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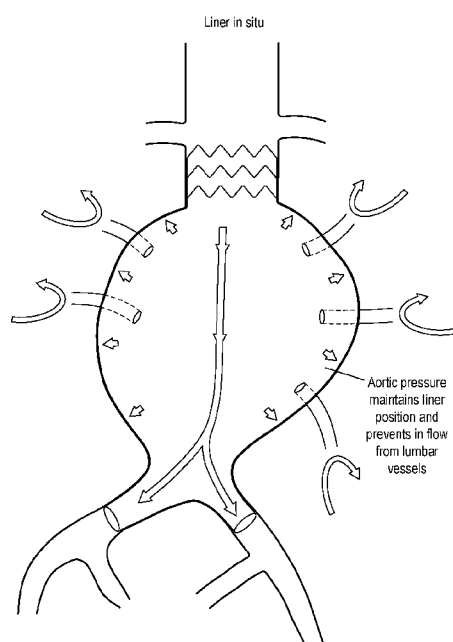


FIG. 4

(57) Abstract: Methods for manufacturing a patient-specific endovas-
cular device comprise creating a 3D model based on spatial dimen-
sions relating to a section of a blood vessel and manufacturing the en-
dovascular device using the 3D model to form a liner. In use the en-
dovascular devices provide a liner which forms a seal against the inner
blood vessel wall or the edge of the blood flow lumen. Correspond-
ing patient-specific endovascular devices and methods for treating a
patient by inserting an endovascular device are also provided.



PATIENT-SPECIFIC ENDOVASCULAR DEVICES

TECHNICAL FIELD

- 5 The present invention relates to customised patient-specific endovascular devices for endovascular repair, methods for manufacturing an endovascular device and methods for treating a patient by inserting an endovascular device.

BACKGROUND

- 10 An abdominal aortic aneurysm (AAA) is a dilatation of the aorta within the abdomen. Abdominal aortic aneurysms (AAA) are a life threatening condition, the incidence of which increases with age. In the UK 8,000 people a year die from ruptured AAA. They affect 2% of men over 70. Open surgical repair was the mainstay of treatment but it is associated with a 3-4% mortality and significant morbidity. Minimally invasive options now exist but have
15 their own limitations

- Although minimally invasive endovascular aneurysm repair (EVAR) reduces mortality and operative risks, the technology as it stands still has a 20% re-intervention rate. Repeat interventions have an economic cost. The 5 year follow up costs for patients with a sealed
20 AAA after EVAR are £2,413, compared to £20,852 for those patients requiring a re-intervention.

- With current EVAR technology a major source of post-operative problems, concern (for physicians and patients) and economic costs are type 2 endoleaks. EVAR relies upon the
25 EVAR stent graft directly opposing the aortic wall, to exclude the aortic sac from arterial pressure. Any flow into the aneurysm sac after EVAR is defined as an endoleak (see Figures 1-3). The stent graft creates a seal with the two common iliac arteries and in the infra-renal aorta, but between this it is not in contact with the dilated aneurysm wall. There are other vessels arising from the abdominal aorta, the lumbar arteries (usually 2 pairs) and
30 the larger inferior mesenteric artery (IMA). Once the stent graft is placed, these vessels receive retrograde flow via a collateral network with blood now passing into the aortic sac (the reverse of the usual situation). This causes continued aneurysm expansion and potentially rupture, despite the presence of the stent graft (see Figure 2).

- 35 Increasingly over the last 2 to 3 years, there is recognition of the fact that whilst type 2 leaks rarely cause AAA rupture alone, they do lead to AAA sac expansion with subsequent aortic neck or iliac dilatation and a sudden type 1A or 1B leak (see Figure 3). This sudden sac re-pressurisation places the patient at high risk of rupture. As EVAR solutions are often modular in nature, and held together simply by the radial force one stent section exerts on
40 another, it is possible for the components to separate from one another and re-pressurise the AAA sac again risking rupture. This is called a type 3 endoleak (see Figure 3).

Nearly all EVAR AAA solutions have focused on simply bridging between healthy blood vessel above and below the AAA, via an endovascular route. However, various alternative approaches are now known.

5 A first approach is provided by devices intended to line the vessel walls of an aneurysm (see WO2004/037116 A2, WO2007/096183 A1, WO2010/0127040 A1 and US2014/0194973 A1).

10 A second approach is the production of a customized device based on the production of a rigid scaffold (see US2010/0016947 and US2015/0209162 A1).

15 A third approach is provided by the Endologix Nellix[®] (Endologix Inc, Irvine, USA) system. This system has a central balloon expandable stent running through the centre of an expandable endobag. These are utilised as a paired device with one stent being delivered into the AAA via the left and right common iliac arteries. The stents here act only as a conduit for the delivery of blood from above the sealing zone to the iliac vessels. The AAA is sealed off by the filling of the endobags with a liquid polymer that sets with a rubber like consistency.

20 There are three main issues with the Nellix[®] system. The first issue is that in order to create a seal, the aortic wall must be pressurised to above normal systolic pressure. This process risks rupturing the AAA because of the pressure used to fill the bags, and this can be a fatal event. As there is often concern about not over-pressurising the bags, physicians can under fill the endobags leaving a non-sealed AAA.

25 The second issue that the Nellix[®] system faces is how to deal with an increase in the size of the aortic neck (proximal sealing zone). As the seal in the Nellix[®] system is created by a rigid structure (i.e. the filled endobags), even a tiny increase in aortic neck diameter leads to a loss of seal and then a dangerous type 1A endoleak.

30 The third problem is that when a proximal endoleak does arise, there are very limited (if any) options to truly reseal the AAA.

35 DESCRIPTION

The invention provides customised patient-specific endovascular devices, methods for manufacturing an endovascular device and methods for treating a patient by inserting an endovascular device of the invention. The endovascular devices of the invention may be used in minimally invasive endovascular repair e.g. in endovascular aortic repair (EVAR).
40 In use the endovascular devices of the invention provide a liner which forms a seal against the inner blood vessel wall (e.g. the inner aortic wall) or the edge of the blood flow lumen (e.g. the edge of the aortic blood flow lumen). The seal may be created by the expansion of the liner of the endovascular device in a blood vessel (e.g. the aorta) by blood pressure (e.g. arterial blood pressure). The seal created by the endovascular device of the invention

may help to prevent endoleaks by compressing the liner of the device against the origin of joining blood vessels. With no flow in the joining blood vessels they may thrombose off permanently.

5 The invention provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first (open-ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) modifying the spatial dimensions of a section of a
10 blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the section of the blood vessel; (b) creating a 3D model based on the modified dimensions; and (c) manufacturing the endovascular device using the 3D model to form the liner.

15 The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first (open-ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) measuring the spatial dimensions of a
20 section of a blood vessel; (b) modifying the spatial dimensions of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the section of the blood vessel; (c) creating a 3D model based on the modified dimensions; and (d) manufacturing the endovascular device using the 3D model to form the liner.

25 The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first (open-ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve
30 portion, and wherein the method comprises: (a) creating a 3D model based on the spatial dimensions of the blood flow lumen of a section of a blood vessel; and (b) manufacturing the endovascular device using the 3D model to form the liner.

The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first (open-
35 ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel; (b) creating a 3D model based on the
40 spatial dimensions; and (c) manufacturing the endovascular device using the 3D model to form the liner.

The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first (open-

ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) modifying the spatial dimensions of the blood flow lumen of a section of a blood vessel to create modified dimensions, wherein the
5 modifying comprises increasing the cross-sectional dimensions of the blood flow lumen; (b) creating a 3D model based on the modified dimensions; and (c) manufacturing the endovascular device using the 3D model to form the liner.

The invention further provides a method for manufacturing an endovascular device,
10 wherein the device comprises a liner that defines a lumen, the liner having a first (open-ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel; (b) modifying the spatial dimensions of the
15 blood flow lumen of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen; (c) creating a 3D model based on the modified dimensions; and (d) manufacturing the endovascular device using the 3D model to form the liner.

20 Preferably, the spatial dimensions that are modified, and optionally measured, are the spatial dimensions of the blood flow lumen. The blood flow lumen may be defined as the space occupied within a blood vessel by flowing blood (e.g. excluding the space occupied by thrombus).

25 Alternatively, the spatial dimensions that are modified, and optionally measured, may be the spatial dimensions of the blood vessel lumen.

Preferably, the spatial dimensions that are modified, and optionally measured, are cross-sectional dimensions. The cross-sectional dimensions corresponding to the body portion
30 may be greater than the cross-sectional dimensions corresponding to the terminal sleeve portions.

The step of measuring may comprise measuring the spatial dimensions by CT, MRI, ultrasound or 3D ultrasound.
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The step of modifying the spatial dimensions may comprise uniformly increasing the cross-sectional dimensions of the blood flow lumen along the length of the section of the blood vessel. The step of modifying the spatial dimensions may not comprise increasing the length of the blood flow lumen of the section of the blood vessel.
40

The step of modifying the spatial dimensions may comprise uniformly increasing the cross-sectional dimensions of the blood vessel lumen along the length of the section of the blood vessel. The step of modifying the spatial dimensions may not comprise increasing the length of the blood vessel lumen of the section of the blood vessel.

5 The step of modifying the spatial dimensions may comprise increasing the spatial dimensions only in the antero-posterior (front-back) and side-side direction, and not in a cranio-caudal (up-down) direction i.e. the spatial dimensions are increased only in the x-y planes and not in the z plane.

10 The step of modifying the spatial dimensions may comprise increasing the cross-sectional dimensions by at least 1%, at least 2%, at least 3%, at least 4% or at least 5%. Preferably, the cross-sectional dimensions are increased by at least 3%.

The step of modifying the spatial dimensions may comprise increasing the cross-sectional dimensions by 1-15%, 1-10%, 1-9%, 2-8%, 3-7%, 4-6% or 5%. Preferably, the cross-sectional dimensions are increased by 3-7%.

