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(54) Title: FLEXIBLE VASCULAR PROSTHESIS, AND METHOD FOR ITS PRODUCTION

(57) Abstract: The invention relates to a method for producing a vascular prosthesis, in which method a vascular prosthesis with an inner surface and outer surface and a wall is sprayed with a liquid containing at least one sealing material, characterized in that the liquid is sprayed onto the outer surface of the prosthesis at a pressure of 0.01 to 1.5 bar in order to generate a sealing impregnation in the prosthesis wall, and/or is sprayed onto the outer surface of the prosthesis at a pressure of 5.0 to 50 bar in order to generate a sealing coating on the outer surface of the prosthesis. The invention further relates to a vascular prosthesis produced or producible by the above method. The invention moreover relates to a vascular prosthesis with an impregnation comprising at least one sealing material in the prosthesis wall and/or with a coating comprising at least one sealing material on the outer surface of the prosthesis, wherein the prosthesis, when subjected to a force of 1 N acting perpendicularly with respect to the outer surface of the prosthesis, is deformed in such a way that the external diameter of the prosthesis decreases, in the direction of the acting force, by 60 to 100% in relation to the original external diameter.

Description

Flexible vascular prosthesis, and method for its production

[0001] The invention relates to a flexible, in particular soft, vascular prosthesis, and to a method for its production.

[0002] Vascular prostheses generally have a porous main structure in order to prevent incorporation of body cells and tissue. This, on the one hand, permits secondary anchoring of the prosthesis after its implantation. On the other hand, the growth of body cells and tissue into the prostheses allows a substantial approximation to the original anatomical circumstances.

[0003] However, the porosity of the prosthesis structure is generally associated with the risk of leaks occurring, which can in turn be the cause of undesired and in particular life-threatening seepage of blood.

[0004] In order to avoid leaks, vascular prostheses can undergo what is called pre-clotting. In this, the vascular prostheses are soaked with the patient's blood before the operation. A vascular prosthesis suitable for this purpose is known from WO 02/094135 A1, for example.

[0005] However, since pre-clotting constitutes a time-consuming preliminary treatment of the vascular prosthesis, it is increasingly common for vascular prostheses to be impregnated or coated with resorbable materials. Vascular prostheses of this kind permit a broader range of application and can in particular also be used for emergency operations.

[0006] For example, a thin and lacquer-like coating with an antithrombogenic action is known, for biomaterials such as stents, from EP 0 652 017 A1.

[0007] A vascular prosthesis which is coated with a synthetic resorbable polymer is the subject matter of DE 10 2006 053 752 A1.

[0008] DE 10 2009 037 134 A1 discloses a vascular prosthesis with a polyurethane coating. US 6,733,768 B2 describes the use of prosthesis-coating compositions that contain polymers and active substances.

[0009] A vascular prosthesis impregnated by means of gelatin, in which substantially the entire prosthesis wall is impregnated, is known from DE 101 49 392 A1.

[0010] Generally, in order to generate a sealing coating, the prostheses undergo an immersion process. The coatings resulting from the latter are often film-shaped and can lead to increased stiffness and hardness of the prosthesis.

[0011] By contrast, if the vascular prostheses are coated by means of a spraying process, a large number of spray cycles is generally needed for the formation of a sealing coating, which can likewise result in stiffer overall prosthesis constructions.

[0012] Stiffer vascular prostheses, however, make handling difficult for the surgeon, since they are more difficult to adapt during the implantation procedure and to sew onto natural tissues.

[0013] Against this background, the object of the present invention is to make available a method by which a vascular prosthesis is produced and which avoids the shortcomings known from the prior art.

[0014] The object of the invention is also to make available a prosthesis that avoids the disadvantages and difficulties arising in conventional vascular prostheses. The vascular prosthesis made available by the invention is intended in particular to be distinguished by improved flexibility and softness, improved ease of handling by the surgeon, and at the same time by a reduced risk of postoperative complications.

[0015] According to a first aspect of the invention, this object is achieved by a method having the features of independent claim 1. Preferred embodiments of the method are the subject matter of dependent claims 2 to 11. A second and third aspect of the invention relates to a vascular prosthesis having the features of claim 12 and also of independent claim 13. Preferred embodiments of the vascular prosthesis protected in claim 13 are set forth in dependent claims 14 to 21. The wording of all the claims is hereby incorporated by express reference into the content of the present description.

[0016] The method according to the invention is a method for producing a vascular prosthesis, in which method a vascular prosthesis with an inner surface and outer surface and a wall is sprayed with a liquid containing at least one sealing material.

[0017] In order to generate a sealing impregnation in the prosthesis wall, the liquid is sprayed onto the outer surface of the prosthesis at a pressure of 0.01 to 1.5 bar.

[0018] Alternatively or in combination, the liquid is sprayed onto the outer surface of the prosthesis at a pressure of 5.0 to 50 bar in order to generate a sealing coating on the outer surface of the prosthesis.

[0019] The present invention is based on the following surprising results:

[0020] If the outer surface of a vascular prosthesis is sprayed with a liquid, containing at least one sealing material, at a pressure of 0.01 to 1.5 bar, a sealing impregnation forms in the prosthesis wall and acts in particular as a kind of substrate or adhesive layer (grounding or priming coat) with respect to a coating optionally present on the outer surface of the prosthesis.

[0021] If, alternatively or in addition, the outer surface of a vascular prosthesis is sprayed with a liquid, containing at least one sealing material, at a pressure of 5.0 to 50 bar, a sealing coating forms on the outer surface of the prosthesis and in particular leads to a prosthesis flexibility, preferably a prosthesis softness, that is much greater than in conventionally coated prostheses with a comparable coating fraction. The flexibility of prostheses that are coated by the method according to the invention is (in some cases) even comparable to the flexibility of uncoated prostheses.

[0022] The greater flexibility, in particular softness, of the prostheses improves their handling by the surgeon. For example, vascular prostheses according to the invention permit easier adaptation to natural blood vessels, which is advantageous especially in bypass operations. The fastening of the prostheses to natural blood vessels is also improved by the greater flexibility.

[0023] Moreover, in vascular prostheses according to the invention, it is possible to do without after-treatment, for example restoration of pleats.

[0024] Finally, the pressure conditions provided according to the invention permit a more efficient spraying process, which is reflected particularly in a reduced number of spray cycles.

