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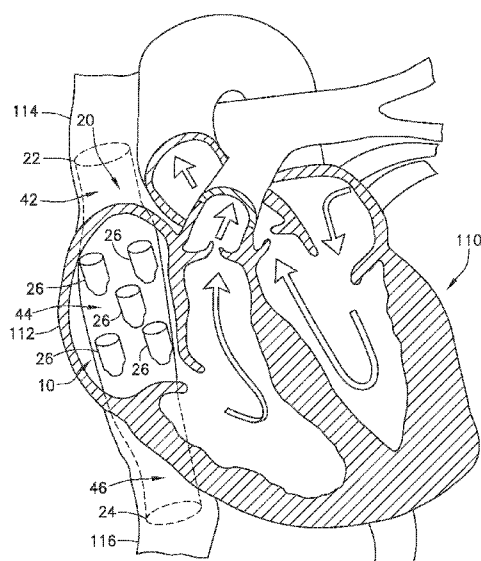


FIG. 1

(57) Abstract: A valved stent device configured to be deployed in a right atrium of a patient's heart includes an expandable frame and a cover on at least a portion of an inside surface and/or an outside surface of the expandable frame. When the frame is expanded, the expanded frame and the cover define a contiguous, sealed passage from a first end to an opposite end of the expanded frame. The frame and the cover of the valved stent device form portions which bias against and/or seal the superior vena cava and the inferior vena cava, and a middle portion which spans the right atrium. The frame and cover also form a plurality of valves in the middle portion of the device. The plurality of valves are configured to permit one-direction flow of a fluid from the passage into the patient's right atrium.

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VALVED STENT FOR THE TREATMENT OF TRICUSPID REGURGITATION

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Provisional Patent Application No. 62/868,275 filed June 28, 2019, entitled “Valved Stent for the Treatment of Tricuspid Regurgitation,” the disclosure of which is hereby incorporated by reference in its entirety.

BACKGROUND

Field of the Invention

[0002] The present disclosure is directed to a valved stent device for use in treating tricuspid valve regurgitation or other tricuspid valve damage or deficiencies, as well as to methods of manufacture of the valved stent device and methods for treating tricuspid valve regurgitation with the valved stent device.

Description of Related Art

[0003] Tricuspid regurgitation (TR) is a dysfunction of the atrio-ventricular valve (e.g., the valve between the right atrium and the right ventricle) in the right side of the heart characterized by incompetence of the valve, resulting in backflow of blood from the right ventricle to the right atrium. The resulting volume overload of the right ventricle can cause ventricular dilatation and dysfunction with decreased cardiac output. Also, increased backpressure can lead to volume overload and systemic congestion with edema, intestinal dysmotility, and hepatic congestion.

[0004] In the United States alone, there are an estimated 1.6 million patients suffering from TR. TR commonly co-exists with left-sided valvular conditions, such as mitral valve disease. About 50% of patients with mitral regurgitation have moderate to severe tricuspid regurgitation. Isolated TR is on the rise with increased prevalence of atrial fibrillation and intracardiac devices (pacemakers and ICDs). However, TR is currently undertreated by surgery. In the United States, surgeons treat only about 5,500 patients for TR per year, with most surgical treatments occurring in conjunction with left heart surgeries. When treated, surgeons choose to repair the valve about 90% of the time (valve replacement is performed about 10% of the time). However, there is a significant gap in the literature about outcomes for surgical intervention for TR and in guidelines for the management of patients with isolated TR. It is believed that the morbidity associated with surgery for treatment of TR is higher than for aortic or mitral valve surgeries. However, patients

with TR are often fairly sick and have additional co-morbidities, which may contribute to overall morbidity for surgical interventions. In any case, it is believed that advanced symptomatic severe TR remains undertreated.

[0005] There are emerging technologies, such as prosthetic valve designs, which can be used for treatment of TR. However, such prosthetic valve devices are often difficult to manipulate and implant percutaneously. In fact, available devices for percutaneously delivering a prosthetic valve may not be suitable for tricuspid valve replacement due to complex anatomy and relatively fragile surrounding tissues. Another known percutaneous solution for symptomatic tricuspid regurgitation is off-label use of a balloon-expandable aortic prosthesis in the superior vena cava and/or in the inferior vena cava. For example, the TricValve® system (P+F Products GmbH, Wessling, Germany) is a transcatheter bicaval approach, in which valves are placed in both the inferior and superior vena cava. While these devices appear to be effective in some instances, simpler and more cost-effective approaches for non-invasive surgical treatment of TR are needed.

SUMMARY

[0006] Provided herein is a valved stent device that, rather than attempting to alter the tricuspid valve itself, functions instead by adding valve(s) upstream from the tricuspid valve in the right atrium. In this way, the valved stent device isolates a portion of the right atrium that is connected to the superior vena cava and the inferior vena cava. The stent device may also include valve covers, flaps, pockets, or leaflets for expelling blood from an interior of the valved stent device into the right atrium, with the goal of reducing the reflux of blood from the right atrium to the superior vena cava and the inferior vena cava. While not intending to be bound by theory, it is believed that the valved stent device provides correction of venous congestion, which may result in decreased right ventricle volume and improved performance.

[0007] By way of comparison, current percutaneous devices for treating tricuspid regurgitation can be difficult to deploy (in particular, annuloplasty devices). Such percutaneous devices also have significant associated morbidity; are not used on patients with ICD/pacemakers in place; are not retrievable; and require extensive expertise with transesophageal echocardiogram (TEE) guidance. The valved stent devices described herein address these shortcomings, being easy to deploy, with no tissue capture or sutures necessary. The valved stent device is also acutely

retrievable in case of poor function and, theoretically, may be used with pacemaker leads in place, since the implantation procedure can be done largely with fluoroscopic guidance.

[0008] According to an aspect of the disclosure, a valved stent device configured to be deployed in a right atrium of a patient's heart includes an expandable frame and a cover on at least a portion of an inside surface and/or an outside surface of the expandable frame. When the frame is expanded, the expanded frame and the cover define a contiguous, sealed passage from a first end to an opposite end of the expanded frame. The frame and the cover of the valved stent device form: a first portion having a first wall portion defining a portion of the passage and configured to bias against an inner circumference of a patient's superior vena cava; a second portion extending axially from the first portion having a second wall portion defining a portion of the passage, the second wall portion being configured to extend through the right atrium between the patient's superior vena cava and inferior vena cava; and a third portion extending axially from the second portion having a third wall portion defining a portion of the passage, configured to extend into the patient's inferior vena cava to bias against the inner circumference of the patient's inferior vena cava. The frame and cover also form a plurality of valves in the second wall portion of the second portion. The plurality of valves are configured to permit one-direction flow of a fluid from the passage into the patient's right atrium.

[0009] According to another aspect of the disclosure, a method of manufacture of the valved stent device is provided. The method includes attaching the cover to the frame by at least one of an adhesive or suturing; cutting portions of the cover to form the openings of the plurality of valves; and attaching flaps to the cover near the openings to form pockets of the valves.

[0010] According to another aspect of the disclosure, a method of treating tricuspid regurgitation in a patient is provided. The method includes a step of deploying the valved stent device into the right atrium of the patient with the first portion biased against the inner circumference of the patient's superior vena cava, the third portion biased against the inner circumference of the patient's inferior vena cava, and the second portion and the plurality of valves in the patient's right atrium.

[0011] Examples of the present disclosure will now be described in the following numbered clauses:

[0012] Clause 1: A valved stent device configured to be deployed in a right atrium of a patient's heart, comprising an expandable frame and a cover on at least a portion of an inside surface and/or

an outside surface of the expandable frame, wherein, when the frame is expanded, the expanded frame and the cover define a contiguous, sealed passage from a first end to an opposite end of the expanded frame, the frame and cover of the valved stent device forming: a first portion comprising a first wall portion defining a portion of the passage and configured to bias against an inner circumference of a patient's superior vena cava; a second portion extending axially from the first portion comprising a second wall portion defining a portion of the passage, the second wall portion being configured to extend through the right atrium between the patient's superior vena cava and inferior vena cava; a third portion extending axially from the second portion comprising a third wall portion defining a portion of the passage, configured to extend into the patient's inferior vena cava to bias against the inner circumference of the patient's inferior vena cava; and a plurality of valves in the second wall portion of the second portion, the plurality of valves being configured to permit one-direction flow of a fluid from the passage into the patient's right atrium.

[0013] Clause 2: The valved stent device of clause 1, wherein the cover comprises a non-bioerodible polymer layer or membrane.

[0014] Clause 3: The valved stent device of clause 1 or clause 2, wherein the first wall portion, the second wall portion, and the third wall portion each comprise at least one of an annular wall, a substantially annular wall, an outwardly convex wall, a spheroidal wall, or a partially spherical wall.

[0015] Clause 4: The valved stent device of any of clauses 1-3, wherein the plurality of valves are arranged substantially equidistantly around a circumference of the second portion on a plane perpendicular to a central and/or longitudinal axis of the second portion.

[0016] Clause 5: The valved stent device of any of clauses 1-3, wherein the plurality of valves comprises at least a first group of valves arranged substantially equidistantly around a circumference of the second portion on a first plane perpendicular to a central and/or longitudinal axis of the second portion, and a second group of valves arranged substantially equidistantly around a circumference of the second portion on a second plane perpendicular to the and/or longitudinal axis of the second portion.

[0017] Clause 6: The valved stent device of any of clauses 1-5, wherein the plurality of valves are arranged such that the valved stent device is symmetrical about a central and/or longitudinal axis of the stent device.

[0018] Clause 7: The valved stent device of any of clauses 1-6, wherein the plurality of valves each comprise an opening in the cover and a flap configured to seal the opening to prevent backflow of fluid from the patient's right atrium into the passage.

[0019] Clause 8: The valved stent device of clause 7, wherein, for the plurality of valves, the flaps are configured to seal the openings during ventricular systole and to be in a neutral position at other times during a cardiac cycle.

[0020] Clause 9: The valved stent device of clause 7 or clause 8, wherein the flaps of the plurality of valves connect to the cover along a substantially straight seam substantially aligned with a circumference of the second portion.

[0021] Clause 10: The valved stent device of clause 7 or clause 8, wherein the flaps of the plurality of valves connect to the cover at a curved seam which forms a pocket.

[0022] Clause 11: The valved stent device of any of clauses 7-10, wherein the openings of the plurality of valves have a total area of from about 1.5 cm² to about 6 cm².

[0023] Clause 12: The valved stent device of any of clauses 7-11, comprising nine valves, each valve having an opening with an area of from about 0.33 cm² to about 0.66 cm².

[0024] Clause 13: The valved stent device of any of clauses 7-12, configured such that, when the stent device is deployed in the right atrium, the flaps are configured to move in an upwards direction towards the first portion of the device and the superior vena cava to seal the openings.

[0025] Clause 14: The valved stent device of any of clauses 7-13, wherein the cover and the flap are formed from a non-bioerodible polymer.

[0026] Clause 15: The valved stent device of clause 14, wherein the non-bioerodible polymer comprises at least one of polyurethane, polytetrafluoroethylene (PTFE), or polyethylene terephthalate (PET).

[0027] Clause 16: The valved stent device of any of clauses 7-13, wherein the cover is formed from a non-bioerodible polymer, and the flaps of the plurality of valves are formed from pericardium tissue.

[0028] Clause 17: The valved stent device of clause 16, wherein the cover is formed from a non-bioerodible polymer and the flaps of the plurality of valves are formed from an electrospun polymer material comprising a urethane monomer.

[0029] Clause 18: The valved stent device of any of clauses 1-17, wherein the cover is connected to the inner surface and/or the outer surface of the frame by at least one of a biocompatible adhesive or suturing.

[0030] Clause 19: The valved stent device of any of clauses 1-18, wherein the cover and/or frame are coated with an antithrombotic coating, such as a coating comprising at least one of polyethylene glycol (PEG) or zwitterionic groups, and/or coated with an anti-clotting agent, such as heparin.

[0031] Clause 20: The valved stent device of any of clauses 1-19, wherein a diameter of the second portion, when expanded, is greater than a diameter of the first portion and/or is greater than a diameter of the third portion.

[0032] Clause 21: The valved stent device of any of clauses 1-20, wherein the frame comprises a balloon-expandable frame.

[0033] Clause 22: The valved stent device of any of clauses 1-20, wherein the frame comprises a self-expanding frame.

[0034] Clause 23: The valved stent device of clause 22, wherein the self-expanding frame comprises a superelastic, shape-memory alloy, such as nickel titanium alloy.

[0035] Clause 24: The valved stent device of any of clauses 1-23, wherein the frame comprises a plurality of flexible elongated tines.

[0036] Clause 25: The valved stent device of clause 24, wherein the plurality of tines are interconnected, thereby forming a closed cell region on the second portion of the valved stent device.

[0037] Clause 26: The valved stent device of any of clauses 1-25, wherein the frame comprises an annular spring positioned in the passage of the valved stent device configured to bias the second portion of the valved stent device radially outwardly.

