to a second density. The process in this example thus produces a ceramic layer at a relatively low density, or high porosity, for ease of drug uptake by the ceramic layer; the subsequent compression results in a denser ceramic layer, with lower porosity for adequately low rate of release of the loaded drugs. The pressure at each stage of compression can be set according to the desired drug uptake and release rates, respectively, for specific applications.

In one respect of the present disclosure, the average size of at least 50 volume percent of the ceramic particles in the ceramic layer is smaller than the average size of at least 50 volume percent of the open pores in the porous layer supporting the ceramic layer. As an example, the average size of at least 50 volume percent of the ceramic particles in the ceramic layer can be less than one tenth of the average size of at least 50 volume percent of the open pores in the porous metal layer or smaller. For example, the surface of a metallic stent body can be treated to produce a porous layer having an average pore size on the order of one-half to one micrometer for at least 50 volume percent of the open pores, and the ceramic particles applied to the porous layer can have an average size on the order of 25 to 50 micrometers for at least 50 volume percent of the ceramic particles. Thus, after the coating and compression steps, some ceramic particles are embedded in the open pores in the porous layer, thereby enhancing the bonding between the ceramic layer and the stent body.

More specific aspects of example methods and configurations are described in the following sections.

A. Surface Treatment of Stent Body

In one aspect of the present disclosure, surface portions of a stent body, such as the abluminal surface 30 of the stent body 26 in Figure 2 is modified to produce a porous layer, such as the porous layer 38. As an example, ion implantation into a surface of a metal can be used to produce a porous surface layer on the metal. In a further example, plasma immersion ion implantation can be used for this purpose. In plasma immersion ion implantation, plasma ions are implanted into a stent body upon pulsed charging to high negative voltages, The energy of the ions impinging upon the surface of the metal at least partially determines the depth

of penetration by the ions into the metal, and thus the thickness of the porous layer. In one aspect of the present disclosure, ion implantation of an element is carried out with a sufficiently high flux, as measured in number of ions per unit area per unit time entering the metal, to result a concentration of the element in the metal exceeding the solubility limit of the element in the metal. Under these conditions, at least portions of the implanted element segregate into pockets of pressurized liquid within the metal. The pockets can migrate and coarsen in the metal, and reshape the surrounding metal when the pockets reach the surface of the metal or each other, thereby producing a porous structure in the metal.

Various elements can be used for creating porous layers on stent bodies. For example, argon, helium and xenon can be used. Formation of porous layers in a target metal can be more efficient with elements having lower solubility limits in the target metal than with elements having higher solubility limits in the target metal. For example, implantations of argon and helium have shown to be effective in forming porous structures in stainless steel. In certain applications, reactive gasses, such as oxygen and nitrogen, can be used as secondary implantation elements in smaller amount than the main implantation elements such as argon, helium and xenon. Chemical reactions between the secondary implanted elements, such as oxygen and nitrogen, with the target metal can also be utilized to achieve beneficial results. For example, oxide or nitride passivation layers can be formed on the surface of certain target metals, such as titanium. According to another aspect of the present disclosure, the secondary implantation elements can be implanted either simultaneously with the main implantation elements or after a porous structure has been formed by the implantation of the main implantation elements.

Processing parameters can be selected to achieve desired open pore sizes in the metal. Processing parameters affecting open pore sizes in a given metal include temperature of the metal, ion type, ion energy and ion flux.

Examples of porous structure produced by argon implantation into a stainless steel substrate are shown in Figures 3(a)-(b). The stainless steel in this case is 316L. Argon implantation was carried out at an energy level of 35 keV, with a dosage of from $1\times10^{18}$ $cm^{-2}$ to $5\times10^{18}$ $cm^{-2}$, and at a substrate temperature of between 300 to 350 °C. The porous layer produced by this example method has

predominantly sub-micrometer-sized and networked stainless steel structures, with open pores of similar dimensions.