15 The step of creating a 3D model based on the modified dimensions may comprise 3D printing or additive manufacturing. The 3D printing may comprise extrusion deposition (e.g. fused deposition modelling (FDM) or fused filament fabrication (FFF)), photopolymerization (e.g. stereolithography (SLA) or digital light processing (DLP)), selective fusion of materials on a granular bed (e.g. powder bed and inkjet head 3D printing (3DP), electron-beam melting (EBM), selective laser melting (SLM), selective heat sintering (SHS), selective laser sintering (SLS) or direct metal laser sintering (DMLS)), lamination (e.g. laminated object manufacturing (LOM)), a powder fed process (e.g. directed energy deposition) or a metal wire process (e.g. electron beam freeform fabrication (EBF)). Preferably, the 3D printing comprises stereolithography.

25 The step of manufacturing the endovascular device using the 3D model to form the liner may result in a liner having spatial dimensions that are within 4%, 3%, 2%, 1%, 0.5% or 0.1% of the modified spatial dimensions. Preferably the liner is manufactured with spatial dimensions that are within 1% of the modified spatial dimensions.

30 The step of manufacturing the device using the 3D model may comprise applying a liner material to the 3D model to produce a liner assembly. For example, the liner may be sprayed onto the 3D model, the liner may be applied by wrapping a layer (or layers) of a liner material onto the 3D model or the liner may be applied to the 3D model by vacuum sealing. Preferably, the liner material is PTFE tape.

40 The 3D model may be solid or hollow. The 3D model may be created having a central void and/or may comprise a crushable material e.g. a material having a porous, sponge or honeycomb structure. These properties may facilitate the chemical and/or physical removal of the 3D model from the liner once formed.

The 3D model may be perforated. In this case, the liner material may be applied to the 3D model by generating a negative pressure inside the 3D model thereby drawing the liner material onto the outer surface of the 3D model.

The 3D model may comprise or be constructed from wax, plastic (e.g. polylactic acid (PLA), acrylonitrile butadiene styrene (ABS), polyvinyl alcohol plastic (PVA) and/or nylon), resin (e.g. epoxy resin), plaster and/or a photopolymer (e.g. wax, plastic and/or resin).
5 Preferably, the 3D model comprises or is constructed from wax.

The liner material may be applied to the 3D model in layers.

10 The step of manufacturing the device using the 3D model may further comprise heating the liner assembly to a temperature sufficient to anneal the layers of the material to form a single layer of material.

15 The 3D model may be constructed of a material that can be removed from the liner once formed. The removal may be achieved by heating (i.e. melting of the 3D model), chemical means (e.g. dissolving the 3D model), by mechanical means, by sound waves or by radiation.

20 For example the 3D model may be removed through the use of robotic tooling. In this process, a robotic arm may be guided by the modified spatial dimensions used to create the 3D model in the first place. A quantity of the 3D model may be removed sufficient to allow mechanical force, applied to the liner and 3D model, to crush the remaining shell of the 3D model enabling it to be removed from the liner.

25 The step of manufacturing the device using the 3D model may comprise producing a solid block containing an impression of one half of the section of the blood vessel (e.g. an AAA) (split vertically), and then a second block containing an impression of the other side. These complimentary blocks may be used to create a complete 3D model of the flow lumen of the blood vessel through use of casting techniques. The 3D model so created may be solid or hollow. Once the liner material has been applied to the 3D model, the 3D model may be
30 mechanically removed, or chemically softened or dissolved.

The step of manufacturing the device using the 3D model may comprise blow moulding the liner material directly into a hollow 3D model to form a liner.

35 The step of manufacturing the endovascular device using the 3D model may comprise: (a) applying a coating to the 3D model; (b) applying a liner material to the coating to produce a liner assembly; and (c) forming the liner from the liner material.

40 The method may comprise: (a) applying layers of the liner material to the coating to produce the liner assembly; and (b) heating the liner assembly to anneal the layers of the material to form a single layer of liner material.

The coating may be applied to the 3D model by electroplating or electroforming. The coating may comprise a metal (e.g. copper or nickel) or ceramic (or ceramic-like material).

The 3D model may have a melting temperature lower than the temperature used to anneal the layers of the liner material to form a single layer.

- 5 The step of heating the liner assembly may further comprise melting the 3D model removing it from the liner assembly.

10 The method may comprise: (a) applying a coating to the 3D model to produce a perforated coating; (b) removing the 3D model from the coating by heating; and (c) applying a liner material to the coating to produce a liner assembly, wherein the liner material is applied to the coating by generating a negative pressure inside the heating resistant coating thereby drawing the liner material onto the outer surface of the coating.

15 The 3D model may be constructed of a material that can be removed from the coating once formed. The removal may be achieved by heating (i.e. melting of the 3D model), chemical means (e.g. dissolving the 3D model), mechanical means (e.g. robotic tooling), sound waves or by radiation.

20 The step of applying a liner material to the coating to produce a liner assembly may comprise heating the liner assembly (to anneal the liner material) while a negative pressure (i.e. a vacuum) is applied inside the coating.

25 The step of applying a liner material to the coating to produce a liner assembly may comprise applying either a single or multiple layers (or sheets) of a liner material to the coating.

30 The perforations (holes) in the coating may be formed by drilling (after removal of the 3D model). Alternatively, if the coating is applied to the 3D model by electroforming, fine extrusions emanating from the surface of the 3D model may not be coated leaving small voids in the surface of the coating when the 3D model is removed.

35 The method may comprise: (a) applying layers of a liner material to the coating to produce the liner assembly; (b) heating the liner assembly to a first temperature, wherein the 3D model melts and is removed from the liner assembly; and (c) heating the liner assembly to a second temperature sufficient to anneal the layers of the liner material to form a single layer of liner material.

40 The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) creating a 3D model based on the spatial dimensions of a section of a blood vessel; (b) applying a coating to the 3D model; (c) applying a liner material to the coating to produce a liner assembly; and (d) forming the liner from the liner material.

5 The invention further provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) measuring the spatial dimensions of a section of a blood vessel; (b) creating a 3D model based on the spatial dimensions of the section of a blood vessel; (c) applying a coating to the 3D model; (c) applying a liner material to the coating to produce a liner assembly; and (d) forming the liner from the liner material.

10

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20 The invention provides a method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises: (a) measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel; (b) creating a 3D model based on the spatial dimensions of the blood flow lumen of a section of a blood vessel; (c) applying a coating to the 3D model; (c) applying a liner material to the coating to produce a liner assembly; and (d) forming the liner from the liner material.

25 30 The step of measuring may comprise measuring the spatial dimensions by CT, MRI, ultrasound or 3D ultrasound.

35 The method may comprise: (a) applying layers of the liner material to the coating to produce the liner assembly; and (b) heating the liner assembly to anneal the layers of the material to form a single layer of liner material.

The 3D model may have a melting temperature lower than the temperature used to anneal the layers of the liner material to form a single layer.

40 The step of heating the liner assembly may further comprise melting the 3D model removing it from the liner assembly.

The method may comprise: (a) applying a coating to the 3D model to produce a perforated coating; (b) removing the 3D model from the coating by heating; and (c) applying a liner

material to the coating to produce a liner assembly, wherein the liner material is applied to the coating by generating a negative pressure inside the heating resistant coating thereby drawing the liner material onto the outer surface of the coating.

- 5 The method may comprise: (a) applying layers of a liner material to the coating to produce the liner assembly; (b) heating the liner assembly to a first temperature, wherein the 3D model melts and is removed from the liner assembly; and (c) heating the liner assembly to a second temperature sufficient to anneal the layers of the liner material to form a single layer of liner material.

10

The method may comprise: (a) modifying the spatial dimensions of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood vessel; and (b) creating the 3D model based on the modified dimensions.

15

The method may comprise: (a) modifying the spatial dimensions of the blood flow lumen of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen; and (b) creating the 3D model based on the modified dimensions.

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The step of modifying the spatial dimensions may be performed in any of the ways described herein.

- 25 The coating may be applied to the 3D model by electroplating or electroforming. The coating may comprise a metal (e.g. copper or nickel) or ceramic (or ceramic-like material).

- 30 The method may comprise removing the coating from the liner assembly after the liner has been formed. This may be necessary as the spatial dimensions (or diameter) of the body portion will in some applications be greater than the spatial dimensions of the terminal sleeve portions. This may be done by dissolution (e.g. in an acid solution such as nitric acid, sulphuric acid or hydrochloric acid), chemical softening, applying a positive pressure, or applying a negative pressure. For example, the coating may be removed by applying external mechanical pressure to the liner assembly to reduce the coating to a size where it can be removed through the lumen (e.g. at the proximal (upper) end) of the liner.
- 35 Alternatively, the coating may be removed by either chemically softening or dissolving it.

The coating may be removed from the liner assembly by applying pressure to the liner assembly thereby deforming the coating enabling it to be removed from the liner assembly.

- 40 The coating may be a heat-resistant coating. The heat-resistant coating may be heat-resistant to at least 100°C, optionally at least 200°C, at least 300°C, at least 325°C, at least 350°C, at least 375°C, at least 400°C, at least 425°C, at least 450°C, at least 475°C or at least 500°C.

The liner may be formed by heating layers of liner on a liner assembly. The heating may be performed in a furnace. If the coating comprises a metal, the liner assembly may be heated by directly heating the coating. A further option is to use localised topical thermal heating (e.g. surface welding).

5

The liner assembly may be heated to at least 300°C, optionally at least 325°C, at least 350°C, at least 375°C or at least 400°C.

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The liner may be capable of being delivered by a catheter, preferably a catheter of 24Fr or less. The liner material may have enough tensile strength to resist expansion when exposed to arterial blood pressure.

15

Generally, the liner is characterised as being made of an impermeable, flexible and/or biocompatible material. The liner may be made of a polymeric material. The polymeric material may be selected from polytetrafluoroethylene (PTFE), polyethylene (PE), polyethylene terephthalate (PET), silicone, polyglycolic acid, polylactic acid and/or polyurethane or other woven fabric materials or polymers. The liner may be made of graphene. Preferably the liner is made of PTFE.

20

Preferably the liner is constructed from a flexible material. In use, this allows the liner to be expanded by arterial pressure until it forms a seal against the inner blood vessel wall.

The liner may not comprise any wires and/or metal structures.

