an implant with a magnesium core to provide a specific degradation time for the core structure.

An endoprosthesis, once expanded in an animal body vessel, is subjected to forces related to the geometry and dynamics of vascular motion. Contraction of the heart myocardium during the cardiac cycle will, for example, generate bending motion, torsion, extension and contraction of the implant in-situ. Further, pulsatile motion in the form of radial pulsation of the vessel will cause repeated increases and decreases in the implant diameter. The combination of physiological forces results in localized strain areas which can occur throughout the body of the implant. To prevent fracture and subsequent incursion of physiological fluids any corrosion barriers applied to the implant would require that the barriers be sufficiently elastic or thin in thickness to overcome dynamic fatigue caused by repeated strain. Inorganic barrier layers such as oxides can be inherently brittle and tend to crack and form fissures that extend into the underlying substrate when exposed to repeated bending, torsion, or lateral displacement. When expanded and placed into a physiological solution, electrolyte ingress into these fissures will begin to invade and corrode the underlying substrate material. It is therefore beneficial to place an additional barrier layer which is very elastic over the first organic or inorganic barrier that will serve to seal and protect any of the fissures which may expose the underlying structure. Such combination of barrier layers may be sufficiently thick to retard corrosion of the implant and yet may not promote excessive inflammation and granuloma reaction within the vessel tissues which surround the implanted device.

The single addition of an inorganic barrier layer to the metallic surface may generally not be sufficient to alone prevent premature corrosion because of cracks which appear in the inherently brittle barrier material during clinical use. The addition of a single thicker elastic barrier layer to the metallic surface may not be sufficient to alone prevent premature corrosion because in many the cases the elastic barrier layer may imbibe physiological fluids and be hydrated, causing subsequent fluid electrolyte ingress to the metallic surface of the implant. A single thick elastic barrier layer such as a biodegradable polymer is undesirable for other reasons. A thick barrier layer will add in dimension to the overall diameter of the implant when it is applied to delivery balloon or system. A larger diameter

mounted implant can be more difficult to deliver to an affected vessel by a clinical specialist. Also, a greater inflammatory response may result from using a thicker biodegradable polymer layer as macrophages and cellular components infiltrate and metabolize the degrading material. The optimum corrosion protection for a biodegradable metallic prosthesis is thus derived using at least a thin elastic organic layer or multiple protective layers as described herein.

Aspects of the invention are defined in the independent claims. Some optional features of the invention are defined in the dependent claims.

It is suggested an expandable prosthesis for vascular placement comprising or consisting of a tubular biodegradable metal structure, a biodegradable organic layer covering the surfaces of the structure and optionally a biodegradable polymer coating covering the organic surface layer.

The invention includes an expandable prosthesis, e.g., stent as a tubular biodegradable metal structure with a base metal structure. The tubular biodegradable metal structure can be formed from suitable biodegradable metals such as magnesium, iron, zinc, aluminum or the like as well as of an alloy of these metals containing a majority by weight percentage of one of the above elements and combined with other trace metals.

The expandable prosthesis may be, e.g., stent with a base metal structure comprised of an alloy of magnesium containing a majority by weight percentage of the element magnesium and combined with other trace metals. One representative material is alloy ZRE1 from Magnesium Elektron UK. This material is an alloy of magnesium containing zinc, zirconium, and rare earth metals. The endoprosthesis is formed from a laser cut tube of the alloy and is subsequently electropolished to a desired geometry.

In a first exemplary experiment the device is then placed into a Thermo-Scientific Inc. model FD1545M furnace which has been heated to 426 degrees C for approximately eight minutes and then removed. An oxide protective layer has now formed on the device surface which has a scaled appearance with a visible boundary surrounding each scale when viewed in a scanning electron microscope at 250X magnification. An alternative surface treatment has also been applied to create a thin protective layer achieved by placing

formulation with a polymer where the ratio of drug to polymer is about five percent to about ninety percent depending on the specific polymer used and also the method of application.

For evaluation, three separate coating sample sets were fabricated. The first sample set included magnesium stents that were 20mm in length and were mounted onto balloon delivery catheters. The second sample set included magnesium stents that were coated by using a spray method with polycaprolactone polymer formulation. These samples were then dried in a vacuum oven at a temperature of 50 deg. C and a vacuum level of 27 inHg for a period of 48 hours. The third set of samples was processed like the second set. However, an additional heat treat process was applied to the bare metal stents before application of the polymer by placing the stent samples into furnace preheated to 426 deg. C with ambient oxygen for a period of five minutes.

Before application of the polycaprolactone polymer measurements of the surface of the unprocessed and processed stents were performed with Auger analysis using a PHI model 600 spectroscopy system with 3 kilovolts applied voltage. Those stents which were not heat treated revealed a minimal oxide layer and those with the heat treatment revealed an oxide layer with surface depth of magnesium oxide of approximately 400 Angstroms.