[0038] Clause 27: The valved stent device of any of clauses 1-26, wherein at least one of the first portion or the third portion of the stent device comprises at least one expandable annular ring independent from other portions of the frame and connected to other portions of the valved stent device by the cover.

[0039] Clause 28: The valved stent device of any of clauses 1-27, configured such that, when deployed in the patient's right atrium, a and/or longitudinal axis of the first portion substantially aligns with a and/or longitudinal axis of a portion of the superior vena cava of the patient, and a

and/or longitudinal axis of the third portion substantially aligns with a and/or longitudinal axis of a portion of the inferior vena cava of the patient.

[0040] Clause 29: The valved stent device of any of clauses 1-28, wherein, when expanded, the second portion has a maximum outer diameter of from about 4 cm to about 8 cm, such as about 6 cm.

[0041] Clause 30: A method of manufacture of the valved stent device of any of clauses 1-29, the method comprising: attaching the cover to the frame by at least one of an adhesive or suturing; cutting portions of the cover to form the openings of the plurality of valves; and attaching flaps to the cover near the openings to form pockets of the valves.

[0042] Clause 31: The method of clause 30, wherein cutting portions of the cover to form the openings comprises cutting openings having a total area of from about 1.5 cm² to about 6 cm².

[0043] Clause 32: The method of clause 30 or clause 31, wherein the flaps are attached to the cover by at least one of a biocompatible adhesive or suturing.

[0044] Clause 33: The method of any of clauses 30-32, wherein the cover is formed from a non-bioerodible polymer, and the flaps of the plurality of valves are formed from pericardium tissue.

[0045] Clause 34: The method of any of clauses 30-32, wherein the cover is formed from a non-bioerodible polymer and the flaps of the plurality of valves are formed from an electrospun polymer material comprising a urethane monomer.

[0046] Clause 35: The method of any of clauses 30-34, further comprising applying a coating to the cover and/or frame of the valved stent device, the coating comprising an antithrombotic coating, comprising an antithrombotic agent, such as polyethylene glycol or molecules comprising zwitterionic groups, or an anticoagulant coating, comprising an anticoagulant agent such as heparin.

[0047] Clause 36: A method of treating tricuspid regurgitation in a patient, comprising: deploying the valved stent device of any of clauses 1-29 into the right atrium of the patient with the first portion biased against the inner circumference of the patient's superior vena cava, the third portion biased against the inner circumference of the patient's inferior vena cava, and the second portion and the plurality of valves in the patient's right atrium.

[0048] Clause 37: The method of clause 36, wherein the valved stent device is deployed percutaneously using a catheter.

[0049] Clause 38: The method of clause 36 or clause 37, wherein positioning of the valved stent device in the right atrium is performed using radiopaque markings as guides.

[0050] Clause 39: The method of any of clauses 36-38, wherein, when the valved stent device is deployed in the right atrium, the flaps are configured to move in an upwards direction towards the first portion of the valved stent device and towards the superior vena cava to seal the openings.

[0051] Clause 40: The method of any of clauses 36-39, further comprising retrieving the valved stent device from the right atrium of the patient about 2 months to about 4 months following implantation of the valved stent device.

BRIEF DESCRIPTION OF DRAWINGS

[0052] These and other features and characteristics of the present disclosure, as well as the methods of operation and functions of the related elements of structures and the combination of parts and economies of manufacture, will become more apparent upon consideration of the following description and the appended claims with reference to the accompanying drawings, all of which form a part of this specification, wherein like reference numerals designate corresponding parts in the various figures. It is to be expressly understood, however, that the drawings are for the purpose of illustration and description only and are not intended as a definition of the limit of the invention.

[0053] FIG. 1 is a schematic drawing of a heart showing an exemplary valved stent device for the treatment of severe TR deployed in a right atrium of the heart;

[0054] FIG. 2 is a schematic drawing of a front view of an exemplary valved stent device;

[0055] FIG. 3A is a front view of a portion of a stent frame of another exemplary valved stent device;

[0056] FIG. 3B is another front view of the stent frame of the valved stent device of FIG. 3A;

[0057] FIG. 4A is a schematic drawing of a portion of a valve of a valved stent device;

[0058] FIG. 4B is a schematic drawing of another embodiment of a valve of a valved stent device;

[0059] FIGS. 5A and 5B are photographs of portions of a stent frame of an embodiment of a valved stent device;

[0060] FIGS. 6A and 6B are photographs an embodiment of a valved stent device including a frame and cover;

[0061] FIGS. 7A-7D are photographs of an embodiment of a valved stent device showing valves in open positions;

[0062] FIG. 8A is a photograph of another embodiment of a valved stent device showing the valves in a closed position; and

[0063] FIG. 8B is a photograph of the valved stent device of FIG. 8A showing the valves in an open position.

DETAILED DESCRIPTION

[0064] The use of numerical values in the various ranges specified in this application, unless expressly indicated otherwise, are stated as approximations as though the minimum and maximum values within the stated ranges are both preceded by the word “about”. In this manner, slight variations above and below the stated ranges can be used to achieve substantially the same results as values within the ranges. Also, unless indicated otherwise, the disclosure of these ranges is intended as a continuous range including every value between the minimum and maximum values.

[0065] As used herein, the terms “right”, “left”, “top”, “bottom”, and derivatives thereof shall relate to devices as they are oriented in the drawing figures and/or in relation to usage of the devices. However, it is to be understood that the invention can assume various alternative orientations and, accordingly, such terms are not to be considered as limiting. Also, it is to be understood that the invention can assume various alternative variations and stage sequences, except where expressly specified to the contrary. It is also to be understood that the specific devices and processes illustrated in the attached drawings, and described in the following specification, are examples. Hence, specific dimensions and other physical characteristics related to the embodiments disclosed herein are not to be considered as limiting. The terms “distal” and “proximal” refer to directions with respect to the devices described herein, and although they also correspond to the relative position, orientation, and/or direction of element(s) of the devices described herein with respect to the end use of the device in typical use as a percutaneous device, those descriptors are provided only to describe the relative position, orientation, and/or direction of element(s) of the devices described herein with regard to the device as a whole, and to elements thereof, and do not require or infer that the elements are located, positioned, oriented, or in any physical relationship with an end user at any given time. Figures are not drawn to scale, but are

drawn in a manner to best depict the relationship between the various elements of the device drawn in the figure.

[0066] As used herein, the terms “comprising,” “comprise” or “comprised,” and variations thereof, are meant to be open ended. The terms “a” and “an” are intended to refer to one or more.

[0067] As used herein, the “treatment” or “treating” of a condition, wound, or defect means administration to a patient by any suitable dosage regimen, procedure and/or administration route of a composition, device or structure with the object of achieving a desirable clinical/medical end-point, including repair and/or replacement of a tricuspid or mitral valve.

[0068] As used herein, the term “patient” or “subject” refers to members of the animal kingdom including but not limited to human beings and “mammal” refers to all mammals, including, but not limited to human beings.

[0069] A polymer composition is “biocompatible” in that the polymer and, where applicable, degradation products thereof, are substantially non-toxic to cells or organisms within acceptable tolerances, including substantially non-carcinogenic and substantially non-immunogenic, and are cleared or otherwise degraded in a biological system, such as an organism (patient) without substantial toxic effect. Non-limiting examples of degradation mechanisms within a biological system include chemical reactions, hydrolysis reactions, and enzymatic cleavage.

[0070] As used herein, the term “polymer composition” is a composition comprising one or more polymers. As a class, “polymers” includes, without limitation, homopolymers, heteropolymers, co-polymers, block polymers, block co-polymers and can be both natural and/or synthetic. Homopolymers contain one type of building block, or monomer, whereas copolymers contain more than one type of monomer. The term “(co)polymer” and like terms refer to either homopolymers or copolymers.

[0071] A polymer “comprises” or is “derived from” a stated monomer if that monomer is incorporated into the polymer. Thus, the incorporated monomer (monomer residue) that the polymer comprises is not the same as the monomer prior to incorporation into a polymer, in that at the very least, certain groups are missing and/or modified when incorporated into the polymer backbone. A polymer is said to comprise a specific type of linkage if that linkage is present in the polymer as a consequence of its normal or intended polymerization and/or cross-linking processes.

[0072] As described herein, a “fiber” is an elongated, slender, thread-like and/or filamentous structure. A “matrix” is any two- or three-dimensional arrangement of elements (e.g., fibers),

either ordered (e.g., in a woven or non-woven mesh) or randomly-arranged (as is typical with a mat of fibers typically produced by electrospinning) and can be isotropic or anisotropic.

[0073] By “biodegradable or “bioerodable”, it is meant that a material, such as a polymer, once implanted and placed in contact with bodily fluids and tissues, will degrade either partially or completely through chemical reactions with the bodily fluids and/or tissues, typically and often over a time period of hours, days, weeks or months. Non-limiting examples of such chemical reactions include acid/base reactions, hydrolysis reactions, and enzymatic cleavage. The biodegradation rate of the polymer matrix may be manipulated, optimized or otherwise adjusted so that the matrix degrades over a useful time period. Bioerodible polymers degrade *in vivo* over a time period. “Non-bioerodible” polymers (e.g., durable polymers) do not degrade to any significant extent *in vivo* over a time period of at least two years, for instance, they do not degrade substantially *in vivo* in five or ten years, and include polyethylene terephthalate (PET, including DACRON®) and PTFE (polytetrafluoroethylene, including expanded PTFE (ePTFE, W.L. Gore), and TEFLON®), which are often used in implantable medical devices. Other non-limiting examples of non-bioerodable polymers include: poly(ethylene-co-vinyl acetate), poly(n-butylmethacrylate), and poly(styrene-b-isobutylene-b-styrene).

[0074] As used herein, “percutaneous” refers to “through the skin.” In the context of the devices provided herein, access to the cardiovascular system is obtained through use of a catheter, for example, and without limitation, by use of the Seldinger technique. Access to the inferior vena cava may be obtained through its branches, for example via the femoral vein, while access to the superior vena cava may be obtained through its branches, for example via the external jugular vein. Access to veins for delivery of an expandable device, e.g., as described herein, is typically achieved using a catheter device, in any useful configuration, as are broadly-known in the medical arts.

Valved stent devices

[0075] With reference to FIGS. 1 and 2, the present disclosure is directed to a valved stent device 10 configured, for example, to be deployed in a right atrium 112 of a patient’s heart 110 (shown in FIG. 1). The present disclosure is also directed, in part, to methods of making and deploying the valved stent device 10 in the right atrium 112 for treatment of tricuspid regurgitation.

[0076] The valved stent device 10 spans the right atrium 112 from the superior vena cava 114 to the inferior vena cava 116. The valved stent device 10 can comprise an expandable frame, identified generally by reference number 12 (shown in FIGS. 2-3B), and a cover, identified

generally be reference number 14 (shown in FIGS. 2-3B), over at least a portion of an inside surface 16 and/or an outside surface 18 of the expandable frame 12. The cover 14 can comprise a non-bioerodible polymer material, layer, fabric, or sheet. When the frame 12 is expanded, the expanded frame 12 and cover 14 can define a contiguous, sealed passage 20 from a first end 22 to an opposing end 24 of the expandable frame 12.

[0077] In some examples and as described in further detail herein, the valved stent device 10 comprises three interconnected portions or sections. A first section or portion 42 of the device 10 is configured to bias against an inner circumference of a patient's superior vena cava 114. A second section or portion 44 of the device 10 extends axially from the first portion 42 and is configured to extend through the right atrium 112 between the patient's superior vena cava 114 and the inferior vena cava 116. A third section or portion 46 of the device 10 extends axially from the second portion 44 and is configured to extend into the patient's inferior vena cava 116 to bias against an inner circumference of the patient's inferior vena cava 116. As used herein, "bias against" means that the portions 42, 46 of the stent device 10 are expanded to contact and exert a biasing force against the superior vena cava 114 and the inferior vena cava 116. In some examples, the biasing force exerted against the superior vena cava 114 and/or the inferior vena cava 116 creates a seal, such that all or substantially all blood flow through the superior vena cava 114 and/or the inferior vena cava 116 passes into the passage 20 of the valved stent device 10. In other examples, the valved stent device 10 may not fully seal the superior vena cava 114 and/or the inferior vena cava 116, meaning that some blood flows into the right atrium 112 without entering the passage 20 of the valved stent device 10.

[0078] The valved stent device 10 further comprises a plurality of valves 26 formed by and/or positioned over openings of the cover 14. The valves 26 are configured to permit one-direction flow of a fluid (e.g., blood) from the passage 20 into the patient's right atrium 112, thereby isolating inflow of fluid (blood) into the right atrium 112. In particular, a substantial portion or all fluid (blood) flows into the right atrium 112 through the valves 26 and not directly from the superior vena cava 114 or inferior vena cava 116. Further, since the valves 26 are one-way valves, fluid (blood) in the right atrium 112 is prevented from reentering the interior or sealed passage 20 defined by the device 10. In this manner, the valved stent device 10 can reduce, control, or eliminate systemic backflow and congestion created by severe TR.

