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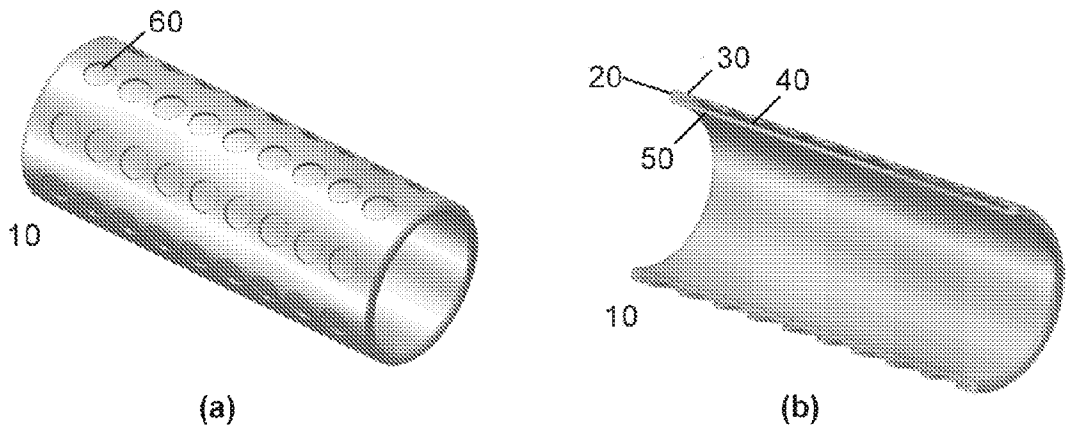

Fig. 1

(57) **Abstract:** The present invention relates to a stent, having a supporting structure of a non-particulate inorganic carbon material.

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Carbon Stents

Field of the invention

The present invention relates to a stent, having a supporting structure of a non-particulate inorganic carbon material.

Background of the invention

Implants are widely used as short-term or long-term devices to be implanted into the human body in different fields of applications, such as orthopedic, cardiovascular or surgical reconstructive treatments. The ongoing development of medical devices including long term implants, such as articular and intravascular prostheses, and short term implants like catheters, has improved the efficacy of surgical and/or interventional treatments. However, the introduction of a 'foreign' material can cause adverse reactions, such as thrombus formation or inflammation. This is generally due to biochemical reactions at the interface between the implant and the patient's body. Conventional materials comprise significant drawbacks in terms of biocompatibility or functionality or efficacy. Significant drawbacks of conventional solutions are related either to biocompatibility of materials, suitability of the used materials for implant design, inability to provide controlled porosities and pore sizes and/or reduced usability to provide and release beneficial agents like drugs.

Different biodegradable and non-degradable implants may be developed for implantation into body passageways to maintain the patency through the passageways. Those passageways that can be treated for maintaining the patency are for example coronary arteries, peripheral arteries, veins, biliary passageways, the tracheal or bronchial passageways, prostate, esophagus or similar passageways. These implants can be deployed in different ways, particularly for vascular stents by introducing them percutaneuously and positioning the devices to the target region and expanding them. Expansion can be assured by mechanical means, like balloon or mandrel expansion, or by using superelastic materials that store the energy for self-expansion. These implants are designed to keep the lumen of the passageway open and remain as a permanent implant within the body.

Conventional stents for different applications comprise monofilament coil wires (U.S. Pat. No. 4,969,458), thin-walled metal cylinders with axial slots (U.S.

Pat. Nos.4,733,665; 4,739,762; and 4,776,337) or welded metal cages (U.S. Pat. Nos. 4,733,665 and 4,776,337). These stents are conventionally made from materials, such as polymers, organic fabrics and metals, such as, stainless steel, gold, silver, tantalum, titanium, magnesium and shape memory alloys, such as Nitinol.

Recently, it was shown that the safety and/or efficacy of a stent can be significantly improved by incorporating beneficial agents, for example drugs that are delivered locally. Implants with drug-releasing coatings are for example disclosed in U.S. Patent Nos. 5,869, 127; 6,099, 563; 6,179, 817; and 6,197,051, particularly for stents with drug elution. EP1466634 describes a stent design with drug reservoirs by introducing through-holes either in metallic or polymeric stents by laser cutting, etching, drilling or sawing or the like. However, the incorporation of beneficial agents can result in beneficial effects like improved safety or efficacy, but after a period of time with the degradation, uptake or release or diffusion of beneficial agents like biologically, pharmacological or therapeutic agents, the underlying implant material can substantially arise as a long-term issue like causing allergic reactions, chronic inflammation or even thrombosis and other severe complications.

Furthermore, stent based local delivery of beneficial agents is used to address various potential issues, the most relevant in connection with vascular stenting is known as re-stenosis. Re-stenosis can occur after stent implantation or angioplasty interventions and is basically an inflammation response of the tissue resulting in cell proliferation, particular of smooth muscle cells, within the vessel wall and re-narrowing of the vessel lumen. To treat this complication, re-intervention and re-vascularisation treatments are necessary that cause again costs for medical care and risks to the patient. With using drugs that can reduce the inflammation or proliferation it was shown that the risk of re-stenosis could be reduced significantly. For example, U.S. Pat. No. 5,716,981 discloses a stent with a surface-coating comprising a composition of a polymer carrier and paclitaxel (a well-known drug that is used in the treatment of cancerous tumors). Surface coatings have some drawbacks with regard to the controlled release of beneficial agents, because the volume of the incorporated beneficial agent is relatively low compared to the surface

area of the stent resulting in a short diffusion way for discharging into the surrounding tissue. The release profiles are typically of a first order kinetics with an initial burst and an asymptotic rapid release. Instead, it is more appropriate and desired to have a linear and constant control over the release of a drug. This disadvantageous effect can be partially compensated by increasing the thickness of a surface coating, but increase of coating thickness, typically above a range of 3-5 μm, increases the stent wall thickness resulting in reduced flow cross-section of the vessel lumen, and furthermore increases the profile of the stent resulting in more traumatic deposition of the stent and difficulties in placing them into small vessels. On the other hand, the use of polymer coatings on stent surfaces can be associated with a higher and significant risk of thrombosis, due to insufficient re-endothelialization of the vessel wall and pertinent presence of less or insufficiently biocompatible material. Recent clinical studies have also revealed that the use of polymers in drug-eluting stents is one of the causes for late thrombosis and a higher risk of myocardial infarction associated with the use of drug-eluting stents.

One conventional solution is disclosed in U.S. Pat. No. 6,241,762. This publication discloses a stent non-deforming strut and link elements that comprise holes without compromising the mechanical properties of the device as a whole. The holes are used as discrete reservoirs for delivering beneficial agents to the device implantation site without the need for a surface coating on the stent. One disadvantage of this design is that due to the mechanical requirements the width and the geometry of the basic stent design disclosed comprises a more traumatic design compared to established bare metal stents. Another significant drawback is that the arrangement of discrete holes contradicts to the requirement of homogeneously distributed drug on the surface of such a device, since it is well known that the homogeneous distribution of the drug is required for sufficient efficacy of drug-release and avoiding toxic accumulation of drug with certain tissue areas. In U.S. Publications No. 2003/0082680 and No. 2004/0073294 a solution to the problem of controlling release kinetics from a stent is described, that allows the deposition of multiple deposits of different polymer only and drug/polymer into discrete hole like

reservoirs to achieve a wide variety of release kinetics which cannot be achieved from a surface coating. A further issue with this conventional approach is also, that the control of the release profile requires a polymer/drug composition. Additionally, the stent is based on metal that in general can also induce adverse effects due to corrosion and release of metal ions in the mid and long term. Moreover, the loading of discrete reservoirs with a drug/polymer composition is complex and costly in terms of manufacturability, in particular because the manufacturing allows no spray or dip coating but requires accurate dispensing technology.

Typically, implants are made of solid materials, either polymers, ceramics or metals. To provide improvements of engraftment or ingrowth of the surrounding tissue or adhesion, or to enable drug-delivery, implants have also been produced with porous structures. Different methods have been established to obtain either completely porous implants, particularly in the orthopaedic field of application, or implants having at least porous surfaces, wherein a drug may be included for in-vivo release.

US2004/220659 discloses endoprosthesis devices including stents, stent-grafts, grafts, vena cava filters, balloon catheters and the like made out of porous PTFE. One significant drawback of this solution is that PTFE in nature is a smooth material that does not allow attachment of cells to promote re-endothelialization or engraftment, that complete removal of siloxane that itself has inflammatory potential is difficult to obtain and that the defects created by the removal of siloxane are inherently very small due to the molecular size of siloxane. Moreover, the hydrophobic nature of PTFE limits the use of less lipophilic drugs due to the surface tension that decreases the adsorption into such like porous structure.

EP1319416 discloses a porous metallic stent coated with a ceramic layer with incorporation of a drug. The metallic pores are induced by electropitting at the surface. One significant disadvantage is that the pore sizes are difficult to control, the pores are inherently provided only at the surface and are not interconnected throughout the complete implant body; furthermore, electropitting can also affect the

mechanical properties of the material resulting in increased fatigue or corrosion of the used implant material.

EP0875218 describes a metallic prosthesis and particularly a stent having a plurality of pores, and a therapeutic medication loaded into the pores of the metallic prosthesis, whereby the metallic implant is made of a sheet or tube based on porous metal wire, a sintered stainless steel, a sintered elemental metal, a sintered noble metal, a sintered refractory metal, and a sintered metal alloy. Significant disadvantages are related to control of the pore sizes and geometries and respective porosities, particularly to control the net shape after the sintering procedure. Moreover, the disclosed solution is based on selection of fibers or particles that are sintered without any fillers so that sintering will result in a higher density of the structural materials.

Applicants WO 2007/003516 discloses medical implants made of a porous composite material which comprises reticulating agents like metals, fibers, fullerenes etc., embedded in a polymeric, i.e. organic matrix. Also described is a thermal treatment of such materials, which may lead under partial decomposition of the polymer to a composite of a porous structure determined by the reticulating agents, hold together by carbonaceous material. In such materials, the porous structure is essentially determined by the geometry of the reticulating agents and their three-dimensional alignment. The drawback of such materials, if the organic matrix is decomposed to a certain extent, is that the mechanical properties are deteriorated, so that such materials with a structure of reticulating agents held together by carbonaceous material cannot be used for supporting structures due to their brittleness.

The requirements for implants are increasingly complex, because the material properties should also meet certain mechanical requirements. Furthermore, the provision of functions, such as drug-release requires a significant drug amount to be released and bio-available. Therefore a sufficient compartment volume for desorption or deposition of drug itself must be provided without affecting the constructive properties of an implant, particularly its physical properties.

Summary of the Invention

There may be an increasing need for porous materials to provide implant functionality with additional properties for drug-release or enhanced biocompatibility or the like.

According to an exemplary embodiment of the invention there is provided an implantable medical device or part thereof, i.e. a stent, having a supporting structure comprising a non-particulate inorganic carbon material.

In an exemplary preferred embodiment, the device is any conventional type of a stent, for example, one of a stent adapted for maintaining the patency of at least one of the esophagus, trachea, bronchial vessels, arteries, veins, biliary vessels and other similar body passageways in animals or human beings.

The stent according to an exemplary embodiment of the invention is expandable from a contracted state suitable for insertion into a vessel to an expanded state in which the stent supports the surrounding tissue, and may be self-expandable.

According to an exemplary embodiment of the invention the non-particulate inorganic carbon material includes at least one of bulk carbon material, a composite material comprising inorganic carbon and a further inorganic material, or a composite material comprising inorganic carbon and a further organic material.

For example, the inorganic carbon material can include at least 20 % by weight of carbon, preferably at least 50 % by weight, more preferred at least 80 % by weight, such as at least 90 % by weight, or at least 95 % by weight. In an exemplary embodiment, the device or stent is entirely consisting of the inorganic carbon material. The inorganic carbon includes at least one of graphite, diamond-like carbon, pyrolytic carbon, turbostratic carbon, glassy or vitreous carbon.

In exemplary preferred embodiments of the present invention, the device or stent has a supporting structure made of or comprising glassy carbon or vitreous carbon, i.e a non-graphitizing type of inorganic carbon material, which combines glassy and ceramic properties with those of graphite. Optionally, the vitreous or

glassy carbon material may include other materials, such as metals, alloys, ceramic, polymers, or the like, preferably in minor amounts.

According to an exemplary embodiment of the invention the inorganic carbon material includes a composite material comprising inorganic carbon as described above, and a further inorganic material selected from, e.g., at least one of a metal, a metal alloy, or a metal compound.

According to a further exemplary embodiment of the invention the inorganic carbon material includes a composite material comprising inorganic carbon as defined above, and a further organic material selected from, e.g. at least one of a polymer, a copolymer, an oligomer, or a polymer composite.

In exemplary embodiments, the supporting structure and/or the inorganic carbon material as defined above is porous, preferably with an open porous structure, e.g. having a plurality of interconnected pores. Open porous means that the pores are interconnected. The supporting structure and/or the inorganic carbon material can have a porosity in the range of 10 to 90%, preferably 30 to 90%, most preferably 50 to 90%, in particular about 60 %., and the average pore size of the pores is in a range of about 5 nanometer (nm) to 5000 micrometer (μm), preferably 10 nm to 1000 μm, most preferably 20 nm to 700 μm. Porosity means the ratio between the net volume of the free available pore space in the structure, and the total volume of the supporting structure including all spaces and pores and the material itself. Porosity, pore sizes and pore size distributions may be measured e.g. by an absorption method, such as N_2-porosimetry. Such porosity may provide a possibility for a large storing capacity with respect to the remaining mass of the stent, or stent section. Also, such pore sizes may allow a structure which is capable of being used for human stents, while obtaining a structure being capable to store an considerable amount of e.g. an active agent, and/or a structure allowing ingrowth of surrounding tissue after implantation.

Such a structure may allow to provide a stent with at least a porous section or being totally made of porous material, which is capable of storing e.g. an active agent without the need to provide a cavity. The size of a particle, a space, a pore or a

polyhedron means its volume or as an alternative the largest dimension. In exemplary embodiments, the interior of the pores is coated with a coating as desired, e.g. to improve biocompatibility or adhesion of active ingredients such that e.g. an active agent may be released in a defined rate.

According to an exemplary embodiment of the invention the pores in a first hierarchy substantially cover a convex polyhedron. Thus, the cavities formed by the pores have an appropriate shape for receiving e.g. an active agent.

According to an exemplary embodiment of the invention at least a part of the pores in a second hierarchy substantially cover a combination of a convex polyhedron and at least one partial convex sub-polyhedron, wherein the size of the polyhedron is larger than or equal to the size of the sub-polyhedron. The pores may also constitute of a plurality of interconnected sub-pores. A convex polyhedron means a polyhedron without pitching in edges.

A pore substantially covering a polyhedron means that each of the particles imaginary is tangent to a plane of the polyhedron covered by the pore. It should be understood that in case of tubular pores the tubes having a cross section of a convex polygon in equivalent interpretation to the convex polyhedron.

Pores may have a first hierarchy substantially covering a fist space, and a second hierarchy covering a space extending over the first space. The second hierarchy may also include further hierarchies in the aforementioned manner.

According to an exemplary embodiment of the invention a ratio between the size of the polyhedron and the at least one sub-polyhedron is in the range of 1:0.5 to 1:0.001, preferably 1: 0.4 to 1:0.01, and most preferred about 1:0.2. Such a ratio may provide an optimal ratio to achieve a good relation between the volume of the material structure, the pores and the stability of the structure.

According to an exemplary embodiment, only parts of the stent is made of the inorganic carbon material, for later assembly of the stent from such and optionally other parts, and said part of the stent determines at least a part of a form of the stent. In such embodiments, the part has a form out of a group consisting of a ring, a torus, a hollow cylinder segment, a tube segment, or a web structure.

According to a further exemplary embodiment of the invention the supporting structure of the stent has a plurality of walls, wherein the walls enclose a lumen for storing at least one active ingredient, and the walls are made of or comprise an inorganic carbon material and which is adapted to allow a fluid communication between the lumen and the exterior of the device for releasing the stored ingredient.

In such embodiments, the material can be non-porous and the walls have at least one opening connecting the enclosed lumen with the exterior of the device, to allow a release of active ingredients. Preferably, the opening is a hole. Alternatively, the material can be porous as defined above, having a plurality of interconnected pores for releasing an active ingredient through porous walls.

In an exemplary embodiment a stent is provided, wherein the lumen has an extension in a longitudinal direction of the stent and along a circumference of the stent, which is substantially larger than a radial extension of the lumen.

In a further exemplary embodiment a stent is provided, comprising a first tube and a second tube concentric to the first tube, wherein the lumen is enclosed between the fist and second concentric tube, and at least a part of the first and/or second tube comprises the carbon material.

In a further exemplary embodiment a stent is provided, comprising a first ribbon helically wound around a tubular space and a second ribbon helically wound around the tubular space corresponding and concentric to the fist ribbon, wherein the lumen is enclosed between the fist and second concentric ribbons, and at least a part of the first and/or second tube comprises the carbon material.

In a further exemplary embodiment a stent is provided, wherein the stent is formed by a plurality of hollow annular elements each having a sub-lumen, which annular elements are arranged such that each annular element circumferences a tubular space and each annular element has a different inclination from an adjacent abutting annular element, wherein adjacent annular elements are joined at an abutting location to form a passage between two abutting annular elements. Optionally, the annular elements comprise openings facing the exterior of the tubular space.

In a further exemplary embodiment a stent is provided, wherein the stent is formed of a brick wall structured mesh of hollow struts, wherein continuous struts extend in a longitudinal direction, which are connected by linking struts. Optionally, the brick walled structure totally circumferences a tubular space, such that the brick walled structure repeats periodically and perpetually along the circumference.

In a further exemplary embodiment a stent is provided, wherein the stent is formed by a plurality of hollow annular wave elements each having a sub-lumen, which annular wave elements are arranged such that each annular element circumferences a tubular space and each annular element abutting an adjacent annular element, wherein adjacent annular elements are joined at an abutting location to form a passage between two abutting annular elements. Optionally, the tubular space has a shape of a bifurcated tube.

According to an exemplary embodiment of the invention the stent includes at least one active ingredient. The active ingredient may provide an active therapy or prophylaxis with an as such passive element of a stent.

According to an exemplary embodiment of the invention the active ingredient is configured to be released in-vivo. Thus, the treatment of diseases requiring a permanent supply of e.g. an active agent is possible without the need to a permanently supplying of said active agent to the human body. Moreover, the active agent is provided in one dose by the stent having stored therein a particular amount of the active agent, but the active agent is continuously released over a wide range of time.

According to an exemplary embodiment of the invention the active ingredient includes at least one of a pharmacologically, therapeutically, biologically or diagnostically active agent or an absorptive agent.

The present invention satisfies a need for porous implants wherein the pore size, the pore distribution and the degree of porosity can be adjusted without deteriorating the physical and chemical properties of the material essentially. For example, with increasing degree of porosity the mechanical properties, such as hardness and strength decrease over-proportionally. This is particularly

disadvantageous in biomedical implants, where anisotropic pore distribution, large pore sizes and a high degree of porosity are required, whereas simultaneously a high long-term stability with regard to biomechanical stresses is necessary.

The present invention further satisfies a need for implant materials with bioactive properties that overcome the drawbacks of corrosive and potentially toxic ion releasing metals or ceramics. In addition, the materials used in the present invention have properties that allow adsorbing and desorbing lipohilic as well as hydrophilic beneficial agents.

The present invention also satisfies a need for providing drug-release function and improving the availability of drug by increasing the overall volume of the porous compartment that contains the drug without affecting adversely the design of the device. E.g., the conventional design of drug-eluting stents is based on non-porous structures that have to be coated resulting in an increase of the stent strut thickness. Increasing the thickness results in adverse properties, such as increasing the profile of the stents within the target vessels, which can limit the use to large vessels, or which can be correlated to mechanically induced, haemodynamic-related thrombosis.