All three sample sets were deployed into silicone tubes with dimensions and physical attributes which would correlate to coronary arteries. The tubes were filled with porcine serum through a heated pumping circuit. The silicone tubes were repeatedly bent at an angle and movement cycle corresponding to a human left anterior descending artery. The implants were visually observed at regular intervals and their appearance was recorded digitally.

The stent samples were maintained cycling in the test apparatus for thirty days, a period of time representing one month of life in a human coronary artery. At the end of this time period the tubes were removed from the apparatus and flushed with deionized water. The vessels with the stents still inside were placed into a test jig and crushed with an Imada model 25 compression tester with a load cell rated at 25 Newtons compressive force.

Those stents which were not treated were broken and did not retain any residual radial force after the first week of testing. The group of stents which were treated with polycaprolactone polymer only retained approximately 2.3 Newtons radial force required to compress the deployed stents to approximately 80% of their deployed diameter. The group of stents which were treated with an initial heat treatment prior to coating with polycaprolactone polymer retained approximately 2.9 Newtons radial force required to compress the deployed stents to approximately 80% of their deployed diameter. The addition of the heat treat step was indicated as responsible for increasing the radial force of stents in this in-vitro test by approximately 26% compared to those stents which were not heat treated.

In another example magnesium stents were first immersed in 1 molar concentration sodium bicarbonate solution at room temperature for a period of three minutes. At this time the surface of the stents was chemically oxidized from a primary magnesium metal alloy content to magnesium hydroxide. The stents were then rinsed in deionized water for one minute to remove residual electrolyte and then dried. They were then placed in an insulated furnace which was preheated to 426 deg. C for five minutes and then removed to cool to room temperature. In the heat treatment process the stent surface magnesium hydroxide material was converted to magnesium oxide and water vapor. Subsequent measurement of the surface of the processed stents with Auger analysis using a PHI model 600 spectroscopy system with 3 kilovolts applied voltage revealed a minimum surface depth of magnesium oxide of 160 Angstroms.

To test the capability of a magnesium oxide surface coating to protect the stent in a corrosive environment the coated samples were placed into glass vials filled with phosphate buffered saline as were samples of untreated stents. The vials were maintained at room temperature. The samples in each container were visually monitored for evidence of corrosion. After one day gas bubbles had formed on the surface of the untreated stents and the stent were visibly tarnished. After two weeks the untreated stents had corroded through the metal in numerous locations on the stent. However, after two weeks the treated stents did not show any visible tarnish, bubbling, or material erosion, indicating that the treatment had provided surface corrosion protection.

In a third example stents twenty millimeters in length and fabricated from magnesium alloy tubes were coated with a surface treatment or thin layer of a siloxane applied using a plasma enhanced chemical vapor deposition process. Siloxane materials, including polydimethylsiloxane (PDMS) and other organosilane compounds are preferred as protective layers because they may be applied uniformly in a plasma process and have a greater degree of ductility when applied as compared to inorganic oxides such as silicon dioxide or as compared to diamond-like carbon coatings. The ductility or flexibility of the siloxanes can be modified or adjusted by varying process parameters which include applied plasma power, the nature of the siloxane precursor, the gas to fluid ratios, time, chamber pressure, and the injection rate. Siloxane materials are also hydrophobic and thus provide an effective barrier for the base metal of the implant device to surrounding fluid electrolytes. Thin layers of siloxane may biodegrade over time, especially in an alkali or base aqueous environment. A Mettler MT5 precision balance was used to determine an average coating layer weight for each stent of approximately 60 micrograms, measuring the weight both before and after the coating deposition.

Subsequent measurement of the surface of the processed stents with Auger analysis using a PHI model 600 spectroscopy system with 3 kilovolts applied voltage revealed a surface depth of the applied coating of approximately three hundred nanometers.

A group of the siloxane coated stents and a group of non- siloxane coated stents were further coated with an additional layer of polycaprolactone biodegradable polymer with a weight of 4 milligrams after drying in a vacuum chamber set to 27 inches of mercury vacuum and 50 degree C for 48 hours and then weighed to determine the weight of the coating material. Yet an additional drug layer of 160 milligrams of polylactic acid polymer and 160 milligrams of the drug rapamycin was applied to both groups. Both stent polymer coatings were applied using a Sono-tek Inc. ultrasonic spray nozzle which directed the spray cone perpendicular to a stent mounted on a mandrel appropriately sized to the inner diameter of the stent. After the coating process was completed the stents were dried in a vacuum chamber set to 27 inches of mercury vacuum and at room temperature for 48 hours and then weighed to determine the weight of the drug coating material.

determined that the combination of both the thin surface treatment layer and the thicker biodegradable polymer layer was responsible for maintaining optimum protection of the base metal from corrosive effects of the porcine plasma over a period of 30 days.