[0025] Within the meaning of the present invention, the expression "at least one sealing material" can signify a sealing material in the sense of a single type of sealing material or a plurality or mixture of different sealing materials.

[0026] Within the meaning of the present invention, the expression "sealing impregnation" or "sealing coating" signifies that the impregnation or coating is leaktight with respect to body fluids, preferably blood.

[0027] Within the meaning of the invention, the expression "impregnation" is to be understood as at least one layer which contains the at least one sealing material and which is formed in the wall of the prosthesis preferably to a depth of at least 1 to 100%, in particular 50 to 100%, preferably 80 to 100%, relative to the wall thickness of the prosthesis. If appropriate, the at least one layer is in addition also formed on the outer surface of the prosthesis. If the impregnation is formed in the prosthesis wall and on the outer surface of the prosthesis, the layer thickness of the impregnation in the prosthesis wall is preferably greater than on the outer surface of the prosthesis. Preferably, the impregnation is formed only, or substantially only, in the prosthesis wall.

[0028] Within the meaning of the invention, the expression "coating" is to be understood as at least one layer which contains the at least one sealing material and which is formed in the wall of the prosthesis preferably to a depth of at most 15%, in particular at most 8 to 12%, preferably at most 9%, relative to the wall thickness of the prosthesis, and is for the rest formed on the outer surface of the prosthesis. If the coating is formed on the outer surface of the prosthesis and in the prosthesis wall, the thickness of the coating on the outer surface of the prosthesis is preferably greater than in the prosthesis wall. Preferably, the coating is formed only, or substantially only, on the outer surface of the prosthesis.

[0029] Within the meaning of the present invention, the "at least one layer" mentioned in the two previous paragraphs can signify one layer or a multiplicity of layers, i.e. at least two or more layers.

[0030] In a preferred embodiment, the liquid for generating the impregnation is sprayed onto the outer surface of the vascular prosthesis at a pressure of 0.02 to 1.5 bar, in particular 0.05 to 0.8 bar, preferably 0.1 to 0.6 bar.

[0031] In an alternative or additional embodiment, the liquid for generating the coating is sprayed onto the outer surface of the vascular prosthesis at a pressure of 5 to 20 bar, in particular 5 to 10 bar, preferably 6 to 9 bar.

[0032] In an expedient embodiment, the liquid is applied to the outer surface of the vascular prosthesis by means of a spraying device controlled by compressed air, preferably a spray gun.

[0033] The outer surface of the vascular prosthesis is preferably sprayed with the liquid at a distance of 1 to 500 mm, in particular 1 to 100 mm, preferably 2 to 70 mm, from the spraying device.

[0034] In principle, 1 to 100 spray cycles can be performed in order to generate the impregnation and/or coating. However, it is preferable to perform only 1 to 20 spray cycles, particularly preferably only 1 to 10 spray cycles. A reduced number of spray cycles means less consumption of material and permits faster and, in particular, less expensive production of the prostheses.

[0035] After the spraying, the vascular prosthesis in a further embodiment is dried, in particular by means of heat. For example, the vascular prosthesis can be dried at a temperature of 15 to 75°C, in particular 15 to 50°C, preferably 15 to 30°C.

[0036] The liquid provided for spraying the vascular prosthesis preferably has, in addition to the at least one sealing material, an organic solvent, which can be a ketone, in particular acetone and/or 3-pentanone, THF, chloroform or a mixture thereof.

[0037] In order to generate the impregnation and/or coating, the outer surface of the vascular prosthesis in a further embodiment is sprayed with a liquid that contains the at least one sealing material in a proportion of 1 to 50% by weight, in particular 5 to 25% by weight, preferably 7 to 15% by weight, relative to the total weight of the liquid.

[0038] In a further embodiment, the liquid has a dynamic viscosity of 20 to 60 mPas, in particular 30 to 45 mPas, preferably 32 to 41 mPas. The aforesaid dynamic viscosity values are preferably measured on the basis of a solution of the at least one sealing material in an acetone solution at 25°C. Preferably, the solution has a concentration (weight/volume; w/v) of the at least one sealing material of 5 to 15 % by weight, in particular 8 to 12 % by weight, preferably 9 to 11 % by weight, relative to the total volume of the solution.

[0039] The at least one sealing material is expediently a biocompatible material, in particular one that seals the prosthesis with respect to body fluids, in particular blood.

[0040] In a preferred embodiment, both an impregnation in the prosthesis wall and also a coating on the outer surface of the prosthesis are generated within the scope of the method according to the invention.

[0041] In principle, the at least one sealing material for generating the impregnation and the at least one sealing material for generating the coating can be different. According to the invention, however, it is preferable if the same at least one sealing material is used to generate the impregnation and the coating.

[0042] The at least one sealing material is preferably resorbable. A sealing material of this kind has, on the one hand, the advantage that the amount of foreign material introduced is reduced again in the mid to long term after the implantation. On the other hand, the inflammatory processes triggered by the resorption process support the secondary anchoring of the vascular prosthesis by contributing to improved encapsulation of the prosthesis by connective tissue.

[0043] Moreover, the at least one sealing material can be a film-forming polymer, in particular a biopolymer.

[0044] In further embodiments, the at least one sealing material can be of biological origin, in particular of animal origin, preferably of bovine, porcine and/or equine origin. Preferably, the at least one sealing material is chosen from the group consisting of collagen, gelatin, albumin and combinations thereof.

[0045] In preferred embodiments, however, the at least one sealing material is of synthetic origin. The at least one sealing material is preferably a synthetic polymer. Examples of suitable polymers are, in particular, synthetic polymers such as polyhydroxy alkanoates and copolymers thereof.

[0046] Within the meaning of the present invention, the term "copolymer" is to be understood as a polymer composed of two or more different types of monomer units. In line with this definition, the expression "copolymer" within the meaning of the present invention can therefore concern a bipolymer, tripolymer, tetrapolymer or the like.

[0047] In a further embodiment, the at least one sealing material is chosen from the group consisting of polyglycolide, polylactide, poly-ε-caprolactone, polytrimethylene carbonate, poly-para-dioxanone, poly-3-hydroxybutyrate, poly-4-hydroxybutyrate, copolymers thereof, stereoi-

somers, in particular diastereomers, thereof, salts thereof, and combinations, in particular blends, thereof.