Furthermore, the present invention satisfies a need for drug-eluting stent which after implantation need to remain permanently in the body to fulfill, e.g., a permanent supporting function.

One aspect of the present invention is to provide a stent made form a bioactive material that comprises improved biocompatibility, facilitates engraftment and reduces inflammatory or adverse long-term effects.

Another aspect of the present invention is to provide a stent that provides at least at the surface that contacts body tissue or physiologic fluids with a carbon-containing bioactive material that comprises improved biocompatibility, facilitates engraftment and reduces inflammatory or adverse long-term effects.

Another aspect of the present invention is to provide a stent with a porous compartment or hollow lumen as a reservoir for incorporation of beneficial agents, for example as a delivery device for release of beneficial agents.

A further aspect of this invention is to provide a stent that can be used as a device for controlled release of biologically active, therapeutically active, diagnostic agents.

Another aspect of the present invention is to provide multifunctional stents that additionally to the foregoing aspects can be modified in the underlying material properties, particularly the physical, chemical and biologic properties, e.g. biodegradability, x-ray and MRI visibility or mechanical strength.

In accordance with another aspect, a stent is comprised according to the other aspects whereby the stent incorporates biologically active, therapeutically active, diagnostic or absorptive agents.

A further object of the present invention is to provide a simple and cost-effective, flexible process for the manufacturing of such-like medical implants.

In accordance with yet a further aspect of the invention, an implantable stent is provided comprising an expandable stent structure, a capillary reservoir and/ or a lumen within the structure and a plurality of openings in the stent structure.

Definitions

The terms "active ingredient", "active agent" or "beneficial agent" as used herein include any material or substance which may be used to add a function to the implantable medical device. Examples of such active ingredients include biologically, therapeutically or pharmacologically active agents, such as drugs or medicaments, diagnostic agents, such as markers, or absorptive agents. The active ingredients may be a part of the first or second particles, such as incorporated into the implant or being coated on at least a part of the implant. Biologically or therapeutically active agents comprise substances being capable of providing a direct or indirect therapeutic, physiologic and/or pharmacologic effect in a human or animal organism. A therapeutically active agent may include a drug, pro-drug or even a targeting group or a drug comprising a targeting group. An "active ingredient" according to the present invention may further include a material or substance which may be activated physically, e.g. by radiation, or chemically, e.g. by metabolic processes.

The term "biodegradable" as used herein includes any material which can be removed in-vivo, e.g. by biocorrosion or biodegradation. Thus, any material, e.g. a metal or organic polymer that can be degraded, absorbed, metabolized, or which is resorbable in the human or animal body may be used either for a biodegradable metallic layer or as a biodegradable template in the embodiments of the present invention. Also, as used in this description, the terms "biodegradable", "bioabsorbable", "resorbable", and "biocorrodible" are meant to encompass materials that are broken down and may be gradually absorbed or eliminated by the body in-vivo, regardless whether these processes are due to hydrolysis, metabolic processes, bulk or surface erosion.

The terms “lumen”, “compartment” or “reservoir” are synonymously used herein to describe a an essentially closed hollow space, other than a pore or pore system, enclosed by walls of the implant material. Examples of a lumen are shown, e.g, in Fig. 1b, wherein the lumen is enclosed between a first and a second concentric tube, in Fig. 2b, wherein the lumen is enclosed between a first and a second concentric ribbon, or in Fig. 3b, wherein the lumen is inside a hollow double helical structure and may either be continuous or discontinuous, i.e. a plurality of not interconnected reservoirs.

The term “porous” as used herein designates a property of a material, which is determined by the presence of a plurality of interconnected pores. The volume of the pores can be assessed by measuring the porosity of the material as further defined herein. “Porous” does not include holes like boreholes or the like.

The term "supporting structure" is used to designate the bulk structure of the device, i.e. the device body. To the contrary, a coating can not be a part of a supporting structure.

The terms "implant", implantable device" and the like are meant to define a stent as described herein.

Brief Description of the Drawings

Exemplary embodiments of the present invention will be described in the following with reference to the following drawings.

Fig. 1. shows a tubular stent structure according to an exemplary embodiment of the present invention.

Fig. 2. shows a helical stent structure according to a further exemplary embodiment of the present invention.

Fig. 3. shows a ring-segmented stent structure according to a further exemplary embodiment of the present invention.

Fig. 4. shows a wall/brick structured stent structure according to a further exemplary embodiment of the present invention.

Fig. 5. shows a variety of strut forms for a stent structure according to a further exemplary embodiment of the present invention.

Fig. 6. shows a punched pattern for a stent structure according to a further exemplary embodiment of the present invention.

Fig. 7 shows a web pattern for a stent structure according to a further exemplary embodiment of the present invention.

Fig. 8 shows an interconnected woven pattern for a stent structure according to a further exemplary embodiment of the present invention.

Fig. 9 shows a bifurcated tube of a stent structure according to a further exemplary embodiment of the present invention.

Fig. 10 shows a cross section of a bifurcated tube of a stent structure according to a further exemplary embodiment of the present invention.

Fig. 11. shows a macro pore structure according to an exemplary embodiment of the present invention.

Fig. 12. shows a macro pore structure having a plurality of hierarchies according to a further exemplary embodiment of the present invention.

Detailed Description of Exemplary Embodiments

The invention will now be described in greater detail with reference to the preferred embodiments illustrated in the accompanying drawings. The following description makes reference to numerous specific details in order to provide a thorough understanding of the present invention. All aspects and features described herein may be combined as desired. However, each and every specific detail needs not to be employed to practice the present invention.

In one preferred embodiment the porous implant comprises a tubular structure with or without an inner lumen along the longitudinal axis. If the stent is made from porous carbon material, the pores are interconnected and constitute a porous compartment or reservoir. In specifically preferred embodiments the structure comprises at least one or a plurality of perforation/s within the porous or non-porous wall, herein referred to as an opening or openings.

Fig. 1a shows an implant or stent 10 with a tubular or essentially cylindrical structure. A cross-sectional view of the implant 10 is shown in Fig. 1b. The tubular structure may comprise in its longitudinal axis an inner lumen 20, whereby the inner wall 50 is closed, and the outer wall 30 of the cylindrical tube comprises at least one opening 60 or a plurality of openings. Between both walls the stent may comprise an inner compartment 40, or respectively a reservoir.

The length of the stent can be depending not he intended use of the stent, e.g. in a range of 100 µm to 100 cm, such as from 1000 µm to 10 cm, or from 5 mm to 60 mm, or even from 7 mm to 40 mm. The diameter can be selected e.g. in a range from 5 nm to 20 cm, such as from 1000 nm to 10 cm, or from 500 µm to 10 mm, or even from 500 µm to 10.000 µm. Furthermore, in a further embodiment the ratio of length to width of the stent tube can be selected from 20:1 to 10:1, more preferred from 8:1 to 5:1 and most preferred from 4:1 to 2:1. However, the ratio is depending on the intended use of the stent and the capacity of the porous compartment or reservoir. The size of the porous compartment, i.e. the overall volume of pores, is not only adjustable by selecting the dimensional sizes of length and width and diameter, but also by appropriate design of pore structure and/or pore volume. The openings can

have a round shape, ellipsoid shape, rectangular shape or any other regular or irregular geometry or any combination thereof. The porous compartment allows the incorporation or release of beneficial agents, such as biologically active, therapeutically active, diagnostic or absorptive agents or any combination thereof. Furthermore, the porous compartment also allows the absorption of compounds from physiologic fluids into the compartment inside the stent structure. A person skilled in the art will easily determine the appropriate option in terms of dimension and embodiment of porous compartments and openings depending on the target area with the body of the living animal or human being. For example, an embodiment for use as an artery or vein graft must have appropriate dimensions for implanting the device. Furthermore, the intended release of a therapeutic agent locally to the surrounding vessel wall may further require appropriate dimensions of the pores to sufficiently absorb and release the beneficial agents.

In another exemplary embodiment the porous stent may have a shape of a helical tube of a band-like or stripe-like structure. The pores in the stent structure are interconnected and constitute a porous compartment or reservoir. The helical structure may allow a flexible distortion of the stent due to the design. The structure may comprise at least one or a plurality of perforation/s within the porous wall, herein referred to as an opening or openings.

Fig. 2a shows a possible stent structure 70 comprising a helical tube of a band-like or stripe-like structure. A cross-sectional view of the implant 70 is shown in Fig. 2b. The band-like or stripe-like structure may be hollow and comprises an inner compartment or reservoir 90. The structure may also comprise at least one opening 80.

For example, in one specific exemplary embodiment for use as a tracheal or bronchial stent the implant must have appropriate dimensions for implanting the device.

In further exemplary embodiments the helical stripe may comprise peaks or serpentines, either symmetrically or asymmetrically, or any desired pattern of peaks and/or serpentines. Also, a plurality of peaks and/or serpentines may be embedded in

any desired combination, whereby also the angles and radius can be different. Furthermore, the peaks and serpentines can be of rectangular shape, either with rounded or without rounded edges of the struts. The struts can have different width and/or depth, i.e. aspect ratios, at different sections along their structures. In some embodiments it can be preferred to have combination of rectangular or rounded peaks and/or serpentines or any combination thereof.

In a further exemplary embodiment the porous implant comprises a stent having a double helical structure of interconnected, helically winded tubes. The pores are interconnected and constitute a porous compartment or reservoir. The structure may comprise at least one or a plurality of perforation/s or openings within the porous wall, as described above.

Fig. 3a shows an implant, e.g. a stent 100 having a double helical structure of interconnected, helically winded tubes. The structure may comprise at least one opening 110. The cross-sectional view of the implant in Fig. 3b illustrates that the double helical structure may be hollow and may comprise a continuous inner compartment 120 or respective reservoir.

In one optional embodiment, the helical tubular stent may comprise more than two helices. The length of the implant can be in a range as described above.

In another exemplary embodiment the porous implant is a mesh-like tube or lattice. One specific exemplary embodiment comprises a rectangular pattern in a two-dimensional view

Fig. 4a shows a rectangular pattern 130 in a two-dimensional view. The lattice structure comprises in longitudinal direction continuous struts 140 that are connected by linking struts 150. The lattice 130 may be formed to a tubular implant 160 as described in Fig. 4b. The struts 140 and 150 may be hollow and comprise an interconnected inner compartment or respective reservoir. The structure may also comprise at least one opening 170 as illustrated in Fig. 4c, which is a magnification of a section of Fig. 4b.

The lattice structure comprises in longitudinal direction continuous struts that are connected by linking struts. The lattice can be formed to a tubular implant as

described in the drawings. The struts are porous and comprise an interconnected porous compartment or respective reservoir. In certain embodiments the structure may also comprise at least one opening.

The length of the implant can be in a range as described above.

A person skilled in the art will easily determine the appropriate option in terms of dimension and embodiment of openings depending on the target area with the body of the living animal or human being. For example, in one specific embodiment for use as a coronary or peripheral stent the implant must have appropriate dimensions for implanting the device. The angle between one linking strut and the continuous struts is 90°, but in other embodiments the angle can be modified to any preferred pattern with angles from 0.1° to 179°. The porous lattice tube may e.g. comprise at least two continuous struts that are linked. The number and distance of continuous and linking struts can be varied according to the intended mechanical properties, the required volume of the porous compartment or respective reservoir. Also, the orientation of the linking struts can be varied. Furthermore, an asymmetric design of linking struts, i.e. identical numbers and/or orientation and/or distances and/or angles, may be used or asymmetric designs with different numbers and/or orientations and/or distances and/or angles. Particularly for expandable stents it is desirable to select an embodiment that is appropriate, whereby a person skilled in the art can easily identify the appropriate design e.g. by using finite element analysis to determine the optimal configuration. The thickness of the struts can play an important role for elastomechanical properties of the implant. For expandable devices, but not limited to strut thicknesses in a range of 10µm up to 500µm, more preferred from 50µm to 400 mm and most preferred from 70µm to 200µm may be used. The thickness can be larger or smaller, depending on the requirements of the implant regarding mechanical or biomechanical stress occurring after implantation. E.g., a person skilled in the art would select larger thicknesses for implants that are used as peripheral stents for arteries in the knee or below the knee.

Also, the aspect ratio, i.e. the ratio between width and depth of a strut, may be varied as appropriate. In applications that require a low profile struts with lower

depth may be used. Therefore, the aspect ratios can be in a range from 20:1 to 1:20, such as from 10:1 to 1:10 or from 2:1 to 1:2.

The drawings illustrate the basic aspects of the invention and are not limited to any of the aforesaid aspects. For example, the edges of the struts can be rounded. In some embodiments, for example in order to increase the overall surface or to optimize the stress distribution for expandable implants, serpentines and peaks may be embedded into the struts. For example, the linking struts may comprise at least one peak or one serpentine with two peaks. The orientation of the peaks or serpentines can be varied, e.g. a left-hand oriented peak or right-hand oriented serpentine with a right-hand oriented peak first and a right-hand oriented peak second or vice versa. In some embodiments the modified linking struts are all of the same design; in other embodiments they can have alternating patterns or any different pattern or combination thereof. In further embodiments the continuous struts may comprise peaks or serpentines, either symmetrically or asymmetrically, or both the continuous struts and the linking struts may comprise any desired pattern of peaks and/or serpentines. The design is not limited to one peak or one serpentine, it is also possible to embed a plurality of peaks and/or serpentines in any desired combination, whereby also the angles and radius can be different.

The drawings in Fig. 5 illustrate several possible strut forms. The edges of the strut can be rectangular 180, the edges of the strut can be rounded 190 or a serpentine can be embedded into the strut 200. The strut can comprise at least one peak 210 or one serpentine with two peaks 220. The orientation of the peaks or serpentines can be varied, e.g. a left-hand oriented peak or right-hand oriented serpentine with a right-hand oriented peak first and a right-hand oriented peak second or vice versa.

The peaks and serpentines can be of rectangular shape, either with rounded or without rounded edges of the struts. Furthermore, the struts can have different width and/or depth, i.e. aspect ratios, at different sections along their structures. In some embodiments it can be preferred to have a combination of rectangular or rounded peaks and/or serpentines or any combination thereof.

In another embodiment the open cells, i.e. the space between the struts, of the above described structure may comprise the struts and the struts comprise the open cells. Therefore, this specific embodiment has to be seen as a "negative" of the aforesaid embodiment.

Fig. 6a shows a open cell pattern 230 in a two-dimensional view. The lattice structure comprises narrow continuous struts 240 connected by broader linking struts 250. Fig. 6b displays a pattern in which the continuous struts 270 and linking struts 280 comprise nodes 290 at their intersections.

In this exemplary embodiment the continuous struts and linking struts comprise nodes at their intersections. The nodes can have different geometric shapes and dimensions. Particularly, the distances between the nodes, distances of linking struts and the segments of continuous struts between the nodes can be modified similar to the above described embodiments. Hence, also the modification of continuous struts and linking struts can be embedded as explained above.

In another exemplary embodiment the porous implant is a mesh-like tube with a rhombic shape of the open cells. The struts are porous and comprise an interconnected inner porous compartment or respective reservoir. The structure may also comprise at least one opening.

Fig. 7a and Fig 7b show mesh-like patterns in a two-dimensional view, wherein the open cells have a square shape 300 and a rhombic shape 310, respectively. The mesh 310 is formed to a tubular implant 320 comprising a mesh-like tube with a rhombic shape of the open cells as illustrated in Fig. 7c. The struts 330 can be optionally hollow, and comprise an interconnected inner compartment or respective reservoir. The structure may also comprise at least one opening 340 as shown in Fig. 7d, which is a magnification of a section of Fig. 7c.

The length and diameter of the implant can be in a range as described above The angle between the struts in the longitudinal axis is 30° to 90°, but the angle can be modified to any preferred pattern with angles from 0.1° to 179°. According to another exemplary embodiment of the present invention, the angle between the struts in the rectangular axis is 20° to 120°. The struts form at their intersections a node,

whereby at least two nodes are comprised. The implant comprises a segment between two nodes, hence, at least on segment is comprised. The struts between the nodes are linking struts. The number and distance of nodes and linking struts can be varied according to the intended mechanical properties, the required volume of the porous compartment or respective reservoir. Also, the orientation of the linking struts can be varied. An asymmetric design of linking struts may also be used, i.e. identical numbers and/or orientation and/or distances and/or angles. Particularly for expandable implants it is desirable to select an embodiment that is appropriate, whereby a person skilled in the art can easily identify the appropriate design e.g. by using finite element analysis to determine the optimal configuration. The thickness of the struts can play an important role for elastomechanical properties of the implant. Strut thickness may be as described above.

Also, the aspect ratio, i.e. the ratio between width and depth of a strut, may be selected as described above.

In another embodiment the porous implant or stent comprises a tube with a parallel lattice with interconnecting links. The struts are porous and comprise an interconnected porous compartment or respective reservoir. In specifically preferred embodiments the structure also comprises at least one opening or a plurality of openings.

Fig. 8a shows an undulated lattice 350 in a two-dimensional view, wherein the parallel, undulated struts 360 are interconnected by linking struts 370. The lattice 350 is formed to a tubular implant 380 as illustrated in Fig. 8b. The structure may comprise at least one opening 390. The cross-sectional view of the implant 380 in Fig. 8c shows that the structure may optionally be hollow, and comprises an interconnected inner compartment 400 or respective reservoir.

In the longitudinal axis at least two continuous struts are interconnected by at least one linking strut. The length and diameter of the implant can be in a range as described above.

The porous compartment allows the incorporation or release of beneficial agents, preferably biologically active, therapeutically active, diagnostic or absorptive

agents or any combination thereof. Furthermore, the porous compartment allows also the absorption of compounds in physiologic fluids into the compartment. A person skilled in the art will easily determine the appropriate option in terms of dimension and embodiment of openings depending on the target area with the body of the living animal or human being. For example, in one embodiment for use as a biliary or coronary stent the implant must have appropriate dimensions for implanting the device. The angle between one linking strut and the continuous struts is 10° to 160°, but the angle can be modified to any preferred pattern with angles from 0,1° to 179°. The number and distance of continuous and linking struts can be varied according to the intended mechanical properties, the required volume of the porous compartment or respective reservoir. The continuous struts may comprise a symmetric or asymmetric pattern of wave-like peaks, whereby the orientation of the peaks can be alternating or non-alternating. The angle of the peaks can be varied from 10° to 179°, such as from 15° to 160°, or from 25° to 120°. Also the orientation of the linking struts can be varied. Furthermore, in specific embodiments it is required to have asymmetric design of linking struts may be used, i.e. identical numbers and/or orientation and/or distances and/or angles.

It has to be understood that the design of different stents is not limited to the above described basic geometric embodiments. For example, implants may also have a combined geometry of the tube, i.e. bifurcated tube at one or more sides or at one lateral end or at both lateral ends and any combination thereof. It could be preferred to implant stents or stent grafts into bifurcated vessels for example, therefore it is useful to have an implant design that follows the natural anatomy of the targeted organ, organ structure or organ vessel.

The drawings in Fig. 9 illustrate three options for implant designs. The implants can have a combined geometry of the tube, i.e. bifurcated tube at one 430 or more sides or at one lateral end 410 or at both lateral ends 420. The implants can have different diameters at the ends or at any section of the implant as shown in Fig. 9.

Moreover, the implants or stents may have different diameters at the ends or at any section of the implant, e.g. to address the anatomy of target vessels that have a narrowing profile. Another embodiment comprises at least one cut out within the structure, e.g. for use in bifurcating vessels or complex anatomical structures. The implants may be used in combination, e.g. to allow the implantation of stent into a bifurcation area of arteries or veins.

Fig. 10 shows an implant 440 comprising a cut out 450 within the structure. The implant 440 can also have a bifurcated tube at one 460 or more sides.

Preferred materials

According to an exemplary embodiment of the invention the supporting structure of the stent, or part thereof comprises an inorganic carbon material, or may optionally consist of the inorganic carbon material.