Additional examples of porous metal produced by ion bombardment are known in the art of metallurgy. For example, M. Tokitani et al., "Desorption of helium from austenitic stainless steel heavily bombarded by low energy He ions", *J. nucl. mater.*, 329-333 (2004) pp. 761-765 discloses formation of porous surface layers in stainless steel under helium radiation. N. Yoshida et al., "Impact of low energy helium irradiation on plasma facing metals", *J. nucl. mater.*, 337-339 (2005) pp. 946-950 discloses formation of porous surface layers in metals including stainless steel and tungsten under helium radiation. Both of the above-mentioned references are incorporated herein by reference.

According to another aspect of the present invention, combinations of processing methods can be used to achieve more complex morphologies of the porous layer. For example, argon implantation can be used first to produce a porous layer with relatively coarse structures. For example, surface structures of 0.1-3.0 micrometers in dimension can be produce by argon implantation. Argon implantation can be followed up with helium implantation to produce surface features of smaller scales on top of the relatively coarse structures. For example, structures of 50 nanometers or less in dimension can be produced by helium implantation on the surface structures produced by argon implantation. Such more complex morphologies further increase the surface areas of the porous layer and can enhance the bonding between the stent body and the ceramic drug reservoir layer.

B. Coating Ceramic Layers

After a porous surface layer has been made in the stent body, one or more coatings of ceramic particles are applied on the porous layer. Ceramic materials are solids that have as their essential component, and are composed in large part of, inorganic nonmetallic materials. Examples of suitable ceramic materials include certain transition metal oxides, such as titanium ($TiO_x$), tantalum oxide ($TaO_x$) and iridium oxide ($IrO_x$). Various methods known in the art of ceramic coating can be used. For example, suspensions of ceramic particles in water or organic solvents, such as ethanol, can be used to apply the ceramic particles. For example, as disclosed in J. Halme et al., "Spray deposition and compression of $TiO_2$

nanoparticle films for dye-sensitized solar cells on plastic substrates", *Solar Energy Materials & Solar Cells* 90 (2006) pp. 887–899 (hereinafter, "the Halme reference"), suspension of titanium oxide particles in ethanol or water can be sprayed, for example, by an airbrush, on a substrate, which can be heated. As another example, H. Lindström, "A new method for manufacturing nanostructured electrodes on glass substrates", *Solar Energy Materials & Solar Cells*, 73 (2002) pp. 91–101 (hereinafter, "the Lindström reference"), discloses applying a suspension of titanium oxide particles in ethanol by a blade. Both the Halme and Lindström references are incorporated herein by reference. In one aspect of the disclosure, Titanium oxide suspensions can be obtained by stirring titanium oxide powers in ethanol or water for several hours. Examples of titanium oxide powders include the commercial product Degussa P25, which is reported to contain predominately anatase and rutile (mineral forms of titanium oxide) particles sized under 100 nm, typically between 20 to 40 nm.

The ceramic suspension applied to the porous surface is then dried. Examples of useful processes for drying the suspension include heating, including heating the stent body material while the suspension is being applied. The drying temperature is set to be sufficiently high to dry the suspension and yet sufficiently low to prevent significant agitation of the ceramic particle in the suspension or driving off a significant portion of any drugs loaded into the layer of ceramic particles before heating. For example, stent body material can be heated to between 80-100°C to dry an ethanol suspension. Additional examples of useful heating processes include convection heating and heating by UV, IR and microwave radiation.

The application and drying of a coating of ceramic particles can be repeated to form a layer of stacked coatings, according to one aspect of the present disclosure. For example, a suspension of ceramic particles can be applied to a piece heated stent body material intermittently, allowing the solvent in the suspension to dry between heating. Forming a layer of ceramic particles from multiple coatings facilitates the formation of a ceramic layer of desirable thickness (e.g., on the order of micrometers) for drug reservoirs in stents while minimizing crack formation in the ceramic layer.