[0079] The valved stent device 10 described herein can be designed for easy deployment in the right atrium 112. Further, the valved stent device 10 can be configured to be easily repositioned or removed if, for example, an echocardiogram or angiography at the time of deployment or later, reveals that the valves 26 are not functioning in an expected manner. As will be appreciated by those skilled in the art, the valved stent devices 10 can be a custom-sized device, tailored, and tested based on the anatomy of an individual patient. In other examples, manufactured stent devices 10 can be sized to fit certain patient populations. In that case, the stent devices 10 may be provided in a limited number of general sizes for patients of particular ages, weights, and/or for use with different anatomical structure.

[0080] In some examples, the valved stent device 10 is configured to be expandable, meaning that the device 10 can be configured to transition from a compressed configuration, for implanting the device 10 through a percutaneous access site, to an expanded configuration, when deployed in the right atrium 112. In the compressed configuration, the device 10 may be sized to fit into a catheter used for percutaneous access to the right atrium 112 by any suitable route. Percutaneous access can be useful for both percutaneous delivery of the device 10 and, where needed, removal of the device 10. In the expanded configuration, the valved stent device 10 extends between the superior vena cave 114 and the inferior vena cava 116 spanning the right atrium 112, as shown in FIG. 1.

[0081] The valved stent device 10 can be a balloon-expandable device formed from a flexible and malleable material. Materials for forming balloon-expandable stents are well-known and may include, for example, stainless steel or cobalt chromium. In order to deploy a balloon-expandable device, the device 10 can be compressed to fit within the lumen of a delivery catheter. For example, the device 10 can be crimped to a balloon catheter and inserted over guidewire through a delivery catheter. The delivery catheter and device 10 can then be advanced to a deployment location and the compressed device is moved through an open distal end of the delivery catheter. Once the valved stent device 10 is released from the delivery catheter to the deployment location (e.g., into the right atrium 112), the balloon catheter can be inflated to cause the valved stent device 10 to transition from the compressed configuration to the expanded configuration. When the balloon catheter is removed, the valved stent device 10 remains in the expanded configuration. Manufacturing techniques and materials for making balloon-expandable stent devices are well-known in the stent field. Further, inflatable and/or balloon catheters for expanding stent devices

are also well-known in the percutaneous device field and are commercially available from numerous sources.

[0082] The valved stent devices 10 described herein can also be self-expanding devices. A self-expanding device can be compressed to fit within the delivery catheter, and is inherently biased to automatically transition to an expanded or deployed configuration once released from the delivery catheter. In particular, the stent device 10 can be biased to automatically adopt the expanded configuration where the device 10 spans the right atrium 112 and extends into both the superior vena cava 114 and the inferior vena cava 116, as shown in FIG. 1. Materials used for self-expanding stents are well-known in the stent field and include, without limitation, shape-memory alloys, such as nickel titanium alloy (e.g., NITINOL). NITINOL is a nickel-titanium alloy comprising a nearly equiatomic intermetallic compound of nickel and titanium. NITINOL exhibits shape memory and superelastic properties related to a reversible temperature or stress-induced martensite phase transition. NITINOL can be deformed to 10% strain and can recover to its original shape when the deformation force is released. *See, e.g.,* Bonsignore, C, Present and future approaches to lifetime prediction of superelastic nitinol, *Theoretical and Applied Fracture Mechanics* 92 (2017) 298–305. Although many shape-memory alloys exist, NITINOL is currently the most common shape memory alloy used in stent preparation and other biomedical applications, because NITINOL exhibits superelastic behavior at body temperature (e.g., 37 °C) with the low transformation temperature within the material.

[0083] Self-expanding devices are produced by heat-setting. Heat-setting comprises heating the device to a setting temperature (about 400°C to 500°C for NITINOL) and, once heated, bending or otherwise conforming the device to the expanded configuration. For example, the device could be bent around a mandrel or mold shaped in the expanded configuration. The device is then subsequently cooled (e.g., quenched), thereby setting the structure to the expanded configuration. After quenching, the device can be deformed at a lower temperature. However, the device returns to the expandable configuration once the device is heated above a transition temperature (e.g., above body temperature for NITINOL) and removed from any constraining structures (e.g., a delivery catheter).

Expandable frame structures

[0084] With reference to FIGS. 2-3B, an exemplary valved stent device 10 can comprise the expandable frame 12 and the cover 14. Photographs of a frame of an expandable frame of a valved

stent device are also shown in FIGS. 5A and 5B. The frame 12 can be a balloon-expandable frame or a self-expanding frame, such as a self-expanding frame comprising a superelastic, shape-memory alloy, such as a nickel titanium alloy (e.g., NITINOL). In some examples, the valved device 10 does not include a ferromagnetic material and, therefore, can be compatible with magnetic resonance imaging (MRI) methods.

[0085] The frame 12 can be formed from and/or can comprise a plurality of interconnected elongated members or tines 28. As will be appreciated by those skilled in the art, the elongated members or tines 28 can be arranged in a variety of configurations and patterns to achieve different mechanical properties. For example, tines 28 can be connected together to form closed cell regions. As used herein, a “closed cell region” refers to a region in which the elongated members or tines 28 are connected together to form enclosed shapes. For example, the elongated members or tines 28 can be connected together to form a series of squares, rectangles, or diamonds extending around a circumference of the device 10. Alternatively or additionally, the elongated members or tines 28 can be arranged to form open cell regions. As used herein, an “open cell region” refers to a pattern of elongated members or tines 28 that do not form enclosed shapes. For example, a region comprising solely of longitudinally extending tines 28 or a helical coil is an open cell region.

[0086] In some examples, the elongated members or tines 28 can be bent to form loops, such as tear-drop shaped loops shown in FIGS. 3A and 3B. In such cases, the elongated members or tines 28 comprise a bent portion 30 positioned, for example, near a middle portion of the device 10 and ends positioned adjacent to one of the ends 22, 24 of the device 10. As shown in FIGS. 2-3B, in the expanded configuration, the bent portions 30 protrude radially outwardly giving the second portion 44 of the device 10 a bulbous structure and appearance relative to the first and third portions 42, 46 of the device 10. Also, bent portions 30 of the tines 28 can be connected together to impart additional structural integrity for portions of the frame 12.

[0087] The frame 12 comprising the elongated members or tines 28 can be produced by a number of different manufacturing techniques used for producing implantable expandable devices, such as stents, filtration devices, and similar endovascular devices. Known manufacturing techniques for producing expandable devices for percutaneous delivery, as are broadly-known with respect to production of stents for the treatment of atherosclerosis, can be employed for manufacturing the expandable frames 12 disclosed herein. For smaller devices, such as neurovascular or cardiovascular stents, laser cutting of a template material, e.g., NITINOL tubing,

can be used, which facilitates rapid and reproducible production of such devices. In other examples, the frame 12 of the valved stent device 10 can be manufactured by chemical etching techniques, or by laser chemical etching. In other examples, the expandable frame 12 can be a wire-based structure produced by winding and twisting of round or flat wire on an appropriate template or mandrel.

[0088] Portions of the elongated members or tines 28 may be physically joined by any useful technique, such as by laser welding, soldering, or mechanical clamping with thin-walled metallic tubes. Numerous publications, patents, and patent documents describe percutaneous stent designs, materials, and manufacturing techniques for both self-expandable and balloon-expandable stents, which may be useful to produce the frame 12 of the device 10. *See, for example and without limitation*, Stoeckel, D. *et al.* Self-expanding nitinol stents: material and design considerations. *Eur Radiol.* 2004 Feb; 14(2): 292-301; Sangiorgi, G., *et al.* Engineering aspects of stents design and their translation into clinical practice *Ann Ist Super Sanità* 2007 Vol. 43, No. 1: 89-100; and United States Patent Nos. 8,728,146 and 8,986,366.

[0089] In some examples, some or all of the elongated members or tines 28 can be coated by a suitable protective material or coating. In particular, elongated members or tines 28 likely to come into contact with blood and/or body tissue can be coated to prevent protein adsorption and/or corrosion. Coatings, materials, and surface treatments for protecting the members or tines 28 and/or for preventing protein adsorption are commonly used in the manufacture of stent devices, and are known to those skilled in the art. In some examples, portion of the tines 28 can be coated with antithrombotic materials or agents, such as polyethylene glycol (PEG) and/or materials comprising zwitterionic groups. The members or tines 28 may also be coated with an anti-clotting agent, such as heparin and/or a nitro-oleic acid or nitro-conjugated linoleic acid.

[0090] In some examples, the valved stent device 10 can further comprise an annular spring 36 positioned in the passageway 20 and configured to bias portions of the expandable frame 12 radially outwardly. The annular spring 36 can be configured to support the expandable frame 12, such that the expandable frame 12 remains in its expanded position when deployed. In some examples, the annular spring 36 comprises a plurality of circumferentially-disposed elongated members or struts connected by alternating peaks 38 and valleys 40 to form a waveform or zig-zag pattern. The peaks 38 and valleys 40 can be configured to move away from one another as the spring 36 expands radially outwardly, thereby supporting the frame 12. In some examples, the

spring 36 can be formed from the same self-expanding and/or shape memory material as the frame 12. In other examples, the spring 36 can be formed from the self-expanding material, while portions of the frame 12 are not formed from self-expanding materials. In such cases, the frame 12 can be made to expand due to the self-expanding characteristics of the spring 36.

[0091] With specific reference to FIGS. 2 and 3B, in some examples, segments of the frame 12 that form the first portion 42 and/or the third portion 46 of the valved stent device 10 may comprise expandable annular rings 56 independent from other portions of the expandable frame 12. As depicted in FIGS. 2 and 3B, the expandable annular rings 56 are connected to other portions of the stent device 10 by the cover 14. The expandable rings 56 are positioned in series with other portions of the valved stent device 10 along a curvilinear, central and/or longitudinal axis X thereof. As used herein, a “central and/or longitudinal axis” can refer to an axis passing through a center of mass and/or axis of rotation of a three-dimensional structure, or to an axis passing through the cross-sections of the three-dimension structure. The “central and/or longitudinal axis” runs lengthwise through (rather than across or transverse to) the three-dimensional structure. The expandable rings 56 can allow the first portion 42 and third portion 46 of the valved stent device 10 to bend by a greater amount than if such rings 56 were not present or if the rings were fixedly connected to other portions of the expandable frame 12 by, for example, elongated struts or tines 28.

[0092] In some examples, the expandable rings 56 can comprise interconnected segments extending circumferentially about the rings 56 in a zig-zag pattern. For example, the rings 56 can comprise alternating peaks 58 and valleys 60 connected together by elongated strut portions 62. As the rings 56 expand, the peaks 58 and valleys 60 can be configured to move circumferentially away from one another, such that a diameter of the ring 56 increases.

[0093] In some examples, portions of the valved stent device 10 or frame 12 can further comprise radiopaque markers 64 (shown in FIG. 2) to facilitate deployment and removal of the valved stent device 10. In such instances, during deployment of stent devices, fluoroscopic x-ray illumination can be used to visualize placement of the device 10. Materials typically used for stent manufacture, such as NITINOL, have poor visibility under fluoroscopic illumination, and as such, radiopaque markers are used for visualization of the device 10. Accordingly, the device 10 can further comprise one or more radiopaque markers 64, such as one or more of tantalum, gold, or platinum-iridium markers, are attached to or incorporated within the structure of the frame 12, to

facilitate fluoroscopic visualization of the valved stent device 10, e.g., during deployment and/or to ascertain placement of the device at any time subsequent to the deployment of the device 10. Radiopaque marker material may be soldered or welded to the device frame 12 at various points, such as at the ends 22, 24 of the device 10, and/or on the middle or second portion 44 of the device 10, such as adjacent to one or more of the valves 26.

[0094] The valved stent device 10 may further comprise a fastener (not shown), such as a hook, screw, nut, other tapped structures, or any suitable connector for attachment to a retrieval device or catheter. In this manner, the valved stent device 10 may be configured to provide temporary treatment for TR and may be retrieved after a period of time, such as about 2 months to 4 months after implantation. The fastener for retrieving the valved stent device 10 may be positioned near an end 22, 24 of the device 10 to facilitate the retrieval and removal of the device 10. The fastener can be configured to be engaged by, for example, a guidewire comprising a loop, ring, collar, locking structure, or similar connector. Once the fastener is engaged, the guidewire can be retracted into, for example, a catheter. Continued retraction of the guidewire draws the device 10 into the catheter, causing the device 10 to contract so that it can be removed in a conventional manner.