The inorganic carbon material for use in the present invention may be any carbon material, which is different from an organic polymer material. Preferably, the inorganic carbon material is a homogenous, i.e. non-particulate material. The inorganic carbon material can, for example, include at least one of a bulk carbon material, a composite material comprising inorganic carbon and a further inorganic material, or a composite material comprising inorganic carbon and a further organic material.

For example, the inorganic carbon material can include at least 20 % by weight of carbon, preferably at least 50 % by weight, more preferred at least 80 % by weight, such as at least 90 % by weight, or at least 95 % by weight.

The inorganic carbon can include at least one of graphite, diamond-like carbon, pyrolytic carbon, turbostratic carbon, glassy or vitreous carbon, amorphous carbon, or the like.

Furthermore, in exemplary embodiments, the inorganic carbon material may be reinforced as conventionally known with minor amounts of e.g. carbon particles, carbon fibers, carbon nanotubes, fullerenes, fullerene onions, metallo-fullerenes, graphite fibers or particles or diamond, e.g. in order to improve the elastomechanical

properties. Preferably, such particulate or fibrous materials are added to the inorganic carbon material in an amount that substantially does not determine or influence the material or pore structure of the inorganic carbon material. Particularly, there are no pores in the inorganic carbon material being determined or confined by an alignment of fillers, fibers or particles as defined herein.

The inorganic carbon material as defined herein is a substantially homogenous, optionally reinforced material, which, if porous, includes pores created by incorporating removable pore-formers into a precursor material and subsequently removing such pore-forming materials from the inorganic carbon material.

In exemplary preferred embodiments of the present invention, the device or stent has a supporting structure comprising or even consisting substantially of glassy carbon or vitreous carbon, i.e. a non-graphitizing type of inorganic carbon material, which combines glassy and ceramic properties with those of graphite. The most important properties of this material are e.g. its biocompatibility, bio-inertness, and resistance to chemical attack. Glassy carbon is a conventional material, widely used e.g. as an electrode material in electrochemistry, and may be produced from organic precursor materials, such as polymers or phenolic resins at temperatures up to 3000 °C by carbonization, and may be widely varied in its physical properties.

Without wishing to be bound to any specific theory, the structure of glassy carbon is 100% sp^2-hybridized carbon, i.e. a graphite or fullerene like structure. Other models assumed that both sp^2 and sp^3 -bonded atoms may be present. A later model was based on the assumption that the molecular orientation of the polymeric precursor material is memorized to some extent after carbonization. Thus, it is assumed that the structure bears some resemblance to that of a polymer, in which the "fibrils" are very narrow curved and twisted ribbons of graphitic, and thus inorganic, carbon. However, more recent research has suggested that glassy carbon has a fullerene-related structure. Basically, glassy or vitreous carbon consists of two-dimensional structural elements (sp^2-C) and does not exhibit 'dangling' bonds, like e.g. amorphous carbon does.

In a further embodiment, the inorganic carbon material may comprise amorphous carbon, i.e. a glassy carbon material that essentially does not have any crystalline structure, but includes a certain amount of sp^3-carbon structural elements. As with all glassy materials, amorphous carbon reveals some short-range order, but there is no long-range pattern of atomic positions.

In further exemplary embodiments the inorganic carbon material may comprise diamond-like carbon (DLC) which is also an amorphous carbon material that displays some of the properties of diamond. Such materials contain significant amounts, for example up to 100 %, of sp^3 hybridized carbon atoms, wherein the carbon atoms may be arranged in a cubic lattice or a hexagonal lattice, or mixtures thereof.

Furthermore, mixtures of amorphous, diamond-like, vitreous, glassy, or other carbon materials may be used for preparing the supporting structure of the devices of the present invention.

Optionally, the inorganic carbon material, such as amorphous, diamond-like, vitreous or glassy carbon material may be mixed with other materials, such as metals, alloys, ceramic, polymers, or the like, preferably in minor amounts, e.g. less than 30 % by weight, preferably less than 10 % by weight.

According to the present invention the, optionally porous, stents contain at minimum a carbon content of 20% by weight, preferably sp^2 carbon or, in specific embodiments, sp^3 carbon or any mixture thereof. Without binding to a specific theory it was demonstrated that inorganic materials with sp^2 carbon or sp^3 carbon contacted with physiologic fluids or living cells or tissue show bioinert or bioactive properties and are superior to other materials in terms of cytotoxicity, haemocompatibility, inflammation or engraftment and respective tissue or cell adhesion.

According to one aspect of the present invention the optionally porous implant comprises the carbon-material at least at one part of the surface contacted with physiologic fluids or cells or tissue. The present invention also contemplates the use of different materials for different sections or parts of the inventive implant.

According to an exemplary embodiment of the invention the inorganic carbon material includes a composite material comprising inorganic carbon as described above, and a further inorganic material selected from, e.g., at least one of a metal, a metal alloy, or a metal compound.

According to one exemplary embodiment the, optionally porous, implant is comprises a combination of carbon materials as described above, and metal or metal alloys, e.g. metals and metal alloys selected from main group metals of the periodic system, transition metals, such as copper, gold and silver, titanium, zirconium, hafnium, vanadium, niobium, tantalum, chromium, molybdenum, tungsten, manganese, rhenium, iron, cobalt, nickel, ruthenium, rhodium, palladium, osmium, iridium or platinum, or from rare earth metals.. The metal compound is selected from any suitable metal or metal oxide or from shape memory alloys any mixture thereof to provide the structural body of the implant. Preferably, the metal compound is selected from the group of zero-valent metals, metal oxides, metal carbides, metal nitrides, metal oxynitrides, metal carbonitrides, metal oxycarbides, metal oxynitrides, metal oxycarbonitrides and the like, and any mixtures thereof. The metals or metal oxides or alloys used in a preferred embodiment of the present invention may be magnetic. Examples are - without excluding others – iron, cobalt, nickel, manganese and mixtures thereof, for example iron, platinum mixtures or alloys, or for example, magnetic metal oxides like iron oxide and ferrite. It may be preferred to use semi-conducting materials or alloys, for example semi-conductors from Groups II to VI, Groups III to V, and Group IV. Suitable Group II to VI semi-conductors are, for example, MgS, MgSe, MgTe, CaS, CaSe, CaTe, SrS, SrSe, SrTe, BaS, BaSe, BaTe, ZnS, ZnSe, ZnTe, CdS, CdSe, CdTe, HgS, HgSe, HgTe, or mixtures thereof. Examples for suitable Group III to V semi-conductors are GaAs, GaN, GaP, GaSb, InGaAs, InP, InN, InSb, InAs, AIAs, AIP, AISb, AIS and mixtures thereof. Examples for Group IV semi-conductors are germanium, lead and silicon. The semi-conductors may also comprise mixtures of semi-conductors from more than one group and all the groups mentioned above are included.

In other embodiments it is preferred to select the metal compound from metals or metal-oxides or alloys that comprise MRI visibility or radiopacity, preferably implants made from ferrite, tantalum, tungsten, gold, silver or any other suitable metal, metal oxide or alloy, like platinum-based radiopaque steel alloys, so-called PERSS (platinum-enhanced radiopaque stainless steel alloys), cobalt alloys or any mixture thereof.

Furthermore, biodegradable metals may be incorporated in carbon composites, which can include, e.g., metals, metal compounds, such as metal oxides, carbides, nitrides and mixed forms thereof, or metal alloys, e.g. particles or alloyed particles including alkaline or alkaline earth metals, Fe, Zn or Al, such as Mg, Fe or Zn, and optionally alloyed with or combined with other particles selected from Mn, Co, Ni, Cr, Cu, Cd, Pb, Sn, Th, Zr, Ag, Au, Pd, Pt, Si, Ca, Li, Al, Zn and/or Fe. Also suitable are, e.g., alkaline earth metal oxides or hydroxides, such as magnesium oxide, magnesium hydroxide, calcium oxide, and calcium hydroxide or mixtures thereof. In exemplary embodiments, the biodegradable metal compound may be selected from biodegradable or biocorrosive metals or alloys based on at least one of magnesium or zinc, or an alloy comprising at least one of Mg, Ca, Fe, Zn, Al, W, Ln, Si, or Y. Furthermore, the implant may be substantially completely or at least partially degradable in-vivo. Examples for suitable biodegradable alloys comprise e.g. magnesium alloys comprising more than 90 % of Mg, about 4-5 % of Y, and about 1.5-4 % of other rare earth metals, such as neodymium and optionally minor amounts of Zr; or biocorrosive alloys comprising as a major component tungsten, rhenium, osmium or molybdenum, for example alloyed with cerium, an actinide, iron, tantalum, platinum, gold, gadolinium, yttrium or scandium.

The metal or metal alloy may include in an exemplary embodiment

(i) 10-98 wt.-%, such as 35-75 wt.-% of Mg, and 0-70 wt.-%, such as 30-40% of Li and 0-12wt.-% of other metals, or

(ii) 60-99wt.-% of Fe, 0.05-6wt.-% Cr, 0.05-7wt.-% Ni and up to 10wt.-% of other metals; or

(iii) 60-96wt.-% Fe, 1-10wt.-% Cr, 0.05-3wt.-% Ni and 0-15wt.-% of other metals,

wherein the individual weight ranges are selected to always add up to 100 wt.-% in total for each alloy.

According to a further exemplary embodiment of the invention the inorganic carbon material includes a composite material comprising inorganic carbon as defined above, and a further organic material selected from, e.g. at least one of a polymer, a copolymer, an oligomer, or a polymer composite. In specifically preferred embodiments the carbon material of the device contains a coating, either partially or completely, to comprise a sandwich-like composite material and preventing the device from particulate formation due to mechanically induced damages or to enhance the elastomechanical properties. This material design consists of the carbon material as the core and the coating material as the shell of the structural implant material. The coating materials are preferably selected from organic compounds.

Preferred organic compounds or materials for such composites include biocompatible polymers, oligomers, or pre-polymerized forms as well as polymer composites. The polymers used may be thermosets, thermoplastics, synthetic rubbers, extrudable polymers, injection molding polymers, moldable polymers, spinnable, weavable and knittable polymers, oligomers or pre-polymerizes forms and the like or mixtures thereof. In a specific embodiment, the organic compounds or materials for such composites are selected from electrically conducting polymers, fluorescent or luminescent polymers. In specific embodiments it is useful to select the organic compound from biodegradable organic materials, for example - without excluding others – collagen, albumin, gelatin, hyaluronic acid, starch, cellulose (methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose-phtalate); furthermore casein, dextrane, polysaccharide, fibrinogen, poly(D,L lactide), poly(D,L-lactide-Co-glycolide), poly(glycolide), poly/hydroxybutylate), poly(alkylcarbonate), poly(orthoester), polyester, poly(hydroxyvaleric acid), polydioxanone, poly(ethylene, terephtalate), poly(maleic

acid), poly(tartaric acid), polyanhydride, polyphosphohazene, poly(amino acids), and all of the copolymers and any mixtures thereof.

In another specific embodiment the material is based on a combination of non-particulate inorganic carbon materials as described above and inorganic composites or organic composites or hybrid inorganic/organic composites. The composite material can also comprise, as a functional additive in small amounts substantially not affecting the performance of the non-particulate inorganic material, e.g. to enhance visibility by diagnostic methods, organic or inorganic micro- or nano-particles or any mixture thereof. Preferably, these additive particles used in the present invention are selected from the group of zero-valent metals, metal oxides, metal carbides, metal nitrides, metal oxynitrides, metal carbonitrides, metal oxycarbides, metal oxynitrides, metal oxycarbonitrides and the like, and any mixtures thereof. The particles used in a preferred embodiment of the present invention may be magnetic. It may be preferred to use semi-conducting particles. In a particularly preferred embodiment, the semiconducting particles used are core/shell particles and have absorption properties for radiation in the wavelength region from gamma radiation up to microwave radiation, or the particles are able to emit radiation, particularly in the region of 60 nm or less, wherein it may be preferred to select the particle size and the diameter of core and shell in such a manner that the emission of light quantums in the region of 20 to 1,000 nm is adjusted. Also, mixtures of such particles may be selected which emit light quantums of different wavelengths when exposed to radiation.

In a particularly preferred embodiment, the selected nanoparticles are fluorescent, particularly preferred without any quenching.

It may further be preferred to select superparamagnetic, ferromagnetic, ferromagnetic metal particles. In a particularly preferred embodiment, the particles are selected from polymers, oligomers or pre-polymeric particles. Examples of suitable polymers for use as particles in the present invention are hompopolymers, copolymers, prepolymeric forms and/or oligomers of poly(meth)acrylate, unsaturated polyester, saturated polyester, polyolefines like polyethylene, polypropylene,

polybutylene, alkyd resins, epoxy-polymers or resins, phenoxy polymers or resins, phenol polymers or resins, polyamide, polyimide, polyetherimide, polyamideimide, polyesterimide, polyesteramideimide, polyurethane, polycarbonate, polystyrene, polyphenole, polyvinylester, polysilicone, polyacetale, cellulosic acetate, polyvinylchloride, polyvinylacetate, polyvinylalcohol, polysulfone, polyphenylsulfone, polyethersulfone, polyketone, polyetherketone, polybenzimidazole, polybenzoxazole, polybenzthiazole, polyfluorocarbons, polyphenylenether, polyarylate, cyanatoester-polymere, and mixtures of any of the foregoing.

Furthermore, polymer particles may be selected from oligomers or elastomers like polybutadiene, polyisobutylene, polyisoprene, poly(styrene-butadiene-styrene), polyurethanes, polychloroprene, or silicone, and mixtures, copolymers and combinations of any of the foregoing.

In a specific embodiment, the particles are selected from electrically conducting polymers, preferably from saturated or unsaturated polyparaphenylene-vinylene, polyparaphenylene, polyaniline, polythiophene, poly(ethylenedioxythiophene), polydialkylfluorene, polyazine, polyfurane, polypyrrole, polyselenophene, poly-p-phenylene sulfide, polyacetylene, monomers oligomers or polymers thereof or any combinations and mixtures thereof with other monomers, oligomers or polymers or copolymers made of the above-mentioned monomers. Particularly preferred are monomers, oligomers or polymers including one or several organic, for example, alkyl- or aryl-radicals and the like or inorganic radicals, like for example, silicone or germanium and the like, or any mixtures thereof. Preferred are conductive or semi-conductive polymers having an electrical resistance between 10^{12} and 10^{12} Ohm·cm. It may particularly be preferred to select those polymers which comprise complexed metal salts.

In other aspects of the preferred embodiment the additive particles are selected from biodegradable particles like for example - without excluding others – collagen, albumin, gelatine, hyaluronic acid, starch, cellulose (methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose-

phtalate); furthermore casein, dextrane, polysaccharide, fibrinogen, poly(D,L lactide), poly(D,L-lactide-Co-glycolide), poly(glycolide), poly/hydroxybutylate), poly(alkylcarbonate), poly(orthoester), polyester, poly(hydroxyvaleric acid), polydioxanone, poly(ethylene, terephtalate), poly(maleic acid), poly(tartaric acid), polyanhydride, polyphosphohazene, poly(amino acids), and all of the copolymers and any mixtures thereof.

Preferably, the carbon phase of the non-particulate inorganic carbon material comprises inorganic sp^2 or sp^3 carbon or any mixture thereof, like graphite, pyrolytic, turbostratic, glassy or vitrous carbon, diamond-like carbon or any mixture thereof.

In further embodiments the implant comprises a supporting structure of a non-particulate inorganic carbon material, i.e. a structural material made out of inorganic sp^2 and/or sp^3 hybridized carbon, whereby, partially or completely, the outer surface or both the outer and inner surface of the supporting structure comprise a non-carbon material.

In an additional preferred embodiment the implant comprises a structural material made out of a composite containing inorganic sp^2 or sp^3 or a mixture of sp^2 and sp^3 hybridized carbon.

Material structure

Fig. 11 schematically shows a pore structure 500 of an exemplary supporting structure of an inorganic carbon material (not shown in detail in Fig. 11), wherein a plurality of pores 510 is embedded in the carbon material, thus forming an open porous structure. The pores may be provided with a coating 511. Although Fig. 11 shows a coating only with respect to a few pores, also the other pores may be coated.

Fig 12 schematically shows a pore system of an exemplary porous supporting structure, in which a plurality of pores are joint to form a pore system having a plurality of hierarchies. In this embodiment, there are provide four hierarchies. The first hierarchy 561, the second hierarchy 562, the third hierarchy 563 and the for the hierarchy 564.

The porous compartment in the carbon material is constituted by a plurality of single pores that are interconnected towards a network of pores.

According to the present invention the pores may also be connected to the surfaces of the implant. Preferably, the degree of porosity of the material is between 10% and 95%, more preferred between 30% and 90% and most preferred between 50% and 90%. The pores can be isotropic or anisotropic and the distribution of pores is preferably homogeneously throughout the implant structure. Preferred pore sizes are in a range of 5nm to 5000µm, more preferred from 10nm to 1000µm and most preferred from 20nm to 700µm. In specific embodiments it is preferred to comprise hierarchical pore designs, i.e. pores with additional pores in the pore defining walls of such-like hierarchically structured pores. In these embodiments the hierarchically structured pores have a larger size than the pores within the walls, whereby the pores in the walls can also be structured hierarchically

According to the present invention a hierarchical pore is referred to as a first level hierarchy pore that has at minimum one or a plurality of a second level hierarchy pore within its wall whereby a second level hierarchy pore can comprise also a hierarchy pore itself. Preferably, the ratio of the radiuses of such like pores between the first level and the second level pore is 1:0,5 to 1:0,001, more preferred 1:0,4 to 1:0,01 and most preferred 1:0,2. A hierarchical design of pores allows to increase the pore volume significantly and the respective surface area within the structural implant body. Furthermore and without binding to a specific theory, the structural design using a hierarchical structure of pores comprises surprisingly a higher mechanical stability compared to a design with similar pore volumes made out of non-hierarchic pores. Another advantage is, that in specific embodiments of the present invention the first level pore can be designed in an dimension that allows tissue ingrowth or a higher contact surface and that the second or further level pores can be used to incorporate and/or release a beneficial agent.

In other embodiments the structural implant body comprises smaller pores on the outer cross-sectional areas of the implant and larger pores at the inner cross-sectional parts or, alternatively, vice versa. Furthermore a gradient can be comprised with increasing or alternatively decreasing the pore sizes along the cross-sectional dimension. In further specific embodiments, there are multiple layers of

interconnected pores, also interconnected across the layers, at least two layers or a plurality of layers, whereby the first layer comprises smaller pores, or optionally an aforesaid gradient of pore sizes, and a second layer comprises larger pores, or optionally an aforesaid gradient of pore size. The layers can subsequently have different pore sizes and gradients, particularly if there is a multitude of layers.

Functionalization

According to this invention, the porous compartments in the inorganic material, if present, or lumens present in the stent structure, can be used to incorporate beneficial agents. Incorporation of beneficial agents may be carried out by any suitable means, preferably by dip-coating, spray coating or the like. The beneficial agent may be provided in an appropriate solvent, optionally using additives. The loading of these agents may be carried out under atmospheric, sub-atmospheric pressure or under vacuum. Alternatively, loading may be carried out under high pressure. Incorporation of the beneficial agent may be carried out by applying electrical charge to the implant or exposing at least a portion of the implant to a gaseous material including the gaseous or vapor phase of the solvent in which an agent is dissolved or other gases that have a high degree of solubility in the loading solvent. In preferred embodiments the beneficial agents are provided using carriers that are incorporated into the compartment of the implant. Carriers can be selected from any suitable group of polymers or solvents.