C. Compression of Layer of Ceramic Particles

According to a further aspect of the present disclosure, after the layer of ceramic particles is formed on the porous surface of the stent body material, the layer is compressed to achieve the desired density of the ceramic layer and strengthen the bonding between the ceramic layer and the stent body material. Compression forces ceramic particles in the ceramic layer into the open pores of the porous layer in the stent body material, as discussed above. Such a process can increase the interface area between the stent body material and the ceramic layer, or result in interlocking structures between the ceramic particles and the porous layer, or both. Bonding between the two materials is thus enhanced. At the same time, compression also reduces the porosity of the ceramic layer, thereby decreasing the drug release rate from the ceramic layer. Compression further increases the integrity of the ceramic layer.

A variety of methods suitable for compressing powdered masses can be used for compressing the layer of ceramic particles. Mechanical presses can be used for this purpose. For example, both the Halme and Lindström references incorporated herein disclose pressing assemblies of titanium oxide films on substrate between solid surfaces of steel plates. Releasing agents, such as Teflon films and aluminum foils, can also be used between a ceramic film-substrate assembly and the plates for releasing the assembly from the plates after compression is complete.

In another example configuration, as shown in Figure 4, a ceramic layer 38 in a tubular stent 20 is compressed between two plates 42, 44 under a compressional force $p$. Each plate 42 or 44 has a recess with a cylindrical wall portion 42a or 44a, respectively, for accommodating a portion of the stent 20 and forming a finite contact area with the ceramic layer 38. The stent 20 is internally supported by a pin 46. Compression of portions of the ceramic layer 38 is thus achieved by the compressive stress applied to the stent by the cylindrical wall portions 42a and 44a and the pin 46. The assembly of the stent 20 and pin 46 can be compressed between the plates 42 and 44 and then released. The steps of compressing and release can be repeated, with the stent 20 rotated about its longitudinal axis between the steps, until the entire ceramic layer 38 has been compressed. Furthermore, the ceramic layer 38 can be compressed in multiple

stages, with the pressing incremented with each successive stage, to gradually compress the ceramic layer 38 to the desired porosity.

In another example configuration, stent 20 can be place relative the compression plates 40 and 42 such that the stent 20 is compressed to a first porosity along only a portion of the length of the stent 20. Portions of the stent 20 can further be compressed along other portions of the stent's length to achieve a second porosity that is different from the first. Thus, a stent 20 with different porosity levels along its length can be produced.

Porosity of the ceramic film generally decreasing with increasing applied pressure. For example, the Lindström reference discloses that the porosity of the titanium oxide film decreases from 70% to 50% when pressure increases from 250 $kg/cm^2$ to 2000 $kg/cm^2$. In one aspect of the present disclosure, the layer of ceramic particles is compressed first to a relatively low pressure to result in a ceramic layer that has sufficient integrity for drug loading and yet a relatively high porosity for efficient absorption of drugs into the ceramic layer. For example, a pressure of 200-300 $kg/cm^2$ can be applied for this purpose. The porosity at this stage can be 60%, 70% or higher. After the drugs is loaded into the ceramic layer (e.g., by contacting the ceramic layer with the drugs in solution), the ceramic layer can be further compressed to a higher pressure to result in a relatively low porosity to achieve a desired drug release rate. In one aspect of the present disclosure, a pressure of 1000-2000 $kg/cm^2$ or higher can be applied to result in a porosity of 50% or lower.

The processes described in the examples above are capable of producing a sufficiently thick ceramic layer on a stent body for storing desired amount of drugs. In one aspect of the present disclosure, a ceramic layer of 1-20 micrometers in final compressed thickness can be produced. In another aspect, the thickness can be 2-15 micrometers. In a further aspect, the thickness can be 5-10 micrometers.

It is noted that the example processes described above, including surface treatment, coating of ceramic layers, compression of the ceramic layers and drug loading, can be carried out on stock material, such as stainless tubes or sheets, used for making stents. Openings in the coated stock material can subsequently be cut out to form the desired patterns of bands and connectors, such as those (22 and

24) shown in Figure 1. For example, lasers, including femtosecond lasers, can be used to cut the stock material. Examples of forming stents by cutting coated metal structure using laser ablation are disclosed in the U.S. Patent No. 6,517,888, which is incorporated herein by reference.