[0048] In a further embodiment, the at least one sealing material is a three-armed polyester having terminal hydroxyl groups from hydroxy acids that are polymerized onto a central trifunctional hydroxy compound, the three arms being tetrapolymers of lactide, ε-caprolactone, trimethylene carbonate and glycolide.

[0049] The lactide is preferably L-lactide.

[0050] The polymer is preferably composed of 30 to 45 mol% lactide, 20 to 40 mol% ε-caprolactone, 10 to 28 mol% trimethylene carbonate, and 3 to 25 mol%, in particular 10 to 25 mol%, glycolide.

[0051] In preferred embodiments, the polymer is a segmented polymer, in particular of three first segments connected to the trifunctional hydroxy compound and of three second segments connected to the free ends of the first segments, wherein the first segments are different from the second segments.

[0052] The first segment is preferably free of lactide. The second segment is preferably free of trimethylene carbonate.

[0053] The first segment is particularly preferably composed of ε–caprolactone, trimethylene carbonate and glycolide.

[0054] The second segment is preferably composed of lactide, glycolide and, optionally, ε-caprolactone.

[0055] The second segment is also preferably free of ε–caprolactone.

[0056] The first segment can contain 30 to 40 mol%, in particular 32 to 35 mol%, ε-caprolactone, relative to the total amount of the monomers in both segments.

[0057] Moreover, the first segment can contain 10 to 20 mol%, in particular 13 to 17 mol%, trimethylene carbonate, relative to the total amount of the monomers in both segments.

[0058] Furthermore, the first segment can contain 7 to 12 mol%, in particular 8 to 11 mol%, glycolide, relative to the total amount of the monomers in both segments.

[0059] The second segment preferably contains 30 to 45 mol%, in particular 32 to 42 mol%, lactide, relative to the total amount of the monomers in both segments.

[0060] The second segment can also be characterized in that it contains 0 to 4 mol%, in particular 1 to 4 mol%, ε-caprolactone, relative to the total amount of the monomers in both segments.

[0061] Moreover, the second segment can contain 1 to 10 mol%, in particular 2 to 8 mol%, glycolide, relative to the total amount of the monomers in both segments.

[0062] As regards further features and advantages of the three-armed polymer described in the preceding embodiments, reference is made to WO 2008/058660 A2, the disclosure of which is incorporated by express reference into the content of the present description.

[0063] To improve or increase the kink stability, provision can also be made according to the invention that the vascular prosthesis undergoes pleating. In principle, the vascular prosthesis can be pleated before and/or after being sprayed with the liquid.

[0064] In a particularly advantageous embodiment, however, the vascular prosthesis undergoes pleating only once, specifically before being sprayed with the liquid. This is because it was discovered that further pleating is no longer needed after the spraying process.

[0065] Further features and advantages of the method according to the invention are set forth in the description below.

[0066] The second aspect of the invention concerns a vascular prosthesis produced or producible by a method according to the present invention. To avoid unnecessary repetition, reference is therefore made to the statements made above in connection with the method according to the invention. For the rest, reference is made to the statements made below.

[0067] In a third aspect, the invention concerns a vascular prosthesis with an inner surface and outer surface, a wall, and a sealing impregnation comprising at least one sealing material in the prosthesis wall and/or a sealing coating comprising at least one sealing material on the outer surface of the prosthesis.

[0068] When subjected to a force of 1 N acting perpendicularly with respect to the outer surface of the prosthesis, the prosthesis is preferably deformable in such a way that the external diameter of the prosthesis decreases, in the direction of the acting force, by 60 to 100%, in particular 50 to 100%, preferably 70 to 100%, more preferably 80 to 100%, in relation to the original external diameter.

[0069] Within the meaning of the present invention, the expression "original external diameter" is to be understood as the external diameter that the vascular prosthesis has in the unloaded state, i.e. without a force acting on it, preferably from the outside.

[0070] In a further embodiment, the impregnation is formed in the wall of the vascular prosthesis to a depth of 1 to 100%, in particular 50 to 100%, preferably 80 to 100%, relative to the wall thickness of the vascular prosthesis.

[0071] As has already been mentioned, the impregnation can particularly advantageously perform the function of an adhesion bed or substrate (grounding or priming coat) for a coating that is optionally present on the outer surface of the vascular prosthesis.

[0072] The inner surface of the vascular prosthesis is preferably free of the at least one sealing material, in particular free of a continuous layer of the at least one sealing material, i.e. a layer partially or completely covering the inner surface of the prosthesis.

[0073] The impregnation and/or coating, in particular the coating, is preferably structured and not smooth, in particular not film-like.

[0074] The impregnation and/or coating, in particular the coating, particularly preferably has fibrous structures. The fibrous structures can have a diameter of 0.1 to 10 µm, in particular 0.4 to 5 µm, preferably 1.5 to 3 µm.

[0075] It is also preferable if the vascular prosthesis comprises the at least one sealing material in a proportion of 10 to 60% by weight, in particular 20 to 50% by weight, preferably 25 to 40% by weight, relative to the total weight of the vascular prosthesis.

[0076] If the vascular prosthesis only has an impregnation within the meaning of the present invention, the vascular prosthesis can then comprise the at least one sealing material in a proportion of 1 to 25% by weight, in particular 5 to 20% by weight, preferably 10 to 15% by weight, relative to the total weight of the vascular prosthesis.

[0077] By contrast, if the vascular prosthesis only has a coating within the meaning of the present invention, the vascular prosthesis can then comprise the at least one sealing material in a proportion of 9 to 35% by weight, in particular 15 to 30% by weight, preferably 15 to 25% by weight, relative to the total weight of the vascular prosthesis.

[0078] As regards further features and advantages, in particular of the impregnation, of the coating and/or of the at least one sealing material, reference is made expressly to the statements made in the context of the first aspect of the invention.

[0079] In an advantageous embodiment, the vascular prosthesis has a water permeability of between 0 and 20 ml/cm^{2}min, in particular of between 0 and 10 ml/cm^{2}min, preferably of between 0 and 5 ml/cm^{2}min.

[0080] In a further embodiment, the coating has a thickness of 5 to 750 µm, in particular 10 to 300 µm, preferably 15 to 100 µm.

[0081] The impregnation and/or the coating consist, in possible embodiments, of the at least one sealing material.