Preferred carriers are polymers like biocompatible polymers, for example. In specific embodiments it can be particularly preferred to select carriers from pH-sensitive polymers, like, for example, however not exclusively: poly(acrylic acid) and derivatives, for example: homopolymers like poly(amino carboxylic acid), poly(acrylic acid), poly(methyl acrylic acid) and their copolymers. This applies likewise for polysaccharides like celluloseacetatephthalate, hydroxylpropylmethyl-cellulose-phthalate,hydroxypropylmethylcellulosesuccinate, cellulose acetate trimellitate and chitosan. In certain embodiments it can be especially preferred to select carriers from temperature sensitive polymers, like for example, however not

exclusively: poly(N-isopropylacrylamide-co-sodium-acrylate-co-n-N-alkylacrylamide),poly(N-methyl-N-n-propylacrylamide), poly(N-methyl-N-isopropylacrylamide), poly(N-N-propylmethacrylamide), poly(N-isopropylacrylamide), poly(N,N-diethylacrylamide), poly(N-isopropylmethacrylamide), poly(N-cyclopropylacrylamide), poly(N-ethylacrylamide), poly(N-ethylmethylacrylamide), poly(N-methyl-N-ethylacrylamide), poly(N-cyclopropylacrylamide). Other polymers suitable to be used as a carrier with thermogel characteristics are hydroxypropylcellulose, methylcellulose, hydroxypropylmethylcellulose, ethylhydroxyethylcellulose and pluronics like F-127, L-122, L-92, L-81, L-61. Preferred carrier polymers include also, however not exclusively, functionalized styrene, like amino styrene, functionalized dextrane and polyamino acids. Furthermore polyamino acids, (poly-D-amino acids as well as poly-L-amino acids), for example polylysine, and polymers which contain lysine or other suitable amino acids. Other useful polyamino acids are polyglutamic acids, polyaspartic acid, copolymers of lysine and glutamine or aspartic acid, copolymers of lysine with alanine, tyrosine, phenylalanine, serine, tryptophan and/or proline.

In an exemplary setup of a typical functionalization, a stent made of a substantially non-porous inorganic carbon material was dipped into a drug solution made out of a 5% paclitaxel in ethanol. After dipping the stent into the solution for 5 minutes, the stent was taken out, dried at room temperature in air and weighed. The increase of weight was approximately 20 µg, visual inspection revealed a paclitaxel crystalline top coat of the stent. When introducing this stent into a 5ml PBS buffer solution to measure the drug release from the surface for 12 hours and measuring the paclitaxel concentration using standard HPLC methods, it could be shown that nearly 50% of paclitaxel wer eluted from the surface of the stent. Repeating the elution test, the sample was again introduced into a 5ml PBS solution for 12 hours and then removed. The measured drug concentration indicated a release of approximately 40% of the remaining drug from the surface. In case of a stent made from a porous carbon material it could be shown that only 15% of paclitaxel wer eluted from the stent, and

upon repeating the elution test, a release of approximately 10% of the remaining drug from the stent could be observed, demonstrating the retention of beneficial agent in the pore system of the stent. Using stent materials having smaller pore sizes, retention can be even more, thus allowing to tailor the release of beneficial agents by tailoring the pore size parameters.

Beneficial agents

Beneficial agents can be incorporated partially or completely into the compartment or reservoir of the implant. Furthermore, it is also one aspect of the present invention to optionally coat the inventive implant with beneficial agents partially or completely.

Biologically, therapeutically or pharmaceutically active agents according to the invention may be a drug, pro-drug or even a targeting group or a drug comprising a targeting group. The active agents may be in crystalline, polymorphous or amorphous form or any combination thereof in order to be used in the present invention.

Suitable therapeutically active agents may be selected from the group of enzyme inhibitors, hormones, cytokines, growth factors, receptor ligands, antibodies, antigens, ion binding agents, such as crown ethers and chelating compounds, substantial complementary nucleic acids, nucleic acid binding proteins including transcriptions factors, toxins etc.. Examples of such active agents are, for example, cytokines, such as erythropoietine (EPO), thrombopoietine (TPO), interleukines (including IL-I to IL-17), insulin, insulin-like growth factors (including IGF-1 and IGF-2), epidermal growth factor (EGF), transforming growth factors (including TGF-alpha and TGF-beta), human growth hormone, transferrine, low density lipoproteins, high density lipoproteins, leptine, VEGF, PDGF, ciliary neurotrophic factor, prolactine, adrenocorticotropic hormone (ACTH), calcitonin, human chorionic gonadotropin, cortisol, estradiol, follicle stimulating hormone (FSH), thyroid-stimulating hormone (TSH), leutinizing hormone (LH), progesterone, testosterone, toxins including ricine and further active agents, such as those included

in Physician's Desk Reference, 58th Edition, Medical Economics Data Production Company, Montvale, N.J., 2004 and the Merck Index, 13th Edition (particularly pages Ther-1 to Ther-29).

In an exemplary embodiment, the therapeutically active agent is selected from the group of drugs for the therapy of oncological diseases and cellular or tissue alterations. Suitable therapeutic agents are, e.g., antineoplastic agents, including alkylating agents, such as alkyl sulfonates, e.g., busulfan, improsulfan, piposulfane, aziridines, such as benzodepa, carboquone, meturedepa, uredepa; ethyleneimine and methylmelamines, such as altretamine, triethylene melamine, triethylene phosphoramide, triethylene thiophosphoramide, trimethylolmelamine; so-called nitrogen mustards, such as chlorambucil, chlornaphazine, cyclophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethaminoxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitroso urea-compounds, such as carmustine, chlorozotocin, fotenmustine, lomustine, nimustine, ranimustine; dacarbazine, mannomustine, mitobranitol, mitolactol; pipobroman; doxorubicin and cis-platinum and its derivatives, etc., combinations and/or derivatives of any of the foregoing.

In a further exemplary embodiment, the therapeutically active agent is selected from the group of anti-viral and anti-bacterial agents, such as aclacinomycin, actinomycin, anthramycin, azaserine, bleomycin, cuctinomycin, carubicin, carzinophilin, chromomycines, ductinomycin, daunorubicin, 6-diazo-5-oxn-1-norieucin, doxorubicin, epirubicin, mitomycins, mycophenolsäure, mogalumycin, olivomycin, peplomycin, plicamycin, porfiromycin, puromycin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, aminoglycosides or polyenes or macrolid-antibiotics, etc., combinations and/or derivatives of any of the foregoing.

In a further exemplary embodiment, the therapeutically active agent may include a radio-sensitizer drug, or a steroidal or non-steroidal anti-inflammatory drug.

In a further exemplary embodiment, the therapeutically active agent is selected from agents referring to angiogenesis, such as e.g. endostatin, angiostatin, interferones, platelet factor 4 (PF4), thrombospondin, transforming growth factor beta, tissue inhibitors of the metalloproteinases -1, -2 and -3 (TIMP-1, -2 and -3), TNP-470, marimastat, neovastat, BMS-275291, COL-3, AG3340, thalidomide, squalamine, combrestastatin, SU5416, SU6668, IFN-[alpha], EMD121974, CAI, IL-12 and IM862 etc., combinations and/or derivatives of any of the foregoing.

In a further exemplary embodiment, the therapeutically-active agent is selected from the group of nucleic acids, wherein the term nucleic acids also comprises oligonucleotides wherein at least two nucleotides are covalently linked to each other, for example in order to provide gene therapeutic or antisense effects. Nucleic acids preferably comprise phosphodiester bonds, which also comprise those which are analogues having different backbones. Analogues may also contain backbones, such as, for example, phosphoramide (Beaucage et al., Tetrahedron 49(10):1925 (1993) and the references cited therein; Letsinger, J. Org. Chem. 35:3800 (1970); Sprinzl et al., Eur. J. Biochem. 81:579 (1977); Letsinger et al., Nucl. Acids Res. 14:3487 (1986); Sawai et al, Chem. Lett. 805 (1984), Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); and Pauwels et al., Chemica Scripta 26:141 91986)); phosphorothioate (Mag et al., Nucleic Acids Res. 19:1437 (1991); and U.S. Pat. No. 5,644,048), phosphorodithioate (Briu et al., J. Am. Chem. Soc. 111:2321 (1989), O-methylphosphoroamidit-compounds (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press), and peptide-nucleic acid-backbones and their compounds (see Egholm, J. Am. Chem. Soc. 114:1895 (1992); Meier et al., Chem. Int. Ed. Engl: 31:1008 (1992); Nielsen, Nature, 365:566 (1993); Carlsson et al., Nature 380:207 (1996), wherein these references are incorporated by reference heierin. further analogues are those having ionic backbones, see Denpcy et al., Proc. Natl. Acad. Sci. USA 92:6097 (1995), or non-ionic backbones, see U.S. Pat. Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi et al., Angew. Chem. Intl. Ed. English 30:423 (1991); Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); Letsinger et al., Nucleoside & Nucleotide 13:1597 (1994); chapters

2 and 3, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y. S. Sanghui and P. Dan Cook; Mesmaeker et al., Bioorganic & Medicinal Chem. Lett. 4:395 (1994); Jeffs et al., J. Biomolecular NMR 34:17 (1994); Tetrahedron Lett. 37:743 (1996), and non-ribose-backbones, including those which are described in U.S. Pat. Nos. 5,235,033 and 5,034,506, and in chapters 6 and 7 of ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y. S. Sanghui and P. Dan Cook. The nucleic acids having one or more carbocylic sugars are also suitable as nucleic acids for use in the present invention, see Jenkins et al., Chemical Society Review (1995), pages 169 to 176 as well as others which are described in Rawls, C & E News, 2 June 1997, page 36,. Besides the selection of the nucleic acids and nucleic acid analogues known in the prior art, also a mixture of naturally occurring nucleic acids and nucleic acid analogues or mixtures of nucleic acid analogues may be used.

In a further embodiment, the therapeutically active agent is selected from the group of metal ion complexes, as described in PCT US95/16377, PCT US95/16377, PCT US96/19900, PCT US96/15527, wherein such agents reduce or inactivate the bioactivity of their target molecules, preferably proteins, such as enzymes.

Therapeutically active agents may also include anti-migratory, anti-proliferative or immune-suppressive, anti-inflammatory or re-endotheliating agents, such as, e.g., everolimus, tacrolimus, sirolimus, mycofenolate-mofetil, rapamycin, paclitaxel, actinomycine D, angiopeptin, batimastate, estradiol, statines and others, their derivatives and analogues.

Active agents or combinations of active agents may further be selected from heparin, synthetic heparin analogs (e.g., fondaparinux), hirudin, antithrombin III, drotrecogin alpha; fibrinolytics, such as alteplase, plasmin, lysokinases, factor XIIa, prourokinase, urokinase, anistreplase, streptokinase; platelet aggregation inhibitors, such as acetylsalicylic acid [aspirin], ticlopidine, clopidogrel, abciximab, dextrans; corticosteroids, such as alclometasone, amcinonide, augmented betamethasone, beclomethasone, betamethasone, budesonide, cortisone, clobetasol, clocortolone, desonide, desoximetasone, dexamethasone, fluocinolone, fluocinonide,

flurandrenolide, flunisolide, fluticasone, halcinonide, halobetasol, hydrocortisone, methylprednisolone, mometasone, prednicarbate, prednisone, prednisolone, triamcinolone; so-called non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, salsalate, sulindac, tolmetin, celecoxib, rofecoxib; cytostatics, such as alkaloides and podophyllum toxins, such as vinblastine, vincristine; alkylating agents, such as nitrosoureas, nitrogen lost analogs; cytotoxic antibiotics, such as daunorubicin, doxorubicin and other anthracyclines and related substances, bleomycin, mitomycin; antimetabolites, such as folic acid analogs, purine analogs or pyrimidine analogs; paclitaxel, docetaxel, sirolimus; platinum compounds, such as carboplatin, cisplatin or oxaliplatin; amsacrin, irinotecan, imatinib, topotecan, interferon-alpha 2a, interferon-alpha 2b, hydroxycarbamide, miltefosine, pentostatin, porfimer, aldesleukin, bexaroten, tretinoin; antiandrogens and antiestrogens; antiarrythmics in particular class I antiarrhythmic, such as antiarrhythmics of the quinidine type, quinidine, dysopyramide, ajmaline, prajmalium bitartrate, detajmium bitartrate; antiarrhythmics of the lidocaine type, e.g., lidocaine, mexiletin, phenytoin, tocainid; class Ic antiarrhythmics, e.g., propafenon, flecainid(acetate); class II antiarrhythmics beta-receptor blockers, such as metoprolol, esmolol, propranolol, metoprolol, atenolol, oxprenolol; class III antiarrhythmics, such as amiodarone, sotalol; class IV antiarrhythmics, such as diltiazem, verapamil, gallopamil; other antiarrhythmics, such as adenosine, orciprenaline, ipratropium bromide; agents for stimulating angiogenesis in the myocardium, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), non-viral DNA, viral DNA, endothelial growth factors: FGF-1, FGF-2, VEGF, TGF; antibiotics, monoclonal antibodies, anticalins; stem cells, endothelial progenitor cells (EPC); digitalis glycosides, such as acetyl digoxin/metildigoxin, digitoxin, digoxin; cardiac glycosides, such as ouabain, proscillaridin; antihypertensives, such as CNS active antiadrenergic substances, e.g., methyldopa, imidazoline receptor agonists; calcium channel blockers of the

dihydropyridine type, such as nifedipine, nitrendipine; ACE inhibitors: quinaprilate, cilazapril, moexipril, trandolapril, spirapril, imidapril, trandolapril; angiotensin II antagonists: candesartancilexetil, valsartan, telmisartan, olmesartanmedoxomil, eprosartan; peripherally active alpha-receptor blockers, such as prazosin, urapidil, doxazosin, bunazosin, terazosin, indoramin; vasodilatators, such as dihydralazine, diisopropylamine dichloracetate, minoxidil, nitroprusside sodium; other antihypertensives, such as indapamide, co-dergocrine mesylate, dihydroergotoxin methanessulfonate, cicletanin, bosentan, fludrocortisone; phosphodiesterase inhibitors, such as milrinon, enoximon and antihypotensives, such as in particular adrenergic and dopaminergic substances, such as dobutamine, epinephrine, etilefrine, norfenefrine, norepinephrine, oxilofrine, dopamine, midodrine, pholedrine, ameziniummetil; and partial adrenoceptor agonists, such as dihydroergotamine; fibronectin, polylysine, ethylene vinyl acetate, inflammatory cytokines, such as: TGF, PDGF, VEGF, bFGF, TNF, NGF, GM-CSF, IGF-a, IL-1, IL 8, IL-6, growth hormone; as well as adhesive substances, such as cyanoacrylates, beryllium, silica; and growth factors, such as erythropoetin, hormones, such as corticotropins, gonadotropins, somatropins, thyrotrophins, desmopressin, terlipressin, pxytocin, cetrorelix, corticorelin, leuprorelin, triptorelin, gonadorelin, ganirelix, buserelin, nafarelin, goserelin, as well as regulatory peptides, such as somatostatin, octreotid; bone and cartilage stimulating peptides, bone morphogenetic proteins (BMPs), in particulary recombinant BMPs , such as recombinant human BMP-2 (rhBMP-2), bisphosphonate (e.g., risedronate, pamidronate, ibandronate, zoledronic acid, clodronsäure, etidronsäure, alendronic acid, tiludronic acid), fluorides, such as disodium fluorophosphate, sodium fluoride; calcitonin, dihydrotachystyrol; growth factors and cytokines, such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), fibroblast growth factors (FGFs), transforming growth factors-b (TGFs-b), transforming growth factor-a (TGF-a), erythropoietin (EPO), insulin-like growth factor-I (IGF-I), insulin-like growth factor-II (IGF-II), interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-a (TNF-a), tumor necrosis factor-b (TNF-b), interferon-g (INF-

g), colony stimulating factors (CSFs); monocyte chemotactic protein, fibroblast stimulating factor 1, histamine, fibrin or fibrinogen, endothelin-1, angiotensin II, collagens, bromocriptine, methysergide, methotrexate, carbon tetrachloride, thioacetamide and ethanol; as well as silver (ions), titanium dioxide, antibiotics and anti-infective drugs, such as in particular β-lactam antibiotics, e.g., β-lactamase-sensitive penicillins, such as benzyl penicillins (penicillin G), phenoxymethylpenicillin (penicillin V); β-lactamase-resistent penicillins, such as aminopenicillins, e.g., amoxicillin, ampicillin, bacampicillin; acylaminopenicillins, such as mezlocillin, piperacillin; carboxypenicillins, cephalosporins, such as cefazoline, cefuroxim, cefoxitin, cefotiam, cefaclor, cefadroxil, cefalexin, loracarbef, cefixim, cefuroximaxetil, ceftibuten, cefpodoximproxetil, cefpodoximproxetil; aztreonam, ertapenem, meropenem; β-lactamase inhibitors, such as sulbactam, sultamicillintosylate; tetracyclines, such as doxycycline, minocycline, tetracycline, chlorotetracycline, oxytetracycline; aminoglycosides, such as gentamicin, neomycin, streptomycin, tobramycin, amikacin, netilmicin, paromomycin, framycetin, spectinomycin; macrolide antibiotics, such as azithromycin, clarithromycin, erythromycin, roxithromycin, spiramycin, josamycin; lincosamides, such as clindamycin, lincomycin; gyrase inhibitors, such as fluoroquinolones, e.g., ciprofloxacin, ofloxacin, moxifloxacin, norfloxacin, gatifloxacin, enoxacin, fleroxacin, levofloxacin; quinolones, such as pipemidic acid; sulfonamides, trimethoprim, sulfadiazine, sulfalene; glycopeptide antibiotics, such as vancomycin, teicoplanin; polypeptide antibiotics, such as polymyxins, e.g., colistin, polymyxin-b, nitroimidazole derivates, e.g., metronidazole, tinidazole; aminoquinolones, such as chloroquin, mefloquin, hydroxychloroquin; biguanids, such as proguanil; quinine alkaloids and diaminopyrimidines, such as pyrimethamine; amphenicols, such as chloramphenicol; rifabutin, dapson, fusidic acid, fosfomycin, nifuratel, telithromycin, fusafungin, fosfomycin, pentamidine diisethionate, rifampicin, taurolidin, atovaquon, linezolid; virus static, such as aciclovir, ganciclovir, famciclovir, foscarnet, inosine-(dimepranol-4-acetamidobenzoate), valganciclovir, valaciclovir, cidofovir, brivudin; antiretroviral active ingredients (nucleoside analog reverse-transcriptase inhibitors

and derivatives), such as lamivudine, zalcitabine, didanosine, zidovudin, tenofovir, stavudin, abacavir; non-nucleoside analog reverse-transcriptase inhibitors: amprenavir, indinavir, saquinavir, lopinavir, ritonavir, nelfinavir; amantadine, ribavirine, zanamivir, oseltamivir or lamivudine, as well as any combinations and mixtures thereof.

In an alternative embodiment of the present invention, the active agents can be encapsulated in polymers, vesicles, liposomes or micelles.

Suitable diagnostically active agents for use in the present invention can be e.g. signal generating agents or materials, which may be used as markers. Such signal generating agents include materials which in physical, chemical and/or biological measurement and verification methods lead to detectable signals, for example in image-producing methods. It is not important for the present invention, whether the signal processing is carried out exclusively for diagnostic or therapeutic purposes. Typical imaging methods are for example radiographic methods, which are based on ionizing radiation, for example conventional X-ray methods and X-ray based split image methods, such as computer tomography, neutron transmission tomography, radiofrequency magnetization, such as magnetic resonance tomography, further by radionuclide-based methods, such as scintigraphy, Single Photon Emission Computed Tomography (SPECT), Positron Emission Computed Tomography (PET), ultrasound-based methods or fluoroscopic methods or luminescence or fluorescence based methods, such as Intravasal Fluorescence Spectroscopy, Raman spectroscopy, Fluorescence Emission Spectroscopy, Electrical Impedance Spectroscopy, colorimetry, optical coherence tomography, etc, further Electron Spin Resonance (ESR), Radio Frequency (RF) and Microwave Laser and similar methods.