D. Additional Example Configurations

Various materials and processes can be used to suit specific stent applications. In one aspect of the present disclosure, various materials can be used for manufacturing stents with at least one layer of ceramic particles compressed on the stent bodies. A stent body, for example, can be made of a variety of materials that are known, or later found, to be suitable for endoluminal implantation applications. For example, a variety of metals that have requisite mechanical properties (such as strength and deformability) are biocompatible and suitable as substrates for forming ceramic coatings can be used. Such metals include various alloys and other metals. In one configuration, the stent body is made of stainless steel.

In another aspect of the present disclosure, specific surface morphologies of the ceramic layer can be created during the compression process for certain stent applications such as promoting cell growth. For example, recesses (such as grooves and pits) or protuberances (such as ridges) can be formed on the surface of the ceramic layer by providing complementary structures in the plates used to compress the ceramic layer. For example, ridges on the compression plates can be used to produce grooves in the ceramic layer.

In another aspect of the present disclosure, at least two stacked ceramic layers can be manufactured by the processes described above, each loaded with a different drug or drug concentration so as to achieve a desired time profile of drug release. Each layer can be compressed to the final density after the drug for the layer is loaded but before the next layer is applied. Alternatively, at least two stacked ceramic layers can be loaded with their respective drugs before the layers are compressed to the final density.

In a further aspect of the present disclosure, drugs can be loaded into the ceramic layer or layers by incorporating the drugs into the suspensions of ceramic particles. This process is particularly useful for drugs that have high

solubility in water or organic solvent (e.g., ethanol) used to make the suspensions and are stable under the conditions for drying the suspension.

In an additional aspect of the present disclosure, other types of particles, including polymeric particles, metal particles and mixtures of any of polymer, metal and ceramic particles can be used to produce the layer or layers over the stent body to suit specific applications.

III. Summary

Thus, according to the present disclosure, at least a surface portion of a stent body material can be made porous by, for example, ion implantation. At least one layer of ceramic or other types of particles can be deposited on the porous surface portion and compressed to form a strong bond with the stent body material. At least one drug can be loaded into the layer of particles. In one aspect, the layer of particles can be compressed to a first density. At least one drug can be loaded into the layer while the layer is at the first density. The layer can then be further compressed to a second density to achieve a desired drug release rate.

The above specification, examples and data provide a complete description of the manufacture and use of the composition of the invention. Since many embodiments of the invention can be made without departing from the spirit and scope of the invention, the invention resides in the claims hereinafter appended.

WE CLAIM:

1. A method of making a stent, the method comprising steps of:

implanting at least one type of ion into a metallic stent body material in at least one surface portion of the stent body material to produce at least one porous layer at the surface portion;

depositing a layer of ceramic particles on the porous layer;

and compressing the layer of ceramic particles.

2. The method of claim 1, wherein the step of depositing a layer of ceramic particles comprises applying at least one suspension of the ceramic particles and drying the applied suspension.

3. The method of claim 2, wherein the step of depositing a layer of ceramic particles comprises successively applying a plurality of stacked coatings of ceramic particles, wherein applying each of the plurality of the coatings comprises applying at least one suspension of ceramic particles and drying the applied suspension.

4. The method of claim 1, wherein the step of implanting at least one type of ion comprises implanting ions of at least one element with a sufficiently high flux to produce concentrations of the element in the stent body material in excess of a solubility limit of the element in the stent body material.

5. The method of claim 1, wherein the step of implanting at least one type of ions comprises implanting at least one of argon, helium, xenon, oxygen and nitrogen into the stent body material.

6. The method of claim 5, wherein the step of implanting at least one type of ions comprises implanting as least argon into a stainless steel portion of the stent body material.