The process of plasma application of thin layer can be suitably modified to obtained desired mechanical and surface properties. A thin layer coating might be optimized for adhesion, moisture barrier properties, surface hardness, or flexibility. The liquid monomer material from which vapor is used to initiate the layer can be chosen from simple organic solvents, fluorinated organic compounds or organosilicon compounds. Also gaseous monomer material can be used such as methane or ethylene. In a preferred arrangement the liquid monomer is chosen from organic solvents and organosilicon compounds, and is chosen most preferred from organosilicon compounds. Suitable organic solvents/compounds can be selected from compounds such as benzene, toluene-2,4-diisocyante, 2-pyrollidone, tetramethyltin, vinyl acetate, styrene, acetylene and p-toluidine. Suitable organosilicon compounds include hexamethyldisiloxane, divinyltetramethyldisiloxane, methyltrimethoxysilane, tetramethylsiloxane, hexamethyldisiloxane, tetramethylsilane, tetramethoxysilane. Fluorinated materials including hexafluorobenzene, tetrafluoroethylene, hexafluoropropylene, chlorotrifluoroethylene, octafluorocyclobutane, perfluorobutene-2, and vinyl fluoride may be applied alone or in combination with organic solvents or organosilicon compounds to enhance ductility or insulating properties. In addition to liquid monomers, gas monomers such as methane and ethylene have been successfully applied to prevent premature corrosion of substrate materials. The monomers mentioned above may be used alone or in combination to achieve desired properties. The amount of the applied layer should be optimized to provide adequate thickness and the lowest residual stress.

According to one aspect of the present invention the biodegradable organic layer comprises or consists of an organic compound applied by injection of monomer vapor into a chamber with an applied plasma. The monomer vapor may be created from the monomer compounds described in the preceding paragraph.

In a preferred arrangement the biodegradable organic layer comprises or consists of a siloxane layer, preferably applied by injection of monomer vapor into a chamber with an

applied plasma, wherein the monomer vapor is preferably created from at least one of the following compounds hexamethyldisiloxane, divinyltetramethyldisiloxane, methyltrimethoxysilane, tetramethylsiloxane, hexamethyldisiloxane, tetramethylsilane and tetramethoxysilane. . In a further preferred arrangement the biodegradable organic layer is a uniform polymethylsiloxane layer applied by injection of HMDSO (hexamethyldisiloxane) or DVTMDSO (divinyltetramethyldisiloxane) vapor into a chamber with an applied plasma. In a further preferred arrangement the biodegradable organic layer is a uniform polymethylsiloxane layer applied by injection of HMDSO (hexamethyldisiloxane) vapor into a chamber with an applied plasma. Yet in another preferred arrangement the biodegradable organic layer is a uniform polymethylsiloxane layer applied by injection of DVTMDSO (divinyltetramethyldisiloxane) vapor into a chamber with an applied plasma.

For applying a biodegradable organic layer plasma enhanced CVD is especially advantageous in comparison to other used methods such as or high temperature CVDs or immersion in a chemical bath because it can occur at very gentle conditions such as low temperatures and in a "dry" process that disfavors corrosion on the surface of the endoprothesis. As a result the underlying material base material of the endoprosthesis is unchanged. Also, many of the use precursors would not survive harsh conditions such as very high temperatures and would decompose before the proper use in the plasma and would thereby form irregular, carbonaceous layers not capable of providing the advantages described herein. Additionally with organic or organosilicon presursors as stated herein PECVD provides a uniform thickness and can be applied to all of the surfaces of complex geometries, like stents. PECVD further creates very dense and continuous layers which totally encapsulate the underlying endoprosthesis like a stent. Moreover, the use of organic or organosilicon precursors with plasma creates coatings which have greater elasticity in comparison when provided by inorganic precursors and/or other harsher methods. Such great elasticity can be enhanced when a layer of biodegradable polymer is applied on the biodegradable organic protection layer.

An endoprosthesis comprising a biodegradable organic layer covering the surfaces of the structure and a biodegradable polymer coating covering the organic surface layer is particularly capable of not only maintaining optimum protection of the base metal, but also

As in prior evaluations the stents from both groups were mounted to 22 millimeter angioplasty balloons using a Blockwise Engineering model RMD crimping device. All of the mounted stents were individually expanded to 18 ATM with a B. Braun indeflation device filled with deionized water into silicone tubes with diameter compliance of 3-5% per 100mm Hg applied pressure. The tubes were filled with porcine serum through a heated pumping circuit. The silicone tubes were repeatedly bent at an angle and movement cycle corresponding to a human left anterior descending artery. The implants were visually observed at regular intervals and their appearance was recorded digitally.

At the end of the 14 day time period the tubes were removed from the apparatus and flushed with deionized water. The vessels with the stents still inside were evaluated under an Olympus model SZ30 optical microscope The group of stents which were treated with the thin surface treatment layer and drug/polymer layer were observed to have an average of 8 fractures occurring over the entire 20mm length of the device. The group of stents which were treated with the thin surface treatment layer, biodegradable polymer layer, and drug/polymer layer were observed to have an average of 2 fractures occurring over the entire 20mm length of the device. Although the mass of the thin layer DVTMDSO-derived layer was dramatically increased, the combination of both the thin surface treatment layer and the thicker biodegradable polymer layer was responsible for maintaining optimum protection of the base metal from corrosive effects of the porcine plasma.