[0082] According to the invention, however, it can be advantageous if the vascular prosthesis, in particular the impregnation and/or coating, has additives, in particular pharmaceutical compositions or medicaments, biologically active compounds, nanoparticles or the like.

[0083] Preferred additives can be chosen from the group consisting of cellular growth factors, cellular differentiation factors, cellular adhesion factors, cellular recruitment factors, antimicrobial substances, in particular antimicrobial metals such as silver, disinfecting substances, anti-inflammatory substances, antithrombogenic substances or anticoagulants, X-ray contrast media and combinations thereof.

[0084] The vascular prosthesis is preferably produced or formed as a textile vascular prosthesis, in particular a woven or knitted vascular prosthesis.

[0085] In a further embodiment, the wall of the vascular prosthesis is formed from a material, in particular polymer, which is preferably chosen from the group consisting of polyester, polyamide, polyethylene, polypropylene, polyvinylidene difluoride, polyhexa-fluoropropylene, polytetrafluoropropylene, polytetra-fluoroethylene, in particular expanded polytetra-fluoroethylene (ePTFE), copolymers thereof, and combinations, in particular blends, thereof.

[0086] Preferred polyesters are chosen from the group consisting of polyethylene terephthalate (PET), polypropylene terephthalate (PPT), polybutylene terephthalate (PBT) and combinations, in particular blends, thereof. Polyethylene terephthalate (PET) is particularly preferred on account of its good biocompatibility and its excellent long-term stability.

[0087] Preferred materials for the wall of a textile vascular prosthesis are non-resorbable polyesters, in particular polyethylene terephthalate.

[0088] In a further embodiment, the vascular prosthesis has an internal diameter of between 2 and 50 mm, in particular 4 and 40 mm.

[0089] Further features and advantages of the present invention will become clear from the following description of preferred embodiments in the form of examples, figures, the associated figure descriptions, and the dependent claims. Here, the features can in each case be implemented singly or in combination with each other.

[0090] In the figures:

[0091] Fig. 1 shows a cross section of the wall of a vascular prosthesis according to the invention with an impregnation in the prosthesis wall,

[0092] Fig. 2 shows a cross section of the wall of a vascular prosthesis according to the invention with a coating on the outer surface of the prosthesis,

[0093] Fig. 3 shows a cross section of the wall of a vascular prosthesis according to the invention with an impregnation in the prosthesis wall and a coating on the outer surface of the prosthesis,

[0094] Fig. 4 shows a graph indicating the results of softness measurements carried out on vascular prostheses.

[0095] Figure descriptions

[0096] Fig. 1 shows the scanning electron microscope image of a PET vascular prosthesis with an impregnation of a tetrapolymer, composed of 40 mol% L-lactide, 30 mol% ε-caprolactone, 26 mol% trimethylene carbonate and 4 mol% glycolide, in the prosthesis wall. To generate the polymer impregnation, the outer surface of the prosthesis was sprayed with an acetone solution containing the tetrapolymer (12.6% w/w) at a pressure of 0.1 bar, wherein one spray cycle was sufficient to generate a sealing impregnation. The prosthesis comprised the polymer in a proportion of ca. 11.5% by weight, relative to the total weight of the prosthesis.

[0097] Fig. 2 shows the scanning electron microscope image of a PET vascular prosthesis, of which the outer surface is coated with a tetrapolymer composed of 40 mol% L-lactide, 30 mol% ε-caprolactone, 26 mol% trimethylene carbonate and 4 mol% glycolide. To generate the polymer coating, the vascular prosthesis was sprayed with an acetone

solution containing the tetrapolymer (12.6% w/w) at a pressure of 7.5 bar. A total of 6 spray cycles were performed. The prosthesis comprised the coating polymer in a proportion of ca. 31.3% by weight, relative to the total weight of the prosthesis.

[0098] Fig. 3 shows the scanning electron microscope image of a PET prosthesis with an impregnation in the prosthesis wall and a coating on the outer surface of the prosthesis. The impregnation and the coating are formed from the same polymer, namely a tetrapolymer composed of 40 mol% L-lactide, 30 mol% ε-caprolactone, 26 mol% trimethylene carbonate and 4 mol% glycolide.

[0099] To form the impregnation, the vascular prosthesis was sprayed, in one spray cycle, with an acetone solution containing the tetrapolymer (12.6% w/w) at a pressure of 0.1 bar. To generate the coating on the outer surface, the prosthesis was sprayed, in 6 cycles and at a pressure of 7.5 bar, with an acetone solution containing the polymer (12.6% w/w).

[0100] Overall, the prosthesis comprised the polymer in a proportion of ca. 29.9% by weight.

[0101] **Examples**

[0102] 1. Softness measurement of vascular prostheses

[0103] The results of the softness measurements are shown in graph form in Figure 4. The ordinate indicates the deformation of the external diameters of the tested prostheses in % under the effect of a force of 1 Newton.

[0104] The softness measurements were carried out using a woven double-velour polyester vascular prosthesis (polyethylene terephthalate, PET; left-hand bar in Figure 4) coated with gelatin in a conventional immersion process, a woven double-velour polyester prosthesis (PET; middle bar in Figure 4) coated with a tetrapolymer of 40 mol% L-lactide, 30 mol% ε-caprolactone, 26 mol% trimethylene carbonate and 4 mol% glycolide in a conventional immersion process, and a double-velour polyester prosthesis (PET; right-hand bar in Figure 4) coated with a tetrapolymer of 40 mol% L-lactide, 30 mol% ε-caprolactone, 26 mol% trimethylene carbonate and 4 mol% glycolide in a method according to the invention.

[0105] To coat the prostheses by means of the immersion process, the prostheses were immersed in an acetone solution containing the coating polymer, having a proportion of the coating polymer of 12.6% by weight, relative to the total weight of the solution.

[0106] To produce the prosthesis coated according to the invention, an acetone solution containing the coating polymer, with a proportion of the coating polymer of 12.6% by weight, relative to the total weight of the solution, was sprayed onto the outer surface of an uncoated polyester prosthesis at a spray pressure of ca. 7.5 bar.

[0107] All of the vascular prostheses had an external diameter of ca. 8 mm.

[0108] In order to measure the softness, the vascular prostheses were fixed horizontally on a sample plate. A sample hammer having a bottom surface area of 10 mm x 50 mm was then moved vertically downwards at a speed of 10 mm/min in the direction of the prostheses and pressed at a defined force of 1 N onto the prostheses. The deformation of the external diameter of the prostheses was measured in mm.