7. The method of claim 1, wherein the step of implanting at least one type of ions comprises implanting ions of a first type to produce a porous layer, and implanting ions of a second type to produce a porous structure within the porous layer

8. The method of claim 7, wherein the step of implanting ions of a first type comprises implanting ions of the first type to produce a first plurality of open pores with a first average pore size for at least 50 volume percent of the first plurality of open pores, and implanting ions of a second type comprises implanting ions of the second type to produce a second plurality of open pores with a second average pore size for at least 50 volume percent of the second plurality of open pores.

9. The method of claim 1, wherein the step of compressing the layer of ceramic particles comprises pressing the layer with a solid surface.

10. The method of claim 1, further comprising loading at least one drug into the layer of ceramic particles.

11. The method of claim 10, wherein the step of compressing the layer of ceramic particles comprises compressing the layer to a first density and further compressing the layer to a second density, and wherein loading at least one drug comprises loading the drug into the layer while the layer is at the first density.

12. The method of claim 9, wherein the step of depositing a layer of ceramic particles on the porous layer comprises depositing the layer of ceramic particles on an abluminal surface of a tubular portion of the stent body material, the method further comprising supporting an adluminal surface portion of the tubular portion.

13. The method of claim 12, wherein the step of pressing the layer of ceramic particles with a solid surface comprises pressing the layer with a cylindrical arch section of a solid surface.

14. The method of claim 1, wherein the step of implanting at least one type of ions to produce at least one porous layer comprises implanting at least one type of ions to produce a plurality of open pores with a first average size for at least 50 volume percent of the open pores, and wherein the step of depositing a layer of ceramic particles on the porous layer comprises depositing a layer of ceramic particles with a second average size for at least 50 volume percent of the ceramic particles, the second average size being smaller than the first average size.

15. The method of claim 14, the second average size being smaller than one tenth of the first average size.

16. The method of claim 10, wherein the step of depositing a layer of ceramic particles comprises applying at least one suspension of the ceramic particles and drying the applied suspension, and wherein loading at least one drug into the layer of ceramic particles comprises incorporating the drug in the suspension.

17. The method of claim 9, further comprising forming a plurality of protuberances or recesses or both on a surface of the layer of ceramic particles, wherein pressing the layer of ceramic particles with a solid surface comprises pressing with a solid surface having a plurality of protuberances or recesses or both.

18. The method claim 1, further comprising creating an opening through the metallic stent body material and the layer of ceramic particles by laser ablation after the implanting, depositing and compressing steps.

19. A method of making a stent, the method comprising steps of:

depositing a layer of ceramic particles on at least one surface portion of a stent body material;

compressing the layer of ceramic particles to a first density;

dispersing at least one drug into the layer of ceramic particles while the layer of ceramic particles is at the first density; and

compressing the layer of ceramic particle to a second density that is higher than the first density.

20. The method of claim 19, further comprising forming a porous surface layer on the at least one surface portion of the stent body material.

21. The method of claim 19, wherein the step of forming a porous surface layer comprises forming the porous surface layer by ion implantation.

22. A method of making a stent, the method comprising:

implanting at least one type of ions into a metallic stent body material in at least one surface portion of the stent body material to produce at least one porous layer at the surface portion;

depositing a layer of particles on the porous layer;

and compressing the layer of ceramic particles.

23. The method of claim 22, wherein the step of depositing a layer of particles on the porous layer comprises depositing at least one type of metal, polymeric and ceramic particles.

24. A stent made by the method of claim 1.

25. A stent made by the method of claim 19.

26. A stent made by the method of claim 22.

27. A stent, comprising:

a stent body having at least one porous surface portion comprising at least 10% of a total surface area of the stent body; and

a layer of ceramic particles having an average porosity of no higher than 50% covering the porous surface portion,

wherein a portion of the ceramic particles are embedded within the porous layer.

28. The stent of claim 27, wherein the porous surface portion is made porous by ion implantation.

29. The stent of claim 28, wherein the layer of ceramic material is made by depositing a layer of ceramic particles on the porous surface portion and compressing the layer of ceramic particles.