It is important to note that simply increasing the thickness of a single surface treatment layer on the base metal, or by increasing the thickness of a single biodegradable polymer layer on the base metal an optimum protection may not be achieved. In one arrangement wherein the thin surface treatment layer is sufficiently flexible that cracks or fissures will not be created in this thin layer during clinical use of the device a subsequent biodegradable polymer layer may not be required. Such sufficient protection can be derived when the thickness of the biodegradable organic layer ranges from about 20 nanometers to about 5 microns. The additional application of a biodegradable polymer may for instance be required to prevent incursion of fluid electrolytes into the base metal of the

stent and initiation of the corrosion process. In such case the endoprosthesis is beneficially provided with additional elasticity and corrosion protection.

Fig. 1 shows a vascular endoprosthesis prior to mounting on a balloon catheter

Fig. 2 illustrates a cross-section of a single filament of an endovascular prosthesis with a primary surface protective layer and an additional polymer passivation coating.

Fig. 3 illustrates a cross-section of a single filament of an endovascular prosthesis with a primary surface protective layer and an additional polymer passivation coating with a yet additional drug-containing coating layer.

Fig. 4 is a schematic representation of the fabrication sequence to generate multiple protective layers noted in an exemplary arrangement.

Fig. 5 is a schematic representation of the plasma enhanced chemical vapor deposition (PECVD) coating onto a surface.

Fig. 6 shows a means of application of a uniform coating layer of polymer passivation material or drug or drug and polymer combination.

Fig. 7 shows a scanning electron microscope image of a single curved portion of a filament of an endovascular prosthesis comprised of magnesium.

Fig. 8 shows a scanning electron microscope image of a single curved portion of a filament of an endovascular prosthesis comprised of magnesium which has an applied surface protection layer which occurs at the outer boundary of the cross section.

Fig. 9 shows a scanning electron microscope image of a single curved portion of a filament of an endovascular prosthesis comprised of magnesium which has an inherent surface protection layer which occurs at the outer boundary of the cross section.

Fig. 10 shows a scanning electron microscope image of a single curved portion of a filament of an endovascular prosthesis comprised of magnesium which has an applied surface protection layer and a polymer passivation layer and a drug eluting polymer layer.

Fig. 11 shows surface elemental analysis of an endovascular prosthesis comprised of a magnesium alloy.

Fig. 12 shows surface elemental analysis of an endovascular prosthesis comprised of a magnesium alloy which has been treated with heat in a controlled environment to produce an inherent surface oxide layer.

Fig. 13 shows surface elemental analysis of an endovascular prosthesis comprised of a magnesium alloy which has been treated a plasma enhanced chemical vapor deposition process to produce an applied surface protection layer with silicon and oxygen in combination.

Fig. 14 shows surface elemental analysis of an endovascular prosthesis comprised of a magnesium alloy which has been treated a plasma enhanced chemical vapor deposition process to produce an applied surface protection layer with carbon, silicon and oxygen in combination.

Fig. 15 shows an angiography image of the left anterior descending artery of a porcine heart in which is deployed an endoprosthesis which has been processed in accordance with methods described herein which is produced after the endoprosthesis has been deployed within the heart for a period of twenty-eight days.

Fig. 16 shows an X-ray image of an endoprosthesis comprised of magnesium with other materials and processed in a manner that does not provide adequate protection to the base material which is provided twenty-eight days after the endoprosthesis has been deployed into a coronary arter of an animal heart.

Fig. 17 shows an X-ray image of an endoprosthesis comprised of magnesium and processed in a manner consistent with methods and processes to provide adequate protection to the base material which is provided twenty-eight days after the endoprosthesis has been deployed into a coronary artery of an animal heart.

Fig. 18 shows a scanning electron microscope image of a single curved portion of a filament of an endovascular prosthesis comprised of magnesium which has an applied surface protection layer of siloxane material. The prosthesis has been expanded to a diameter of 3.0mm and cracks in the protection layer are revealed

Fig. 19 is a magnified image of a single crack in the protection layer which was previously applied to the surface of an endoprosthesis comprised of magnesium. The device has been expanded to a diameter of 3.0mm.

Fig. 20 shows a scanning electron microscope image of an expanded endoprosthesis comprised of magnesium which has been coated with a siloxane material coated by plasma deposition using the monomer DVTMDSO.

Fig. 21 shows a comparison of the radial strength of endoprostheses comprised of magnesium and with different coating configurations after undergoing bending and pulsatile repetitive cycling in a physiologically relevant environment for a period of twenty-eight days.

which is obtained from Magnesium Elektron UK of Manchester, England. This material is comprised of magnesium with a 2.0%-3.0% zinc, 0.4%-1.0% zirconium, and 2.5%-4.0% of rare earth elements. The tensile strength of 160 MPa and yield strength of 110 MPa of this metal provide sufficient strength to create an endoprosthesis to support the radial support requirements of an endovascular device. Such materials may be further modified through metallurgical means to provide optimized corrosion resistance or tensile properties. Work hardening and heat tempering are exemplary means to manipulate or orient metallic grains in a preferential manner to increase fatigue life or tensile strength of a given bioabsorbable metal or metal alloy. The geometry of the device is developed so that it will support physiological radial loads over a range of deployed diameters. Flexibility, bioabsorption rate, potential drug delivery characteristics, and physical size of the device in a vascular delivery system are also other design considerations in development of the device design.