Signal generating agents can be metal-based from the group of metals, metal oxides, metal carbides, metal nitrides, metal oxynitrides, metal carbonitrides, metal oxycarbides, metal oxynitrides, metal oxycarbonitrides, metal hydrides, metal alkoxides, metal halides, inorganic or organic metal salts, metal polymers, metallocenes, and other organometallic compounds.

Preferred metal-based agents are e.g. nanomorphous nanoparticles from metals, metal oxides semiconductors as defined above as the metal-based particles, or mixtures thereof. In this regard, it may be preferred to select at least a part of the metal-based particles from those materials capable of functioning as signal generating agents, for example to mark the implant for better visibility and localization in the body after implantation.

Further, signal producing metal-based agents can be selected from salts or metal ions, which preferably have paramagnetic properties, for example lead (II), bismuth (II), bismuth (III), chromium (III), manganese (II), manganese (III), iron (II), iron (III), cobalt (II), nickel (II), copper (II), praseodymium (III), neodymium (III), samarium (III), or ytterbium (III), holmium (III) or erbium (III) etc.. Based on especially pronounced magnetic moments, especially gadolinium (III), terbium (III), dysprosium (III), holmium (III) and erbium (III) are mostly preferred. Further one can select from radioisotopes. Examples of a few applicable radioisotopes include H 3, Be 10, O 15, Ca 49, Fe 60, In 111, Pb 210, Ra 220, Ra 224 and the like. Typically such ions are present as chelates or complexes, wherein for example as chelating agents or ligands for lanthanides and paramagnetic ions compounds, such as diethylenetriamine pentaacetic acid ("DTPA"), ethylenediamine tetra acetic acid ("EDTA"), or tetraazacyclododecane-N,N', N",N'"-tetra acetic acid ("DOTA") are used. Other typical organic complexing agents are for example published in Alexander, Chem. Rev. 95:273-342 (1995) and Jackels, Pharm. Med. Imag, Section III, Chap. 20, p645 (1990). Other usable chelating agents may be found in U.S. Patents 5,155,215; 5,087,440; 5,219,553; 5,188,816; 4,885,363; 5,358,704; 5,262,532, and Meyer et al., Invest. Radiol. 25: S53 (1990), further U.S. Patents 5,188,816, 5,358,704, 4,885,363, and 5,219,553. Also, salts and chelates from the lanthanide group with the atomic numbers 57-83 or the transition metals with the atomic numbers 21-29, or 42 or 44 may be incorporated into the implants of exemplary embodiments of the present invention.

Also suitable can be paramagnetic perfluoroalkyl containing compounds which for example are described in German laid-open patents DE 196 03 033, DE 197 29

013 and in WO 97/26017, further diamagnetic perfluoroalkyl containing substances of the general formula:

R<PF>-L<II>-G<III>,

wherein R<PF> represents a perfluoroalkyl group with 4 to 30 carbon atoms, L<II> stands for a linker and G<III> for a hydrophilic group. The linker L is a direct bond, an -SO2- group or a straight or branched carbon chain with up to 20 carbon atoms which can be substituted with one or more -OH, -COO<->, -SO3-groups and/or if necessary one or more -O-, -S-, -CO-, -CONH-, -NHCO-, -CONR-, -NRCO-, -SO2-, -PO4-, -NH-, -NR-groups, an aryl ring or contain a piperazine, wherein R stands for a C1 to C20 alkyl group, which again can contain and/or have one or a plurality of O atoms and/or be substituted with -COO<-> or SO3- groups.

The hydrophilic group G<III> can be selected from a mono or disaccharide, one or a plurality of -COO<-> or -SO3<->-groups, a dicarboxylic acid, an isophthalic acid, a picolinic acid, a benzenesulfonic acid, a tetrahydropyranedicarboxylic acid, a 2,6- pyridinedicarboxylic acid, a quaternary ammonium ion, an aminopolycarboxcylic acid, an aminodipolyethyleneglycol sulfonic acid, an aminopolyethyleneglycol group, an SO2-(CH2)2-OH-group, a polyhydroxyalkyl chain with at least two hydroxyl groups or one or a plurality of polyethylene glycol chains having at least two glycol units, wherein the polyethylene glycol chains are terminated by an -OH or -OCH3- group, or similar linkages.

In exemplary embodiments paramagnetic metals in the form of metal complexes with phthalocyanines may be used to functionalize the implant, especially as described in Phthalocyanine Properties and Applications, Vol. 14, C. C. Leznoff and A. B. P. Lever, VCH Ed.. Examples are octa(1,4,7,10-tetraoxaundecyl)Gd-phthalocyanine, octa(1,4,7,10-tetraoxaundecyl)Gd-phthalocyanine, octa(1,4,7,10-tetraoxaundecyl)Mn-phthalocyanine, octa(1,4,7,10-tetraoxaundecyl)Mn-phthalocyanine, as described in U.S. 2004/214810.

Super-paramagnetic, ferromagnetic or ferrimagnetic signal generating agents may also be used. For example among magnetic metals, alloys are preferred, among ferrites, such as gamma iron oxide, magnetites or cobalt-, nickel- or manganese-

ferrites, corresponding agents are preferably selected, especially particles as described in WO83/03920, WO83/01738, WO85/02772 and WO89/03675, in U.S. Pat. 4,452,773, U.S. Pat. 4,675,173, in WO88/00060 as well as U.S. Pat. 4,770,183, in WO90/01295 and in WO90/01899.

Further, magnetic, paramagnetic, diamagnetic or super paramagnetic metal oxide crystals having diameters of less than 4000 Angstroms are especially preferred as degradable non-organic diagnostic agents. Suitable metal oxides can be selected from iron oxide, cobalt oxides, iridium oxides or the like, which provide suitable signal producing properties and which have especially biocompatible properties or are biodegradable. Crystalline agents of this group having diameters smaller than 500 Angstroms may be used. These crystals can be associated covalently or non-covalently with macromolecular species. Further, zeolite containing paramagnets and gadolinium containing nanoparticles can be selected from polyoxometallates, preferably of the lanthanides, (e.g., K9GdW10O36).

For optimizing the image producing properties the average particle size of the magnetic signal producing agents may be limited to 5 μm at maximum, such as from about 2 nm up to 1 μm, e.g. from about 5 nm to 200 nm. The super paramagnetic signal producing agents can be chosen for example from the group of so-called SPIOs (super paramagnetic iron oxides) with a particle size larger than 50 nm or from the group of the USPIOs (ultra small super paramagnetic iron oxides) with particle sizes smaller than 50 nm.

Signal generating agents for imparting further functionality to the implants of embodiments of the present invention can further be selected from endohedral fullerenes, as disclosed for example in U.S. Patent 5,688,486 or WO 93/15768, or from fullerene derivatives and their metal complexes, such as fullerene species, which comprise carbon clusters having 60, 70, 76, 78, 82, 84, 90, 96 or more carbon atoms. An overview of such species can be gathered from European patent application 1331226A2. Metal fullerenes or endohedral carbon-carbon nanoparticles with arbitrary metal-based components can also be selected. Such endohedral fullerenes or endometallo fullerenes may contain for example rare earths, such as

cerium, neodymium, samarium, europium, gadolinium, terbium, dysprosium or holmium. The choice of nanomorphous carbon species is not limited to fullerenes, other nanomorphous carbon species, such as nanotubes, onions, etc. may also be applicable.

In another exemplary embodiment fullerene species may be selected from non-endohedral or endohedral forms which contain halogenated, preferably iodated, groups, as disclosed in U.S. Patent 6,660,248.

Generally, mixtures of such signal generating agents of different specifications can also used, depending on the desired properties of the signal generating material properties. The signal producing agents used can have a size of 0.5 nm to 1,000 nm, preferably 0.5 nm to 900 nm, especially preferred from 0.7 to 100 nm, and the may partly replace the metal-based particles. Nanoparticles are easily modifiable based on their large surface to volume ratios. The nanoparticles can for example be modified non-covalently by means of hydrophobic ligands, for example with trioctylphosphine, or be covalently modified. Examples of covalent ligands are thiol fatty acids, amino fatty acids, fatty acid alcohols, fatty acids, fatty acid ester groups or mixtures thereof, for example oleic cid and oleylamine.

In exemplary embodiments of the invention the active ingredients, such as signal producing agents can be encapsulated in micelles or liposomes with the use of amphiphilic components, or may be encapsulated in polymeric shells, wherein the micelles/liposomes can have a diameter of 2 nm to 800 nm, preferably from 5 to 200 nm, especially preferred from 10 to 25 nm. The micelles/liposomes may be added to the suspension before molding, to be incorporated into the implant. The size of the micelles/liposomes is, without committing to a specific theory, dependant on the number of hydrophobic and hydrophilic groups, the molecular weight of the nanoparticles and the aggregation number. In aqueous solutions the use of branched or unbranched amphiphilic substances, is especially preferred in order to achieve the encapsulation of signal generating agents in liposomes/micelles. The hydrophobic nucleus of the micelles hereby contains in a exemplary embodiment a multiplicity of hydrophobic groups, preferably between 1 and 200, especially preferred between 1

and 100 and mostly preferred between 1 and 30 according to the desired setting of the micelle size.

Such signal generating agents encapsulated in micelles and incorporated into the porous implant can moreover be functionalized, while linker (groups) are attached at any desired position, preferably amino-, thiol, carboxyl-, hydroxyl-, succinimidyl, maleimidyl, biotin, aldehyde- or nitrilotriacetate groups, to which any desired corresponding chemically covalent or non-covalent other molecules or compositions can be bound according to the prior art. Here, especially biological molecules, such as proteins, peptides, amino acids, polypeptides, lipoproteins, glycosaminoglycanes, DNA, RNA or similar biomolecules are preferred especially.

Signal generating agents may also be selected from non-metal-based signal generating agents, for example from the group of X-ray contrast agents, which can be ionic or non-ionic. Among the ionic contrast agents are included salts of 3-acetyl amino-2,4-6-triiodobenzoic acid, 3,5-diacetamido-2,4,6-triiodobenzoic acid, 2,4,6-triiodo-3,5-dipropionamido-benzoic acid, 3-acetyl amino-5-((acetyl amino)methyl)-2,4,6-triiodobenzoic acid, 3-acetyl amino-5-(acetyl methyl amino)-2,4,6-triiodobenzoic acid, 5-acetamido-2,4,6-triiodo-N-((methylcarbamoyl)methyl)-isophthalamic acid, 5-(2-methoxyacetamido)-2,4,6-triiodo-N-[2-hydroxy-1-(methylcarbamoyl)-ethoxy l]-isophthalamic acid, 5-acetamido-2,4,6-triiodo-N-methylisophthalamic acid, 5-acetamido-2,4,6-triiodo-N-(2-hydroxyethyl)-isophthalamic acid 2-[[2,4,6-triiodo-3[(1-oxobutyl)-amino]phenyl]methyl]-butanoic acid, beta-(3-amino-2,4,6-triiodophenyl)-alpha-ethyl-propanoic acid, 3-ethyl-3-hydroxy-2,4,6-triiodophenyl-propanoic acid, 3-[[(dimethylamino)-methyl]amino]-2,4,6-triiodophenyl-propanoic acid (see Chem. Ber. 93: 2347 (1960)), alpha-ethyl-(2,4,6-triiodo-3-(2-oxo-1-pyrrolidinyl)-phenyl)-propanoic acid, 2-[2-[3-(acetyl amino)-2,4,6-triiodophenoxy]ethoxymethyl]butanoic acid, N-(3-amino-2,4,6-triiodobenzoyl)-N-phenyl-.beta.-aminopropanoic acid, 3-acetyl-[(3-amino-2,4,6-triiodophenyl)amino]-2-methylpropanoic acid, 5-[(3-amino-2,4,6-triiodophenyl)methyl amino]-5-oxypentanoic acid, 4-[ethyl-[2,4,6-triiodo-3-(methyl amino)-phenyl]amino]-4-oxo-butanoic acid, 3,3'-oxy-bis[2,1-ethanediyloxy-(1-oxo-

2,1-ethanediyl)imino]bis-2,4,6-triiodobenzoic acid, 4,7,10,13-tetraoxahexadecane-1,16-dioyl-bis(3-carboxy-2,4,6-triiodoanilide), 5,5'-(azelaoyldiimino)-bis[2,4,6-triiodo-3-(acetyl amino)methyl-benzoic acid], 5,5'-(apidoldiimino)bis(2,4,6-triiodo-N-methyl-isophthalamic acid), 5,5'-(sebacoyl-diimino)-bis(2,4,6-triiodo-N-methylisophthalamic acid), 5,5 -[N,N-diacetyl-(4,9-dioxy-2,11-dihydroxy-1,12-dodecanediyl)diimino]bis(2,4 ,6-triiodo-N-methyl-isophthalamic acid), 5,5'5"-(nitrilo-triacetyltriimino)tris(2,4,6-triiodo-N-methyl-isophthalamic acid), 4-hydroxy-3,5-diiodo-alpha-phenylbenzenepropanoic acid, 3,5-diiodo-4-oxo-1(4H)-pyridine acetic acid, 1,4-dihydro-3,5-diiodo-1-methyl-4-oxo-2,6-pyridinedicarboxylic acid, 5-iodo-2-oxo-1(2H)-pyridine acetic acid, and N-(2-hydroxyethyl)-2,4,6-triiodo-5-[2,4,6-triiodo-3-(N-methylacetamido)-5- (methylcarbomoyl)benzamino]acetamido]-isophthalamic acid, and the like, especially preferred, as well as other ionic X-ray contrast agents suggested in the literature, for example in J. Am. Pharm. Assoc., Sci. Ed. 42:721 (1953), Swiss Patent 480071, JACS 78:3210 (1956), German patent 2229360, U.S. Patent 3,476,802, Arch. Pharm. (Weinheim, Germany) 306: 11 834 (1973), J. Med. Chem. 6: 24 (1963), FR-M-6777, Pharmazie 16: 389 (1961), U.S. Patents 2,705,726, U.S. Patent 2,895,988, Chem. Ber. 93:2347(1960), SA-A-68/01614, Acta Radiol. 12: 882 (1972), British Patent 870321, Rec. Trav. Chim. 87: 308 (1968), East German Patent 67209, German Patent 2050217, German Patent 2405652, Farm Ed. Sci. 28: 912(1973), Farm Ed. Sci. 28: 996 (1973), J. Med. Chem. 9: 964 (1966), Arzheim.-Forsch 14: 451 (1964), SE-A-344166, British Patent 1346796, U.S. Patent 2,551,696, U.S. Patent 1,993,039, Ann 494: 284 (1932), J. Pharm. Soc. (Japan) 50: 727 (1930), and U.S. Patent 4,005,188.

Examples of applicable non-ionic X-ray contrast agents in accordance with the invention are metrizamide as disclosed in DE-A-2031724, iopamidol as disclosed in BE-A-836355, iohexol as disclosed in GB-A-1548594, iotrolan as disclosed in EP-A-33426, iodecimol as disclosed in EP-A-49745, iodixanol as in EP-A-108638, ioglucol as disclosed in U.S. Patent 4,314,055, ioglucomide as disclosed in BE-A-846657, ioglunioe as in DE-A-2456685, iogulamide as in BE-A-882309, iomeprol as in EP-A-26281, iopentol as EP-A-105752, iopromide as in DE-A-2909439, iosarcol

as in DE-A-3407473, iosimide as in DE-A-3001292, iotasul as in EP-A-22056, iovarsul as disclosed in EP-A-83964 or ioxilan in WO87/00757.

Agents based on nano-particle signal generating agents may be selected to impart functionality to the implant, which after release into tissues and cells are incorporated or are enriched in intermediate cell compartments and/or have an especially long residence time in the organism.

Such particles can include water-insoluble agents, a heavy element, such as iodine or barium, PH-50 as monomer, oligomer or polymer (iodinated aroyloxy ester having the empirical formula C19H23I3N2O6, and the chemical names 6-ethoxy-6-oxohexy-3, 5-bis (acetyl amino)-2,4,6-triiodobenzoate), an ester of diatrizoic acid, an iodinated aroyloxy ester, or combinations thereof. Particle sizes which can be incorporated by macrophages may be preferred. A corresponding method for this is disclosed in WO03/039601 and suitable agents are disclosed in the publications U.S. Patents 5,322,679, 5,466,440, 5,518,187, 5,580,579, and 5,718,388. Nanoparticles which are marked with signal generating agents or such signal generating agents, such as PH-50, which accumulate in intercellular spaces and can make interstitial as well as extrastitial compartments visible, can be advantageous.

Signal generating agents may also include anionic or cationic lipids, as disclosed in U.S. Patent 6,808,720, for example, anionic lipids, such as phosphatidyl acid, phosphatidyl glycerol and their fatty acid esters, or amides of phosphatidyl ethanolamine, such as anandamide and methanandamide, phosphatidyl serine, phosphatidyl inositol and their fatty acid esters, cardiolipin, phosphatidyl ethylene glycol, acid lysolipids, palmitic acid, stearic acid, arachidonic acid, oleic acid, linoleic acid, linolenic acid, myristic acid, sulfolipids and sulfatides, free fatty acids, both saturated and unsaturated and their negatively charged derivatives, etc.. Moreover, halogenated, in particular fluorinated anionic lipids can be preferred in exemplary embodiments. The anionic lipids preferably contain cations from the alkaline earth metals beryllium (Be<+2>), magnesium (Mg<+2>), calcium (Ca<+2>), strontium (Sr<+2>) and barium (Ba<+2>), or amphoteric ions, such as aluminum (Al<+3>), gallium (Ga<+3>), germanium (Ge<+3>), tin (Sn+<4>) or

lead (Pb<+2 > and Pb<+4>), or transition metals, such as titanium (Ti<+3 > and Ti<+4>), vanadium (V<+2 > and V<+3>), chromium (Cr<+2 > and Cr<+3>), manganese (Mn<+2 > and Mn<+3>), iron (Fe<+2 > and Fe<+3>), cobalt (Co<+2 > and Co<+3>), nickel (Ni<+2 > and Ni<+3>), copper (Cu<+2>), zinc (Zn<+2>), zirconium (Zr<+4>), niobium (Nb<+3>), molybdenum (Mo<+2 > and Mo<+3>), cadmium (Cd<+2>), indium (In<+3>), tungsten (W<+2 > and W<+4>), osmium (Os<+2> , Os<+3 > and Os<+4>), iridium (Ir<+2> , Ir<+3 > and Ir<+4>), mercury (Hg<+2>) or bismuth (Bi<+3>), and/or rare earths, such as lanthanides, for example lanthanum (La<+3>) and gadolinium (Gd<+3>). Cations can include calcium (Ca<+2>), magnesium (Mg<+2>) and zinc (Zn<+2>) and paramagnetic cations, such as manganese (Mn<+2>) or gadolinium (Gd<+3>).

Cationic lipids may include phosphatidyl ethanolamine, phospatidylcholine, Glycero-3-ethylphosphatidylcholine and their fatty acid esters, di- and tri-methylammoniumpropane, di- and tri-ethylammoniumpropane and their fatty acid esters, and also derivatives, such as N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride ("DOTMA"); furthermore, synthetic cationic lipids based on for example naturally occurring lipids, such as dimethyldioctadecylammonium bromide, sphingolipids, sphingomyelin, lysolipids, glycolipids, such as, for example, gangliosides GM1, sulfatides, glycosphingolipids, cholesterol and cholesterol esters or salts, N-succinyldioleoylphosphattidyl ethanolamine, 1,2,-dioleoyl-sn- glycerol, 1,3-dipalmitoyl-2-succinylglycerol, 1,2-dipalmitoyl-sn-3-succinylglycerol, 1-hexadecyl-2-palmitoylglycerophosphatidyl ethanolamine and palmitoyl-homocystein, and fluorinated, derivatized cationic lipids, as disclosed in U.S. 08/391,938. Such lipids are furthermore suitable as components of signal generating liposomes, which especially can have pH- sensitive properties as disclosed in U.S. 2004197392 and incorporated herein explicitly.