25

In the methods of the invention, the section of the blood vessel may comprise an aneurysm or dissection (e.g. an aortic dissection). The aneurysm may be an aortic aneurysm, a popliteal aneurysm, a cerebral aneurysm, a renal aneurysm, a hepatic aneurysm or a splenic aneurysm. The aortic aneurysm may be an abdominal aortic aneurysm or a thoracic aortic aneurysm. Additionally or alternatively, the section of the blood vessel may

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be a section to which a (conventional) EVAR stent graft has been previously inserted and subsequently failed.

35

The method may further comprise the step of applying radiopaque markers to the endovascular device that are specific to the section of the blood vessel from which the spatial dimensions are derived.

The markers may be added by applying dots to the 3D model (e.g. by 3D printing) and then applying the radiopaque markers to the liner of the device.

40

The sites at which the radiopaque markers are placed on the liner may be recorded on a 3D digital image used to create the 3D model and the liner. This data relating to the marker position may then be uploaded to a 3D overlay fluoroscopic system, and the correct sites for the markers may be seen on the screen during insertion, expansion and fixation of the

device. These digital guides may be aligned with the actual markers on the liner as it is being inserted.

5 The method may comprise adding a barcode, unique ID or readable chip to the endovascular device to enable later identification of the patient for whom it has been manufactured.

10 The method may further comprise manufacturing a set of endovascular devices for insertion into the blood vessel section in layers. The use of a set of endovascular devices may enable each individual endovascular device to be thinner enabling it to be delivered using a small diameter delivery system. The set of endovascular devices can be used to provide the appropriate tensile strength for endovascular repair.

15 The set of endovascular devices may comprise at least two, at least three, at least four, at least five, at least six or at least seven endovascular devices as defined herein. In such a method, each of the endovascular devices of the set may be manufactured by any of the methods of the invention.

20 Each endovascular device of the set of endovascular devices may comprise a coupling means enabling it to be fixed to another of the endovascular devices when inserted into a blood vessel. The coupling means may be a hook or a barb.

25 The invention provides an endovascular device comprising a liner that defines a lumen, the liner having a first (open-ended) terminal sleeve portion, a second (open-ended) terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, wherein the endovascular device is obtainable by any of the methods described herein.

30 The liner may be branched and have at least a third (open-ended) terminal sleeve portion.

The first, second and third sleeve portions of the liner may have a Y-like configuration.

35 The liner may have a bifurcated shape, with the first terminal sleeve portion at one end, and the second and third terminal sleeve portions at the opposite end, relative to the body portion.

The device may comprise an anchor attached to the first terminal sleeve portion.

40 The device may comprise an anchor attached to the second terminal sleeve portion.

The anchor may be an expandable stent. The expandable stent may be sized to allow an expansion of the cross-sectional dimensions of the section of the blood vessel (e.g. by up to 15%, 5-15% or 10-15%).

A coil or helix (e.g. a nitinol coil or helix) may be wound around the body portion of the device. This may provide greater protection against type 2 endoleaks or device collapse should a type 1 endoleak develop and a dissection-like true/false lumen pressurisation situation occur.

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The invention further provides an endovascular device as described herein, the customised device further comprising a stent graft inserted through the lumen, wherein the terminal sleeve portions are sealed to the body of the stent graft forming a fillable structure between the liner of the endovascular device and the stent graft. The device may further comprise a conduit (or tube) connected to the fillable structure. In use the fillable structure may be filled with a filling medium e.g. by passing the filling medium through the conduit (or tube) into the fillable structure. The filling of the fillable structure may enable the liner to form a seal against the inner blood vessel wall. The filling medium may be capable of hardening or curing in situ. Preferably, the filling medium is a flowable polymer e.g. a polymer comprising polyethylene glycol (PEG), polyurethane and/or collagen.

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The invention provides a method for inserting an endovascular device as described herein, wherein the method comprises: (a) inserting the endovascular device in a collapsed condition into a section of a blood vessel; (b) expanding the endovascular device in the blood vessel; and (c) fixing the endovascular device in the blood vessel by expansion of at least one anchor.

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The liner of the endovascular device may be expanded by blood pressure so that it forms a seal with the wall of the blood vessel.

25

Two or more endovascular devices may be inserted into the blood vessel section in layers. This allows each individual endovascular device to be thinner enabling it to be delivered using a small diameter delivery system. The use of two or more endovascular devices can be used to provide the appropriate tensile strength for endovascular repair.

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When multiple endovascular devices are inserted in layers, several options are available for fixing endovascular devices inserted after the first endovascular device. One option is to have each endovascular device offset from the other(s) such that each endovascular device can be fixed in the blood vessel. Alternatively, a further endovascular device can be fixed by interacting with the already expanded endovascular device (e.g. hooks or barbs on the expanded endovascular device).

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The method may further comprise inserting a further endovascular device as described herein comprising: (a) inserting the further endovascular device in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel; (b) expanding the further endovascular device in the expanded endovascular device; and (c) fixing the further endovascular device in the expanded endovascular device.

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The further endovascular device may be fixed by expansion of at least one anchor.

The steps (a)-(c) may be repeated to insert at least two, at least three, at least four, at least five, at least six or at least seven endovascular devices as defined herein in layers in the blood vessel.

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The section of the blood vessel may include an aneurysm or dissection (e.g. an aortic dissection). The aneurysm may be an aortic aneurysm, a popliteal aneurysm, a cerebral aneurysm, a renal aneurysm, a hepatic aneurysm or a splenic aneurysm. The aortic aneurysm may be an abdominal aortic aneurysm or a thoracic aortic aneurysm. Additionally or alternatively, the section of the blood vessel may be a section to which a (conventional) EVAR stent graft has been previously inserted and subsequently failed.

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The endovascular device may be inserted into the abdominal aorta at the site of an abdominal aortic aneurysm and the body portion of the liner may be expanded so that it forms a seal with the wall of the aneurysm.

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The endovascular device may be inserted across the point at which the abdominal aorta bifurcates into the left and right common iliac arteries.

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The method may comprise: (a) inserting, expanding and fixing a first endovascular device as described herein between a portion of the abdominal aorta and a portion of only one of the iliac arteries; and (b) inserting, expanding and fixing a second endovascular device in the expanded first endovascular device, wherein the second endovascular device is inserted in the portion of the expanded first endovascular device that is fixed in the abdominal aorta, the expanded first endovascular device is punctured at the point of bifurcation enabling the second endovascular device to be inserted into a portion of the other iliac artery, and the second endovascular device is expanded and fixed between the portion of the expanded first endovascular device that is fixed in the abdominal aorta and the portion of the other iliac artery.

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The second endovascular device may be an endovascular device as described herein or a (conventional) endovascular aneurysm repair (EVAR) stent graft.

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Whilst the endovascular devices described herein can be used in isolation in endovascular repair, they may also be used in combination with a convention endovascular aneurysm repair (EVAR) stent graft.

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The method may comprise: (a) inserting a endovascular device as described herein in a collapsed condition into a section of a blood vessel; (b) expanding the endovascular device in the blood vessel; (c) fixing the endovascular device in the blood vessel by expansion of at least one anchor; (d) inserting an endovascular aneurysm repair stent graft in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel; (e) expanding the endovascular aneurysm repair stent graft in the expanded endovascular

device; and (f) fixing the endovascular aneurysm repair stent graft in the expanded endovascular device.

5 The endovascular aneurysm repair stent graft may have an opening in its wall which allows blood to pass through such that in use blood pressure expands the body portion of the liner sealing it with the wall of the blood vessel. The endovascular device and the endovascular aneurysm repair stent graft may be inserted during the same procedure. The opening in the wall of the endovascular aneurysm repair stent graft may be closed in a subsequent procedure. The opening in the wall of the endovascular aneurysm repair stent graft may have a closure, and the closure may be used in the subsequent procedure to seal the opening (e.g. the closure may be operated by a wire).

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BRIEF DESCRIPTION OF THE DRAWINGS

15 The present disclosure will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 illustrates blood flow in an untreated AAA.

20 Figure 2 illustrates blood flow in an AAA after the insertion of a conventional EVAR stent graft.

Figure 3 illustrates the different types of endoleaks that may occur after insertion of a conventional EVAR stent graft.

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Figure 4 illustrates blood flow in an AAA after the insertion of an endovascular device of the invention.

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Paragraphs of the invention

1. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:
 - a. modifying the spatial dimensions of the blood flow lumen of a section of a blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen;
 - b. creating a 3D model based on the modified dimensions; and
 - c. manufacturing the endovascular device using the 3D model to form the liner.
2. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:
 - a. measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel;
 - b. modifying the spatial dimensions of the blood flow lumen of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen;
 - c. creating a 3D model based on the modified dimensions; and
 - d. manufacturing the endovascular device using the 3D model to form the liner.
3. The method of paragraph 2, wherein the step of measuring comprises measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel by CT, MRI or 3D ultrasound.
4. The method of any one of paragraphs 1-3, wherein the step of modifying the spatial dimensions does not comprise increasing the length of the blood flow lumen of the section of the blood vessel.
5. The method of any one of paragraphs 1-4, wherein the step of modifying the spatial dimensions comprises increasing the cross-sectional dimensions of the blood flow lumen by 1-9%.
6. The method of any one of paragraphs 1-5, wherein the step of manufacturing the device using the 3D model comprises applying a liner material to the 3D model to produce a liner assembly.
7. The method of paragraph 6, wherein the 3D model is perforated and the liner material is applied to the 3D model by generating a negative pressure inside the 3D model thereby drawing the liner material onto the outer surface of the 3D model.