[0109] The measurement results obtained are shown in graph form in Fig. 4.

[0110] The measurement results shown in graph form in Figure 4 illustrate that the external diameter of the prosthesis coated according to the invention deformed to a significantly greater extent, under the effect of the force of 1 N, than in the conventionally coated vascular prostheses. In other words, the prosthesis coated according to the invention is significantly softer than the conventionally coated prostheses.

[0111] Table 1 below contains some of the parameters used to characterize some of the prostheses used in the preceding series of tests:

Prosthesis: (Coating method)	Double-velour prosthesis (Immersion process)	Double-velour prosthesis (High-pressure spraying method)
Prosthesis diameter:	8 mm	8 mm
Coating content:	33.2%	34.9%

Blood leak-tightness:	present	present

[0112] Table 1: Characterization of some vascular prostheses

[0113] Table 1 shows that the vascular prosthesis according to the invention also has the blood leaktightness required for vascular prostheses.

Claims

1. Method for producing a vascular prosthesis, in which method a vascular prosthesis with an inner surface and outer surface and a wall is sprayed with a liquid containing at least one sealing material, characterized in that the liquid is sprayed onto the outer surface of the prosthesis at a pressure of 0.01 to 1.5 bar in order to generate a sealing impregnation in the prosthesis wall, and/or is sprayed onto the outer surface of the prosthesis at a pressure of 5.0 to 50 bar in order to generate a sealing coating on the outer surface of the prosthesis.

2. Method according to claim 1, characterized in that the liquid for generating the impregnation is sprayed onto the outer surface of the prosthesis at a pressure of 0.02 to 1.5 bar, in particular 0.05 to 0.8 bar, preferably 0.1 to 0.6 bar.

3. Method according to claim 1 or 2, characterized in that the liquid for generating the coating is sprayed onto the outer surface of the prosthesis at a pressure of 5 to 20 bar, in particular 5 to 10 bar, preferably 6 to 9 bar.

4. Method according to one of the preceding claims, characterized in that the outer surface of the prosthesis is sprayed with a liquid that contains the at least one sealing material in a proportion of 1 to 50% by weight, in particular 5 to 25% by weight, preferably 7 to 15% by weight, relative to the total weight of the liquid.

5. Method according to one of the preceding claims, characterized in that, in order to generate the impregnation, the same at least one sealing material is used as for generating the coating.

6. Method according to one of the preceding claims, characterized in that the at least one sealing material is resorbable.

7. Method according to one of the preceding claims, characterized in that the at least one sealing material is a film-forming polymer, in particular a biopolymer.

8. Method according to one of the preceding claims, characterized in that the at least one sealing material is of biological origin, in particular of animal origin, preferably chosen from the group consisting of collagen, gelatin, albumin and combinations thereof.

9. Method according to one of claims 1 to 7, characterized in that the at least one sealing material is of synthetic origin, preferably chosen from the group consisting of polyglycolide, polylactide, poly-ε-caprolactone, polytrimethylene carbonate, poly-para-dioxanone, poly-3-hydroxybutyrate, poly-4-hydroxybutyrate, copolymers thereof and combinations thereof.

10. Method according to one of claims 1 to 7 or 9, characterized in that the at least one sealing material is a three-armed polyester having terminal hydroxyl groups from hydroxy acids that are polymerized onto a central trifunctional hydroxy compound, the three arms being tetrapolymers of lactide, ε-caprolactone, trimethylene carbonate, and glycolide.

11. Method according to one of the preceding claims, characterized in that the prosthesis undergoes pleating only before the liquid is applied.

12. Vascular prosthesis, produced or producible by a method according to one of the preceding claims.

13. Vascular prosthesis with an impregnation comprising at least one sealing material in the prosthesis wall and/or with a coating comprising at least one sealing material on the outer surface of the prosthesis, characterized in that the prosthesis, when subjected to a force of 1 N acting perpendicularly with respect to the outer surface of the prosthesis, is deformed in such a way that the external diameter of the prosthesis decreases, in the direction of the acting force, by 60 to 100% in relation to the original external diameter.

14. Vascular prosthesis according to claim 12 or 13, characterized in that the impregnation is formed in the wall of the prosthesis to a depth of 1 to 100%, in particular 50 to 100%, preferably 80 to 100%, relative to the wall thickness of the prosthesis.

15. Vascular prosthesis according to one of the claims 12 to 14, characterized in that the impregnation in the prosthesis wall acts as an adhesion bed or substrate for the coating on the outer surface of the prosthesis.

16. Vascular prosthesis according to one of claims 12 to 15, characterized in that the coating on the outer surface of the prosthesis is structured and not smooth, in particular not film-like.

17. Vascular prosthesis according to one of claims 12 to 16, characterized in that the coating on the outer surface of the prosthesis has fibrous structures.

18. Vascular prosthesis according to claim 17, characterized in that the fibrous structures have a diameter of 0.1 to 10 µm, in particular of 0.4 to 5 µm, preferably of 1.5 to 3 µm.

19. Vascular prosthesis according to one of claims 12 to 18, characterized in that the vascular prosthesis comprises the at least one

sealing material in a proportion of 10 to 60% by weight, in particular 20 to 50% by weight, preferably 25 to 40% by weight, relative to the total weight of the vascular prosthesis.

20. Vascular prosthesis according to one of claims 12 to 19, characterized in that the prosthesis has a water permeability of between 0 and 20 ml/cm^{2}min, in particular of between 0 and 10 ml/cm^{2}min, preferably of between 0 and 5 ml/cm^{2}min.

21. Vascular prosthesis according to one of claims 12 to 20, characterized in that the coating on the outer surface of the prosthesis has a thickness of 5 to 750 µm, in particular of 10 to 300 µm, preferably of 15 to 100 µm.