Signal generating agents may also include so-called micro bubbles or micro balloons, which contain stable dispersions or suspensions in a liquid carrier substance. Suitable gases may include air, nitrogen, carbon dioxide, hydrogen or noble gases, such as helium, argon, xenon or krypton, or sulfur-containing

fluorinated gases, such as sulfur hexafluoride, disulfurdecafluoride or trifluoromethylsulfurpentafluoride, or for example selenium hexafluoride, or halogenated silanes, such as methylsilane or dimethylsilane, further short chain hydrocarbons, such as alkanes, specifically methane, ethane, propane, butane or pentane, or cycloalkanes, such as cyclopropane, cyclobutane or cyclopentane, also alkenes, such as ethylene, propene, propadiene or butene, or also alkynes, such as acetylene or propyne. Further ethers, such as dimethylether may be selected, or ketones, or esters or halogenated short-chain hydrocarbons or any desired mixtures of the above. Examples further include halogenated or fluorinated hydrocarbon gases, such as bromochlorodifluoromethane, chlorodifluoromethane, dichlorodifluoromethan, bromotrifluoromethane, chlorotrifluoromethane, chloropentafluoroethane, dichlorotetrafluoroethane, chlorotrifluoroethylene, fluoroethylene, ethyl fluoride, 1,1-difluoroethane or perfluorohydrocarbons, such as for example perfluoroalkanes, perfluorocycloalkanes, perfluoroalkenes or perfluorinated alkynes. Especially preferred are emulsions of liquid dodecafluoropentane or decafluorobutane and sorbitol, or similar, as disclosed in WO-A-93/05819.

Preferably such micro bubbles are selected, which are encapsulated in compounds having the structure R1-X-Z; R2-X-Z; or R3-X-Z' wherein R1, R2 comprises and R3 hydrophobic groups selected from straight chain alkylenes, alkyl ethers, alkyl thiolethers, alkyl disulfides, polyfluoroalkylenes and polyfluoroalkylethers, Z comprises a polar group from CO2-M<+>, SO3<-> M<+>, SO4<-> M<+>, PO3<-> M<+>, PO4<-> M<+> 2, N(R)4<+> or a pyridine or substituted pyridine, and a zwitterionic group, and finally X represents a linker which binds the polar group with the residues.

Gas-filled or in situ out-gassing micro spheres having a size of < 1000 µm can be further selected from biocompatible synthetic polymers or copolymers which comprise monomers, dimers or oligomers or other pre-polymer to pre-stages of the following polymerizable substances: acrylic acid, methacrylic acid, ethyleneimine, crotonic acid, acryl amide, ethyl acrylate, methylmethacrylate, 2-

hydroxyethylmethacrylate (HEMA), lactonic acid, glycolic acid, [epsilon]caprolactone, acrolein, cyanoacrylate, bisphenol A, epichlorhydrin, hydroxyalkylacrylate, siloxane, dimethylsiloxane, ethylene oxide, ethylene glycol, hydroxyalkylmethacrylate, N-substituted acryl amide, N-substituted methacrylamides, N-vinyl-2-pyrrolidone, 2,4-pentadiene-1-ol, vinyl acetate, acrylonitrile, styrene, p-aminostyrene, p-aminobenzylstyrene, sodium styrenesulfonate, sodium-2-sulfoxyethylmethacrylate, vinyl pyridine, aminoethylmethacrylate, 2-methacryloyloxytrimethylammonium chloride, and polyvinylidenes, such as polyfunctional cross-linkable monomers, such as for example N,N'-methylene-bis-acrylamide, ethylene glycol dimethacrylate, 2,2'-(p-phenylenedioxy)-diethyldimethacrylate, divinylbenzene, triallylamine and methylene-bis-(4-phenyl-isocyanate), including any desired combinations thereof. Preferred polymers contain polyacrylic acid, polyethyleneimine, polymethacrylic acid, polymethylmethacrylate, polysiloxane, polydimethylsiloxane, polylactonic acid, poly([epsilon]-caprolactone), epoxy resins, poly(ethylene oxide), poly(ethylene glycol), and polyamides (e.g. Nylon) and the like, or any arbitrary mixtures thereof. Preferred copolymers contain among others polyvinylidene-polyacrylonitrile, polyvinylidene-polyacrylonitrile-polymethylmethacrylate, and polystyrene-polyacrylonitrile and the like, or any desired mixtures thereof. Methods for manufacture of such micro spheres are published for example in Garner et al., U.S. Patent 4,179,546, Garner, U.S. Patent 3,945,956, Cohrs et al., U.S. Patent 4,108,806, Japan Kokai Tokkyo Koho 62 286534, British Patent 1,044,680, Kenaga et al., U.S. Patent 3,293,114, Morehouse et al., U.S. Patent 3,401,475, Walters, U.S. Patent 3,479,811, Walters et al., U.S. Patent 3,488,714, Morehouse et al., U.S. Patent 3,615,972, Baker et al., U.S. Patent 4,549,892, Sands et al., U.S. Patent 4,540,629, Sands et al., U.S. Patent 4,421,562, Sands, U.S. Patent 4,420,442, Mathiowitz et al., U.S. Patent 4,898,734, Lencki et al., U.S. Patent 4,822,534, Herbig et al., U.S. Patent 3,732,172, Himmel et al., U.S. Patent 3,594,326, Sommerville et al., U.S. Patent 3,015,128, Deasy, Microencapsulation and Related Drug Processes, Vol. 20, Chapters. 9 and 10, pp. 195-240 (Marcel Dekker, Inc., N.Y., 1984), Chang et al.,

Canadian J of Physiology and Pharmacology, Vol 44, pp. 115-129 (1966), and Chang, Science, Vol. 146, pp. 524-525 (1964).

Other signal generating agents can be selected from agents, which are transformed into signal generating agents in organisms by means of in-vitro or in-vivo cells, cells as a component of cell cultures, of in-vitro tissues, or cells as a component of multicellular organisms, such as for example fungi, plants or animals, in exemplary embodiments from mammals, such as mice or humans. Such agents can be made available in the form of vectors for the transfection of multicellular organisms, wherein the vectors contain recombinant nucleic acids for the coding of signal generating agents. In exemplary embodiments this may be done with signal generating agents, such as metal binding proteins. It can be preferred to choose such vectors from the group of viruses for example from adeno viruses, adeno virus associated viruses, herpes simplex viruses, retroviruses, alpha viruses, pox viruses, arena-viruses, vaccinia viruses, influenza viruses, polio viruses or hybrids of any of the above.

Such signal generating agents may be used in combination with delivery systems, e.g. in order to incorporate nucleic acids, which are suitable for coding for signal generating agents, into the target structure. Virus particles for the transfection of mammalian cells may be used, wherein the virus particle contains one or a plurality of coding sequence/s for one or a plurality of signal generating agents as described above. In these cases the particles can be generated from one or a plurality of the following viruses: adeno viruses, adeno virus associated viruses, herpes simplex viruses, retroviruses, alpha viruses, pox viruses, arena-viruses, vaccinia viruses, influenza viruses and polio viruses.

These signal generating agents can be made available from colloidal suspensions or emulsions, which are suitable to transfect cells, preferably mammalian cells, wherein these colloidal suspensions and emulsions contain those nucleic acids which possess one or a plurality of the coding sequence(s) for signal generating agents. Such colloidal suspensions or emulsions can include macromolecular complexes, nano capsules, micro spheres, beads, micelles, oil-in–

water- or water-in-oil emulsions, mixed micelles and liposomes or any desired mixture of the above.

Also, cells, cell cultures, organized cell cultures, tissues, organs of desired species and non-human organisms can be chosen which contain recombinant nucleic acids having coding sequences for signal generating agents. In exemplary embodiments organisms can include mouse, rat, dog, monkey, pig, fruit fly, nematode worms, fish or plants or fungi. Further, cells, cell cultures, organized cell cultures, tissues, organs of desired species and non-human organisms can contain one or a plurality of vectors as described above.

Signal generating agents can be produced in vivo from proteins and made available as described above. Such agents can be directly or indirectly signal producing, while the cells produce (direct) a signal producing protein through transfection, or produce a protein which induces (indirect) the production of a signal producing protein. These signal generating agents are e.g. detectable in methods, such as MRI while the relaxation times T1, T2, or both are altered and lead to signal producing effects which can be processed sufficiently for imaging. Such proteins can include protein complexes, such as metalloprotein complexes. Direct signal producing proteins can include such metalloprotein complexes which are formed in the cells. Indirect signal producing agents can include proteins or nucleic acids, for example, which regulate the homeostasis of iron metabolism, the expression of endogenous genes for the production of signal generating agents, and/or the activity of endogenous proteins with direct signal generating properties, for example Iron Regulatory Protein (IRP), transferrin receptor (for the take-up of Fe), erythroid-5-aminobevulinate synthase (for the utilization of Fe, H-Ferritin and L-Ferritin for the purpose of Fe storage). In exemplary embodiments both types of signal generating agents, that is direct and indirect, may be combined with each other, for example an indirect signal generating agent, which regulates the iron-homeostasis and a direct agent, which represents a metal binding protein.

In embodiments, where metal-binding polypeptides are selected as indirect agents, it can be advantageous if the polypeptide binds to one or a plurality of metals

which possess signal generating properties. Metals with unpaired electrons in the Dorf orbitals may be used, such as for example Fe, Co, Mn, Ni, Gd etc., wherein especially Fe is available in high physiological concentrations in organisms. Such agents may form metal-rich aggregates, for example crystalline aggregates, whose diameters are larger than 10 picometers, preferably larger than 100 picometers, 1 nm, 10 nm or specially preferred larger than 100 nm.

Also, metal-binding compounds, which have sub-nanomolar affinities with dissociation constants of less than 10-15 M, 10-2 M or smaller may be used to impart functionality for the implant. Typical polypeptides or metal-binding proteins are lactoferrin, ferritin, or other dimetallocarboxylate proteins, or so-called metal catcher with siderophoric groups, such as hemoglobin. A possible method for preparation of such signal generating agents, their selection and the possible direct or indirect agents which are producible in vivo and are suitable as signal generating agents is disclosed in WO 03/075747.

Another group of signal generating agents can be photo physically signal producing agents which consist of dyestuff–peptide-conjugates. Such dyestuff–peptide-conjugates can provide a wide spectrum of absorption maxima, for example polymethin dyestuffs, such as cyanine-, merocyanine-, oxonol- and squarilium dyestuffs. From the class of the polymethin dyestuffs the cyanine dyestuffs, e.g. the indole structure based indocarbo-, indodicarbo- and indotricarbocyanines, can be suitable. Such dyestuffs can be substituted with suitable linking agents and can be functionalized with other groups as desired, see also DE 19917713.

The signal generating agents can further be functionalized as desired. The functionalization by means of so-called "Targeting" groups is meant to include functional chemical compounds which link the signal generating agent or its specifically available form (encapsulation, micelles, micro spheres, vectors etc.) to a specific functional location, or to a determined cell type, tissue type or other desired target structures. Targeting groups can permit the accumulation of signal-producing agents in or at specific target structures. Therefore the targeting groups can be selected from such substances, which are principally suitable to provide a purposeful

enrichment of the signal generating agents in their specifically available form by physical, chemical or biological routes or combinations thereof. Useful targeting groups can therefore include antibodies, cell receptor ligands, hormones, lipids, sugars, dextrane, alcohols, bile acids, fatty acids, amino acids, peptides and nucleic acids, which can be chemically or physically attached to signal-generating agents, in order to link the signal-generating agents into/onto a specifically desired structure. Exemplary targeting groups may include those which enrich signal-generating agents in/on a tissue type or on surfaces of cells. Here may not be necessary for the function, that the signal generating agent be taken up into the cytoplasm of the cells. Peptides can be targeting groups, for example chemotactic peptides that are used to visualize inflammation reactions in tissues by means of signal generating agents; see also WO 97/14443.

Antibodies can be used, including antibody fragments, Fab, Fab2, Single Chain Antibodies (for example Fv), chimerical antibodies, moreover antibody-like substances, for example so-called anticalines, wherein it may not be important whether the antibodies are modified after preparation, recombinants are produced or whether they are human or non-human antibodies. Humanized or human antibodies may be used, such as chimerical immunoglobulines, immunoglobulin chains or fragments (such as Fv, Fab, Fab', F(ab'')2 or other antigen-binding subsequences of antibodies, which may partly contain sequences of non-human antibodies; humanized antibodies may include human immunoglobulines (receptor or recipient antibody), in which groups of a CDR (Complementary Determining Region) of the receptor are replaced through groups of a CDR of a non-human (spender or donor antibody), wherein the spender species for example, mouse, rabbit or other has appropriate specificity, affinity, and capacity for the binding of target antigens. In a few forms the Fv framework groups of the human immunglobulines are replaced by means of corresponding non-human groups. Humanized antibodies can moreover contain groups which either do not occur in either the CDR or Fv framework sequence of the spender or the recipient. Humanized antibodies essentially comprise substantially at least one or preferably two variable domains, in which all or

substantial components of the CDR components of the CDR regions or Fv framework sequences correspond with those of the non-human immunoglobulin, and all or substantial components of the FR regions correspond with a human consensus-sequence. Targeting groups can also include hetero-conjugated antibodies. The functions of the selected antibodies or peptides include cell surface markers or molecules, particularly of cancer cells, wherein here a large number of known surface structures are known, such as HER2, VEGF, CA15-3, CA 549, CA 27.29, CA 19, CA 50, CA242, MCA, CA125, DE-PAN-2, etc.

Moreover, targeting groups may contain the functional binding sites of ligands and which are suitable for binding to any desired cell receptors. Examples of target receptors include receptors of the group of insulin receptors, insulin-like growth factor receptor (e IGF-1 and IGF-2), growth hormone receptor, glucose transporters (particularly GLUT 4 receptor), transferrin receptor (transferrin), Epidermal Growth Factor receptor (EGF), low density lipoprotein receptor, high density lipoprotein receptor, leptin receptor, estrogen receptor; interleukin receptors including IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12, IL-13, IL-15, and IL-17 receptor, VEGF receptor (VEGF), PDGF receptor (PDGF), Transforming Growth Factor receptor (including TGF-[alpha] and TGF-[beta]), EPO receptor (EPO), TPO receptor (TPO), ciliary neurotrophic factor receptor, prolactin receptor, and T-cell receptors.

Also, hormone receptors may be used, especially for hormones, such as steroidal hormones or protein- or peptide-based hormones, for example, epinephrines, thyroxines, oxytocine, insulin, thyroid-stimulating hormone, calcitonine, chorionic gonadotropine, corticotropine, follicle stimulating hormone, glucagons, leuteinizing hormone, lipotropine, melanocyte-stimulating hormone, norepinephrines, parathyroid hormone, Thyroid-Stimulating Hormone (TSH), vasopressin's, encephalin, serotonin, estradiol, progesterone, testosterone, cortisone, and glucocorticoide. Receptor ligands include those which are on the cell surface receptors of hormones, lipids, proteins, glycol proteins, signal transducers, growth factors, cytokine, and other bio molecules. Moreover, targeting groups can be

selected from carbohydrates with the general formula: Cx(H2O)y, wherein herewith also monosaccharides, disaccharides and oligo- as well as polysaccharides are included, as well as other polymers which consist of sugar molecules which contain glycosidic bonds. Carbohydrates may include those in which all or parts of the carbohydrate components contain glycosylated proteins, including the monomers and oligomers of galactose, mannose, fructose, galactosamine, glucosamine, glucose, sialic acid, and the glycosylated components, which make possible the binding to specific receptors, especially cell surface receptors. Other useful carbohydrates include monomers and polymers of glucose, ribose, lactose, raffinose, fructose and other biologically occurring carbohydrates especially polysaccharides, for example, arabinogalactan, gum Arabica, mannan etc., which are suitable for introducing signal generating agents into cells, see U.S. Patent 5,554,386.

Furthermore, targeting groups can include lipids, fats, fatty oils, waxes, phospholipids, glycolipids, terpenes, fatty acids and glycerides, and triglycerides, or eicosanoides, steroids, sterols, suitable compounds of which can also be hormonese prostaglandins, opiates and cholesterol etc.. All functional groups can be selected as the targeting group, which possess inhibiting properties, such as for example enzyme inhibitors, preferably those which link signal generating agents into/onto enzymes.

Targeting groups can also include functional compounds which enable internalization or incorporation of signal generating agents in the cells, especially in the cytoplasm or in specific cell compartments or organelles, such as, for example, the cell nucleus. For example, such a targeting group may contains all or parts of HIV-1 tat-proteins, their analogs and derivatized or functionally similar proteins, and in this way allows an especially rapid uptake of substances into the cells. As an example refer to Fawell et al., PNAS USA 91:664 (1994); Frankel et al., Cell 55:1189,(1988); Savion et al., J. Biol. Chem. 256:1149 (1981); Derossi et al., J. Biol. Chem. 269:10444 (1994); and Baldin et al., EMBO J. 9:1511 (1990).

Targeting groups can further include the so-called Nuclear Localisation Signal (NLS), which include positively charged (basic) domains which bind to specifically targeted structures of cell nuclei. Numerous NLS and their amino acid sequences are

known including single basic NLS, such as that of the SV40 (monkey virus) large T Antigen (pro Lys Lys Lys Arg Lys Val), Kalderon (1984), et al., Cell, 39:499-509), the teinoic acid receptor-[beta] nuclear localization signal (ARRRRP); NFKB p50 (EEVQRKRQKL; Ghosh et al., Cell 62:1019 (1990); NFKB p65 (EEKRKRTYE; Nolan et al., Cell 64:961 (1991), as well as others (see for example Boulikas, J. Cell. Biochem. 55(1):32-58 (1994), and double basic NLS's, such as for example xenopus (African clawed toad) proteins, nucleoplasmin (Ala Val Lys Arg Pro Ala Ala Thr Lys Lys Ala Gly Gln Ala Lys Lys Lys Lys Leu Asp), Dingwall, et al., Cell, 30:449-458, 1982 and Dingwall, et al., J. Cell Biol., 107:641-849, 1988. Numerous localization studies have shown that NLSs, which are built into synthetic peptides which normally do not address the cell nucleus or were coupled to reporter proteins, lead to an enrichment of such proteins and peptides in cell nuclei. Exemplary references are made to Dingwall, and Laskey, Ann, Rev. Cell Biol., 2:367-390, 1986; Bonnerot, et al., Proc. Natl. Acad. Sci. USA, 84:6795-6799, 1987; Galileo, et al., Proc. Natl. Acad. Sci. USA, 87:458-462, 1990. Targeting groups for the hepatobiliary system may be selected, as suggested in U.S. Patents 5,573,752 and 5,582,814.

In exemplary embodiments the implant comprises absorptive agents, e.g. to remove compounds from body fluids. Suitable absorptive agents include chelating agents, such as penicillamine, methylene tetramine dihydrochloride, EDTA, DMSA or deferoxamine mesylate, any other appropriate chemical modification, antibodies, and micro beads or other materials containing cross linked reagents for absorption of drugs, toxins or other agents.

In some specifically preferred embodiments biologically active agents are selected from cells, cell cultures, organized cell cultures, tissues, organs of desired species and non-human organisms.

In specific embodiments the beneficial agents comprise metal based nano-particles that are selected from ferromagnetic or superparamagnetic metals or metal-alloys, either further modified by coating with silanes or any other suitable polymer or not modified, for interstitial hyperthermia or thermoablation.

In another embodiment it can be desirable to coat the implant on the outer surface or inner surface with a coating to enhance engraftment or biocompatibility. Such coatings may comprise carbon coatings, metal carbides, metal nitrides, metal oxides e.g. diamond-like carbon or silicon carbide, or pure metal layers of e.g. titanium, using PVD, Sputter-, CVD or similar vapor deposition methods or ion implantation.

In further embodiments it is preferred to produce a porous coating onto at least one part of the inventive implant in a further step, such as porous carbon coatings as disclosed in WO 2004/101177, WO 2004/101017 or WO 2004/105826, or porous composite-coatings as disclosed previously in PCT/EP2006/063450, or porous metal-based coatings as disclosed in WO 2006/097503, or any other suitable porous coating.