Within Figs. 2 and 3 two protective layers (6, 7) are provided to prevent premature corrosion of the endoprosthesis. Corrosion protection of magnesium and aluminum is a well-established science. Dichromate treatments conforming to standard ASTM D1732 class 1 and galvanic anodize treatments conforming to standard ASTM D1732 class 2 are standard industrial treatments for magnesium under the trade names Dow #7 and Dow #9. The HAE process for magnesium provides good abrasion resistance and excellent corrosion resistance for coated devices as measured by hours of exposure to salt spray in industry standard testing. The Tagnite® process is an anodize process I which surface penetration and buildup of a dense magnesium oxide coating which covers the base metal surface to protect from environmental and potential galvanic corrosion. These traditional passivation treatments can be effective for application to static or nondeformable components that are generally not for implantable medical applications. Several requirements of implantable endoprosthesis devices preclude the use of traditional and well established magnesium passivation methods. First, any process material which is considered toxic, inflammatory, thrombogenic, or prevents tissue healing is not suitable for implant use. These materials would include chromates, nickel, and permanganate compounds. Second, an endoprosthesis is subject to plastic deformation and dynamic motion during manufacturing, deployment, and implant duration. Any coating or protective

layer that would inhibit effective motion or deformation of the device through hardness or excessive thickness requirements would be prohibitive. Finally, in a device designed to be biodegradable or bioabsorbable the coating may be eventually be metabolized by the host animal along with the base material from which the device is constructed.

The protective layer (6) is considered a thin and dense passivation layer which provides primary protection of the base material (5) against corrosion by means of preventing fluid ingress from surrounding animal tissue. The protective layer is considered primarily a passivation means to prevent premature corrosion of the implantable device. In this regard this primary layer is nonporous and contiguous, covering the entire surface of the implant to provide complete corrosion protection. It is not used to deliver a drug or to enhance adhesion properties or promote the release of a drug by another coating layer or the base device itself. Thickness of this layer (6) can be measured by one or more methods used to measure thin layers commonly found in the electronics industry. Scanning electron microscope imaging of a sectioned device can reveal the dimensions of external coatings and layers. Spectroscopic means such as Auger elemental surface analysis can be utilized to determine layer depth. Interferometric or spectral reflectance means can also be used to determine the coating thickness of some transparent coatings. As an example, the model F40 layer thickness measurement tool from Filmetrics, Inc. (San Diego, CA) can be used to measure coating depths on areas as small as 1 micron diameter on the surface of a vascular implant. An effective thickness of layer (6) would range from about 20 nanometers to about 5 microns, and was found to be particularly effective from about 20 nanometers to about 1 micron.

The layer (6) may be deposited or may involve penetration or conversion of the base material to a more stable, yet bioerodable layer. It is required that the layer (6) provide adequate protection to the base metal for a temporary and predetermined time period before degradation. Those familiar with vascular implants will appreciate that a dense layer (6) should be only sufficiently thick enough to provide an effective temporary barrier and not more so. Increasing thickness of the layer (6) will increase the interface stresses which occur when the substrate undergoes bending movement which will increase the potential for delamination or cracking of this layer and subsequent exposure of the base material(5).

of the base material (5). In clinical usage the deployed device may be subject to bending movement, pulsatile motion, stretching, and torsion depending on the anatomical location of deployment. These physiological motions may further exacerbate any crack or fissure which may be present. Cracking and subsequent exposure of the base material (5) may occur to a higher extent if the thin protective layer (6) does not exhibit sufficient elasticity.

It is therefore beneficial to place a biodegradable polymer layer (7) which will further protect the device and create a flexible seal over the thin protective layer (6) in the event of cracks which may occur during deployment and clinical usage. Representative examples of polymers that may be used to create polymer layer (7) to coat a bioabsorbable endoprosthesis include, but are not limited to poly(caprolactone), polyvinyl esters, poly(D,L lactic acid), poly(L-lactide), poly(lactid-co-glycolide), polyorthoester, polyanhydride, poly(trimethylene carbonate), poyurethanes, silicones, oils, and fatty acids. The polymer layer (7) should be biocompatible and not induce inflammation when implanted into an animal body. The polymer should be soluble in standard solvents which may be later evaporated from the device by vacuum drying in a heated environment. The polymer should have a glass transition point T_g which is higher than any process used to fabricate the finished device, including the sterilization process. The polymer layer (7) should have suitable flexibility to maintain its consistency and not produce cracks upon deployment of the device or during clinical usage of the device. It should also have sufficient mechanical strength to maintain its shape and not deform during manufacturing processes, deployment, or clinical life of the device. Finally, the polymer must be biodegradable within the predetermined clinical usage life of the device.