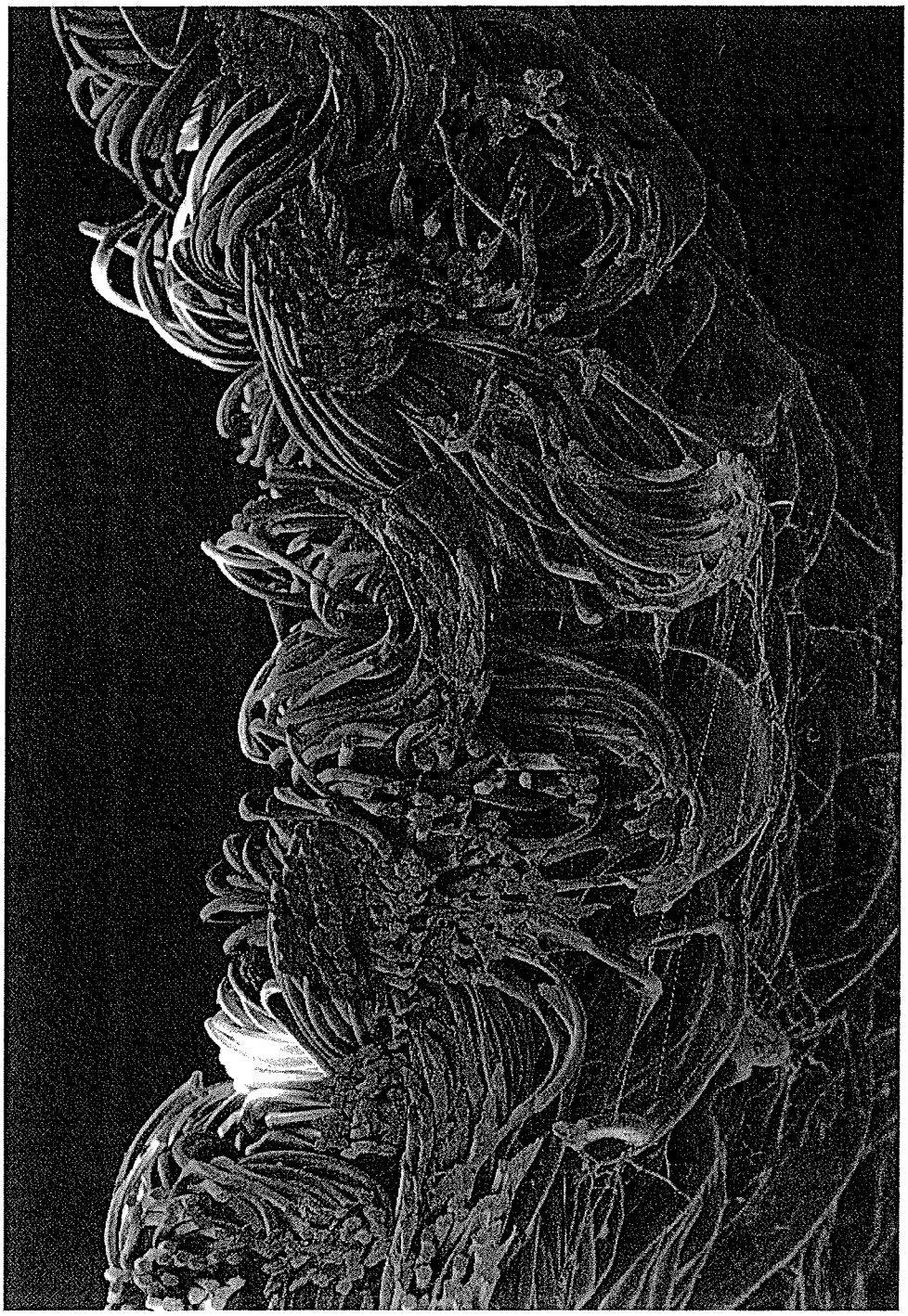


Fig.1

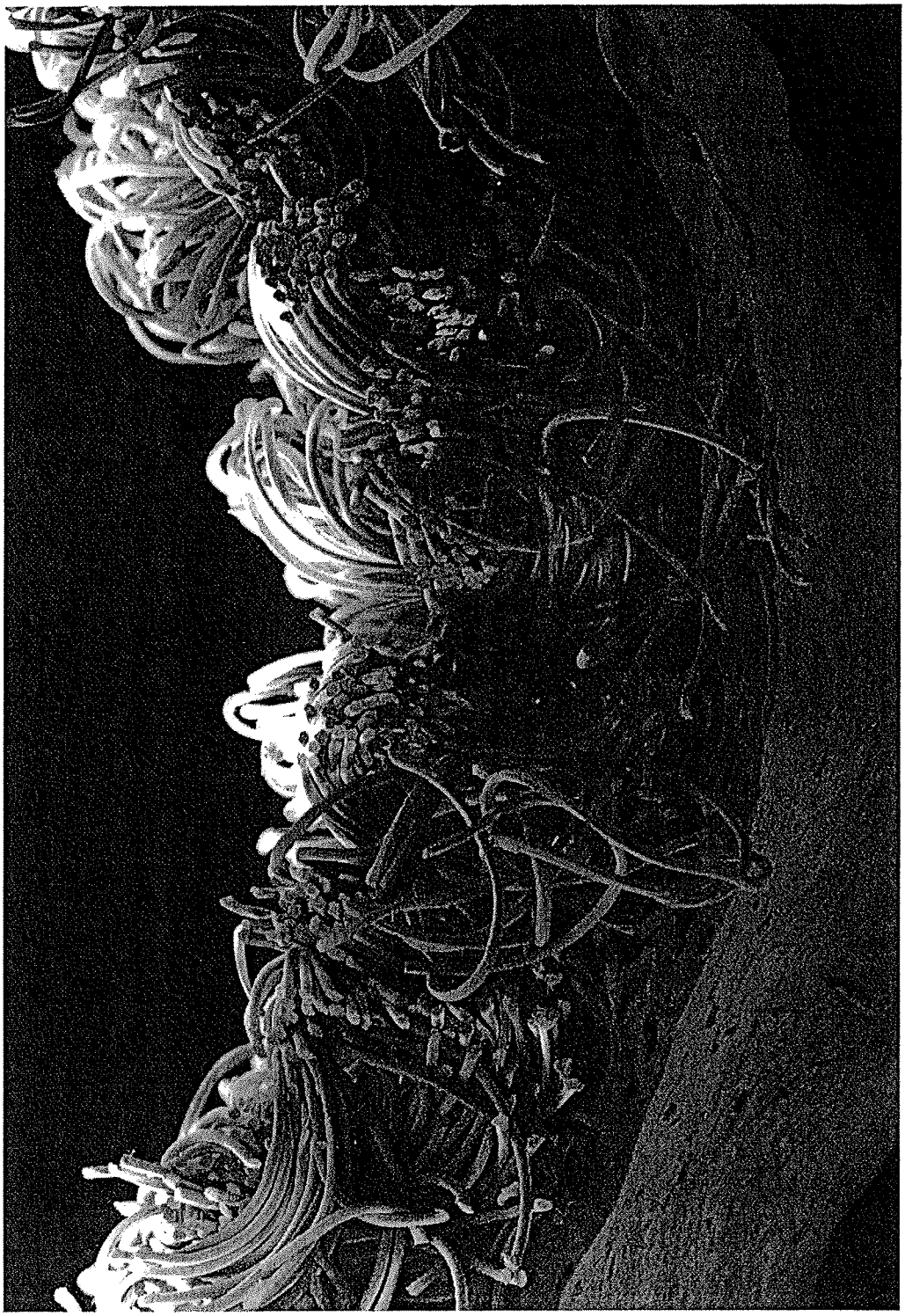