In further embodiments a sol/gel-based beneficial agent can be incorporated into the inventive implant or a sol/gel-based coating that can be dissolvable in physiologic fluids may be applied to at least a part of the implant, as disclosed e.g. in WO 2006/077256 or WO 2006/082221.

In some exemplary embodiments it can be desirable to combine two or more different functional modifications as described above to obtain a functional implant.

Preferred methods of manufacturing

The inventive implants can be manufactured in one seamless part or with seams from multiple parts. The inventive implants may be manufactured using known implant manufacturing techniques. Particularly, appropriate manufacturing methods include, but are not limited to, laser cutting, chemical etching or stamping of tubes. Another preferred option is the manufacturing by laser cutting, chemically etching, and stamping flat sheets, rolling of the sheets and, as a further option, welding the sheets. Other appropriate manufacturing techniques include electrode discharge machining or molding the inventive implant with the desired design. A further option is to weld individual sections together. Any other suitable implant manufacturing process may also be applied and used.

Further appropriate methods for manufacturing the inventive implant is to use a semi-finished part or the net-shaped part which provides a structural implant body material that can be carbonized appropriately. Such manufacturing methods for producing inorganic carbon material shapes are e.g. disclosed in applicants prior PCT-application WO2005/021462 A1, specifically methods for introducing porosity into carbon materials produced by carbonization of organic polymer precursors.

One specifically preferred option for manufacturing e.g. stents is to use tubes or sheets. The tubes or sheets comprise a chemically or physically connected phase of structural material as well as removable fillers, preferably fibrous or spherical or any other regularly or irregularly shaped particles, that also can be chemically or physically connected. The removable fillers are referred to as a template for generating the porous compartment or respective reservoir. Removal of templates results in formation of the porous compartment within the implant. Preferably the template material or filler can be removed by using appropriate solvents, particularly if the template material is an organic compound, a salt or the like. Suitable solvents are for example, (hot) water, diluted or concentrated inorganic or organic acids, bases or organic solvents, and the like. Another preferred method comprises a thermolytic degradation or vaporization of a filler or template material at elevated temperatures. The temperatures are preferably in the range of 100°C to 1500°C, most preferably in the range of 300°C to 800°C. Preferably, the thermal degradation occurs after manufacturing the desired implant design using e.g. tubes or sheets.

An exemplary method for manufacturing the implantable device of the present invention includes the structuring of a precursor material, e.g. a polymer, a phenolic resin, mesophase pitch, tar, or the like, into a net-shape of the implant supporting structure and subsequent treatment thereof at elevated temperatures to convert the precursor material into an inorganic carbon material as described above. Non-carbon material additives to produce composites and/or removable fillers or templates for generating pores may be added to the precursor materials as desired before the high temperature treatment. Precursor materials may be structured to a mixture of structural materials and template materials of the desired implant design in a suitable

way by folding, embossing, punching, pressing, extruding, gathering, injection molding, or any other conventional technique. In this way, certain implant structures of a regular or irregular type can be provided as a net shape precursor of the implants according to this invention, which are subsequently converted to the inorganic carbon implants of the invention at elevated temperatures. Other known methods of structuring may include, e.g. wet or dry spinning methods, electro-spinning and the like, or knitting, weaving and any other known method to produce woven or non-woven articles or forms of regular or irregular forms.

Another preferred method is to provide first an organic precursor material that can be shaped into sheets or tubes, optionally with multiple layers, or molded into semi-finished parts or the final shape of the desired implant.

Organic or polymeric precursor materials for producing the inorganic carbon material of the implant by high temperature treatment, such as carbonization can include homopolymers, copolymers prepolymeric forms and/or oligomers of aliphatic or aromatic polyolefines, such as polyethylene, polypropylene, polybutene, polyisobutene, polypentene; polybutadiene; polyvinyls, such as polyvinyl chloride, polyvinylacetate, or polyvinyl alcohol, polyacrylates, such as poly(meth)acrylic acid, polymethylmethacrylate (PMMA), polyacrylocyano acrylate; polyacrylonitril, polyamide, polyester, polyurethane, polystyrene, polytetrafluoroethylene; polyethylene vinyl acetate, silicones; poly(ester urethanes), poly(ether urethanes), poly(ester ureas), polyethers, such as polyethylene oxide, polypropylene oxide, pluronics, polytetramethylene glycol; polyvinylpyrrolidone, poly(vinyl acetate phthalate), or shellac, and combinations of these.

In further exemplary embodiments, the polymer for producing the implant of inorganic carbon material can include unsaturated or saturated polyesters, alkyd resins, epoxy-polymers, epoxy resins, phenoxy resins, nylon, polyimide, polyetherimide, polyamideimide, polyesterimide, polyesteramideimide, polyurethane, polycarbonate, polystyrene, polyphenol, polyvinylester, polysilicon, polyacetal, cellulose acetate, polysulfone, polyphenylsulfone, polyethersulfone, polyketone, polyetherketone, polyetheretherketone, polyetherketonketones,

polybenzimidazole, polybenzoxazole, polybenzthiazole, polyfluorocarbons, polyphenylenether, polyarylate, cyanatoester-polymers, copolymers or mixtures of any of these.

Suitable polyacrylates also comprise aliphatic unsaturated organic compounds, e.g. polyacrylamide and unsaturated polyesters from condensation reactions of unsaturated dicarboxylic acids and diols, as well as vinyl-derivatives, or compounds having terminal double bonds. Examples include N-vinylpyrrollidone, styrene, vinyl-naphthalene or vinylphtalimide. Methacrylamid-derivatives include N-alkyl- or N-alkylen-substituted or unsubstituted (meth)acrylamide, such as acrylamid, methacrylamide, N-methacrylamide, N-methylmethacrylamide, N-ethylacrylamide, N,N-dimethylacrylamide, N,N-dimethylmethacrylamide, N,N-diethylacrylamide, N-ethylmethacrylamide, N-methyl-N-ethylacrylamide, N-isopropylacrylamide, N-n-propylacrylamide, N-isopropylmethacrylamide, N-n-propylmethacrylamide, N-acryloyloylpyrrolidine, N-methacryloylpyrrolidine, N-acryloylpiperidine, N-methacryloylpiperidine, N-acryloylhexahydroazepine, N-acryloylmorpholine or N-methacryloylmorpholine.

Further suitable polymers can include unsaturated and saturated polyesters, particularly also including alkyd resins. The polyesters may contain polymeric chains, a varying number of saturated or aromatic dibasic acids and anhydrides, or epoxy resins, which may be used as monomers, oligomers or polymers, optionally crosslinked as desired, can be selected, particularly those which comprise one or several oxirane rings, one aliphatic, aromatic or mixed aliphatic-aromatic molecular structural element, or exclusively non-benzoid structures, i.e., aliphatic or cycloaliphatic structures with our without substituents, such as halogen, ester groups, ether groups, sulfonate groups, siloxane groups, nitro groups, or phosphate groups, or any combination thereof.

In preferred exemplary embodiments of the invention, the precursor material may include epoxy resins, for example of the glycidyl-epoxy type, such as those equipped with the diglycidyl groups of bisphenol A. Further epoxy resins include amino derivatized epoxy resins, particularly tetraglycidyl diaminodiphenyl methane,

triglycidyl-p-aminophenol, triglycidyl-m -maminophenole, or triglycidyl aminocresole and their isomers, phenol derivatized epoxy resins, such as, for example, epoxy resins of bisphenol A, bisphenol F, bisphenol S, phenol-novolac, cresole-novolac or resorcinole, phenoxy resins, as well as alicyclic epoxy resins. Furthermore, halogenated epoxy resins, glycidyl ethers of polyhydric phenols, diglycidylether of bisphenol A, glycidylethers of phenole-formaldehyde-novolac resins and resorcinole diglycidylether, as well as further epoxy resins as described in US Patent No. 3,018,262, herewith incorporated by reference, may be used. These materials may be easily structured, worked, and solidified or cured e.g. thermally or by radiation or cross linking, before being converted into the inorganic carbon material.

For example, in exemplary embodiments of the invention, a stent may be produced from a suitable polymeric precursor material, such as one of those described above, e.g. a phenol-formaldehyde novolac resin, which may optionally be mixed with a porogen (is porosity of the inorganic carbon material is desired). The porogen could be any material easily decomposable during carbonization, for example, polyethylene beads of a suitable size, such as 100µm size. A typical example for a suitable porogen may be polyethylene beads, such as "micro scrub", commercially available from Micro Powders Inc. If no porosity is desired, the porogen is simply left out. Alternatively, porosity may be produced by applying the precursor material onto a thermally decomposable template material such as polyethylene. in such instance, pores can be produced during carbonization from the decomposition products of the template, which flow through the carbonizing polymeric precursor. To the precursor or its mixture with the porogen in a suitable ratio, such as 3:1 (wt/wt), optionally a cross-linker or other additives, such as hexamethylene tetramine in case of a phenolic resin used, can be added in a suitable amount, e.g. to obtain 10% cross-linker content, and mixed, e.g. a conventional stirrer at 20 rpm and filled into a mould, e.g. a metal mould. The mould comprising the precursors can then be cured or dried, whatever is necessary for the particular materials selected, for example by heating at 150°C for 4 hours. The resulting hollow

polymeric precursor shape. e.g. a hollow tube, such as a phenolic resin tube, can then subsequently conventionally be carbonized into the inorganic carbon material.

In an exemplary setup using phenolic resin and polyethylene beads, such a precursor tube had a wall thickness of 4,5mm, a length of 81cm and a lumen diameter of 10,5mm. Subsequently, this tube was carbonized in a standard tube reactor at 2000°C in nitrogen atmosphere (flow rate 2000ml/min) using a heating ramp of 1K/min, the dwell time was 8 hours. During carbonization the tube was supported by a stainless steel spit. The resulting carbonized tube shrunk to a 0,5mm wall thickness, an inner lumen diameter of 1,5mm and a length of 65 cm.

The carbonized stent green bodies can then be patterned with any suitable conventional method as described above. In the exemplary setup hereinbefore described, a conventional laser cutting was carried out by cutting a 3-D coronary stent pattern out of the tube. The surface of the carbon tube and respective stent was matt, indicating porosity. A field emission scanning electron microscope at 5,000 x magnification showed a porous carbon with a pore size of approx. 1 μm.

Having thus described in detail several exemplary embodiments of the present invention, it is to be understood that the invention described above is not to be limited to particular details set forth in the above description, as many apparent variations thereof are possible without departing from the spirit or scope of the present invention. The embodiments of the present invention are disclosed herein or are obvious from and encompassed by the detailed description. The detailed description, given by way of example, but not intended to limit the invention solely to the specific embodiments described, may best be understood in conjunction with the accompanying Figures.

The foregoing applications, and all documents cited therein or during their prosecution ("appln. cited documents") and all documents cited or referenced in the appln. cited documents, and all documents cited or referenced herein ("herein cited documents"), and all documents cited or referenced in the herein cited documents, together with any manufacturer's instructions, descriptions, product specifications,

and product sheets for any products mentioned herein or in any document incorporated by reference herein, are hereby incorporated herein by reference, and may be employed in the practice of the invention.

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Claims:

1. A stent or part thereof, having a supporting structure consisting of a non-particulate inorganic carbon material.

2. The stent of claim 1, adapted for maintaining the patency of at least one of the esophagus, trachea, bronchial vessels, arteries, veins, biliary vessels and other passageways in the body of a patient.

3. The device of any one of the previous claims, wherein the non-particulate inorganic carbon material includes at least one of bulk carbon material, a composite material comprising inorganic carbon and a further inorganic material, or a composite material comprising inorganic carbon and a further organic material.

4. The device of claim 3, wherein the inorganic carbon material includes at least 50 % by weight of inorganic carbon, preferably at least 60 % by weight, more preferred at least 80 % by weight.

5. The device of claim 3 or 4, wherein said inorganic carbon material includes at least one of graphite, diamond-like carbon, pyrolytic carbon, turbostratic carbon, carbon obtained from carbonization of a polymeric material, glassy or vitrous carbon.

6. The stent of claim 3, wherein said further inorganic material includes at least one of a metal, a metal alloy, or a metal compound.

7. The stent of claim 3, wherein said further organic material includes at least one of a polymer, a copolymer, an oligomer, or a polymer composite.

8. The stent of any one of the previous claims, wherein the supporting structure and/or the non-particulate inorganic carbon material is porous.

9. The stent of claim 8, wherein the porous supporting structure and/or the non-particulate inorganic carbon material has a plurality of interconnected pores.

10. The stent of claim 8 or 9, wherein the supporting structure and/or the inorganic carbon material has a porosity in the range of 10 to 90%, preferably 30 to 90%, most preferably 50 to 90%, in particular about 60 %.

11. The stent of any one of claims 8 to 10, wherein a pore size of the pores is in a range of about 5 nm to 5000 μm, preferably 10 nm to 1000 μm, most preferably 20 nm to 700 μm.

12. The stent of any one of the previous claims, wherein the interior of the pores is coated with a coating.

13. The stent of any one of the previous claims, wherein the pores in a first hierarchy substantially cover a convex polyhedron.

14. The stent of any one of the previous claims, wherein at least a part of the pores in a second hierarchy substantially cover a combination of a convex polyhedron and at least one partial convex sub-polyhedron, wherein the size of the polyhedron is larger than or equal to the size of the sub-polyhedron.

15. The stent of claim 14, wherein a ratio between the size of the polyhedron and the at least one sub-polyhedron is in the range of 1:0.5 to 1:0.001, preferably 1: 0.4 to 1:0.01, and most preferred about 1:0.2.

16. The stent of any one of the previous claims, wherein the part of the stent determines at least a part of a form of the stent.

17. The stent of claim 16, wherein the part has a form selected from the group consisting of a ring, a torus, a hollow cylinder segment, a tube segment, or a web structure.

18. The stent of any one of claims 1 to 7, wherein:

the supporting structure has a plurality of walls,

the walls enclosing a lumen for storing at least one active ingredient, wherein the walls consist of a non-particulate inorganic carbon material and which is adapted to allow a fluid communication between the lumen and the exterior of the device for releasing the stored ingredient.

19. The stent of claim 18, wherein the inorganic carbon material is non-porous and the walls have at least one opening connecting the enclosed lumen with the exterior of the stent.

20. The stent of claim 18, wherein the material is porous having a plurality of interconnected pores.

21. The stent of claim 19, having at least one opening to allow a fluid communication between the lumen and the exterior of the stent for releasing the stored ingredient.

22. The stent of claim 21, wherein the opening is a hole.

23. The stent of any one of claims 18 to 22, wherein the lumen has an extension in a longitudinal direction of the stent and along a circumference of the stent, which is substantially larger than a radial extension of the lumen.

24. The stent of any one of claims 18 to 22, wherein the stent comprises a first tube and a second tube concentric to the first tube, wherein the lumen is enclosed between the first and second concentric tube, and at least a part of the first and/or second tube comprises the porous material.

25. The stent of any one of claims 18 to 22, wherein the stent comprises a first ribbon helically wound around a tubular space and a second ribbon helically wound around the tubular space corresponding and concentric to the fist ribbon, wherein the lumen is enclosed between the first and second concentric ribbons, and at least a part of the first and/or second tube comprises the porous material.

26. The stent of any one of claims 18 to 22, wherein the stent is formed by a plurality of hollow annular elements each having a sub-lumen, which annular elements are arranged such that each annular element circumferences a tubular space and each annular element has a different inclination from an adjacent abutting annular element, wherein adjacent annular elements are joined at an abutting location to form a passage between two abutting annular elements.

27. The stent of any one of claims 18 to 22, wherein the annular elements comprise openings facing the exterior of the tubular space.

28. The stent of any one of claims 18 to 22, wherein the stent is formed from a brick wall structured mesh of hollow struts, wherein continuous struts extend in a longitudinal direction, which are connected by linking struts.

29. The device of claim 28, wherein the brick walled structure totally circumferences a tubular space, such that the brick walled structure repeats periodically and perpetually along the circumference.

30. The stent of any one of claims 18 to 22, wherein the stent is formed by a plurality of hollow annular wave elements each having a sub-lumen, which annular wave elements are arranged such that each annular element circumferences a tubular space and each annular element abutting an adjacent annular element, wherein adjacent annular elements are joined at an abutting location to form a passage between two abutting annular elements.

31. The stent of claim 30, wherein the tubular space has a shape of a bifurcated tube.

32. The stent of any one of claims 1 to 31, including at least one active ingredient.

33. The stent of claim 32, wherein the active ingredient is configured to be released from the device in-vivo.

34. The stent of claim 30 or 31, wherein the active ingredient includes at least one of a pharmacologically, therapeutically, biologically or diagnostically active agent or an absorptive agent.