Cover structure and materials

[0095] With continued reference to the exemplary device depicted in FIG. 2, the valved stent device 10 can further comprise the cover 14. Photographs of a valved stent device including a cover mounted to and fully enclosing the frame are also provided in FIGS. 6A and 6B. In some examples, the cover 14 can be connected to the inside surface 16 and/or the outside surface 18 of the expandable frame 12. Cover(s) 14 may also be attached to both the inside surface 16 and the outside surface 18 of the frame 12. The cover 14 can be attached to the frame 12 using conventional connecting and fastening techniques, such as using either a biocompatible polymer adhesive or fine suturing materials, as are known in the art. In some examples, the cover 14 can comprise a non-bioerodible polymer material, such as a layer, membrane, sheet, film, mesh, matrix, fabric, or surface of the non-bioerodible polymer material. For example, the non-bioerodible polymer material can comprise and/or can be composed of PTFE, e.g., ePTFE. In other examples, the non-bioerodible polymer material can comprise or is composed of PET, e.g., DACRON®. In other examples, the cover 14 can comprise an electrospun polymer material, such as an electrospun polymer material comprising urethane monomers.

[0096] The cover 14 can be coated with, impregnated with, and/or formed from a non-thrombogenic or anti-fouling material, such as a non-thrombogenic polyurethane. The coating can comprise functional groups comprising, for example, anti-thrombogenic groups, such as zwitterionic groups. An exemplary and suitable coating comprising zwitterionic groups, which can be used with the frame 12 and/or cover 14 of the valved stent device 10, is disclosed in U.S. Patent No. 9,808,560 to Hong et al., which is incorporated by reference herein in its entirety. A polyurethane material, which can be used for forming portions of the cover 14 including anti-thrombogenic groups, is disclosed in Hong et al., *Synthesis, Characterization, and Paclitaxel Release from a Biodegradable, Elastomeric, Poly(ester urethane)urea Bearing Phosphorylcholine Groups for Reduced Thrombogenicity*, BioMacromolecules 2012, 13, 3686-3694. Other nonthrombogenic polymer materials are disclosed in Sang-Ho et al., *Nonthrombogenic, Biodegradable Elastomeric Polyurethanes with Variable Sulfobetaine Content*, ACS Appl. Mater. Interfaces 2014, 6, 22796–22806. In some examples, the antithrombotic material can comprise polyethylene glycol. The cover 14 can also be coated with an anticoagulant agent or material, such as heparin and/or nitro-fatty acids, such as nitro-oleic acid or nitro-conjugated linoleic acid.

[0097] In some examples, the expandable frame 12 and cover 14 can collectively form or define an expandable tubular structure including the first portion 42, the second portion 44, and the third portion 46. In some examples, the first, second, and third portions 42, 44, 46 formed by the frame 12 and cover 14 are aligned along the central and/or longitudinal axis X of the device 10, as shown in FIGS. 1 and 2. The axis X is not necessarily linear. Instead, the axis X can extend in a line or curve depending on an orientation of the device 10 in the right atrium 112 of the patient's heart 110. As shown in FIG. 1, when the device 10 is deployed in the right atrium 112 and expanded, the axis X generally extends from and is co-extensive with a central and/or longitudinal axis of the superior vena cava 114 or a central and/or longitudinal axis of the inferior vena cava 116. In some examples, a central and/or longitudinal axis of the first portion 42 substantially aligns with the central and/or longitudinal axis of a portion of the superior vena cava 114 and a central and/or longitudinal axis of the third portion 46 substantially aligns with the central and/or longitudinal axis of a portion of the inferior vena cava 116.

[0098] The covered first, second, and third portions 42, 44, 46 of the valved stent device 10 may be tubular structures comprising annular walls or wall portions formed by the frame 12 and cover 14, which define the lumen or passageway 20 for permitting passage of fluid (e.g., blood)

through the device 10, when expanded. The walls or wall portions of the first, second, and third portions 42, 44, 46 can have a variety of shapes or curvatures. For example, the walls of the first, second, and third portions 42, 44, 46 can comprise one or more of an annular wall, a substantially or partially annular wall, an outwardly convex wall, a spheroidal wall, a partially spherical wall, or combinations thereof. The portions 42, 44, 46 are generally longitudinally-flexible, such that the portions 42, 44, 46 flex along the axis X. For example, the portions 42, 44, 46 may bend or flex relative to one another, such that the axis X of the stent device 10 adopts the curved and/or curvilinear configuration. Accordingly, blood flowing through the passageway 20 of the valved stent device 10 would travel in a curved or curvilinear flow path.

[0099] As shown in exemplary FIG. 1, the first portion 42 of the stent device 10 is positioned in and configured to bias against the inner circumference of a patient's superior vena cava 114. When expanded, the first portion 42 of the stent device 10 can seal the superior vena cava 114, such that blood flows into the right atrium 112 only through the passageway 20 of the device 10. The second portion 44 extends axially from the first portion 42. As used herein, "extending axially from" means that the second portion 44 is connected to and extends from an end of the first portion 42. The first portion 42 and the second portion 44 are arranged such that a central and/or longitudinal axis of the first portion 42 is co-extensive with a central and/or longitudinal axis of the second portion 44. In a similar manner, the third portion 46 is connected to and extends axially from the second portion 44. The third portion 46 is configured to extend into the patient's inferior vena cava 116. When deployed, the third portion 46 biases against and seals the inner circumference of the inferior vena cava 116, such that at least a portion, or a substantial portion, of blood from the inferior vena cava 116 enters the right atrium 112 only through the passageway 20 of the valved stent device 10.

[00100] When expanded, the second portion 44 can be a bulbous and/or convex portion which extends or protrudes radially outwardly relative to the first portion 42 and the third portion 46. The first, second, and third portions 42, 44, 46 of the valved stent device 10 are generally sized to span in the right atrium 112 protruding into the superior vena cava 116 and into the inferior vena cava 114. The length L2 and diameter D2 can be selected to maximize or optimize sizes of the valves 26 within the right atrium of the patient. As shown in the exemplary device 10 in FIGS. 1-3B, the first portion 42 and the third portion 46 can have narrower outer diameters D1, D3 sized to seal the superior vena cava 116 and the inferior vena cava 114.

[00101] In some examples, the stent device 10 can have a total length L of from about 10 cm to about 20 cm, or about 12 cm, for standard sized patients. In an expanded state, the outer diameter D1, D3 of the first portion 42 and the third portion 46 can be about 1 cm to about 2 cm. The maximum outer diameter D2 of the second portion 44, when expanded, can be greater than the diameters D1, D2. For example, the outer diameter D2 of the second portion 44, when expanded, can be from about 2 cm to about 10 cm, or about 6 cm. In a contracted or delivery state, the valved stent device 10 can be configured to fit within a delivery catheter of about 20 Fr to about 24 Fr (e.g., a delivery catheter having an outer diameter of from about 6 mm to about 8 mm).

Valve configuration and placement

[00102] Referring to exemplary FIG. 1, the valved stent device 10 further comprises the plurality of valves 26. Photographs of a valved stent device including valves in an open position are shown in FIGS. 7A-7D. Photographs of another example of a valved stent device showing valves in a closed position (FIG. 8A) and in an open position (FIG. 8B) are shown in FIGS. 8A and 8B. As shown in FIG. 2, the valves 26 can be positioned on the second portion 44 of the device 10. The valves 26 can be configured to permit one-direction flow of fluid from the valved stent device 10 (e.g., from the passageway 20 of the stent device 10 into the patient's right atrium 112).

[00103] The plurality of valves 26 can be provided in a variety of positions and orientations on the second portion 44. For example, one or more of the valves 26 can be located at lower positions of the second portion 44 (e.g., closer to the third portion 46 than to the first portion 42). When deployed in the right atrium 112, these lower valves 26 are located closer to the inferior vena cava 116 than to the superior vena cava 114. Other valves 26 can be positioned in a middle of the second portion 44, an equal distance from the first portion 42 and the third portion 46. Other valves 26 are located at an upper position of the second portion 44 (e.g., closer to the first portion 42 than to the third portion 46). When the valved stent device 10 is deployed in the right atrium 112, these upper valves 26 are located closer to the superior vena cava 114 than to the inferior vena cava 116.

[00104] As shown in FIGS. 1 and 2, the valved stent device 10 includes nine valves 26 arranged generally in three rows extending about the circumference of the second portion 44. Some, but not necessarily all, of the valves 26 in a row can be axially aligned with valves 26 in other rows. However, the arrangement of valves 26 in FIGS. 1 and 2 is not intended to be limiting. In some examples, the device 10 can include more than or fewer than nine valves 26. Also, valves 26 can

be arranged in more than or fewer than three rows extending about the circumference of the second portion 44.

[00105] In some examples, the valves 26 can be positioned so that the device 10 is direction-independent, meaning that the device 10 can be deployed in the right atrium 112 with valves 26 facing in any direction. Similarly, the valves 26 may be arranged such that the device 10 is symmetrical about the central and/or longitudinal axis X. Beneficially, a direction-independent or symmetrical device does not need to be rotated (e.g., rotated about the axis X) and aligned during deployment, to ensure that certain valves 26 or certain portions of the device 10 are positioned near to specific regions of the right atrium 112 and/or heart 110. Instead, the device 10 can be positioned in the right atrium 112 in any orientation since the valves 26 are dispersed about the annular sidewall of the second portion 44.

[00106] When deployed in the right atrium 112 and expanded, the valved stent device 10 can be orientated such that the valves 26 face upwards (e.g., towards the first portion 42 of the device 10 and the patient's superior vena cava 116). As used herein, "face upwards" means that the valves 26 are shaped to direct fluid in a particular direction. For example, the valves 26 can include flaps 48 that direct fluid in the desired direction. In some examples, when the valved stent device 10 is expanded and deployed in the right atrium 112, blood in the passageway 20 can flow through the valves 26 in a substantially upward direction (based on the orientation of the heart 110 in FIG. 1) towards the superior vena cava 114, so that backflow caused by tricuspid regurgitation doesn't force open the valves 26. As discussed previously, blood exiting the valved stent device 10 through the valves 26 generally does not pass into the superior vena cava 114, because the superior vena cava 114 is sealed or at least partially sealed by the first portion 42 of the valved stent device 10. Similarly, blood exiting the valved stent device 10 through the valves 26 does not pass into the inferior vena cava 116, because the inferior vena cava 116 is sealed or partially sealed by the third portion 46 of the stent device 10.

[00107] In some examples, the valves 26 can comprise or define an opening 50 in the cover 14. The flap 48 can be positioned to cover and/or seal the opening 50 to prevent backflow of fluid from the patient's right atrium 112 into the passageway 20. The opening 50 can be a circle, semicircle, ellipse, square, triangle, longitudinal slot, circumferential slot, or any other convenient shape. In some aspects, openings 50 for each of the valves 26 are a same shape and size. In other examples, openings 50 for the valves 26 can be different shapes and/or sizes. The openings 50

can be any convenient size selected to provide sufficient blood flow into the right atrium 112. In some examples, an opening 50 has an area of from 0.15 cm^2 to 1.5 cm^2 , or about 0.33 cm^2 to 0.66 cm^2 . A circular opening 50 can have a diameter of from about 0.50 cm to about 1.25 cm.

[00108] In exemplary FIGS. 1 and 2, the flap 48 can be configured to seal the opening 50 to prevent blood from reentering the passageway 20 of the device 10 from the right atrium 112. For example, the flap 48 can travel in an upwards direction shown by arrow A1 (in FIGS. 2 and 4A-4B) to cover and seal the opening 50. In some examples, the flap 48 can seal the opening 50 during ventricular systole due to upwardly directed fluid flow from tricuspid regurgitation. The flap 48 may also seal the opening 50 due to kinetic (e.g., due to angulation) and/or static (e.g., due to right atrium pressure rise) energy leading to interruption of reflux in the superior vena cava 114 and/or the inferior vena cava 116. The flap 48 can be configured to be in a neutral and/or open position at other times. In some examples, the flap 48 can be integral with the cover 14. For example, the opening 50 and flap 48 can be cut out of a single sheet of cover material.

[00109] In other examples, the flap 48 can be a separate layer or membrane, such as a small piece of natural, synthetic, or polymeric material, mounted, attached, connected, or fused to the cover 14 by, for example, an adhesive or suturing, and positioned to seal the opening 50 of the valve 26. Flaps 48 configured to be attached to cover the openings 50 can be made by various techniques used, for example, for forming valve leaflets of prosthetic heart valve devices and similar implantable devices. For example, the flaps 48 can be formed from pieces of pericardium tissue to mimic opening and closing characteristics of native heart valves. In other examples, the flaps 48 can be formed from synthetic polymer fibers produced to mimic pericardium tissue, such as electrospun polymer fibers including, for example and without limitation, one or more of the following biocompatible, biodegradable elastomeric (co)polymers materials: polyurethane, poly(ester urethane) urea (PEUU), poly(ether ester urethane)urea (PEEUU), poly(ester carbonate)urethane urea (PECUU) and poly(carbonate)urethane urea (PCUU). Beneficially, flaps 48 formed from synthetic polymers by electrospinning techniques can be shaped to provide improved function. For example, rather than forming flat sheets, electrospinning processes can be used to form flaps 48 with curved surfaces which mimic a shape of a valve leaflet of a native heart valve. In particular, the flaps 48 can be adapted to conform to a curved pocket shape to better cover and seal the openings 50 when the valves 26 are closed. Polymer materials and methods for forming prosthetic heart valves by, for example, electrospinning valve leaflets from such polymer

materials are further described in PCT Publication No. WO 2016/138416, entitled “Double Component Mandrel for Electrospun Stentless, Multi-Leaflet Valve Fabrication,” which is incorporated by reference herein in its entirety.