Fig.2

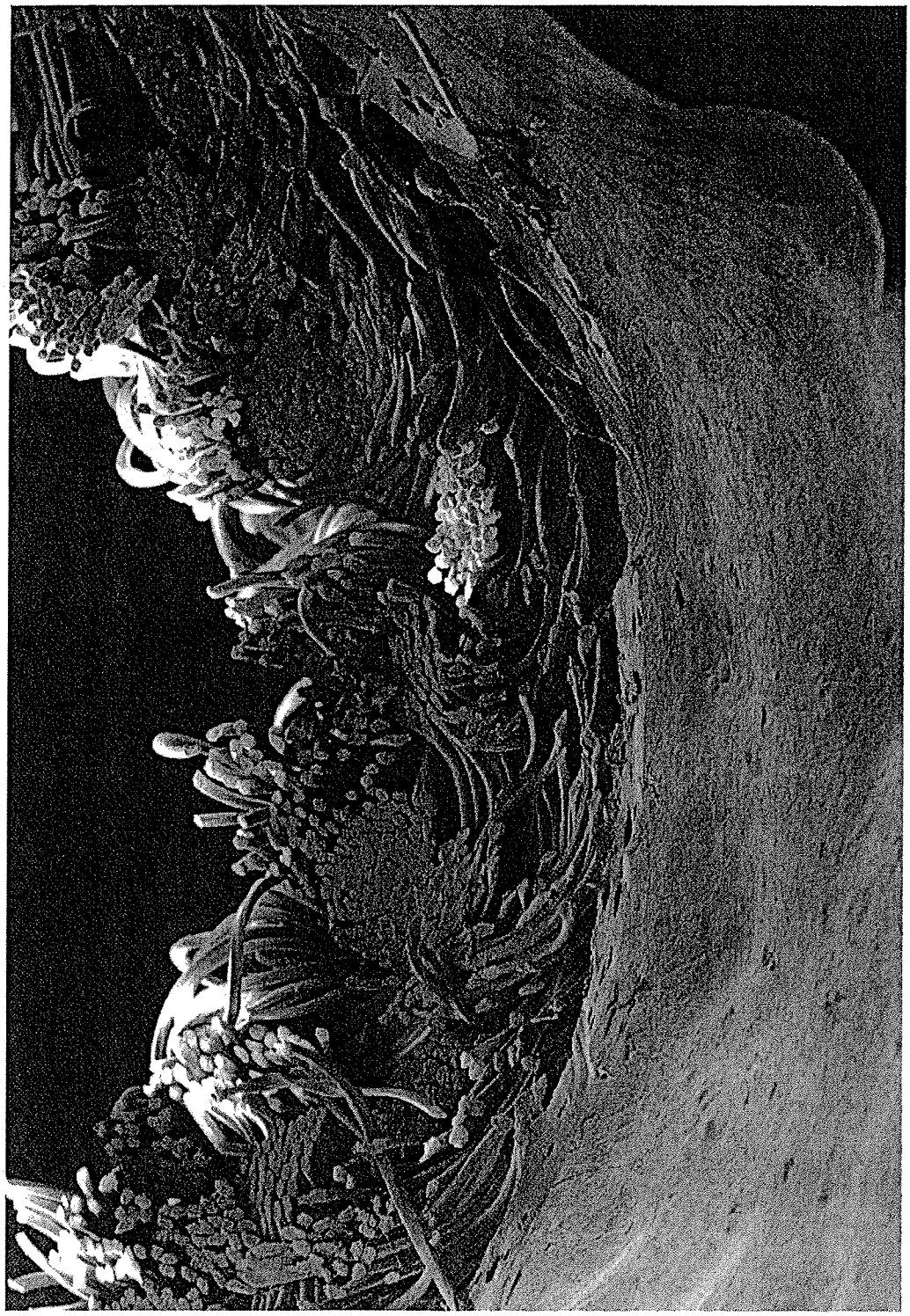
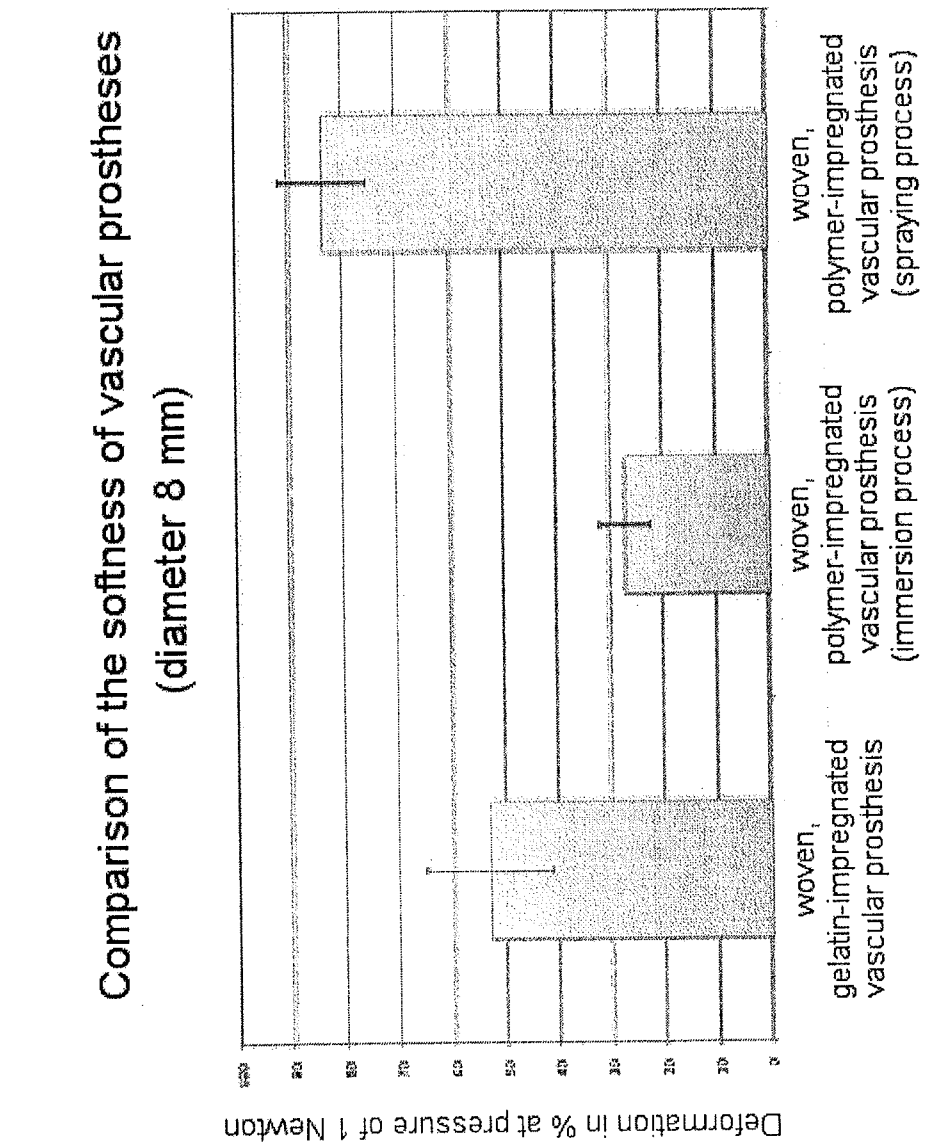