An exemplary polymer layer (7) is formed of PC-12 polycaprolactone which has a tensile modulus of elasticity in the range of 0.2-0.3GPa, a tensile strength of 25-30 MPa, a value for elongation to break of greater than 300%, and a degradation time of 12 – 24 months. In an arrangement a blend of polymers may be used. Blending a flexible polymer such as polycaprolactone with a more rigid polymer such as poly L- lactide may yield a better combination of properties which include mechanical strength, flexibility, elongation at break, or degradation time which are relevant to the particular

application of the device. Further, it is possible to blend or to copolymerize biodegradable polymers to optimize the beneficial properties required.

A therapeutic drug may be added to polymer layer (7) or an additional drug or drug and polymer combination layer (8) may be applied to polymer layer (7). It is known that a therapeutic drug may be beneficial to reduce the incidence of restenosis of a vascular lesion in which an endovascular prosthesis has been placed. Appropriate drugs include but are not limited to those with antiproliferative, immunosuppressive, antineoplastic, antithrombogenic, or other clinically beneficial properties. Exemplary anti-platelet, fibrinolytic, or thrombolytic agents are heparin, aspirin, hirudin, ticlopidine, urokinase, and mixtures thereof. Macrocyclic triene molecules of the rapamycin family are commonly used in drug eluting stent applications. This class of drugs includes alone or in combination with a biodegradable polymer coating those selected from a group which includes the compounds Rapamycin, Biolimus A9, Everolimus, Zotarolimus, CRC-015, Novolimus, Tacrolimus, and Myolimus and combinations thereof. Anticancer drugs for drug eluting endoprosthesis use include taxol, paclitaxol, doxorubicin, antisense compounds and combinations thereof.

The drug may be incorporated into polymer layer (7) as a drug matrix. After implantation, the drug diffuses out of the polymer matrix and preferably into the surrounding tissue over a period lasting at least 4 weeks, and in some cases up to 3 months or longer, ideally matching the time course of restenosis, smooth muscle cell proliferation, thrombosis, or a combination thereof. In addition to diffusion, the drug may also be released as the polymer degrades or dissolves, making the drug more readily available to the surrounding tissue. The ratio of drug to polymer used in the matrix can range from preferably 0 percent to 70 percent by weight depending on the potency and mode of action of the drug and the physical character of the polymer material which is used. If a drug is contained in polymer layer (7) then any additives may affect the properties of the polymer and increasing the drug to polymer ration may impart a reduction in the degradation time or structural integrity of the material and its ability to adequately cover and seal the thin protective layer (6) and base material(5). Some arrangements would have an additional drug or drug and polymer combination (8). In this configuration the drug or drug and

polymer combination (8) is completely independent of polymer layer (7) and the drug release kinetics would not affect the properties of polymer layer (7) below. Representative examples of polymers that may be used to create a drug and polymer layer(8) include, but are not limited to poly(caprolactone), polyvinyl esters, poly(D,L lactic acid), poly(L-lactide), poly(lactid-co-glycolide), polyorthoester, polyanhydride, poly(trimethylene carbonate), poyurethanes, silicones, oils, and fatty acids. The thickness of polymer layer (7) is preferably from 1 micron to 30 microns. The thickness of the drug or drug and polymer combination (8) is preferably from 1 to 10 microns. It should not be necessary to add an additional diffusion-controlling layer to the polymer layer (7) or polymer layer (8).

A sequence of fabrication steps is required. The schematic representation of Fig 4 illustrates the sequence of steps required to create one exemplary. A weight measurement step is included between each process to assist in evaluation of the mass generated by each step.

Fig. 5 illustrates a schematic diagram of typical equipment used to deposit a thin protective layer (6) in one arrangement where the layer is created from monomer units as suggested herein, for example of liquid monomer solution of hexamethyldisiloxane (HMDSO), injected into a plasma chamber. An inert gas (9) such as nitrogen or argon is used as a carrier gas and to create a gas vapor from a reservoir of the exemplary chosen liquid HMDSO (11), while the other herein suggested monomer compounds will work all the like. Mass flow controllers (10) are used to regulate the gas flow. The combined vapor and carrier gas are introduced into a plasma enclosure (12). Within this enclosure (12) one or more endoprosthesis (18) is placed between two electrodes (19). One electrode is connected to an alternating power source (16) and the other electrode is connected to ground through resistor (17). A pressure gauge (13) measures internal chamber pressure which can be regulated by adjustment of gas through the mass flow controllers (10) and the vacuum pump (15) across valve (14). Power is applied across the electrodes to generate a plasma at near atmospheric pressure with subsequent deposition of for example dimethylsiloxane molecules and molecular radicals and combinations of these molecules. The thickness of the layer deposition is dependent on the applied power, the monomer concentration within the carrier gas, and the rate of gas flow among other factors. For

example, a siloxane layer with a thickness of 200 nM to 400 nM will have a typical tensile strength of 25 MPa and a resulting value of 130 to 150 strain% at break. Siloxane layers are known to those familiar with medical device coatings to be effective moisture barriers with limited ductility.