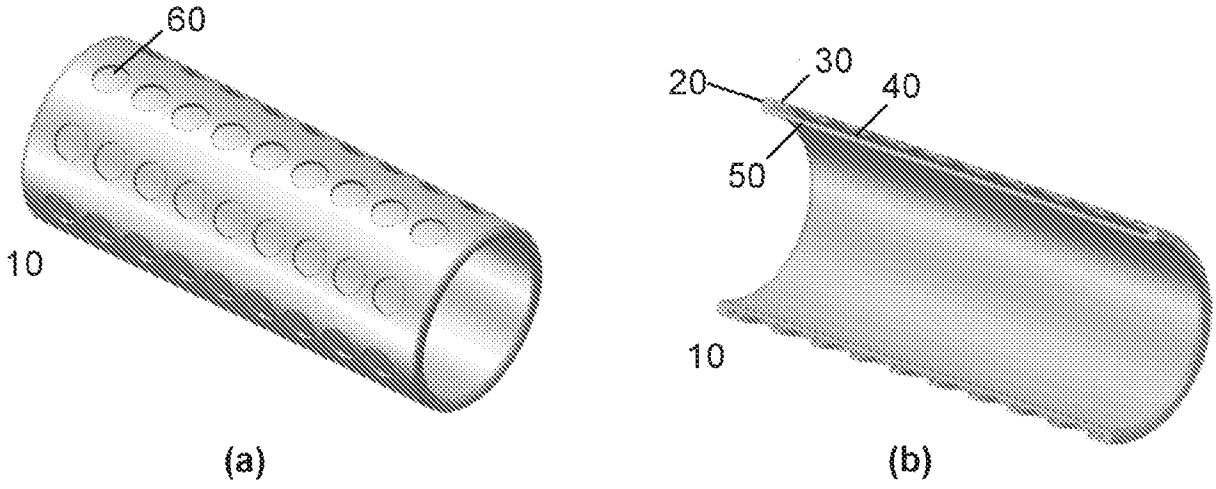

Fig. 1

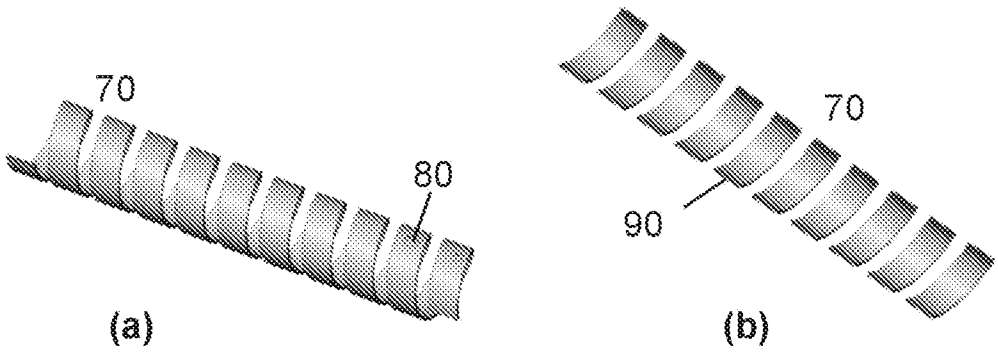

Fig. 2

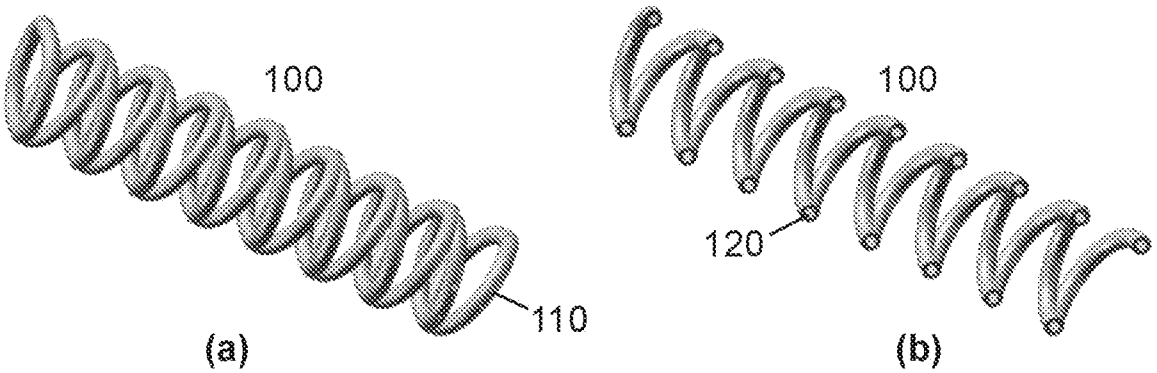

Fig. 3

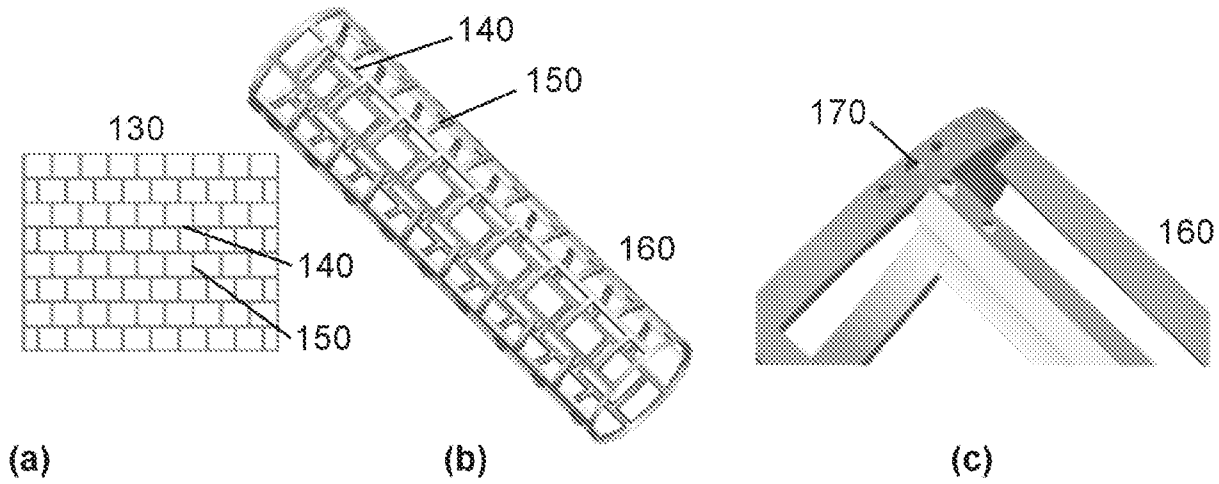

Fig. 4

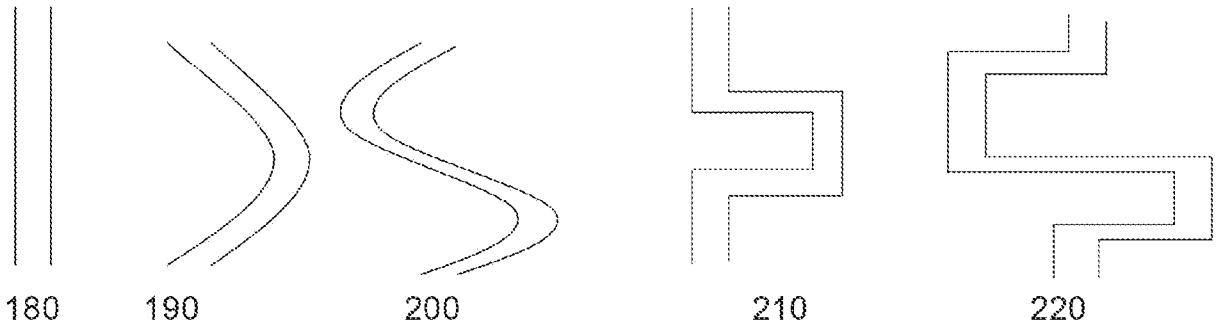

Fig. 5

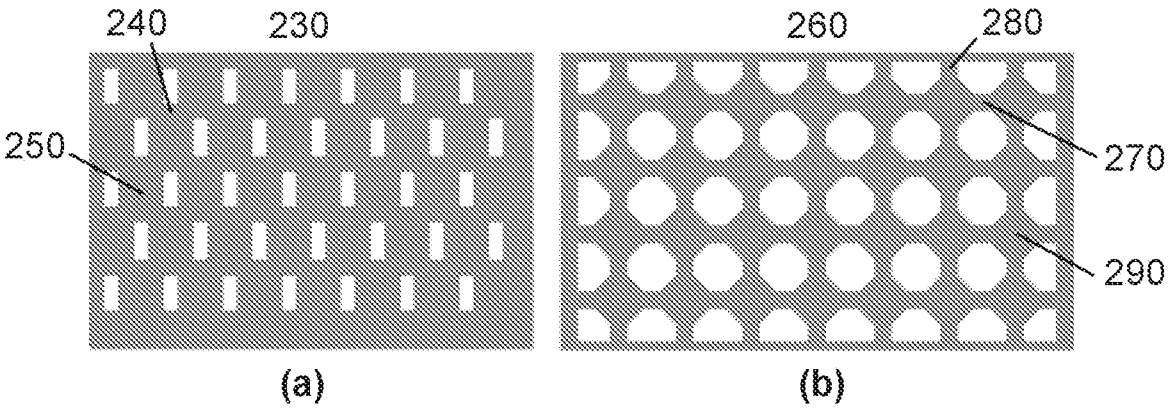

Fig. 6

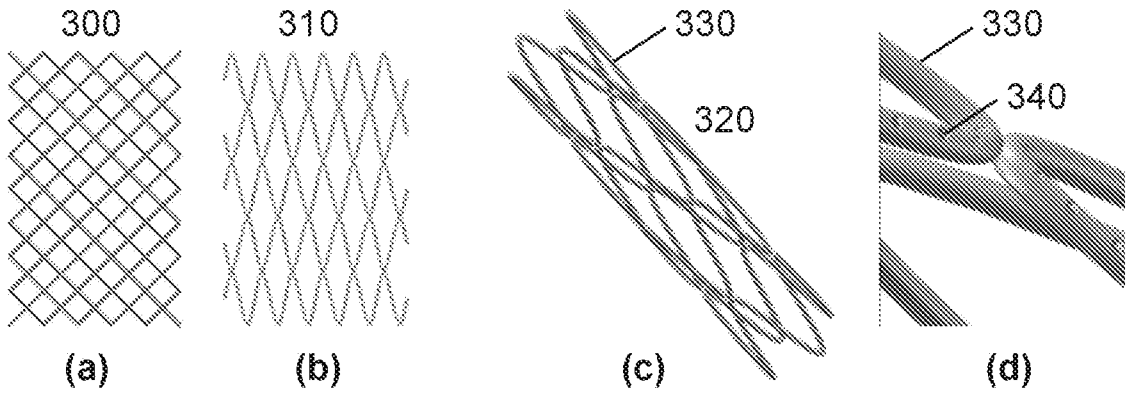

Fig. 7

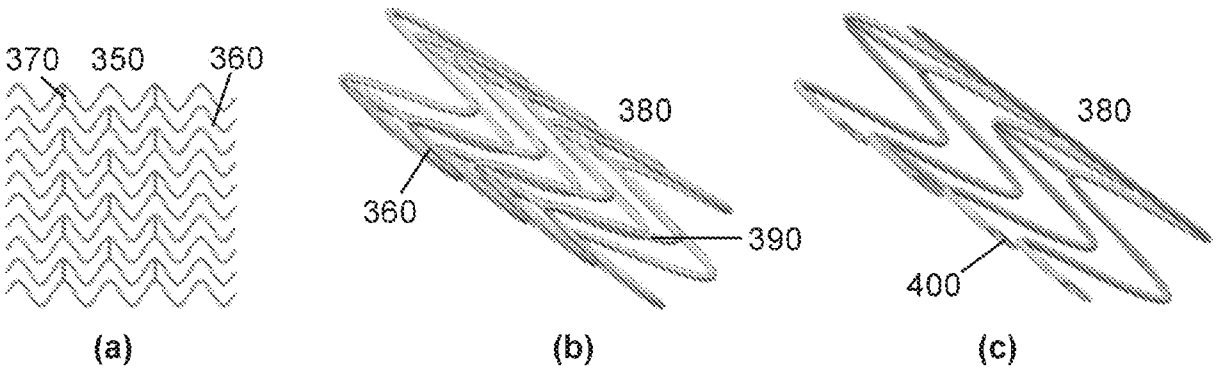

Fig. 8

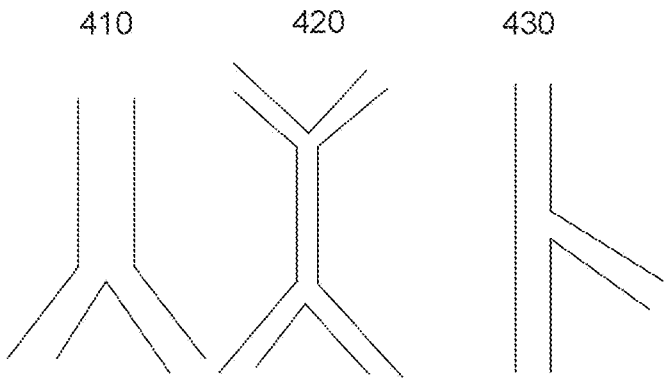

Fig. 9

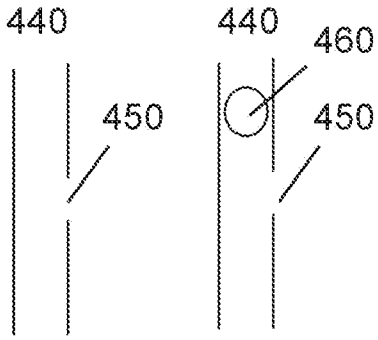

Fig. 10

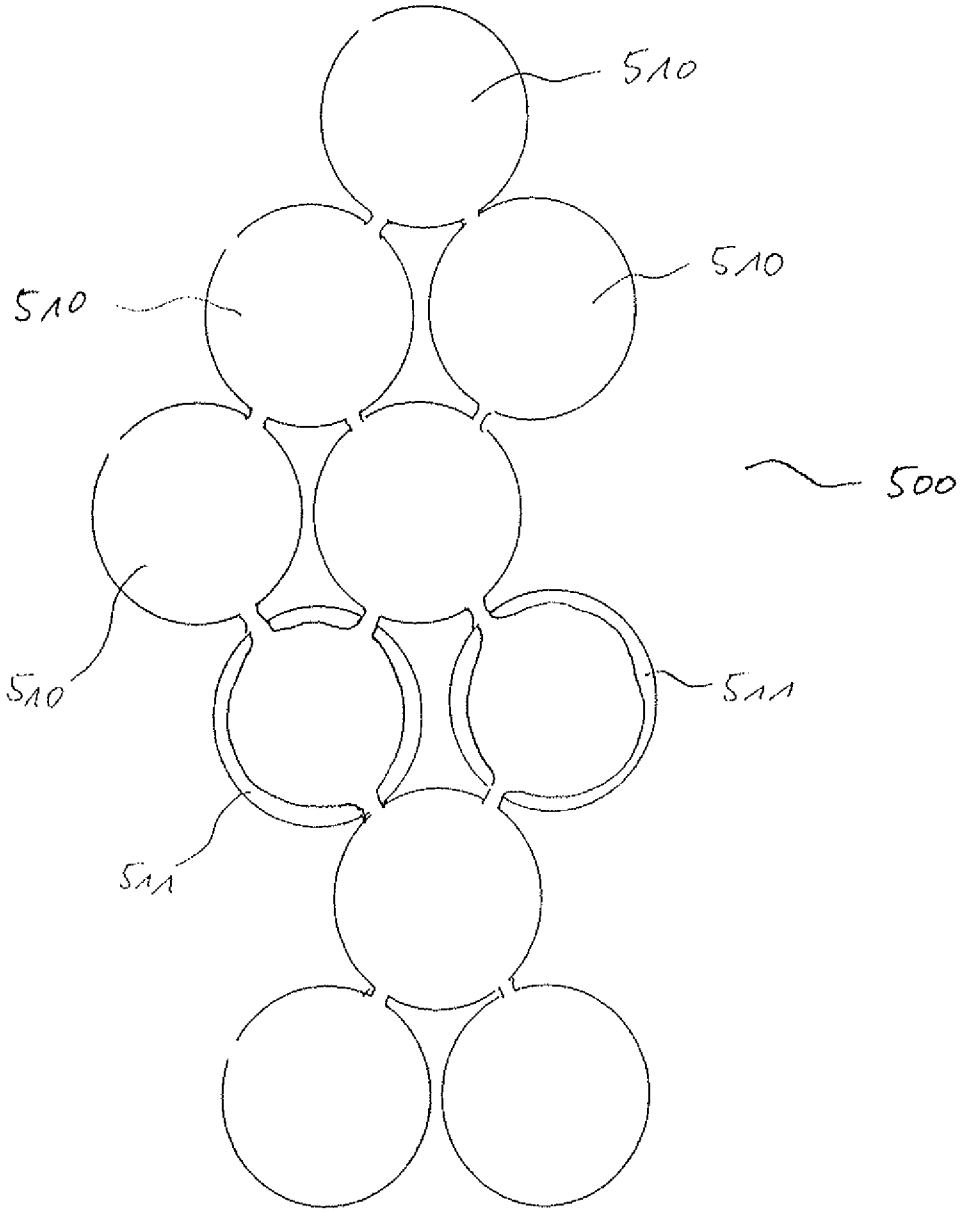

Fig. 11

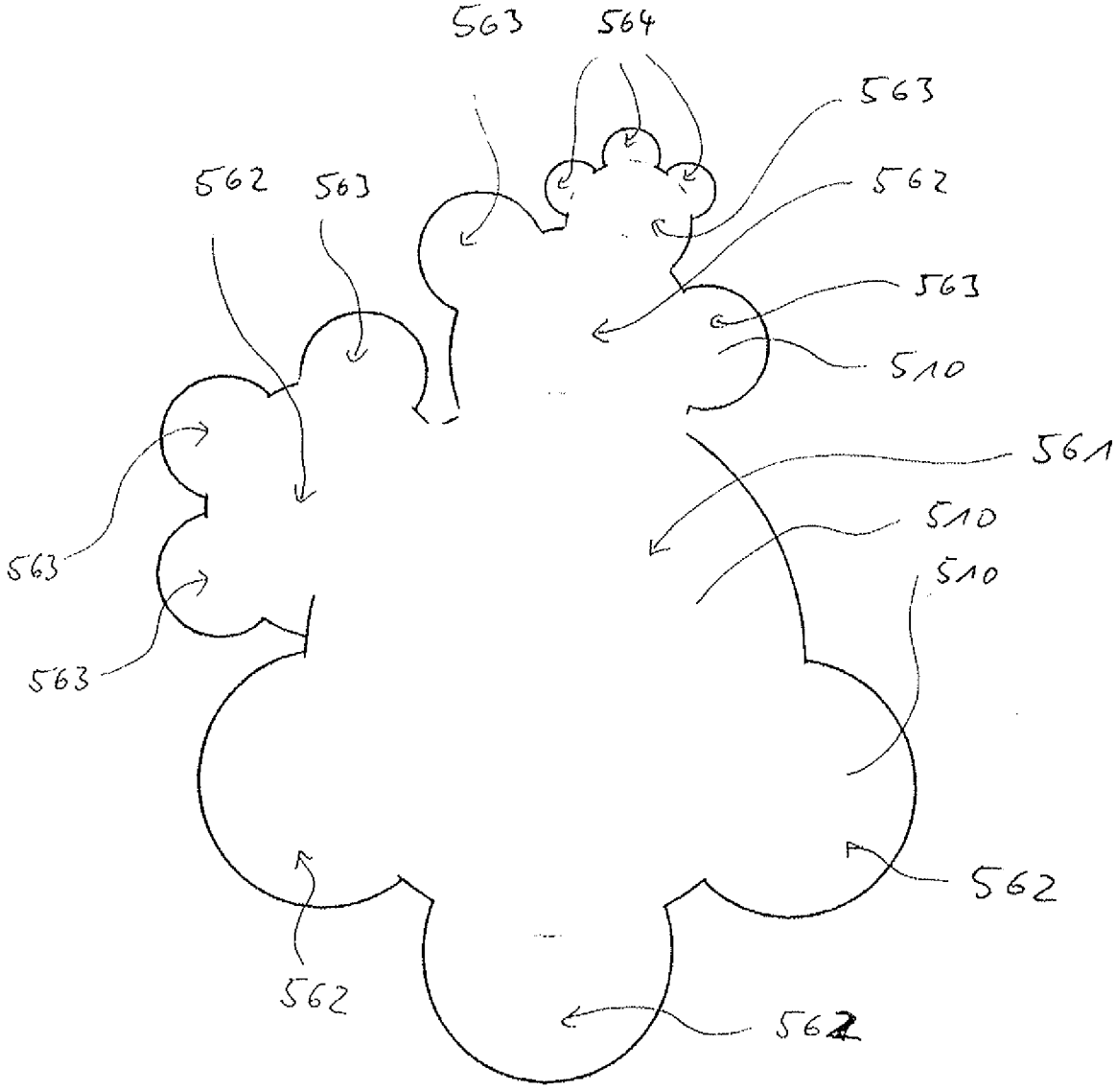

Fig. 12

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/051907

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L27/08 A61L31/12 A61F2/82

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61L A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/260355 A1 (WEBER JAN [US] ET AL) 24 November 2005 (2005-11-24) paragraph [0029] paragraph [0047] paragraphs [0050] - [0052] claims 1-32	1-4, 6-12, 17-24
X	US 7 008 446 B1 (AMIS JAMES PETER [US] ET AL) 7 March 2006 (2006-03-07) column 17, lines 63-67	1-4,6-17
Y	column 21, lines 25-40 column 23, lines 40-55 claims 4,27	18-34

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 April 2008	25/04/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Cismaru, L

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/051907

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2001/021870 A1 (EDWIN TARUN J [US] ET AL EDWIN TARUN J [US] ET AL) 13 September 2001 (2001-09-13) paragraph [0009] paragraph [0012]	1-4,6-25
Y	paragraph [0039] claims 1,2	18-34
X	EP 0 004 299 A (SIGRI ELEKTROGRAPHIT GMBH [DE]) 3 October 1979 (1979-10-03) claims 1-5	1-17
X	US 3 526 906 A (LASZLO HENRY G DE) 8 September 1970 (1970-09-08) column 2, lines 20-50	1-17
X	GB 2 105 197 A (BENTLEY LAB [US]) 23 March 1983 (1983-03-23) page 2, lines 15-44	1-17
Y	claims 14-20	18-34
Y	US 3 936 887 A (HODOSH MILTON) 10 February 1976 (1976-02-10) column 2, lines 25-47 claim 1	18-34

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/051907

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2005260355 A1	24-11-2005	CA 2569027 A1	01-12-2005
		EP 1747030 A2	31-01-2007
		JP 2007537837 T	27-12-2007
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