8. The method of paragraph 6 or paragraph 7, wherein the liner material is applied to the 3D model in layers.
- 5 9. The method of paragraph 8, wherein the step of manufacturing the device using the 3D model further comprises heating the liner assembly to a temperature sufficient to anneal the layers of the material to form a single layer of material.
- 10 10. The method of any one of paragraphs 1-6, wherein the step of manufacturing the endovascular device using the 3D model comprises:
 - a. applying a coating to the 3D model;
 - b. applying a liner material to the coating to produce a liner assembly; and
 - c. forming the liner from the liner material.
- 15 11. The method of paragraph 10, wherein the method comprises:
 - a. applying layers of the liner material to the coating to produce the liner assembly; and
 - b. heating the liner assembly to anneal the layers of the material to form a single layer of liner material.
- 20 12. The method of paragraph 11, wherein the 3D model has a melting temperature lower than the temperature used to anneal the layers of the liner material to form a single layer.
- 25 13. The method of paragraph 11 or paragraph 12, wherein the step of heating the liner assembly further comprises melting the 3D model removing it from the liner assembly.
- 30 14. The method of paragraph 10 or paragraph 11, wherein the method comprises:
 - a. applying a coating to the 3D model to produce a perforated coating;
 - b. removing the 3D model from the coating by heating; and
 - c. applying a liner material to the coating to produce a liner assembly, wherein the liner material is applied to the coating by generating a negative pressure inside the coating thereby drawing the liner material onto the outer surface of the coating.
- 35 15. The method of any one of paragraphs 10-13, wherein the method comprises:
 - a. applying layers of a liner material to the coating to produce the liner assembly;
 - b. heating the liner assembly to a first temperature, wherein the 3D model melts and is removed from the liner assembly; and
 - c. heating the liner assembly to a second temperature sufficient to anneal the layers of the liner material to form a single layer of liner material.
- 40 16. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second

terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:

- a. creating a 3D model based on the spatial dimensions of the blood flow lumen of a section of a blood vessel;
- 5 b. applying a coating to the 3D model;
- c. applying a liner material to the coating to produce a liner assembly; and
- d. forming the liner from the liner material.

10 17. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:

- a. measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel;
- 15 b. creating a 3D model based on the spatial dimensions of the blood flow lumen of a section of a blood vessel;
- c. applying a coating to the 3D model;
- d. applying a liner material to the coating to produce a liner assembly; and
- 20 e. forming the liner from the liner material.

20 18. The method of paragraph 17, wherein the step of measuring comprises measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel by CT, MRI or 3D ultrasound.

25 19. The method of any one of paragraphs 16-18, wherein the method comprises:

- a. applying layers of the liner material to the coating to produce the liner assembly; and
- b. heating the liner assembly to anneal the layers of the material to form a single layer of liner material.

30 20. The method of paragraph 19, wherein the 3D model has a melting temperature lower than the temperature used to anneal the layers of the liner material to form a single layer.

35 21. The method of paragraph 19 or paragraph 20, wherein the step of heating the liner assembly further comprises melting the 3D model removing it from the liner assembly.

40 22. The method of any one of paragraphs 16-19, wherein the method comprises:

- a. applying a coating to the 3D model to produce a perforated coating;
- b. removing the 3D model from the coating by heating; and
- c. applying a liner material to the coating to produce a liner assembly, wherein the liner material is applied to the coating by generating a negative pressure inside the heating resistant coating thereby drawing the liner material onto the outer surface of the coating.

23. The method of any one of paragraphs 16-21, wherein the method comprises:
- a. applying layers of a liner material to the coating to produce the liner assembly;
 - b. heating the liner assembly to a first temperature, wherein the 3D model melts and is removed from the liner assembly; and
 - c. heating the liner assembly to a second temperature sufficient to anneal the layers of the liner material to form a single layer of liner material.
24. The method of any one of paragraphs 16-23, wherein the method comprises:
- a. modifying the spatial dimensions of the blood flow lumen of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen; and
 - b. creating the 3D model based on the modified dimensions.
25. The method of paragraph 24, wherein the step of modifying the spatial dimensions does not comprise increasing the length of the blood flow lumen of the section of the blood vessel.
26. The method of paragraph 24 or paragraph 25, wherein the step of modifying comprises increasing the cross-sectional dimensions of the blood flow lumen by 1-9%.
27. The method of any one of paragraphs 10-26, wherein the coating is removed from the liner assembly by dissolution in an acid solution.
28. The method of any one of paragraphs 10-27, wherein the coating is removed from the liner assembly by applying a positive or negative pressure.
29. The method of paragraph 28, wherein the coating is removed from the liner assembly by applying pressure to the liner assembly thereby deforming the coating enabling it to be removed from the liner assembly.
30. The method of any one of paragraphs 10-29, wherein the step of applying a coating to the 3D model is performed using electroplating or electroforming.
31. The method of any one of paragraphs 6-30, wherein the liner assembly is heated to at least 300°C, optionally at least 325°C, at least 350°C, at least 375°C or at least 400°C.
32. The method of any one of paragraphs 1-31, wherein the 3D model comprises a wax.
33. The method of any one of paragraphs 1-32, wherein the 3D model is solid or hollow.
34. The method of any one of paragraphs 1-33, wherein the step of creating a 3D model based on the modified dimensions comprises 3D printing.

35. The method of any one of paragraphs 1-34, wherein the body portion of the liner is made of PTFE.
- 5 36. The method of any one of paragraphs 1-35, wherein the section of the blood vessel comprises an aneurysm.
- 10 37. The method of paragraph 36, wherein the aneurysm is an aortic aneurysm, optionally wherein the aortic aneurysm is an abdominal aortic aneurysm or a thoracic aortic aneurysm.
38. The method of paragraph 36, wherein the aneurysm is a cerebral aneurysm.
- 15 39. The method of any one of paragraphs 1-38, wherein the method further comprises the step of applying radiopaque markers to the endovascular device that are specific to the section of the blood vessel from which the spatial dimensions are derived.
- 20 40. An endovascular device comprising a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, wherein the endovascular device is obtainable by the method of any one of paragraphs 1-39.
- 25 41. The endovascular device of paragraph 40, wherein the liner is branched and has at least a third terminal sleeve portion.
- 30 42. The endovascular device of paragraph 41, wherein the first, second and third sleeve portions of the liner have a Y-like configuration.
43. The endovascular device of paragraph 41, wherein the liner has a bifurcated shape, with the first terminal sleeve portion at one end, and the second and third terminal sleeve portions at the opposite end, relative to the body portion.
- 35 44. The endovascular device of any one of paragraphs 40-43, wherein the device comprises an anchor attached to the first terminal sleeve portion.
45. The endovascular device of any one of paragraphs 40-44, wherein the device comprises an anchor attached to the second terminal sleeve portion.
- 40 46. The endovascular device of paragraph 44 or paragraph 45, wherein the anchor is an expandable stent.
47. The endovascular device of any one of paragraphs 40-46, wherein the device further comprises a stent graft inserted through the lumen, and wherein the terminal sleeve

portions are sealed to the body of the stent graft forming a fillable structure between the liner and the stent graft.

- 5 48. The endovascular device of paragraph 47, wherein the device further comprises a conduit connected to the fillable structure, and wherein in use the fillable structure may be filled with a filling medium by passing the filling medium through the conduit into the fillable structure.
- 10 49. A method for inserting an endovascular device as defined in paragraph 47 or paragraph 48, wherein the method comprises:
- a. inserting the endovascular device in a collapsed condition into a section of a blood vessel;
 - b. fixing the endovascular device in the blood vessel by expansion of at least one anchor; and
 - 15 c. filling the fillable structure with a filling medium thereby expanding the liner until it forms a seal against the inner wall of the blood vessel.
50. The method of paragraph 49, wherein the filling medium comprises a flowable polymer.
- 20 51. The method of paragraph 49 or paragraph 50, wherein the filling medium comprises polyethylene glycol (PEG), polyurethane and/or collagen.
52. The method of any one of paragraphs 49-51, wherein the filling medium is hardened or cured in situ in the fillable structure.
- 25 53. The method of any one of paragraphs 49-52, wherein the fillable structure is filled with filling medium by passing the filling medium through the conduit into the fillable structure.
- 30 54. A method for inserting an endovascular device as defined in any one of paragraphs 40-46, wherein the method comprises:
- a. inserting the endovascular device in a collapsed condition into a section of a blood vessel;
 - b. expanding the endovascular device in the blood vessel; and
 - 35 c. fixing the endovascular device in the blood vessel by expansion of at least one anchor.
55. The method of paragraph 54, wherein the method further comprises inserting a further endovascular device as defined in any one of paragraphs 40-46 comprising:
- 40 a. inserting the further endovascular device in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel;
 - b. expanding the further endovascular device in the expanded endovascular device; and

c. fixing the further endovascular device in the expanded endovascular device.

56. The method of paragraph 55, wherein the further endovascular device is fixed by expansion of at least one anchor.

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57. The method of paragraph 55 or paragraph 56, wherein steps (a)-(c) of paragraph 54 are repeated to insert at least two, at least three, at least four or at least five endovascular devices as defined in any one of paragraphs 40-46 in layers in the blood vessel.

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58. The method of any one of paragraphs 54-57, wherein the section of the blood vessel includes an aneurysm.

59. The method of paragraph 58, wherein the aneurysm is an aortic aneurysm, optionally wherein the aortic aneurysm is an abdominal aortic aneurysm or a thoracic aortic aneurysm.

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60. The method of paragraph 58, wherein the aneurysm is a cerebral aneurysm.

61. The method of any one of paragraphs 54-57, wherein the endovascular device is inserted into the abdominal aorta at the site of an abdominal aortic aneurysm and wherein the body portion of the liner is expanded and forms a seal with the wall of the aneurysm.

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62. The method of paragraph 61, wherein the endovascular device is inserted across the point at which the abdominal aorta bifurcates into the left and right common iliac arteries.

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63. The method of paragraph 62, wherein the method comprises:

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a. inserting, expanding and fixing a first endovascular device as defined in any one of paragraphs 40-46 between a portion of the abdominal aorta and a portion of only one of the iliac arteries; and

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b. inserting, expanding and fixing a second endovascular device in the expanded first endovascular device, wherein the second endovascular device is inserted in the portion of the expanded first endovascular device that is fixed in the abdominal aorta, the expanded first endovascular device is punctured at the point of bifurcation enabling the second endovascular device to be inserted into a portion of the other iliac artery, and the second endovascular device is expanded and fixed between the portion of the expanded first endovascular device that is fixed in the abdominal aorta and the portion of the other iliac artery.

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64. The method of paragraph 63, wherein the second endovascular device is an endovascular device as defined in any one of paragraphs 40-46.