[00110] For examples where the flap 48 is attached to the cover 14, the flap 48 connects to and/or extends from the cover 14 along a seam 52, 54. The seam 52 can be a substantially straight line. For example, the seam 52 can be a straight line substantially aligned with a circumference of the second portion 44, as shown in FIG. 4A. Alternatively, the seam 54 can be a curved or arcuate seam that forms a pocket. An example of a valve 26 including a curved seam 54 is shown in FIG. 4B.

[00111] The valves 26 and openings 50 are generally sized to permit or provide sufficient blood flow through the device 10 and into the right atrium 112. Accordingly, a number of valves 26 and dimensions of the valves 26 can be selected to optimize blood flow, while also preventing backflow of blood from the right atrium 112 into the device 10. Particularly, the plurality of valves 26 should have a total area sufficient to permit good flow into the right atrium 112 without producing high pressure in the passage 20 of the device 10. For example, openings 50 of the valves 26 can have a total area ranging from about 1.5 cm² to about 6 cm². Therefore, for a valved stent device 10 having nine substantially identical valves 26, the area of the opening 50 for each valve 26 is about 0.33 cm² to about 0.66 cm². For valved stent devices 10 having fewer than nine valves 26, the area of the opening 50 of each valve 26 will generally be larger than 0.66 cm².

[00112] Another exemplary arrangement of valves is shown by the photographs in FIGS. 7A-7D. As shown by the photographs in FIGS. 7A-7D, an exemplary stent device includes multiple valves disposed substantially equidistantly around a circumference of the second portion in a single row. Accordingly, the valves shown in FIGS. 7A-7D are co-planar (e.g., positioned on a common plane, such as a plane perpendicular to the central and/or longitudinal axis of the device 10).

Manufacturing method

[00113] Exemplary methods of manufacture of a valved stent device 10 are also provided by the present disclosure. An exemplary method of manufacture can comprises providing a frame 12 according to any aspect, example, or embodiment described herein. For example, as previously described, the frame 12 can be formed by cutting or etching portions of an elongated tube to form the frame structure. In other examples, wires, tines, or flexible members can be bent, twisted, and/or woven together to form the frame structure. The method can further comprise attaching the

cover 14 to the frame 12 by any convenient process or technique. In some examples, the cover 14 can be connected to the frame 12 by a suitable biocompatible adhesive. Alternatively or in addition, the cover 14 can be connected to the frame 12 by, for example, fine suturing. Openings 50 for the valves 26 can be cut into the cover 14 by any convenient process at various locations on the second portion 44 of the device 10. For example, a blade or scalpel can be used for cutting openings 50 into the cover 14. As discussed previously, openings 50 are generally cut at various positions around the circumference of the second portion 44 so that the valved stent device 10 is symmetrical about the axis X or, at least, is direction-independent and can be deployed in the right atrium 112 in any orientation.

[00114] In some examples, the method further comprises attaching the flaps 48 to the cover 14 to seal the openings 50. For example, a small piece of pericardium tissue or polymer membrane can be attached to the cover 14 to form a pocket extending over the opening 50. In some examples, the small piece of tissue or polymer membrane can be a flat sheet. In other examples, as discussed previously, pieces of polymer membrane can comprise curved surfaces to form deeper and/or more robust pockets. In other examples, as discussed previously, the flap 48 is integral with the cover 14 and is formed by cutting out the opening 50 to include the flap 48.

Deployment methods

[00115] Exemplary methods for implanting a valved stent device 10 and for using the valved stent device 10 for treatment of a patient are also provided herein. In some examples, the valved stent devices 10 can be configured to be delivered percutaneously through a delivery catheter assembly. The delivery catheter assembly can comprise a sheath, a guidewire, and the valved stent device 10 according to any aspect, example, or embodiment described herein. The valved stent device 10 can be disposed within the sheath and advanced through the sheath over the guidewire to a deployment location, such as to the right atrium 112 of a patient for treatment of tricuspid regurgitation.

[00116] In some examples, a method of treating tricuspid regurgitation can comprise providing the catheter assembly and the valved stent device 10 according to any aspect, example, or embodiment described herein. In order to deploy the valved stent device 10 into the right atrium 112 of the patient, the catheter can be introduced into the body by a transfemoral access procedure. A distal end of the catheter can then be advanced to the right atrium 112 via a transfemoral route. Angiographic and fluoroscopic guidance can be used to assist in advancing

the catheter device. The delivery can be about 20-24 French which, given the fact that it is done via femoral venous access, is believed to be well tolerated by most patients.

[00117] Once the delivery catheter and valved stent device 10 are advanced to the right atrium 112, the method can further comprise expanding the valved stent device 10 in the patient's right atrium 112. If the valved stent device 10 is self-expanding, it may expand automatically when advanced into the right atrium 112 through the distal end of the delivery catheter. Alternatively, a balloon catheter can be used to manually expand the valved stent device 10. For example, the valved stent device 10 can be crimped to the balloon catheter. Once the valved stent device 10 is released into the right atrium 112 through the sheath of the catheter assembly, the balloon catheter can be inflated, which causes the valved stent device 10 to transition from the compressed configuration to the expanded configuration. As discussed previously, when expanded, the valved stent device 10 can be sized to seal the superior vena cava 114 and the inferior vena cava 116, so that blood enters the right atrium 112 exclusively or substantially exclusively through the passageway 20 of the valved stent device 10. The only way for blood to exit the passageway 20 into the right atrium 112 is through the plurality of valves 26. Thus, as previously discussed, the valved stent device 10 disclosed herein uncouples the right atrium 112 from the systemic venous circulation by the valve(s) 26, thus reducing the blood reflux in the venous circulation.

[00118] In some examples, the valved stent device 10 can be configured to be and/or is used as a temporary implant. Accordingly, the method for treating tricuspid regurgitation can further comprise retrieving the valved stent device 10 after a period of time. Retrieval of the valved stent device 10 can be performed percutaneously. For example, retrieval can comprise inserting a catheter assembly through a percutaneous access site and advancing the catheter assembly and guidewire to the right atrium 112. Once the catheter assembly advances to the right atrium 112, the retrieval method can comprise attaching a loop, ring, collar, or locking structure of the guidewire to a corresponding fastener (e.g., a hook, screw, or similar protruding structure) of the valved stent device 10. Once secured to the guidewire, the valved stent device 10 can be retracted into the catheter assembly and removed from the body. In some examples, the valved stent device 10 may be retrieved and removed about 2 months to about 4 months after being implanted in the right atrium 112.

[00119] The present invention has been described with reference to certain exemplary embodiments. However, it will be recognized by those of ordinary skill in the art that various substitutions, modifications or combinations of any of the exemplary embodiments may be made without departing from the spirit and scope of the invention. Thus, the invention is not limited by the description of the exemplary embodiments.

WHAT IS CLAIMED IS:

1. A valved stent device configured to be deployed in a right atrium of a patient's heart, comprising an expandable frame and a cover on at least a portion of an inside surface and/or an outside surface of the expandable frame, wherein, when the frame is expanded, the expanded frame and the cover define a contiguous, sealed passage from a first end to an opposite end of the expanded frame, the frame and cover of the valved stent device forming:

a first portion comprising a first wall portion defining a portion of the passage and configured to bias against an inner circumference of a patient's superior vena cava;

a second portion extending axially from the first portion comprising a second wall portion defining a portion of the passage, the second wall portion being configured to extend through the right atrium between the patient's superior vena cava and inferior vena cava;

a third portion extending axially from the second portion comprising a third wall portion defining a portion of the passage, configured to extend into the patient's inferior vena cava to bias against the inner circumference of the patient's inferior vena cava; and

a plurality of valves in the second wall portion of the second portion, the plurality of valves being configured to permit one-direction flow of a fluid from the passage into the patient's right atrium.

2. The valved stent device of claim 1, wherein the cover comprises a non-bioerodible polymer layer or membrane.

3. The valved stent device of claim 1, wherein the first wall portion, the second wall portion, and the third wall portion each comprise at least one of an annular wall, a substantially annular wall, an outwardly convex wall, a spheroidal wall, or a partially spherical wall.

4. The valved stent device of claim 1, wherein the plurality of valves are arranged substantially equidistantly around a circumference of the second portion on a plane perpendicular to a central and/or longitudinal axis of the second portion.

5. The valved stent device of claim 1, wherein the plurality of valves comprises at least a first group of valves arranged substantially equidistantly around a circumference of the second portion on a first plane perpendicular to a central and/or longitudinal axis of the second portion, and a second group of valves arranged substantially equidistantly around a circumference of the second portion on a second plane perpendicular to the and/or longitudinal axis of the second portion.

6. The valved stent device of claim 1, wherein the plurality of valves are arranged such that the valved stent device is symmetrical about a central and/or longitudinal axis of the stent device.

7. The valved stent device of claim 1, wherein the plurality of valves each comprise an opening in the cover and a flap configured to seal the opening to prevent backflow of fluid from the patient's right atrium into the passage.

8. The valved stent device of claim 7, wherein, for the plurality of valves, the flaps are configured to seal the openings during ventricular systole and to be in a neutral position at other times during a cardiac cycle.

9. The valved stent device of claim 7, wherein the flaps of the plurality of valves connect to the cover along a substantially straight seam substantially aligned with a circumference of the second portion.

10. The valved stent device of claim 7, wherein the flaps of the plurality of valves connect to the cover at a curved seam which forms a pocket.

11. The valved stent device of claim 7, wherein the openings of the plurality of valves have a total area of from about 1.5 cm² to about 6 cm².

12. The valved stent device of claim 7, comprising nine valves, each valve having an opening with an area of from about 0.33 cm² to about 0.66 cm².

13. The valved stent device of claim 7, configured such that, when the stent device is deployed in the right atrium, the flaps are configured to move in an upwards direction towards the first portion of the device and the superior vena cava to seal the openings.

14. The valved stent device of claim 7, wherein the cover and the flap are formed from a non-bioerodible polymer.

15. The valved stent device of claim 14, wherein the non-bioerodible polymer comprises at least one of polyurethane, polytetrafluoroethylene (PTFE), or polyethylene terephthalate (PET).

16. The valved stent device of claim 7, wherein the cover is formed from a non-bioerodible polymer, and the flaps of the plurality of valves are formed from pericardium tissue.

17. The valved stent device of claim 16, wherein the cover is formed from a non-bioerodible polymer and the flaps of the plurality of valves are formed from an electrospun polymer material comprising a urethane monomer.

18. The valved stent device of claim 1, wherein the cover is connected to the inner surface and/or the outer surface of the frame by at least one of a biocompatible adhesive or suturing.

19. The valved stent device of claim 1, wherein the cover and/or frame are coated with an antithrombotic coating, such as a coating comprising at least one of polyethylene glycol (PEG) or zwitterionic groups, and/or coated with an anti-clotting agent, such as heparin.

20. The valved stent device of claim 1, wherein a diameter of the second portion, when expanded, is greater than a diameter of the first portion and/or is greater than a diameter of the third portion.

21. The valved stent device of claim 1, wherein the frame comprises a balloon-expandable frame.

22. The valved stent device of claim 1, wherein the frame comprises a self-expanding frame.

23. The valved stent device of claim 22, wherein the self-expanding frame comprises a superelastic, shape-memory alloy, such as nickel titanium alloy.

24. The valved stent device of claim 1, wherein the frame comprises a plurality of flexible elongated tines.

25. The valved stent device of claim 24, wherein the plurality of tines are interconnected, thereby forming a closed cell region on the second portion of the valved stent device.

26. The valved stent device of claim 1, wherein the frame comprises an annular spring positioned in the passage of the valved stent device configured to bias the second portion of the valved stent device radially outwardly.

27. The valved stent device of claim 1, wherein at least one of the first portion or the third portion of the stent device comprises at least one expandable annular ring independent from other portions of the frame and connected to other portions of the valved stent device by the cover.

28. The valved stent device of claim 1, configured such that, when deployed in the patient's right atrium, a and/or longitudinal axis of the first portion substantially aligns with a and/or longitudinal axis of a portion of the superior vena cava of the patient, and a and/or longitudinal axis of the third portion substantially aligns with a and/or longitudinal axis of a portion of the inferior vena cava of the patient.

29. The valved stent device of claim 1, wherein, when expanded, the second portion has a maximum outer diameter of from about 4 cm to about 8 cm, such as about 6 cm.