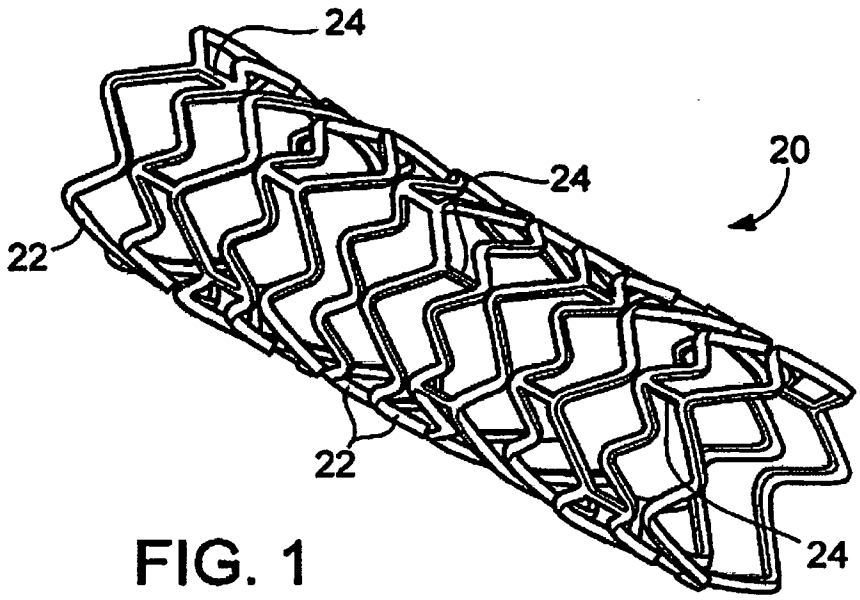


FIG. 1

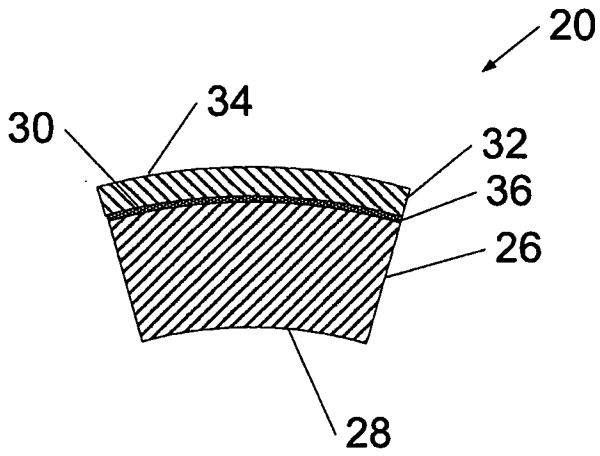


Fig. 2