65. The method of paragraph 63, wherein the second endovascular device is an endovascular aneurysm repair stent graft.

- 5 66. The method of any one of paragraphs 54-62, wherein the method further comprises:
- a. inserting an endovascular aneurysm repair stent graft in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel;
 - b. expanding the endovascular aneurysm repair stent graft in the expanded endovascular device; and
 - 10 c. fixing the endovascular aneurysm repair stent graft in the expanded endovascular device.

15 67. The method of paragraph 66, wherein the endovascular aneurysm repair stent graft has an opening in its wall which allows blood to pass through such that blood pressure expands the body portion of the liner sealing it with the wall of the blood vessel.

68. The method of paragraph 67, wherein the endovascular device and the endovascular aneurysm repair stent graft are inserted during the same procedure.

20 69. The method of paragraph 68, wherein the opening in the wall of the endovascular aneurysm repair stent graft is closed in a subsequent procedure.

25 70. The method of paragraph 69, wherein the opening in the wall of the endovascular aneurysm repair stent graft has a closure, and wherein the closure is used in the subsequent procedure to seal the opening.

EXAMPLE

30 An endovascular device described herein may be used to line an AAA. The device may form an impermeable lining that forms a complete seal with the walls of the aortic blood flow lumen. Here the aortic pressure will always be higher than the flow in the smaller vessels (lumbar, IMA, median sacral and possible accessory renal vessels) and as such it will compress the liner against the origin of those vessels. With no flow in the vessels they will thrombose off permanently.

35 The liner may not need to have great tensile strength because of the following: the growth rate of AAAs is relatively low, often in the region of 5mm/yr. This would indicate only a small mismatch in the ability of the aortic wall to resist expansion versus the expansatile action of the blood pressure peaks created by the cardiac cycle. A relatively thin liner, or liners, may shift the balance back in favour of the aortic wall resisting further expansion.

40 The patient with an AAA would undergo a high resolution arterial and portal phase CT or MRI scan with contrast, or a 3D ultrasound scan. From this a 3D reconstruction of the blood flow lumen (not the external morphology of the AAA) from directly below a line joining the inferior border of the renal arteries down to just above the common iliac bifurcation

(origin of the hypogastric vessels) is created. This model is then expanded by a very small amount, around 3-8% (e.g. 5%) and recreated by a 3D printer. The expansion of the 3D model will only take place in an antero-posterior and side-side direction, not in a cranio-caudal direction. This is so that the body of the device is slightly oversized to ensure sealing against the aortic wall or edge of the flow lumen, whilst not extending vertically to cover the renal or internal iliac vessels. Some degree of model surface smoothing may be required, either at the time of the computer simulation or as a post-processing step after printing. It is possible that the CT or MRI scan may not give a clear picture of the blood flow lumen of the aorta and in this scenario the use of conventional ultrasound scan (USS), or even 3D USS, may be beneficial in generating additional data to inform the construct of the 3D model.

The current description relates to the formation of a device extending from below the renal arteries to above the internal iliac arteries. It will also be possible using this technique to generate unique, patient specific stent-graft liners that incorporate a one or more branches to supply named blood vessels arising from the aorta. This model would obviously potentially work for any anatomy, such as the thoracic aorta and even visceral vessels. For aortic dissection, unique liners may be created for both the true and false lumens.

The 3D model of the section of the aorta may also be marked with anterior and posterior markers to allow siting of radiopaque markers for device orientation during insertion. In addition, the proximal aortic and distal iliac lumens may be extended by a tube 5-10cm long. These will be used to aid handling and manipulation of the device during manufacture. The junction between the actual aortic lumen model and the extensions may be marked with a ridge around the 3D structure (indicating where the liner should be constructed to).

Two approaches are provided, by way of example only, for the manufacture of the liner.

In a first approach, a 3D model will be created by 3D printing from the 3D digital reconstruction described above. This model will have a smooth surface but an underlying porous structure that is soluble in water. The model will then be spray coated with the liner material to form a thin, impermeable and non-elastic membrane that does not rupture when exposed to aortic pressure.

Once the proximal and distal self-expanding stents have been incorporated between layers of the membrane, and the structure has fully cured the model will be dissolved away. The liner is then mounted onto the delivery system.

In a second approach, a 3D model will be created by 3D printing from the 3D digital reconstruction described above. This will be printed as a wax core which is then electroplated with a thin layer of copper and a final nickel surface. The assembly will then be wrapped with a layer of PTFE tape, the proximal and distal balloon expandable stents incorporated and then an outer layer of PTFE added.

The assembly will then be kept vertical and heated to a temperature at which all of the wax will melt and run away from the remaining metal-PTFE structure. Once this is done, the structure is heated to 390°C to anneal the PTFE. After cooling, the metal liner is then dissolved away with nitric acid. After being thoroughly washed, the PTFE liner is then mounted onto the delivery system.

In both approaches, during the printing of the 3D model, dots will be added to mark the anterior and posterior sections of the blood vessel. Multiple small radiopaque markers will then be incorporated into the fabric of the liner on its anterior surface and a longer one onto the posterior surface. These markers will form a line when the device is correctly orientated under fluoroscopic guidance when the device is being implanted. To further aid in correct positioning markers will also be placed across the neck of the liner and at the origin of the ipsilateral limb, and also the distal end of the contralateral limb.

As correct positioning of the graft will play an important role in its long term durability, additional steps may be taken to optimise siting the liner in the aorta. The sites at which all the radiopaque markers are placed on the graft will also be recorded on the 3D digital image used to create the liner in the first place. This data relating to the marker position can then be uploaded to a 3D overlay fluoroscopic system, and the correct sites for the markers will be seen on the screen during implantation. These digital guides will be aligned with the actual markers on the liner as it is being inserted.

The proximal neck section of the liner may be built using a balloon expandable stent, or an existing self-expanding bare stent and hook configuration to create a fixation zone proximal to the start of the liner. This could be incorporated into the main body construct. For example, in accordance with the second approach described above, a number of layers of PTFE may be added before the stent is attached and then more layers of PTFE applied. Once the wrapping is complete, the assembly will be heated to anneal the layers of PTFE to form a single layer and this will also seal the stent into position.

A proximal seal is created through the use of a self-expanding stent placed in a normal portion of the aorta above the AAA. The proximal stent is sized to allow a further expansion of the aortic neck by around 10-15%, that is to say that the diameter of the aortic neck is measured and then a stent chosen that is 10-15% larger than this. If the aortic neck expands beyond the 10-15% of oversize allowed for, then fenestrated aortic cuffs, or branched stent graft technology, may be used to create a new more proximal sealing zone.

One-piece liner

The ideal configuration of the liner would be to have both iliac limbs (ipsilateral and contralateral) constructed at the same time as the main body forming a single bifurcated liner. Creating the liner from a single piece would reduce the risk of type3 endoleaks as there will be no modularity to the device and therefore no junctions which could leak.

The liner will also have to be delivered into the aortic lumen and then deployed. In the case of a single piece design, this will require the contralateral limb being delivered down into the contralateral iliac vessel from above. The contralateral limb would be constrained in a thin plastic sheath would be snared and pulled down into the iliac vessel. To enable this to happen, the main body will need to remain constrained whilst the distal end of the contralateral limb is sited above the origin of the contralateral iliac artery. Once the iliac limb is delivered into place then the main body can be unsheathed. One solution to this would be to use 2 sheaths of different diameters and lengths. The longer, inner sheath would contain the main body and ipsilateral limb but its proximal section will be split along a length great enough to allow the contralateral limb to be placed outside the inner sheath. The inner sheath and contralateral limb would then be packed into a shorter, outer sheath of greater diameter than the first. Once the whole dual sheath system has been inserted far enough into the aorta that the markers on the distal end of the contralateral limb are above the aortic bifurcation, the outer sheath would be retracted to allow release of the limb. This limb would be snared and pulled down into the iliac artery and would be held in position whilst the remainder of the aortic liner was uncovered.

Modular liner

An alternative approach would be to have no contralateral limb aperture at all on the main body. The main body would have an ipsilateral outflow and the liner would be sealed over across the origin of the contralateral iliac. The main body would be deployed down to the origin of the ipsilateral iliac limb and the top of the main body deployed and fixed into position. A sheath would then be inserted via the contralateral femoral artery. A new sheath would need to be designed with a high volume, low pressure external balloon at its most proximal segment. The sheath diameter would only need to be large enough to accept the constrained contralateral limb when it was ready to be sited. The reason for the balloon is that this would centre the sheath in the iliac lumen, as well as fixing it into position. A stiff wire or hollow flexible needle would then be used to puncture the endolining of the main body. An 8mm angioplasty balloon would then be used to dilate the puncture made in the endolining. A new iliac limb would then be placed into position and then a final angioplasty to dilate the puncture hole to the size of the stent would be undertaken.

A variation on the previous paragraph would be again to construct a liner with no contralateral limb, but in this case the 3D model on which the liner is based is created with a deep indentation or hole in it which corresponds to the origin of the contralateral limb. Once the liner has been created, and annealed if necessary, but before the 3D model is removed, an opening will be cut into the liner over the indentation or hole. The cutting technique may weld the edges of the liner. This opening may then be reinforced by having a loop of nitinol, or similar material, sutured into position around the edges of the opening. Two options then exist for completion of the aortic sealing. The first would be to create a new limb with a proximal inflatable seal. This would be inserted and the inflatable section used to seal against the liner. Instead of an inflatable seal, an internal flange could be produced on the new graft limb to create overlap against the internal liner surface. The second option would be to create a second liner very similar to the first, but this time the

limb that is preserved, and therefore becomes the ipsilateral limb on the second liner, is the limb that was previously the contralateral limb on the first. This new liner would be inserted through the hole created in the first and it would have a corresponding opening for the now contralateral limb on the other side. This would double line the aortic lumen and provide a secure distal seal.

A number of alternative options exist for the construction of the contra-lateral limb. The first of these is to continue the construction of the 3D model to include the first 2-3cm of the contra-lateral limb. Prior to the sheathing process during production, the contralateral limb is inverted inside the main body. Once the device is deployed the contralateral limb is cannulated and the inverted limb then everted using an angioplasty balloon. The contralateral seal is then completed by the use of a conventional iliac stent-graft.