30. A method of manufacture of the valved stent device of claim 1, the method comprising:

attaching the cover to the frame by at least one of an adhesive or suturing;
cutting portions of the cover to form the openings of the plurality of valves; and
attaching flaps to the cover near the openings to form pockets of the valves.

31. The method of claim 30, wherein cutting portions of the cover to form the openings comprises cutting openings having a total area of from about 1.5 cm² to about 6 cm².

32. The method of claim 30, wherein the flaps are attached to the cover by at least one of a biocompatible adhesive or suturing.

33. The method of claim 30, wherein the cover is formed from a non-bioerodible polymer, and the flaps of the plurality of valves are formed from pericardium tissue.

34. The method of claim 30, wherein the cover is formed from a non-bioerodible polymer and the flaps of the plurality of valves are formed from an electrospun polymer material comprising a urethane monomer.

35. The method of claim 30, further comprising applying a coating to the cover and/or frame of the valved stent device, the coating comprising an antithrombotic coating, comprising an antithrombotic agent, such as polyethylene glycol or molecules comprising zwitterionic groups, or an anticoagulant coating, comprising an anticoagulant agent such as heparin.

36. A method of treating tricuspid regurgitation in a patient, comprising:
deploying the valved stent device of claim 1 into the right atrium of the patient with the first portion biased against the inner circumference of the patient's superior vena cava, the third

portion biased against the inner circumference of the patient's inferior vena cava, and the second portion and the plurality of valves in the patient's right atrium.

37. The method of claim 36, wherein the valved stent device is deployed percutaneously using a catheter.

38. The method of claim 36, wherein positioning of the valved stent device in the right atrium is performed using radiopaque markings as guides.

39. The method of claim 36, wherein, when the valved stent device is deployed in the right atrium, the flaps are configured to move in an upwards direction towards the first portion of the valved stent device and towards the superior vena cava to seal the openings.

40. The method of claim 36, further comprising retrieving the valved stent device from the right atrium of the patient about 2 months to about 4 months following implantation of the valved stent device.