The thin protective layer (6) alone may provide effective corrosion protection to the base material (5) of the endoprosthesis. In a preferred arrangement an additional polymer layer (7) may be applied which partially or fully covers the protective layer (6). An apparatus to apply the polymer layer (7) is illustrated in Fig. 6. The coating formulation can be applied by spray coating, dip coating, casting, vapor deposition, manual application with a syringe, or other means. In a preferred arrangement a 120kHz Micromist nozzle(22) from Sono-tek Inc., (Milton, New York), is used to deposit a coating of between 10 and 35 microns depth of polymer coating onto all surfaces of the device. A solution of polymer and solvent (21) is applied to an appropriate spray nozzle (22) by pressure means. The concentration of polymer in solvent solution may range from 10 mg/ml to 100 mg/ml. which may be adjusted to obtain an optimum droplet size. Compressed air or an inert gas may be used to direct the spray droplets or to segregate droplets within the spray stream. The solvent chosen for the formulation should preferably dissolve the polymer completely to create a clear solution without the appearance of undissolved matter. Solvents with high vapor pressures permit ease of removal from the sprayed polymer when placed in a heated vacuum chamber such as Model 1410M from VWR International (Sheldon Manufacturing, Cornelius, OR) set to a temperature between 25 °C and 55 °C and an applied vacuum which ranges from 15 inHg to 29 inHg for a time period of between 1 hour and 72 hours.

Solvents should be chosen with preference to those which do not exhibit a toxic or inflammatory response in vascular tissue. Examples of solvents which may be considered for use include but are not limited to acetone, chloroform, ethyl lactate, dichloromethane, methylene chloride and combinations thereof. The droplets of polymer in solvent (23) are uniformly dispensed on all of the surfaces of a prosthesis device which has been positioned and subsequently rotated or translated to the correct position to accept the droplets to create a uniform surface coating. A therapeutic drug may be added to the solution of polymer and solvent (21).

Figs. 7 through 10 are scanning electron microscope images of a preferred arrangement during various stages of assembly. Fig. 7 is an image of a feature of an endoprosthesis fabricated from a magnesium alloy. Fig. 8 is an image of a feature of an endoprosthesis fabricated from a magnesium alloy which has been coated with a thin protective layer of dimethylsiloxane molecules which is approximately 250 nM in thickness. Fig. 9 is an image of a feature of an endoprosthesis fabricated from a magnesium alloy which also incorporates a thin protective layer. This layer was created by immersing the device in a sodium bicarbonate solution at room temperature for a period of five minutes followed by rinsing in deionized water and drying to complete dryness. The device was then heated in an oven for five minutes at 426°C to produce a stable oxide layer over the surfaces of the device. Fig. 10 is an image of a feature of an endoprosthesis fabricated from a magnesium alloy which contains multiple protective layers which include in this example a thin protective layer (6) a polymer layer (7) and a drug-containing polymer layer (8).

Figs. 11 through 14 show surface elemental analysis scans of the surface of a magnesium alloy stent and stents which have been processed sequentially in accordance with a preferred arrangement. The surface scans were performed with a PHI model 600 spectroscope from Physical Electronics, Inc. (Chanhassen, MN) with an applied voltage of 3 kV. Fig. 11 shows the surface scan of an untreated endoprosthesis fabricated from a magnesium alloy. The predominant element on the device surface is magnesium. Fig. 12 shows the surface scan of an endoprosthesis fabricated from a magnesium alloy which has been placed into a heated chamber at 426°C for a period of five minutes. An oxide layer of approximately 200 Angstroms thickness is evident from the surface scan as noted by the presence of elemental oxygen that is not apparent in the surface scan of the untreated magnesium alloy stent. Fig. 13 shows the scan of the surface of an endoprosthesis fabricated from a magnesium alloy which has been placed into a plasma chamber and subjected to active gas plasma in the presence of silicon and oxygen molecules for a period of fifteen minutes. A glass-like layer of SiO_x of approximately 1 to 2 microns thickness is evident from the surface scan as noted by the presence of silicon and oxygen that is not apparent in the surface scan of the untreated magnesium stent. Fig. 14

shows the surface of an endoprosthesis fabricated from a magnesium alloy which has been placed into a plasma chamber and subjected to active gas plasma in the presence of silicon, carbon, and oxygen atoms for a period of fifteen minutes. A layer of siloxane molecules of approximately 500 nM to 800 nM in thickness is evident from the surface scan as noted by the presence of carbon, silicon, and oxygen that is not apparent in the surface scan of the untreated magnesium stent.

Fig. 15 shows an angiogram of the left anterior descending coronary artery of a living porcine heart in which is deployed an endoprosthesis which has been processed in accordance with methods described herein. The implanted device was fabricated by first coating a stent made from a magnesium alloy with a protective layer of polycaprolactone polymer using materials and methods described herein. It was then coated with a drug and polymer coating layer comprised of the rapamycin derivative drug CRC-015 combined with the polymer d,l PLA. After removal of all solvents in a heated vacuum chamber the device was mounted on a delivery balloon and packaged in protective foil packaging and then sterilized with ethylene oxide gas.