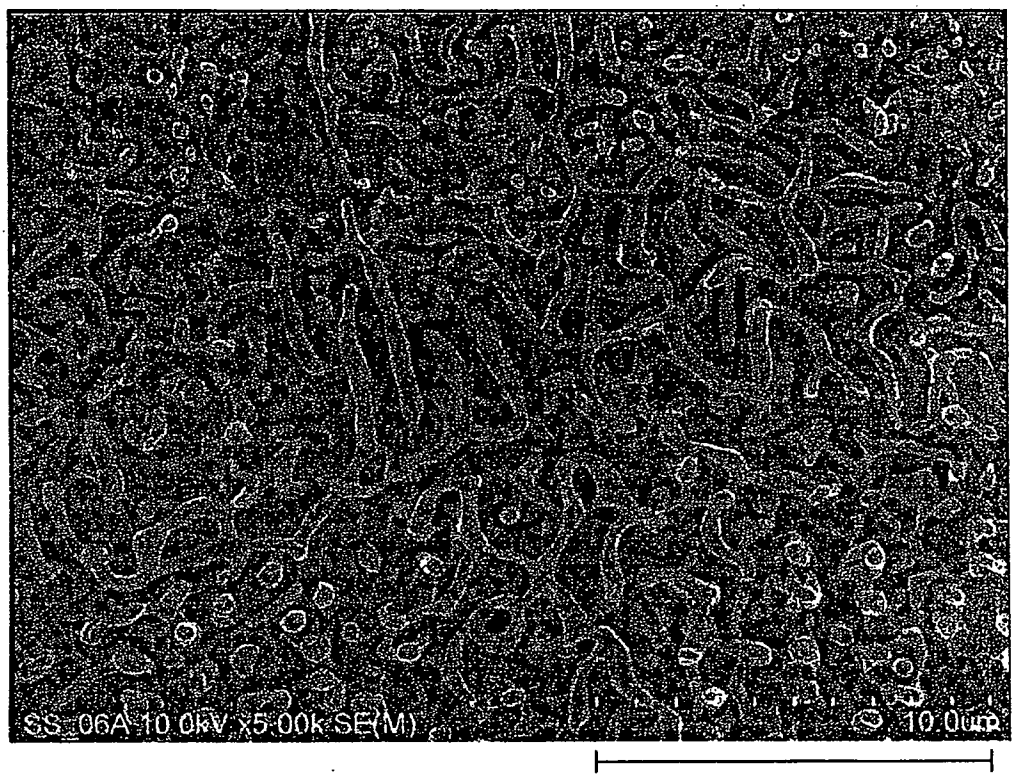


FIG. 3(a)

FIG. 3(b)

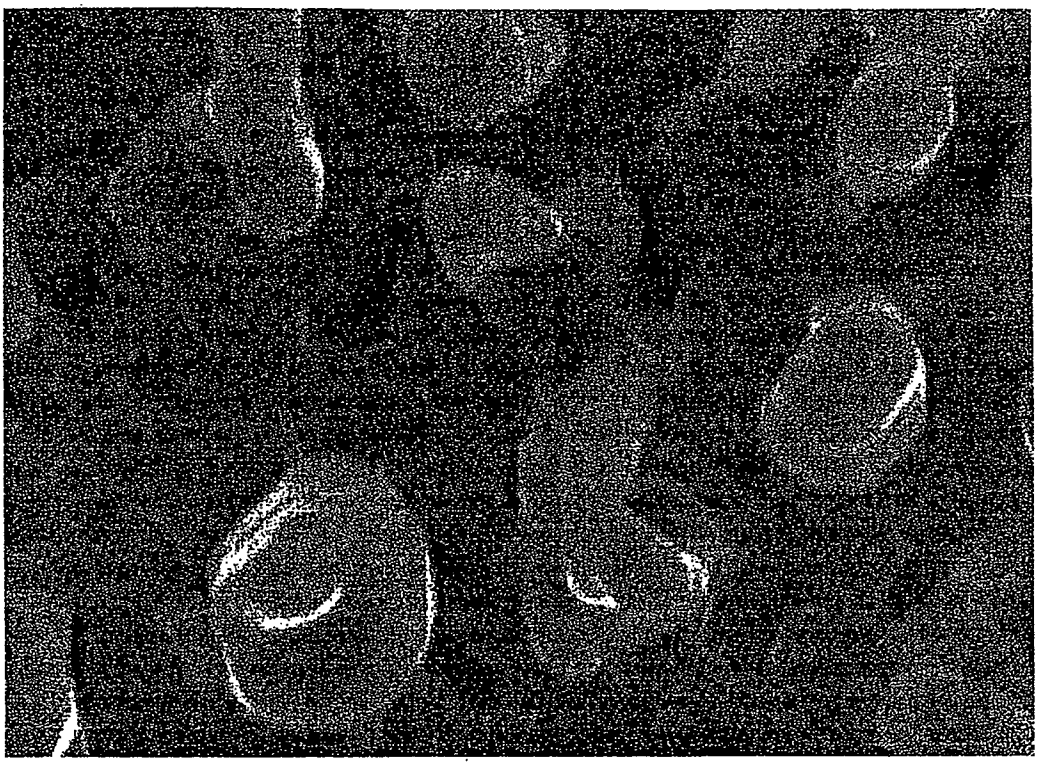

FIG. 3(c)

FIG. 4