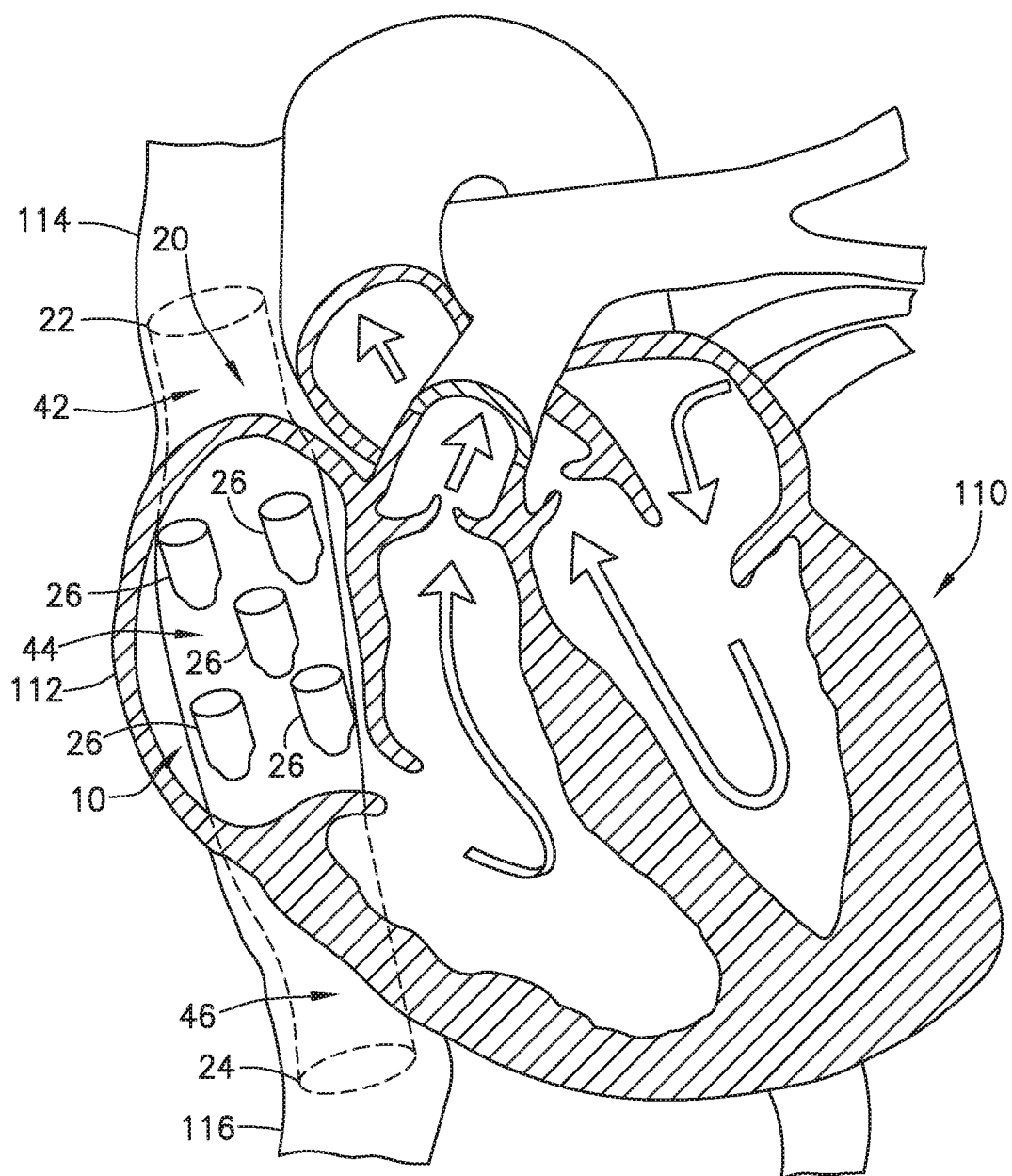


FIG. 1

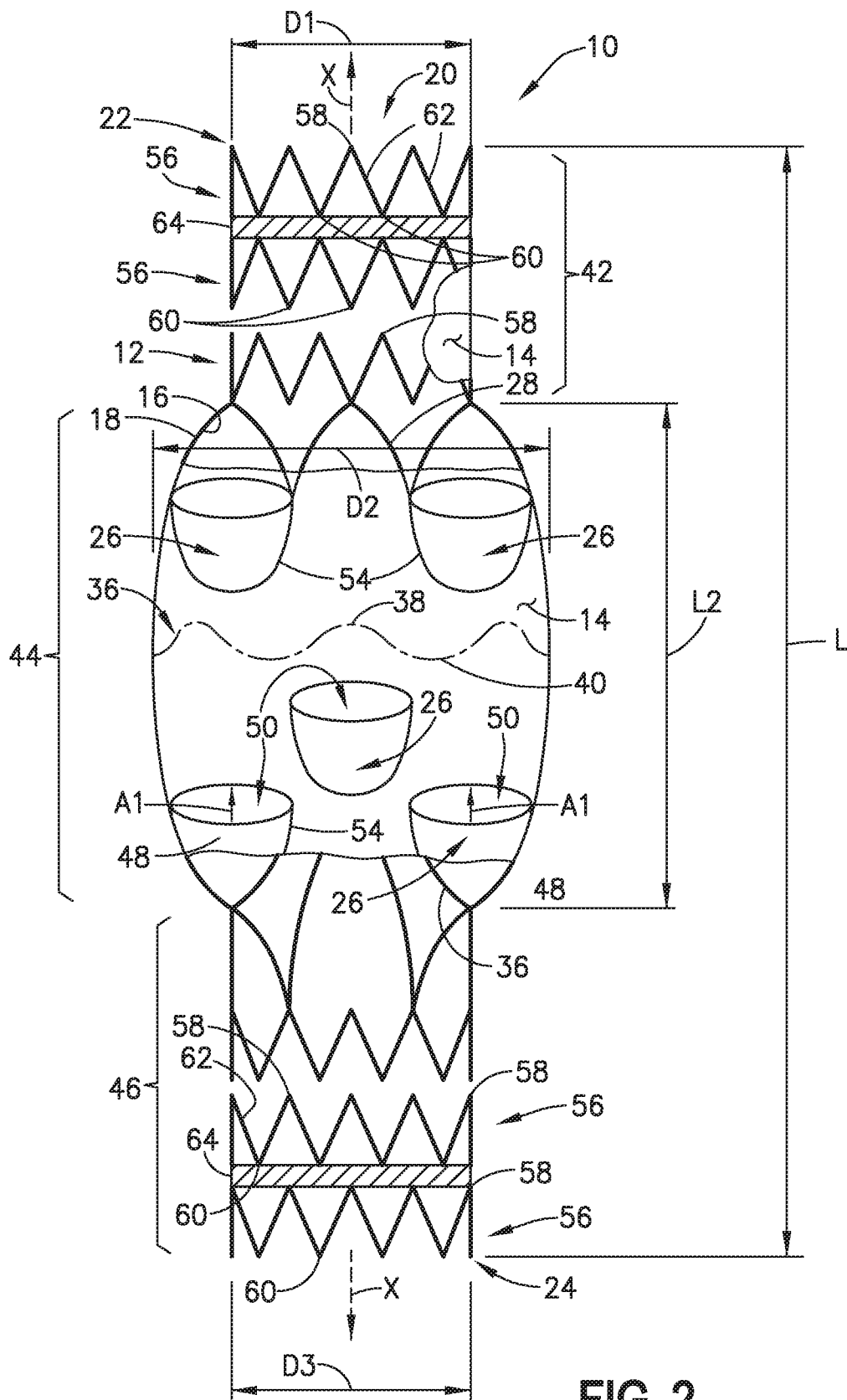


FIG. 2

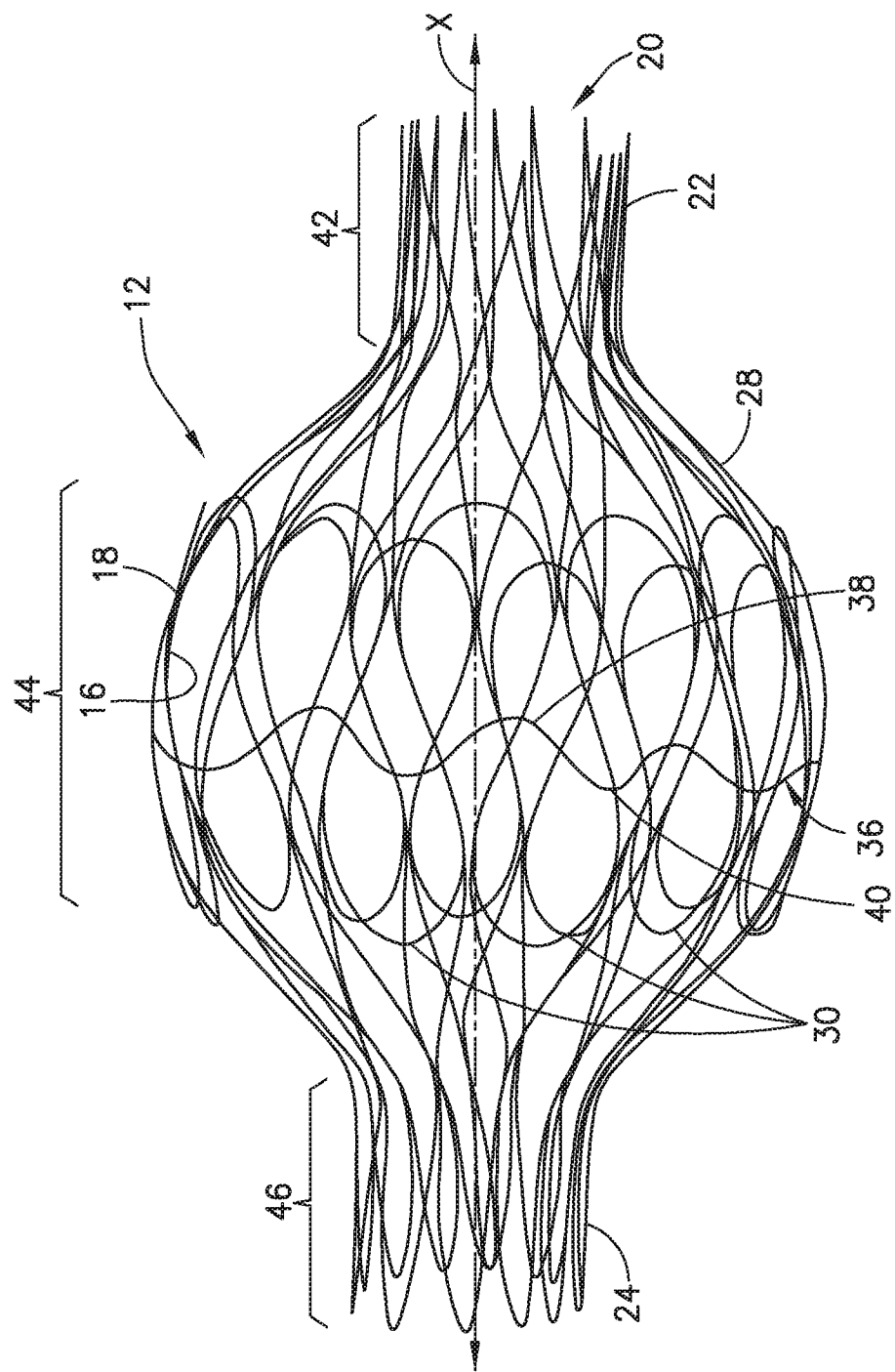


FIG. 3A

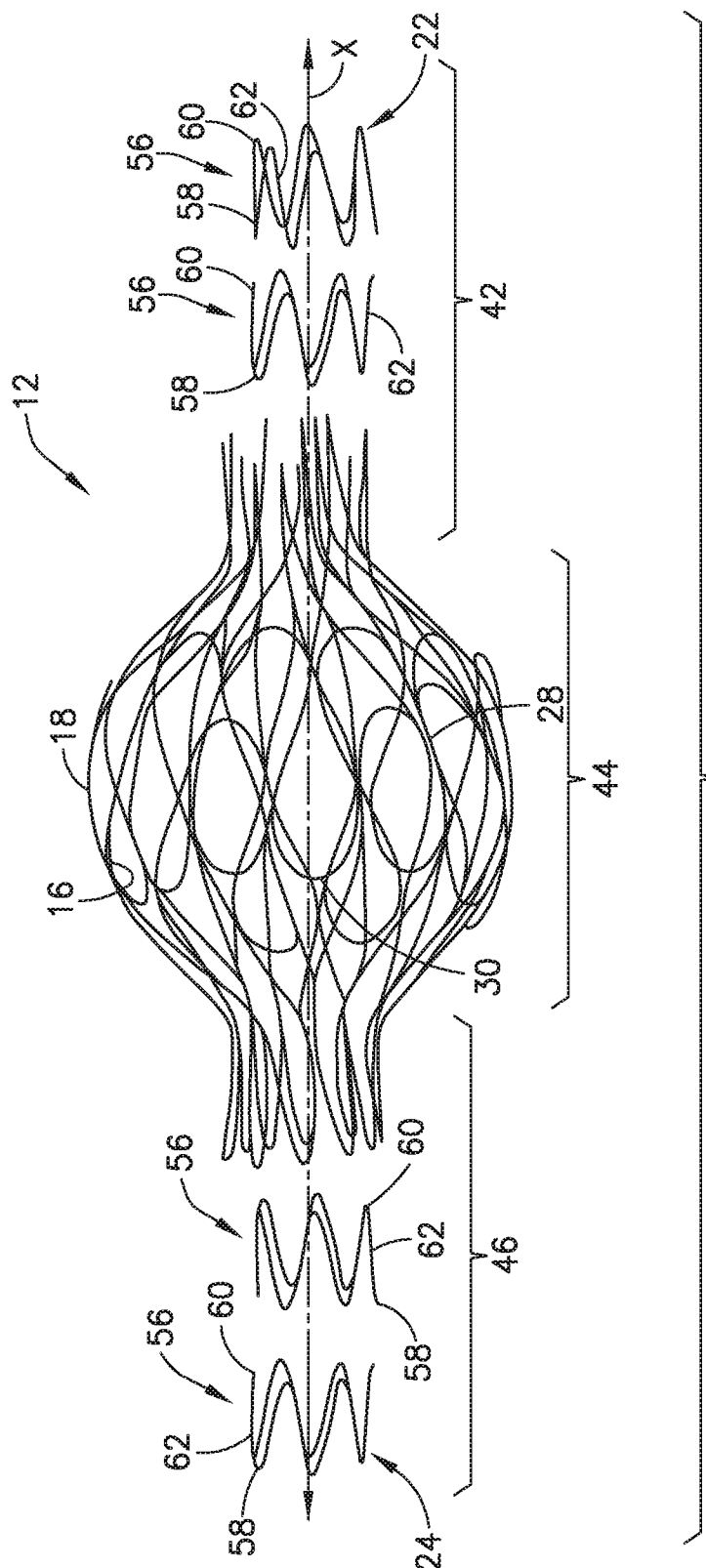


FIG. 3B

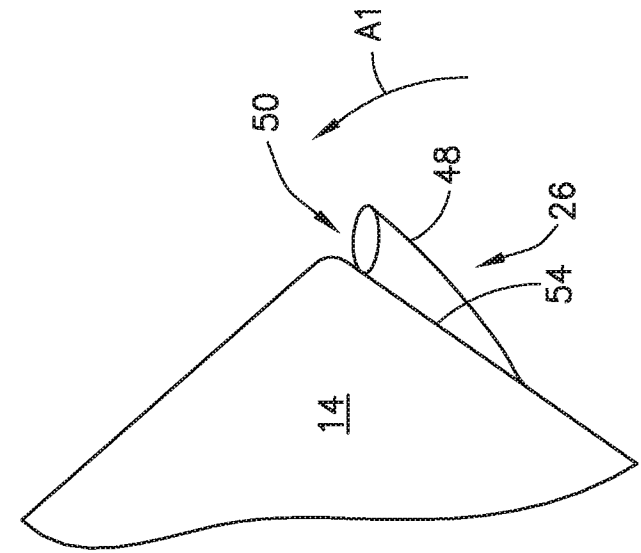


FIG. 4B

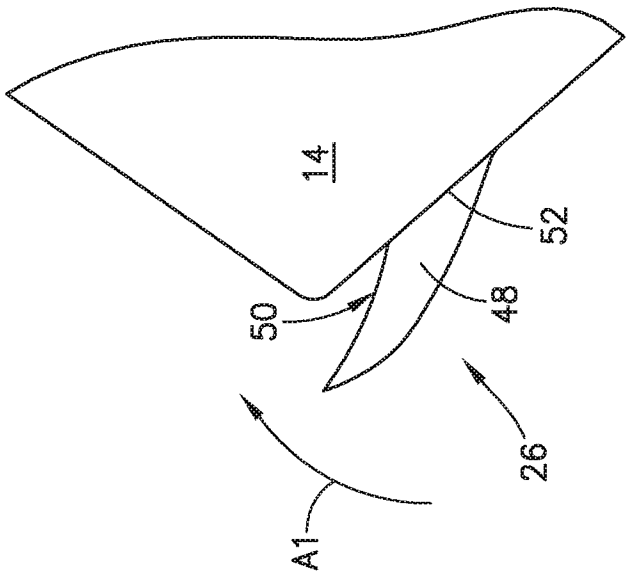


FIG. 4A

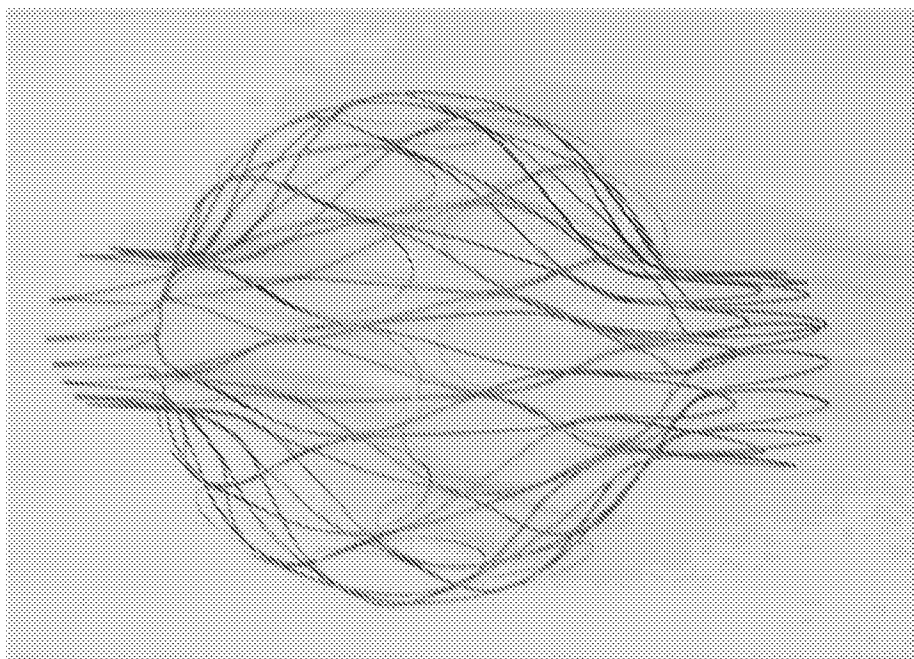


FIG. 5A

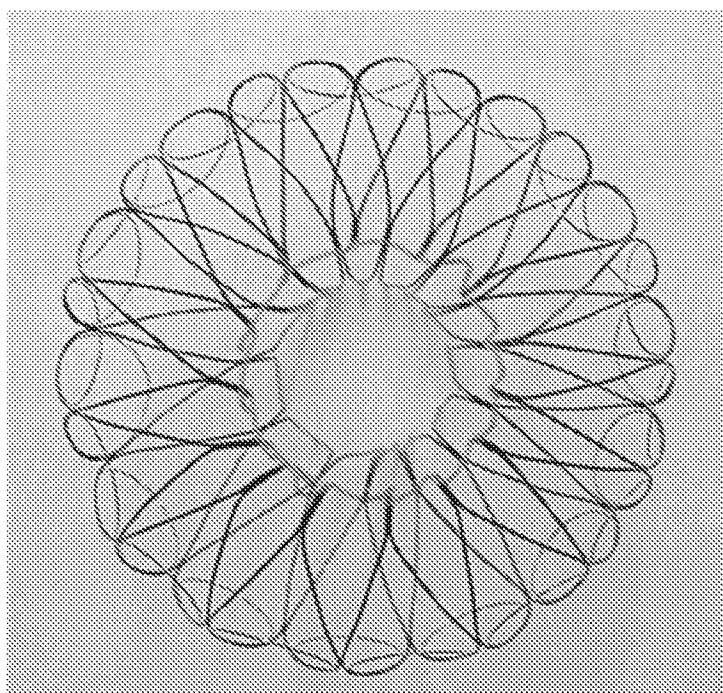


FIG. 5B

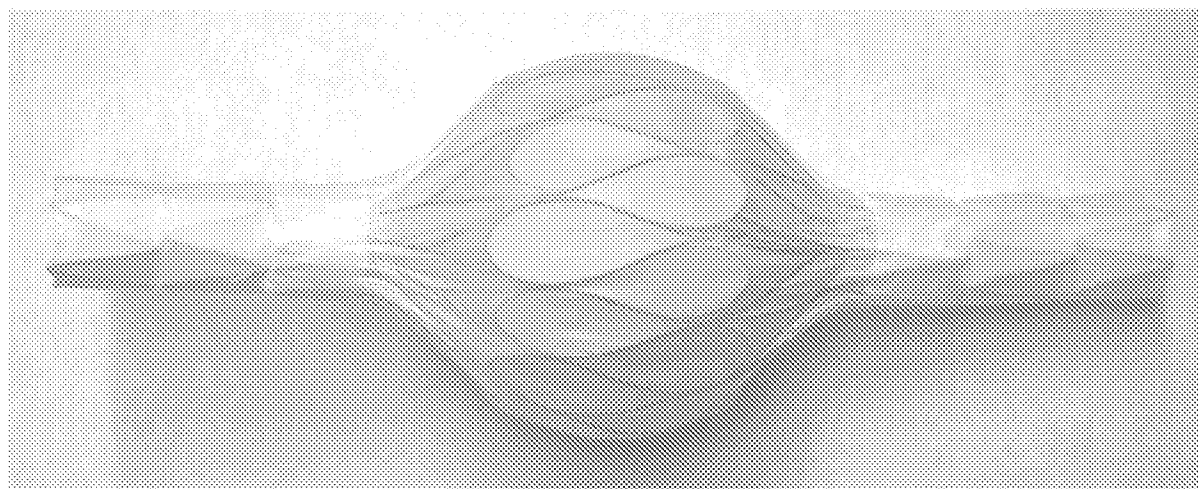


FIG. 6A



FIG. 6B

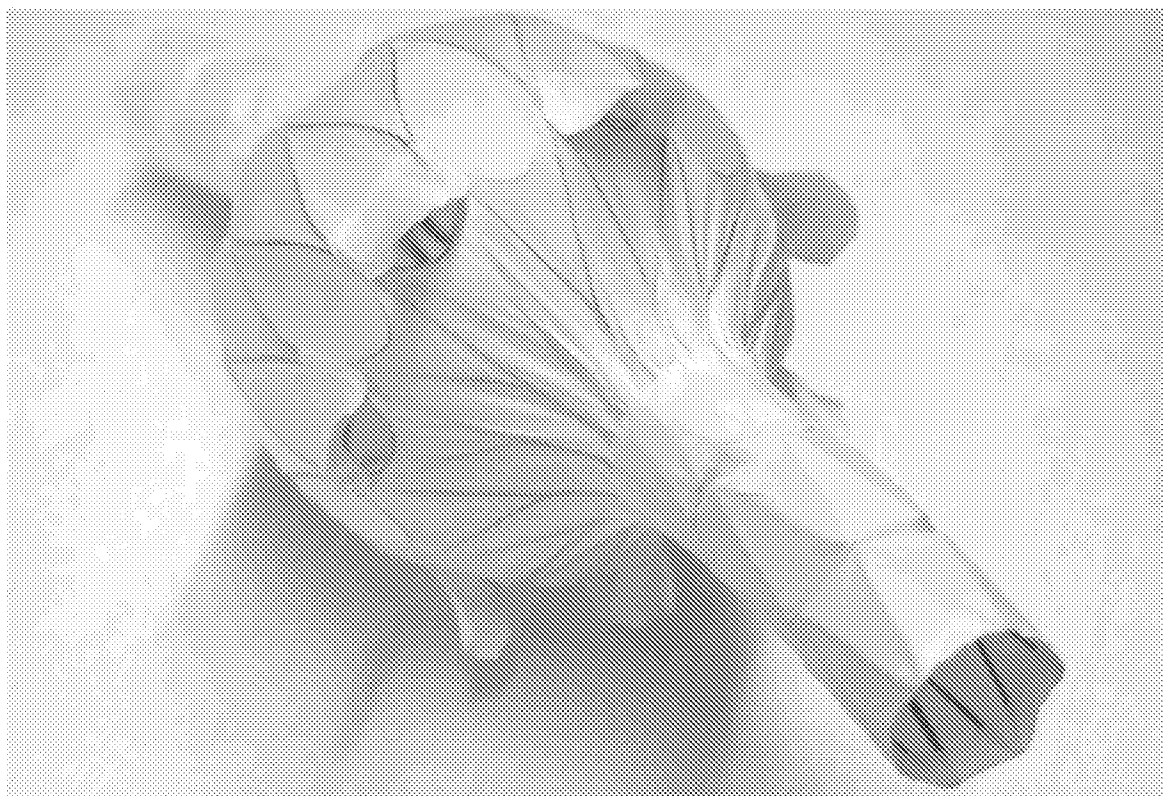


FIG. 7A

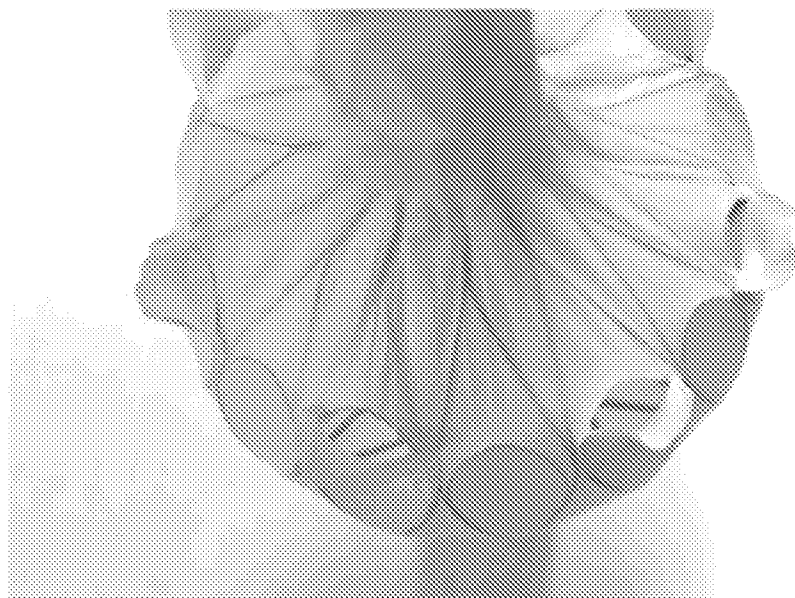


FIG. 7B

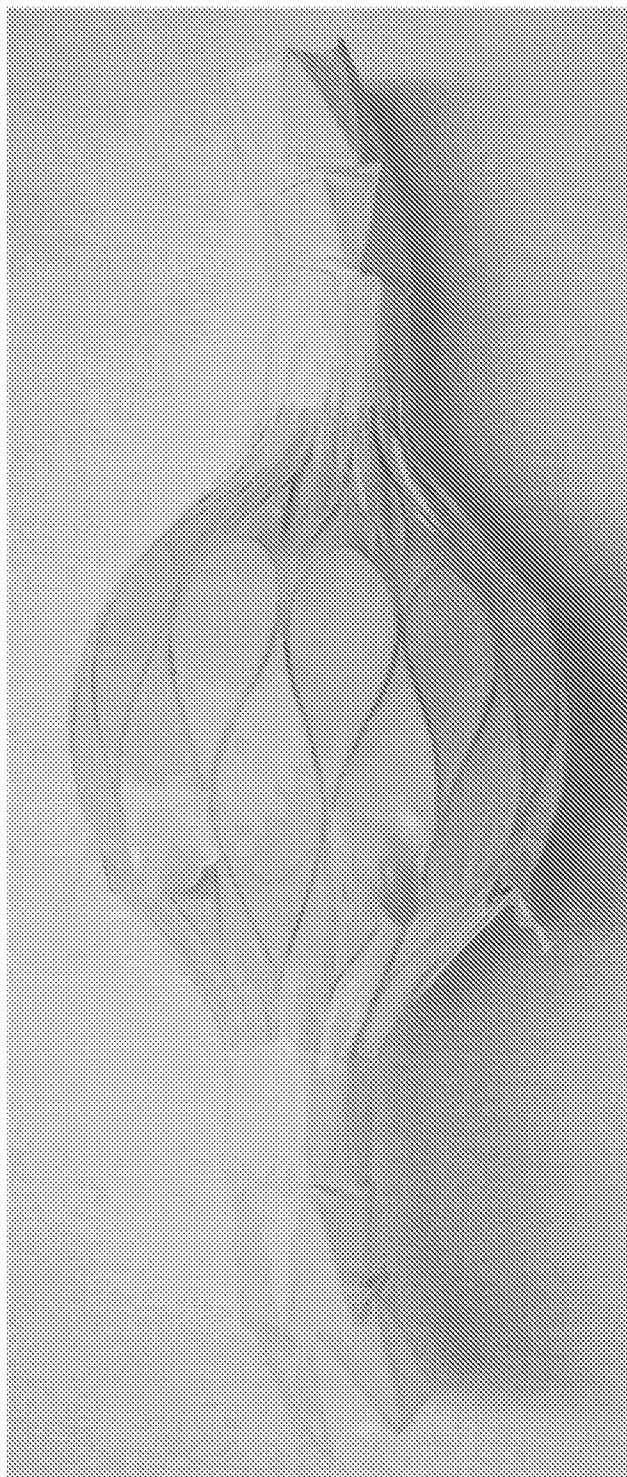


FIG. 7C



FIG. 7D

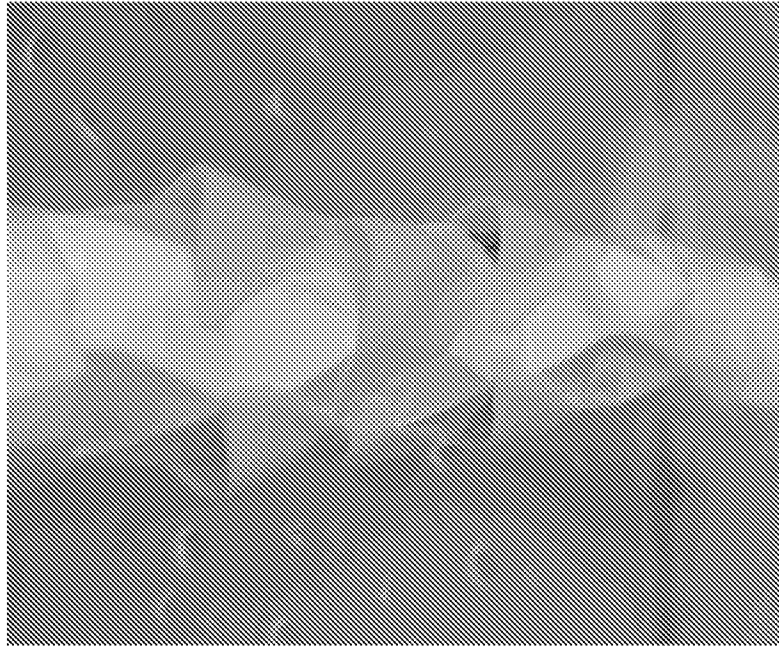


FIG. 8B

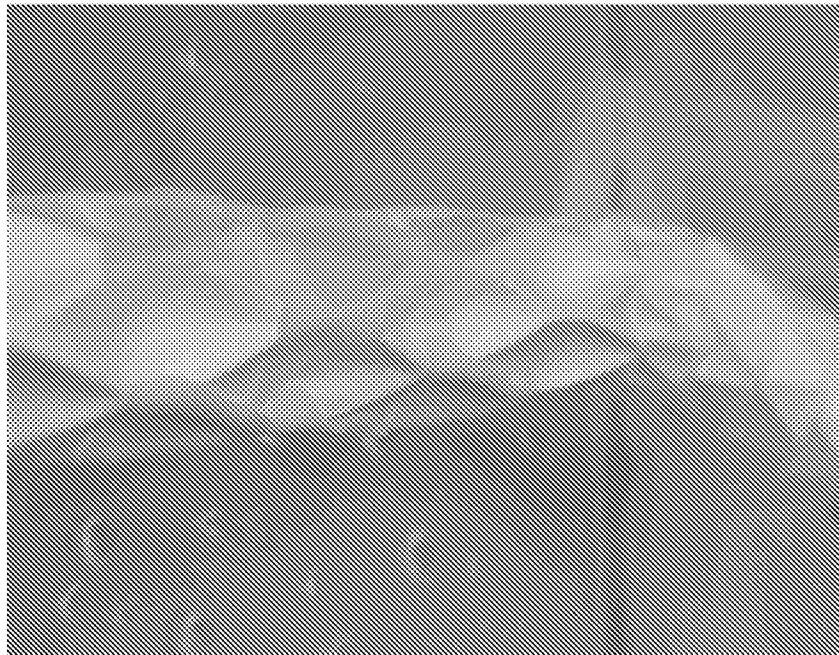


FIG. 8A

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/039583

A. CLASSIFICATION OF SUBJECT MATTER IPC (20200101) A61F 2/24, A61F 2/06, A61F 2/86 CPC (20130101) A61F 2/2412, A61F 2/06, A61F 2/86 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) IPC (20200101) A61F 2/24, A61F 2/06, A61F 2/86 CPC (20130101) A61F 2/2412, A61F 2/06, A61F 2/86 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) Databases consulted: Google Patents, PatBase, Orbit		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/0021130 A1 (INNOVENTRIC LTD. [IL]) 25 Jan 2018 (2018/01/25) the whole document (particularly, figures 4A-B, 6, 7)	1-19,21-40
Y		20
Y	CN 107212947 A (LIU JIAN [CN]) 29 Sep 2017 (2017/09/29) the whole document	20
A		1-19,21-40