In theory, if the liner has been placed correctly, the contralateral limb may just open into the iliac vessel, particularly if the outflow on the ipsilateral side is occluded with a balloon. This may not occur and there is a potential danger that the limb could fold on itself and then be very difficult to cannulate in order to then use a balloon to pull it into the correct position. A solution to this would be to temporarily hold the limb inverted to allow cannulation to occur and guide the limb into the correct position. When the graft was being constructed, the contra limb would have 3 small loops created along its distal edge. These loops would then be held inverted by having the central core or lock wire pass through them. This should facilitate cannulation.

Rather than having to cannulate the contralateral limb from the contra side, it would be possible to have a pre-loaded catheter and wire within the main body, passing out through the contra limb. Before the graft is fully deployed, the pre-loaded wire is passed down into the contra iliac artery where it can be snared and femoral access secured. This would marginally add to the device diameter but it should be possible to use an .018 or even .014 system to keep this to a minimum.

A further alternative to cannulation would be to have a permanent internal section. This would be a standard diameter stent-graft section (12mm) that was built to face internally into the main body by 2cm. The main body would be deployed just until the contra limb was out of the main sheath. As the liner would be expanded by the arterial pressure it would provide a target for standard contralateral limb cannulation and once this was achieved then the rest of the main body could be deployed. As this would add to the complexity of the build, a variation of this would be to create a self-expanding ring at the origin of the contra common iliac. This could be cannulated in the same way as the internal stent.

Use of multiple layers

For larger diameter aortic flow lumens the liner may be created in a number of thinner liner layers, each of which is then inserted into the patient separately. The thinner layers will take up less volume, and so can be delivered through a small delivery system, but with the multiple layers providing the appropriate tensile strength.

If multiple layers are used, differing stent configurations may be used on each liner. The first option is the use of overlapping stents, with the outer stent likely to be a balloon expandable stent and then the stent on the inner liner a self-expanding one. The second
5 option is to have the stents set at varying distances from the proximal end of the liner, such that there is a gap between the stents on one liner that the stent on the next liner will fit into. A third option is to hold the secondary liners in place using a first liner (that has been inserted) with a number of inward facing, upward slanting, hooks or barbs. When the
10 secondary liners are inserted, they will be captured by these hooks, and the need for a stent may be avoided.

Lastly, in the case of modular liner approach described above, the secondary liners may not need the distal limbs adding to them. For example, in a setting where there is a single
15 infrarenal aneurysm with normal iliac vessels, simply reinforcing the liner section of the main body of the aneurysm through the use of a liner without iliac limbs may enable more rapid treatment of the aneurysm.

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein
20 will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims. Moreover, all embodiments of the invention described herein are considered to be broadly applicable and combinable with any and all other consistent
25 embodiments, as appropriate.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

CLAIMS

1. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:
 - a. modifying the spatial dimensions of the blood flow lumen of a section of a blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen;
 - b. creating a 3D model based on the modified dimensions; and
 - c. manufacturing the endovascular device using the 3D model to form the liner.
2. A method for manufacturing an endovascular device, wherein the device comprises a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, and wherein the method comprises:
 - a. measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel;
 - b. modifying the spatial dimensions of the blood flow lumen of the section of the blood vessel to create modified dimensions, wherein the modifying comprises increasing the cross-sectional dimensions of the blood flow lumen;
 - c. creating a 3D model based on the modified dimensions; and
 - d. manufacturing the endovascular device using the 3D model to form the liner.
3. The method of claim 2, wherein the step of measuring comprises measuring the spatial dimensions of the blood flow lumen of a section of a blood vessel by CT, MRI or 3D ultrasound.
4. The method of any one of claims 1-3, wherein the step of modifying the spatial dimensions does not comprise increasing the length of the blood flow lumen of the section of the blood vessel.
5. The method of any one of claims 1-4, wherein the step of modifying the spatial dimensions comprises increasing the cross-sectional dimensions of the blood flow lumen by 1-9%.
6. The method of any one of claims 1-5, wherein the step of manufacturing the device using the 3D model comprises applying a liner material to the 3D model to produce a liner assembly.
7. The method of claim 6, wherein the 3D model is perforated and the liner material is applied to the 3D model by generating a negative pressure inside the 3D model thereby drawing the liner material onto the outer surface of the 3D model.

8. The method of claim 6 or claim 7, wherein the liner material is applied to the 3D model in layers.
- 5 9. The method of claim 8, wherein the step of manufacturing the device using the 3D model further comprises heating the liner assembly to a temperature sufficient to anneal the layers of the material to form a single layer of material.
- 10 10. The method of any one of claims 1-6, wherein the step of manufacturing the endovascular device using the 3D model comprises:
- a. applying a coating to the 3D model;
 - b. applying a liner material to the coating to produce a liner assembly; and
 - c. forming the liner from the liner material.
- 15 11. The method of claim 10, wherein the method comprises:
- a. applying layers of the liner material to the coating to produce the liner assembly; and
 - b. heating the liner assembly to anneal the layers of the material to form a single layer of liner material.
- 20 12. The method of claim 11, wherein the 3D model has a melting temperature lower than the temperature used to anneal the layers of the liner material to form a single layer.
- 25 13. The method of claim 11 or claim 12, wherein the step of heating the liner assembly further comprises melting the 3D model removing it from the liner assembly.
- 30 14. The method of claim 10 or claim 11, wherein the method comprises:
- a. applying a coating to the 3D model to produce a perforated coating;
 - b. removing the 3D model from the coating by heating; and
 - c. applying a liner material to the coating to produce a liner assembly, wherein the liner material is applied to the coating by generating a negative pressure inside the coating thereby drawing the liner material onto the outer surface of the coating.
- 35 15. The method of any one of claims 10-13, wherein the method comprises:
- a. applying layers of a liner material to the coating to produce the liner assembly;
 - b. heating the liner assembly to a first temperature, wherein the 3D model melts and is removed from the liner assembly; and
 - c. heating the liner assembly to a second temperature sufficient to anneal the layers of the liner material to form a single layer of liner material.
- 40 16. The method of any one of claims 10-15, wherein the coating is removed from the liner assembly by dissolution in an acid solution.

17. The method of any one of claims 10-16, wherein the coating is removed from the liner assembly by applying a positive or negative pressure.
- 5 18. The method of claim 17, wherein the coating is removed from the liner assembly by applying pressure to the liner assembly thereby deforming the coating enabling it to be removed from the liner assembly.
- 10 19. The method of any one of claims 10-18, wherein the step of applying a coating to the 3D model is performed using electroplating or electroforming.
20. The method of any one of claims 6-19, wherein the liner assembly is heated to at least 300°C, optionally at least 325°C, at least 350°C, at least 375°C or at least 400°C.
- 15 21. The method of any one of claims 1-20, wherein the 3D model comprises a wax.
22. The method of any one of claims 1-21, wherein the 3D model is solid or hollow.
- 20 23. The method of any one of claims 1-22, wherein the step of creating a 3D model based on the modified dimensions comprises 3D printing.
24. The method of any one of claims 1-23, wherein the body portion of the liner is made of PTFE.
- 25 25. The method of any one of claims 1-24, wherein the section of the blood vessel comprises an aneurysm.
26. The method of claim 25, wherein the aneurysm is an aortic aneurysm, optionally wherein the aortic aneurysm is an abdominal aortic aneurysm or a thoracic aortic aneurysm.
- 30 27. The method of claim 25, wherein the aneurysm is a cerebral aneurysm.
28. The method of any one of claims 1-27, wherein the method further comprises the step of applying radiopaque markers to the endovascular device that are specific to the section of the blood vessel from which the spatial dimensions are derived.
- 35 29. An endovascular device comprising a liner that defines a lumen, the liner having a first terminal sleeve portion, a second terminal sleeve portion and a body portion extending between the first terminal sleeve portion and the second terminal sleeve portion, wherein the endovascular device is obtainable by the method of any one of claims 1-28.
- 40 30. The endovascular device of claim 29, wherein the liner is branched and has at least a third terminal sleeve portion.