The device was deployed into the animal heart and the angiogram was produced twenty-eight days after the initial procedure. At this later time point the endoprosthesis provided adequate vessel patency as indicated by the contrast image of the vessel cross-section of the proximal portion of the left anterior descending coronary artery of the animal heart.

A biodegradable endoprosthesis which does not maintain adequate support for the period of time required for vessel healing may fracture and exhibit compression and loss of diameter. The vessel lumen may be reduced as a direct consequence of the stent compression Fig. 16 shows an X-ray image of an implanted endoprosthesis comprised of magnesium with other materials and processed in a manner that does not provide adequate protection to the base material which is provided twenty-eight days after the endoprosthesis has been deployed into a coronary artery of an animal heart. In contrast, a biodegradable endoprosthesis which does maintain adequate support for the period of time required for complete vessel healing will maintain its diameter and should begin to fracture after completed healing of the vessel. Fig. 17 shows an X-ray image of an endoprosthesis

CLAIMS

1. An expandable prosthesis for vascular placement comprising, a tubular biodegradable metal structure, a biodegradable organic layer covering the surfaces of the structure, and a biodegradable polymer coating covering the organic surface layer, wherein the biodegradable organic layer comprises an organic compound applied by injection of monomer vapor into a chamber with an applied plasma and wherein thickness of the biodegradable organic layer ranges from 20 nanometers to 5 micrometers (microns), wherein the biodegradable organic layer is a siloxane layer.

2. The expandable prosthesis of claim 1, wherein the optional biodegradable polymer coating contains a therapeutic drug.

3. The expandable prosthesis of claim 1 or 2, wherein the biodegradable polymer coating contains a therapeutic drug selected from a group which includes the compounds Rapamycin, Biolimus A9, Everolimus, Zotarolimus, CRC-015, Novolimus, Tacrolimus, and Myolimus.

4. The expandable prosthesis according to any of the preceding claims, wherein the optional polymer coating contains a therapeutic drug selected from the group which includes paclitaxel and paclitaxel derivative compounds.

5. The expandable prosthesis according to any of the preceding claims, wherein the monomer vapor is preferably created from at least one of the following compounds hexamethyldisiloxane, divinyltetramethyldisiloxane, methyltrimethoxysilane, tetramethylsiloxane, hexamethyldisiloxane, tetramethylsilane and tetramethoxysilane.

6. The expandable prosthesis of claim 5, wherein the biodegradable organic layer is a uniform polymethylsiloxane layer applied by injection of HMDSO (hexamethyldisiloxane) vapor into a chamber with an applied plasma.

7. The expandable prosthesis of claim 5, wherein the biodegradable organic layer is a uniform polymethylsiloxane layer applied by injection of DVTMDSO (divinyltetramethyldisiloxane) vapor into a chamber with an applied plasma.

8. The expandable prosthesis according to any of the preceding claims, wherein the biodegradable metal is magnesium or a metallic alloy of magnesium.

9. The expandable prosthesis according to any of the preceding claims, wherein the optional polymer coating is selected from a group which includes the compounds cellulose, collagen, albumen, casein, polysaccharides, polylactide (PLA), poly-L-lactide(PLLA), poly-d,l-Lactide (PDLLA), polyglycol (PGA), polycaprolactone (PCL), poly-d,l-lactide-co-glycolide (PDLLA-PGA), polyhydroxybuteric acid (PHB), polyhydroxyvaleric acid (PHV), polyalkyl carbonates, polyorthoesters, polyethylene terepthalate (PET), polymalonic acid (PML), polyanhydrides, polyphosphazenes, polyaminoacids and their copolymers, hylauronic acid, and blends of the aforementioned compounds.

10. The expandable prosthesis according to any of the preceding claims, wherein the prosthesis is a stent and the therapeutic drug is contained on the surface of the biodegradable polymer layer.

11. The expandable prosthesis according to any of the preceding claims, wherein the prosthesis is a stent and the therapeutic drug is dispersed in the biodegradable polymer layer in a drug-to-polymer ratio of 10 percent by weight to 70 percent by weight.

12. The expandable prosthesis according to any of the preceding claims, wherein the prosthesis is a stent and the therapeutic drug is dispersed in the drug-containing polymer layer in a drug-to-polymer ratio of 10 percent by weight to 70 percent by weight.

13. A method of producing a biodegradable stent comprising
coating a tubular biodegradable metal structure with a biodegradable organic layer, and

coating the organic layer with a biodegradable polymer coating, wherein the biodegradable organic layer is a siloxane layer.

14. The method of claim 13, wherein the biodegradable organic layer is coated with a polymer coating containing a therapeutic drug.

15. The method of claim 13 or 14, wherein coating the tubular biodegradable metal structure with a biodegradable organic layer comprises coating the metal structure with a siloxane compound by a plasma enhanced chemical vapor deposition process.