A	US 2015/0282958 A1 (NVT AG [DE]) 08 Oct 2015 (2015/10/08) the whole document	1-40
P,X	WO 2019/234755 A2 (INNOVENTRIC LTD. [IL]) 12 Dec 2019 (2019/12/12) the whole document	1-19,21-40
☐ 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 "D" document cited by the applicant in the international application "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 27 Sep 2020		Date of mailing of the international search report 30 Sep 2020
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Email address: pctoffice@justice.gov.il		Authorized officer SEGAL Liviu Telephone No. 972-73-3927134

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2020/039583

Patent document cited search report			Publication date	Patent family member(s)			Publication Date
US	2018/0021130	A1	25 Jan 2018	US	2018021130	A1	25 Jan 2018
				AU	2017218708	A1	23 Aug 2018
				CA	3013861	A1	17 Aug 2017
				CN	109069268	A	21 Dec 2018
				EP	3402440	A1	21 Nov 2018
				EP	3402440	B1	27 May 2020
				JP	2019504739	A	21 Feb 2019
				WO	2017137868	A1	17 Aug 2017
CN	107212947	A	29 Sep 2017	CN	107212947	A	29 Sep 2017
US	2015/0282958	A1	08 Oct 2015	US	2015282958	A1	08 Oct 2015
				US	10028821	B2	24 Jul 2018
				CN	104970901	A	14 Oct 2015
				CN	104970901	B	02 Oct 2018
				EP	2929860	A1	14 Oct 2015
				EP	2929860	B1	28 Jun 2017
				ES	2635438	T3	03 Oct 2017
				JP	2015198914	A	12 Nov 2015
				JP	6560507	B2	14 Aug 2019
				PL	2929860	T3	31 Jan 2018
WO	2019/234755	A2	12 Dec 2019	WO	2019234755	A2	12 Dec 2019
				WO	2019234755	A3	14 May 2020