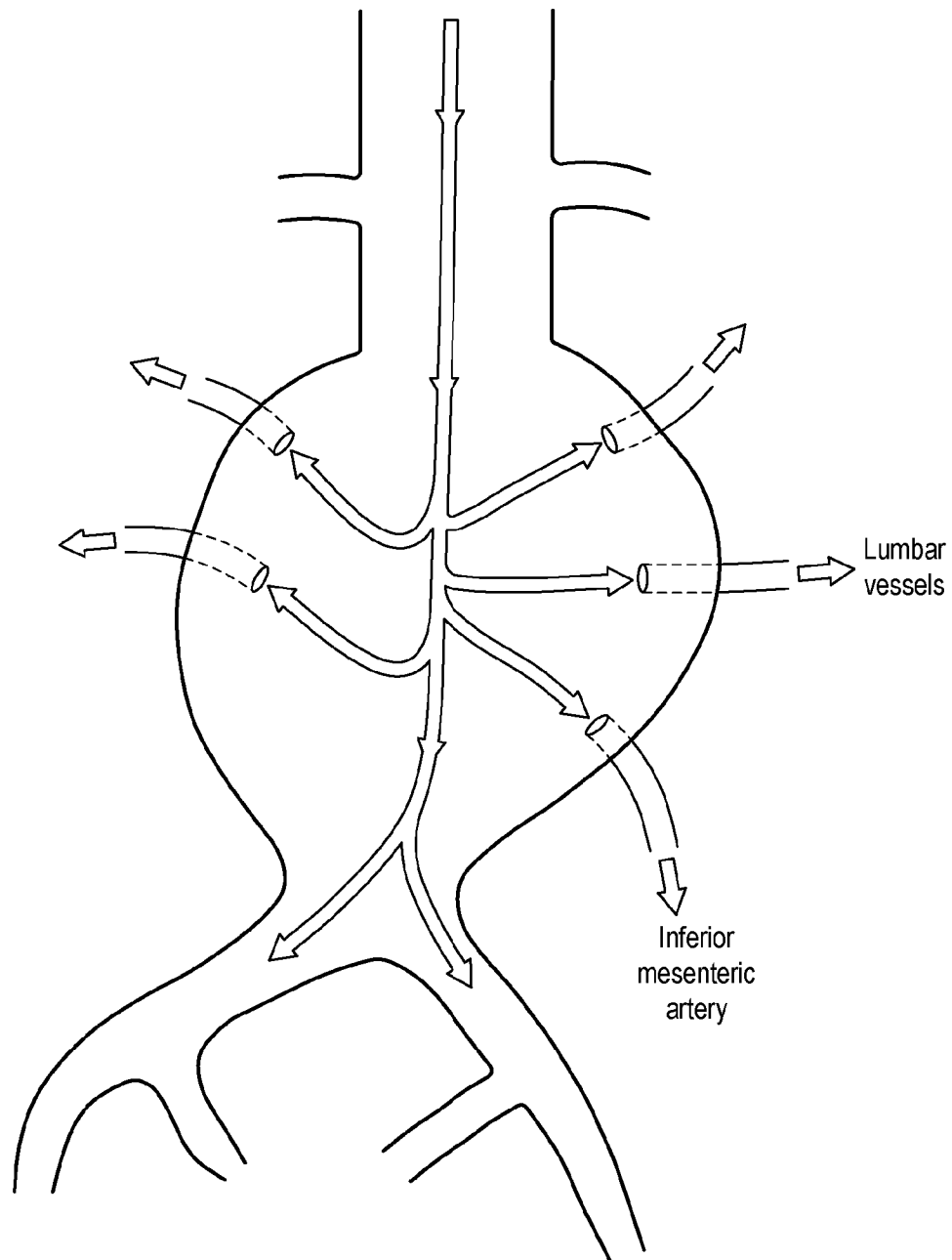
31. The endovascular device of claim 30, wherein the first, second and third sleeve portions of the liner have a Y-like configuration.
- 5 32. The endovascular device of claim 30, wherein the liner has a bifurcated shape, with the first terminal sleeve portion at one end, and the second and third terminal sleeve portions at the opposite end, relative to the body portion.
- 10 33. The endovascular device of any one of claims 29-32, wherein the device comprises an anchor attached to the first terminal sleeve portion.
34. The endovascular device of any one of claims 29-33, wherein the device comprises an anchor attached to the second terminal sleeve portion.
- 15 35. The endovascular device of claim 33 or claim 34, wherein the anchor is an expandable stent.
- 20 36. The endovascular device of any one of claims 29-35, wherein the device further comprises a stent graft inserted through the lumen, and wherein the terminal sleeve portions are sealed to the body of the stent graft forming a fillable structure between the liner and the stent graft.
- 25 37. The endovascular device of claim 36, wherein the device further comprises a conduit connected to the fillable structure, and wherein in use the fillable structure may be filled with a filling medium by passing the filling medium through the conduit into the fillable structure.
- 30 38. A method for inserting an endovascular device as defined in claim 36 or claim 37, wherein the method comprises:
a. inserting the endovascular device in a collapsed condition into a section of a blood vessel;
b. fixing the endovascular device in the blood vessel by expansion of at least one anchor; and
c. filling the fillable structure with a filling medium thereby expanding the liner until it forms a seal against the inner wall of the blood vessel.
- 35 39. The method of claim 38, wherein the filling medium comprises a flowable polymer.
- 40 40. The method of claim 38 or claim 39, wherein the filling medium comprises polyethylene glycol (PEG), polyurethane and/or collagen.
41. The method of any one of claims 38-40, wherein the filling medium is hardened or cured in situ in the fillable structure.

42. The method of any one of claims 38-41, wherein the fillable structure is filled with filling medium by passing the filling medium through the conduit into the fillable structure.
43. A method for inserting an endovascular device as defined in any one of claims 29-35, wherein the method comprises:
- a. inserting the endovascular device in a collapsed condition into a section of a blood vessel;
 - b. expanding the endovascular device in the blood vessel; and
 - c. fixing the endovascular device in the blood vessel by expansion of at least one anchor.
44. The method of claim 43, wherein the method further comprises inserting a further endovascular device as defined in any one of claims 29-35 comprising:
- a. inserting the further endovascular device in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel;
 - b. expanding the further endovascular device in the expanded endovascular device; and
 - c. fixing the further endovascular device in the expanded endovascular device.
45. The method of claim 44, wherein the further endovascular device is fixed by expansion of at least one anchor.
46. The method of claim 44 or claim 45, wherein steps (a)-(c) of claim 43 are repeated to insert at least two, at least three, at least four or at least five endovascular devices as defined in any one of claims 29-35 in layers in the blood vessel.
47. The method of any one of claims 43-46, wherein the section of the blood vessel includes an aneurysm.
48. The method of claim 47, wherein the aneurysm is an aortic aneurysm, optionally wherein the aortic aneurysm is an abdominal aortic aneurysm or a thoracic aortic aneurysm.
49. The method of claim 47, wherein the aneurysm is a cerebral aneurysm.
50. The method of any one of claims 43-46, wherein the endovascular device is inserted into the abdominal aorta at the site of an abdominal aortic aneurysm and wherein the body portion of the liner is expanded and forms a seal with the wall of the aneurysm.
51. The method of claim 50, wherein the endovascular device is inserted across the point at which the abdominal aorta bifurcates into the left and right common iliac arteries.
52. The method of claim 51, wherein the method comprises:

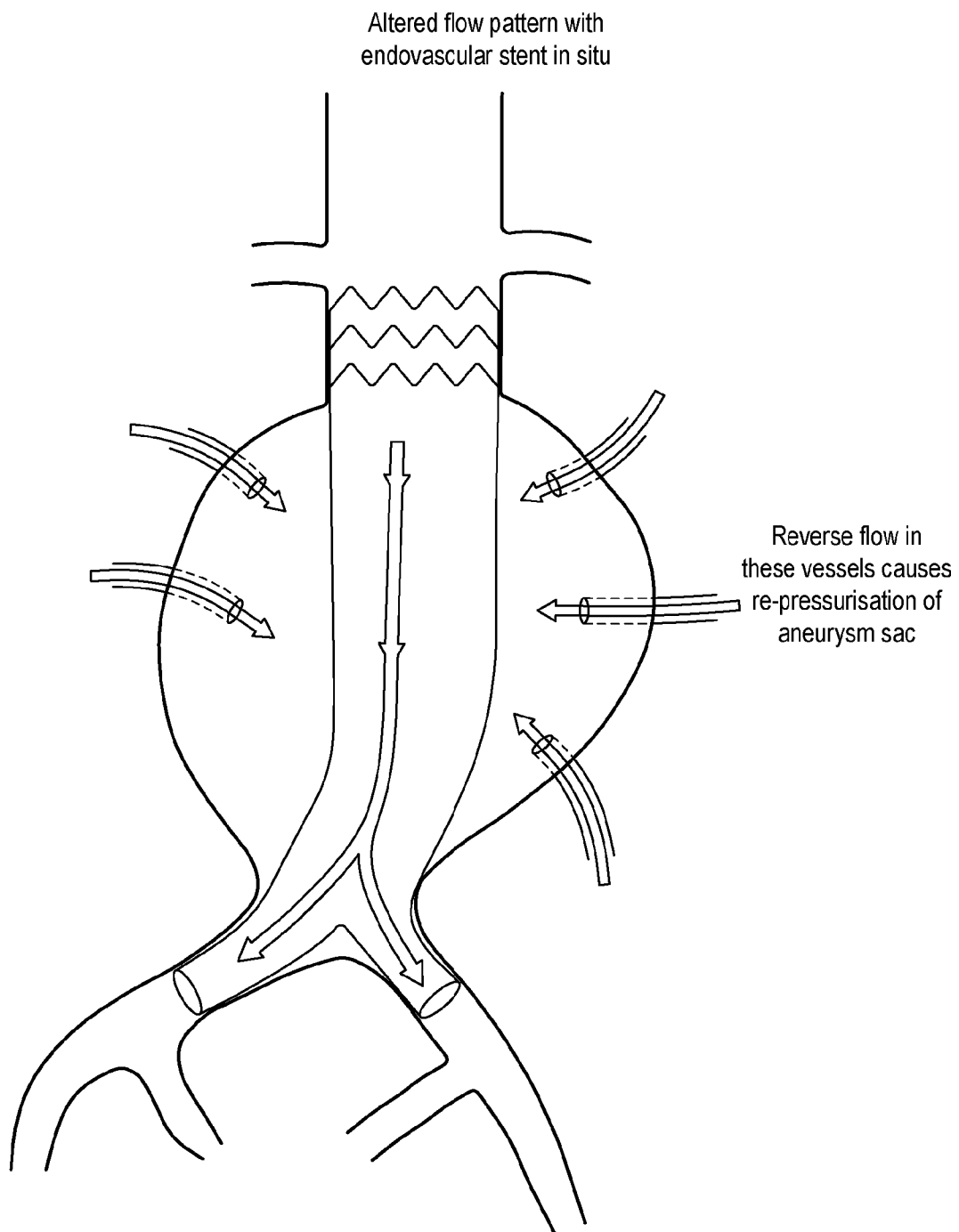
- 5 a. inserting, expanding and fixing a first endovascular device as defined in any one of claims 29-35 between a portion of the abdominal aorta and a portion of only one of the iliac arteries; and
- 10 b. inserting, expanding and fixing a second endovascular device in the expanded first endovascular device, wherein the second endovascular device is inserted in the portion of the expanded first endovascular device that is fixed in the abdominal aorta, the expanded first endovascular device is punctured at the point of bifurcation enabling the second endovascular device to be inserted into a portion of the other iliac artery, and the second endovascular device is expanded and fixed between the portion of the expanded first endovascular device that is fixed in the abdominal aorta and the portion of the other iliac artery.
- 15 53. The method of claim 52, wherein the second endovascular device is an endovascular device as defined in any one of claims 40-46.
54. The method of claim 52, wherein the second endovascular device is an endovascular aneurysm repair stent graft.
- 20 55. The method of any one of claims 43-51, wherein the method further comprises:
- a. inserting an endovascular aneurysm repair stent graft in a collapsed condition into the expanded endovascular device that is fixed in the blood vessel;
- b. expanding the endovascular aneurysm repair stent graft in the expanded endovascular device; and
- 25 c. fixing the endovascular aneurysm repair stent graft in the expanded endovascular device.
56. The method of claim 55, wherein the endovascular aneurysm repair stent graft has an opening in its wall which allows blood to pass through such that blood pressure expands the body portion of the liner sealing it with the wall of the blood vessel.
- 30 57. The method of claim 56, wherein the endovascular device and the endovascular aneurysm repair stent graft are inserted during the same procedure.
- 35 58. The method of claim 57, wherein the opening in the wall of the endovascular aneurysm repair stent graft is closed in a subsequent procedure.
- 40 59. The method of claim 58, wherein the opening in the wall of the endovascular aneurysm repair stent graft has a closure, and wherein the closure is used in the subsequent procedure to seal the opening.