Fig.3

Fig.4


Comparison of the softness of vascular prostheses
(diameter 8 mm)
Deformation in % at pressure of 1 Newton
woven, gelatin-impregnated vascular prosthesis
woven, polymer-impregnated vascular prosthesis (immersion process)
woven, polymer-impregnated vascular prosthesis (spraying process)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2013/051364

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 13(completely); 14-21(partially)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/051364

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L27/34 A61L27/50 B05D1/00
ADD.

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)
B05D A61L

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 practicable, 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	WO 2011/012178 A2 (AESCULAP WERKE AG [DE]; GOLDMANN HELMUT [DE]; MERCKLE CHRISTOF [DE]; P) 3 February 2011 (2011-02-03) cited in the application	1,2,4,5, 7,9,12, 14-18,21
Y	page 1, paragraph 3 page 2, paragraph 2-4 page 3, paragraph 3 page 5, paragraph 3 page 6, paragraphs 2,3 page 8, paragraph 2-3 page 15 page 16, paragraph 5 page 17, paragraph 2 example 1	1-12, 14-21

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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 :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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
21 May 2013	31/05/2013

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, Fax: (+31-70) 340-3016	Sierra Gonzalez, M

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/051364

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2009/234442 A1 (GOLDMANN HELMUT [DE] ET AL) 17 September 2009 (2009-09-17) cited in the application paragraphs [0003], [0007], [0022], [0023], [0029] - [0032], [0035], [0036]; claim 1 -----	1-12, 14-21
A	US 2004/109892 A1 (SHALABY SHALABY W [US]) 10 June 2004 (2004-06-10) the whole document -----	1-12, 14-21

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2013/051364

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011012178 A2	03-02-2011	DE 102009037134 A1	03-02-2011
		EP 2459241 A2	06-06-2012
		US 2012130483 A1	24-05-2012
		WO 2011012178 A2	03-02-2011
US 2009234442 A1	17-09-2009	DE 102006053752 A1	15-05-2008
		DE 202007019314 U1	04-10-2011
		EP 2089074 A2	19-08-2009
		ES 2389738 T3	31-10-2012
		JP 2010508923 A	25-03-2010
		US 2009234442 A1	17-09-2009
		WO 2008058660 A2	22-05-2008
US 2004109892 A1	10-06-2004	NONE	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12(completely); 14-21(partially)

   Method for producing a vascular prosthesis and vascular prosthesis produced by said method

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2. claims: 13(completely); 14-21(partially)

   Vascular prosthesis characterized by having a particular reduced diameter after the application of a force of 1 N.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 13(completely); 14-21(partially)

1 The European Patent Office acting as ISA considers that the present application fails to such an extent to comply with the requirements of the PCT that is impossible to carry out a meaningful search regarding the state of the art (PCT Guidelines 9.34 and 9,35).
2 The requirements of the PCT referred to in the previous paragraph are the requirements of Article 5 PCT concerning lack of disclosure but also the requirements of Rule 13.1 and 13.2 PCT concerning lack of unity. The reasons behind this objection can be seen under Item IV of the Written Opinion of International Searching Authority.
3 In what the requirements of Article 5 PCT are concerned, independent claim 13 refers to a impregnated or coated vascular prosthesis defined solely by a parameter, namely by the property that"when the prosthesis is subjected to a force of 1 N acting perpendicularly with respect to the outer surface of the prosthesis, said prosthesis is deformed in such a way that the external diameter of the prosthesis decreases, in the direction of the acting force, by 60 to 100% in relation to the original external diameter". 3.1 Insofar as the parameters are concerned, claims 13-21 and the description seem not to meet the requirements of Article 5 PCT . In order to be able to carry out the alleged invention of the present application, one skilled in the art will have to perform extensive tests to find out whether or not the given vascular prosthesis have the particular reduced diameter after the application of a force of 1 N. The skilled person has to find from an almost unlimited number of vascular prosthesis those which meet the conditions of this particular force test. Furthermore, the skilled person would not have adequate information from either the present description or from common general knowledge which would lead towards success through the evaluation of initial failures. Description refers to any sealing material, polymeric or not, of biological origin or not, of synthetic origin or not, as the only originally limiting selecting features. This trial and error procedure seems to place an undue burden on the skilled person and requires a research project on its own. Accordingly, the subject-matter of claim 13 is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. The requirements of Article 5 PCT are thus not fulfilled.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.