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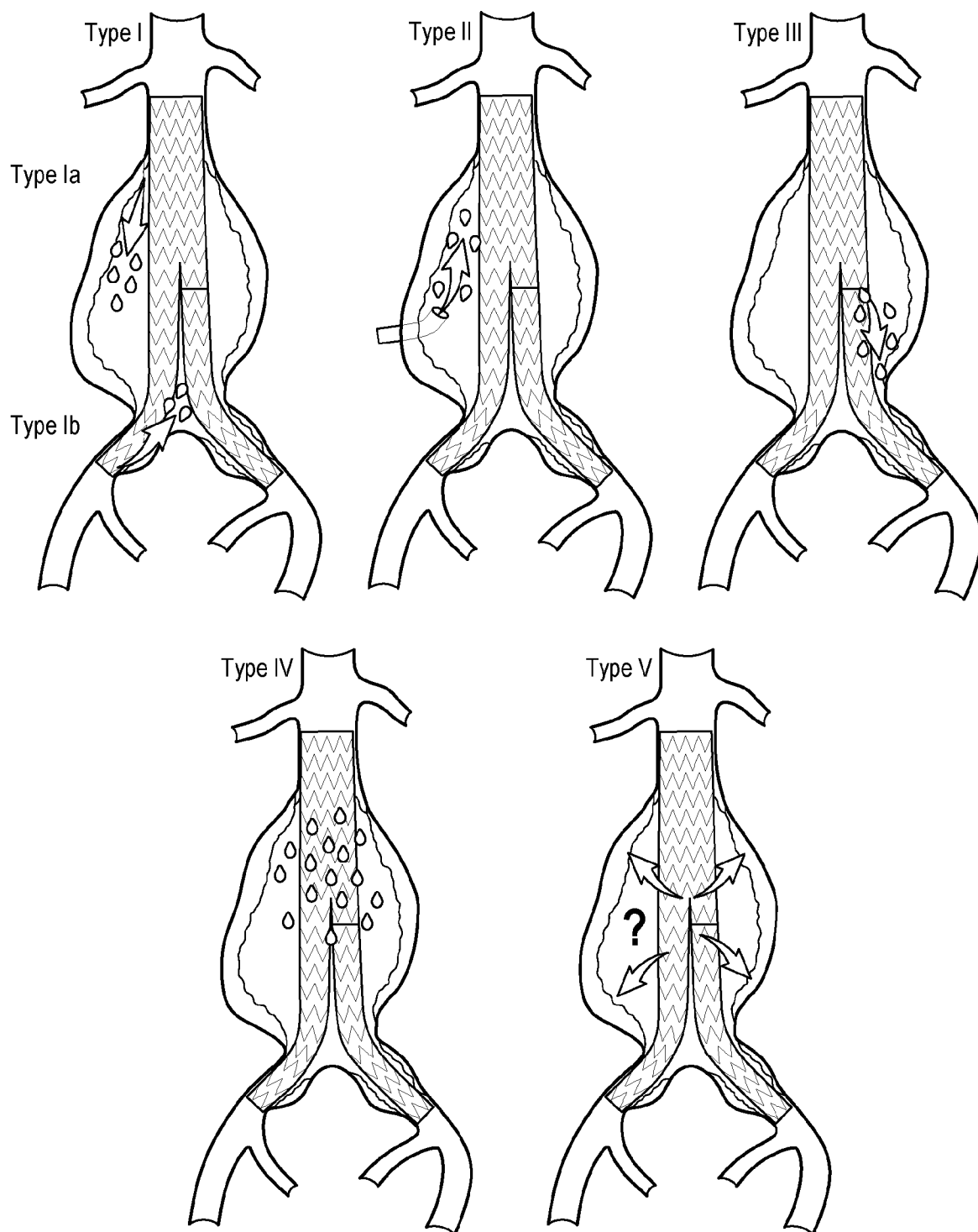
Flow pattern in aortic aneurysm

**FIG. 1**

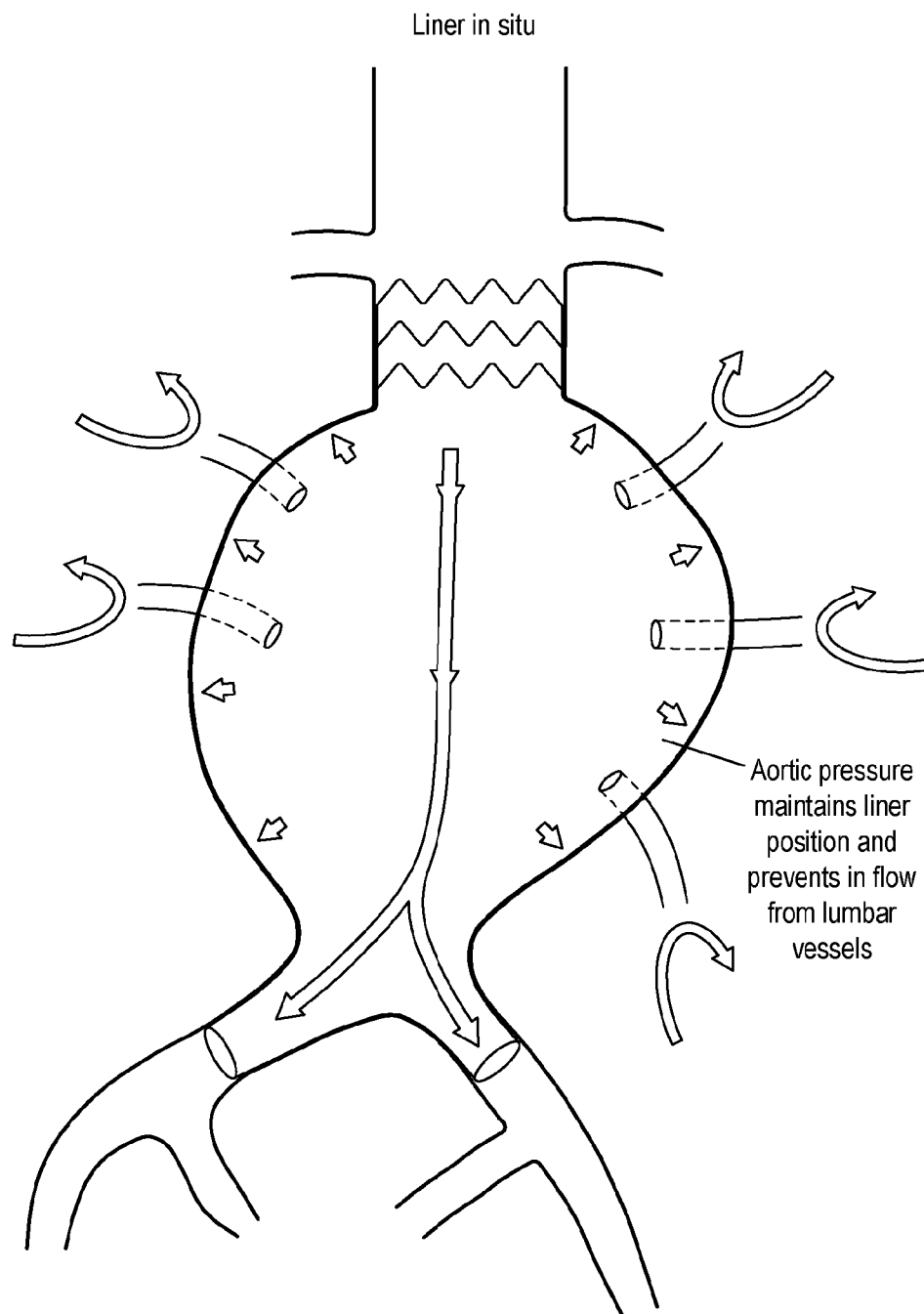
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**FIG. 2**

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**FIG. 3**

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**FIG. 4**

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2017/051169

A. CLASSIFICATION OF SUBJECT MATTER INV. A61F2/07 A61B5/02 G09B23/30 G06T17/00 ADD. B29C67/00 A61F2/06		
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) A61F A61B G09B B29C G06T		
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 2004/026183 A2 (NELLIX INC [US]; TAYLOR CHARLES S [US]; ZARINS CHRISTOPHER [US]; GESHL) 1 April 2004 (2004-04-01) page 3, line 24 - line 38; figures page 7, line 16 - page 8, line 9 -----	29-35
X	WO 2007/096183 A1 (ANGIOMED AG [DE]; BERKHOFF WOLFGANG [DE]) 30 August 2007 (2007-08-30) page 8, paragraph 4 - page 9, paragraph 2; claims; figures -----	29-35
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☒ Further documents are listed in the continuation of Box C. ☒ 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 11 July 2017		Date of mailing of the international search report 18/07/2017
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Neumann, Elisabeth

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2017/051169

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 2012/259406 A1 (SCHRECK STEFAN [US] ET AL) 11 October 2012 (2012-10-11) paragraphs [0060], [0070], [0077]; figures -----	29,33-37
X	DE 10 2006 020687 A1 (AESCULAP AG & CO KG [DE]; TUTECH INNOVATION GMBH [DE]; UNIV HAMBURG HA) 8 February 2007 (2007-02-08) paragraphs [0028], [0029], [0033], [0034] -----	29,33-36
X	US 2007/293936 A1 (DOBAK JOHN D III [US]) 20 December 2007 (2007-12-20) paragraphs [0007], [0014], [0016]; figures -----	29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2017/051169

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.: 1-28, 38-59
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:
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:
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:

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

Information on patent family members

International application No

PCT/GB2017/051169

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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